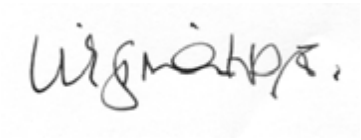
RECOMMENDATION FOR SEASONAL INFLUENZA VACCINE COMPOSITION FOR NEW ZEALAND FOR 2013



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Recommendations

The Australian Influenza Vaccine Committee (AIVC) met with New Zealand representatives (Appendix 1) in Melbourne on 3 October 2012 to consult on the influenza vaccine composition for 2013 for New Zealand, Australia and South Africa. The recommended composition was:

- A(H1N1) an A/California/7/2009 (H1N1)pdm09 - like virus
- A(H3N2) an A/Victoria/361/2011 (H3N2) - like virus
- B a B/Wisconsin/1/2010 - like virus

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RECOMMENDATION FOR SEASONAL INFLUENZA VACCINE COMPOSITION FOR 2013

It is known that influenza viruses frequently go through antigenic changes in their surface proteins, haemagglutinin (HA) and neuraminidase (NA). Protection by vaccines against influenza infection depends on achieving a good match between the vaccine strains and the circulating viruses, particularly for the HA antigen. A combination of antigenic and genetic analyses is used to identify emergent antigenic variants of potential future epidemic importance and for consideration of their inclusion in vaccines. Antigenic relationships among contemporary viruses and vaccine strains are of prime importance in determining vaccine composition. These relationships are evaluated mainly in haemagglutination-inhibition (HI) tests using post-infection ferret sera against egg and/or cell grown reference and vaccine viruses using red blood cells principally from turkeys but also from other species, as appropriate. Virus neutralisation tests provide complementary data. Antigenic cartography is used as an additional analytical tool to visualise and integrate antigenic data. Phylogenetic analyses of HA and NA genes help to define the genetic relatedness of antigenic variants to their predecessors and to elucidate the molecular basis for antigenic drift. The spread of antigenic variants associated with influenza outbreaks in different countries is also an important criterion for selection of epidemiologically relevant vaccine candidates.

The World Health Organization (WHO) makes twice-yearly recommendations to guide national/regional authorities on the formulation of influenza vaccines. One recommendation is made in February for the northern hemisphere winter and another recommendation is made in September for the southern hemisphere winter. The recommendation for the southern hemisphere is published in the 12 October issue of the *Weekly Epidemiological Record, 2012 87(41):389-400 (Appendix 6)*.

It should be noted that the WHO recommendations are made with respect to reference strains which may or may not be suitable for vaccine production. Thus, even where the WHO recommendation is adopted, it is necessary for country/regional authorities to approve the specific vaccine strains to be used and this, in turn, requires the preparation of specific reagents for vaccine standardisation.

Since 1969, the Australian Influenza Vaccine Committee (AIVC), with representatives from New Zealand, Australia and South Africa, has met annually in October to approve or update the WHO recommended formulation for influenza vaccines intended for the following winter (March to September of the following year) for these countries. New Zealand uses the influenza vaccine strains recommended by AIVC in the subsequent year.

The AIVC met with New Zealand representatives (Appendix 1) on 3 October 2012 to consult on the seasonal influenza vaccine composition for New Zealand, Australia and South Africa for 2013. The recommended composition (Table 1) was:

- A(H1N1) an A/California/7/2009 (H1N1)pdm09 - like virus
- A(H3N2) an A/Victoria/361/2011 (H3N2) - like virus
- B a B/Wisconsin/1/2010 - like virus

TABLE 1. Influenza Vaccine Recommendations for New Zealand, 1991-2013

Formulation Recommendations		Vaccine used for	A H3N2	A H1N1	B
NZ & WHO*	2012	2013	A/Victoria/361/2011	A/California/7/2009	B/Wisconsin/1/2010
NZ & WHO*	2011	2012	A/Perth/16/2009	A/California/7/2009	B/Brisbane/60/2008
NZ & WHO*	2010	2011	A/Perth/16/2009	A/California/7/2009	B/Brisbane/60/2008
NZ & WHO*	2009	2010	A/Perth/16/2009	A/California/7/2009	B/Brisbane/60/2008
NZ & WHO*	2008	2009	A/Brisbane/10/2007	A/Brisbane/59/2007	B/Florida/4/2006
NZ & WHO*	2007	2008	A/Brisbane/10/2007	A/Solomon Islands/3/2006	B/Florida/4/2006
NZ & WHO*	2006	2007	A/Wisconsin/67/2005	A/New Caledonia/20/99	B/Malaysia/2506/2004
NZ & WHO*	2005	2006	A/California/7/2004	A/New Caledonia/20/99	B/Malaysia/2506/2004
NZ & WHO*	2004	2005	A/Wellington/1/2004	A/New Caledonia/20/99	B/Shanghai/361/2002
NZ & WHO*	2003	2004	A/Fujian/411/2002	A/New Caledonia/20/99	B/Hong Kong/330/2001
NZ & WHO*	2002	2003	A/Moscow/10/99	A/New Caledonia/20/99	B/Hong Kong/330/2001
NZ & WHO*	2001	2002	A/Moscow/10/99	A/New Caledonia/20/99	B/Sichuan/379/99
NZ	2000	2001	A/Sydney/5/97	A/New Caledonia/20/99	B/Beijing/184/93
WHO*	2000	2001	A/Moscow/10/99	A/New Caledonia/20/99	B/Beijing/184/93
NZ & WHO*	1999	2000	A/Sydney/5/97	A/Beijing/262/95	B/Beijing/184/93
NZ	1998	1999	A/Sydney/5/97	A/Bayern/7/95	B/Beijing/184/93
WHO**	1997-98		A/Wuhan/359/95	A/Bayern/7/95	B/Beijing/184/93
NZ	1997	1998	A/Wuhan/359/95	A/Texas/36/91	B/Beijing/184/93
WHO**	1996-97		A/Wuhan/359/95	A/Singapore/6/86***	B/Beijing/184/93
NZ	1996	1997	A/Johannesburg/33/94	A/Texas/36/91	B/Beijing/184/93
WHO**	1995-96		A/Johannesburg/33/94	A/Singapore/6/86	B/Beijing/184/93
NZ	1995	1996	A/Guangdong/25/93	A/Texas/36/91	B/Panama/45/90
WHO**	1994-95		A/Shangdong/9/93	A/Singapore/6/86	B/Beijing/184/93
NZ	1994	1995	A/Beijing/32/92	A/Texas/36/91	B/Panama/45/90
WHO**	1993-94		A/Beijing/32/92	A/Singapore/6/86	B/Panama/45/90
NZ	1993	1994	A/Shanghai/24/90	A/Texas/36/91	B/Panama/45/90
WHO**	1992-93		A/Beijing/353/89	A/Singapore/6/86	B/Yamagata/16/88 or B/Panama/45/90
NZ	1992	1993	A/Beijing/353/89	A/Victoria/36/88	B/Yamagata/16/88 or B/Panama/45/90
WHO**	1991-92		A/Beijing/353/89	A/Singapore/6/86	B/Yamagata/16/88 or B/Panama/45/90
NZ	1991	1992	A/Beijing/353/89	A/Victoria/36/88	B/Yamagata/16/88
WHO**	1990-91		A/Guizhou/54/89	A/Singapore/6/86	B/Yamagata/16/88

* WHO recommendations are for the Southern Hemisphere winter;
* * WHO recommendations are for the Northern Hemisphere winter
*** USA selected the variant A/Texas/36/91

1. INFLUENZA EPIDEMIOLOGY

1.1 World-wide influenza activity, February to September 2012

Between February and September 2012, influenza was active worldwide and reported in Africa, the Americas, Asia, Europe and Oceania. Activity in individual countries was low or moderate to high and was due to circulation of influenza A(H1N1)pdm09, A(H3N2) and B viruses. (Appendix 6)

In the northern hemisphere, influenza activity increased in February and March, started to decline in April, and remained low since May. For the southern hemisphere in general, activity increased from May and had declined by September. In tropical areas, activity was variable throughout the period. (Appendix 6)

Influenza type A(H1N1)pdm09
Generally, influenza type A(H1N1)pdm09 activity was low, notably so in Africa, Europe and Oceania. In other regions it was reported as the predominant or co-dominant subtype (with A(H3N2) viruses) in some countries. For Asia, India reported regional outbreaks in March and April, while China Hong Kong Special Administrative Region reported regional outbreaks in May and June. In the Americas, northern hemisphere countries, areas and territories reporting widespread and/or regional outbreaks in the timeframe February to April were Colombia, French Guiana, Guatemala and the United States of America, while southern hemisphere countries Argentina, the Plurinational State of Bolivia, Brazil, El Salvador and Paraguay reported such outbreaks from June to August.

Influenza A(H3N2)
Influenza A(H3N2) activity was reported in most countries during this period. In the northern hemisphere widespread and/or regional outbreaks were reported in Europe, the Russian Federation, parts of Asia, northern Africa, Canada and the United States of America in February-April, extending into May in Japan and the United States of America. Regional outbreaks in May and June were reported by China, Hong Kong Special Administrative Region and widespread or regional outbreaks were reported by the Dominican Republic from May to July. In many parts of the southern hemisphere, A(H3N2) viruses caused widespread and regional outbreaks between May and August, notably in Chile (June-August) and Brazil (July). In Australia and New Zealand widespread outbreaks were reported in July to August and August respectively. South Africa reported regional outbreaks in August.

Influenza B
Widespread and regional influenza B activity was reported in many countries, areas and territories in the northern hemisphere over the period February to July including the American continent (Canada, Cuba, El Salvador, Panama and the United States of America), Asia (China, Israel, Japan and the Republic of Korea), and Europe (Austria, Belgium, Croatia, Estonia, Hungary and the Russian Federation). For the southern hemisphere, widespread and regional influenza B activity was reported in the Plurinational State of Bolivia, Ecuador, Paraguay and Peru between June and August. Within Oceania, Australia reported regional outbreaks in August. In South Africa, influenza B activity increased from July to become regional in August.

Zoonotic influenza infections caused A(H5N1), A(H3N2) variant (v), A(H1N1)v, A(H1N2)v and A(H7N3) viruses
From 23 February to 18 September 2012, 17 confirmed human cases of A(H5N1), 10 of which were fatal, were reported by Bangladesh, Cambodia, China Hong Kong Special Administrative Region, Egypt, Indonesia, and Viet Nam where highly pathogenic avian influenza A(H5N1) is present in poultry and/or wild birds. Since December 2003, a total of 608 cases with 359 deaths have been

confirmed in 15 countries. To date there has been no evidence of sustained human-to-human transmission.

Human cases of influenza A(v) viruses have been detected since February 2012 in the United States of America where a total of 305 infections caused by A(H3N2)v viruses have been reported. One of these infections was fatal. A single case of A(H1N1)v and three cases of A(H1N2)v have also been detected.

Two human cases of conjunctivitis due to A(H7N3) have been reported by Mexico. These cases had exposure to A(H7N3) infected poultry.[1]

No human cases of influenza A(H9N2) were detected during the period 23 February to 18 September 2012.
(Abridged from the Weekly Epidemiological Record, 2012 87(41): 457-468)

The WHO Collaborating Centre for Reference and Research on Influenza in Melbourne, Australia (Melbourne WHOCC) analysed influenza isolates received from 1 March to 12 September 2011. Influenza A(H3N2) virus was the predominant strain which accounted for 68.5% (1076/1572) of isolates, while 30.3% (476/1572) were influenza B and 1.3% (20/1527) were A(H1N1)pdm09 (Table 2.1 in Appendix 2).

1.2 Influenza activity in Australia, March to September 2012

Influenza activity in Australia in 2012 was medium with some regional variations regarding influenza activities and types/subtypes. There are 10 forms of influenza surveillance system in Australia, which can be divided into three categories.

- **Influenza-like-illness surveillance**
  - **Australian Sentinel Practice Research Network (ASPREN).** This system has general practitioners (GPs) who report influenza-like illness (ILI) presentation rates in New South Wales, South Australia, Victoria, Queensland, Tasmania, Western Australia and the Northern Territory. As jurisdictions joined ASPREN at different times and the number of GPs reporting has changed over time, the representativeness of ASPREN data in 2012 may be different from that of previous years. The national case definition for ILI is presentation with fever, cough and fatigue. Overall, there was an earlier increase and higher peak in ILI consultation rates compared with the seasonal peaks reported in 2010 and 2011.

  - **Emergency department surveillance.** Emergency departments across New South Wales and Western Australia participated in influenza surveillance. Both Western Australia and New South Wales emergency department surveillance indicated that influenza activity in 2012 was higher than in 2010 and 2011.

  - **FluTracking.** FluTracking is an online health surveillance system to detect influenza epidemics. It involves participants from around Australia completing a simple online weekly survey, which collects data on the rate of ILI symptoms in communities. Overall, FluTracking activity in 2012 was higher than in 2010 and 2011, but lower than that of 2008-2009.

[1] http://www.cdc.gov/mmwr/pdf/wk/mm6136.pdf

- **Laboratory surveillance:**
  - **National Notifiable Disease Surveillance System (NNDSS).** In Australia, laboratory-confirmed cases of influenza became nationally notifiable from 1 January 2001. All laboratory-confirmed cases are required to be reported to state and territory health departments. From January to 31 August 2012, there have been 36,321 laboratory-confirmed notifications of influenza diagnosed and reported to NNDSS. Of these, 29,744 (82%) cases were reported as influenza A (63% influenza A (unsubtyped), 18% A(H3N2) and 1% A(H1N1)pdm09) and 6,489 (18%) were influenza B. A further 41 (<1%) were type A&B and 3 (<1%) were type C. In addition, the age distribution of influenza notifications has shown a bimodal trend with peaks in those aged 0-4 years and in those aged 70 years and over, with a small peak among those aged 30-44 years. Overall, the 2012 notification data are higher than that of 2011 and 2010.

  - **WHOCC Laboratory Surveillance.** This is conducted by the Melbourne WHOCC. A total of 1297 influenza viruses from Australia were received for analysis at the Melbourne WHOCC (Appendix 2) from 1 March to 12 September 2012. Eight hundred and seventy-five A(H3N2) viruses (67.5%, 875/1297) were isolated with the majority relating antigenically to the A/Perth/16/2009-lik and A/Victoria/361/2011-like strains. Sixteen (1.2%, 16/1297) of the isolates were influenza A(H1N1)pdm09 viruses and antigenically closely related to A/California/7/2009 (H1N1)-like strain. Four hundred and six (31.3%, 406/1297) influenza B viruses were isolated with most of them belonging to the B/Victoria lineage. Regarding oseltamivir-resistant viruses, between 1 January to 3 September 2012, one influenza A(H1N1)pdm09 virus (out of 810 tested) have shown resistance to NA inhibitor oseltamivir by enzyme inhibition assay. This virus also had the H275Y mutation known to confer resistance to oseltamivir.

  - **Sentinel Laboratory Surveillance.** Laboratory testing data are provided weekly directly from the three National Influenza Centres (PathWest (WA), VIDRL (VIC) and ICPMR (NSW) and also from Tasmanian laboratories. Additionally, approximately 30% of all ILI patients presenting to ASPREN-based sentinel GPs are swabbed for laboratory testing, and the results of ASPREN ILI laboratory respiratory viral tests now include Western Australia. From the fortnight ending 18 August to 31 August 2012, a total of 25.1% of the specimens have been positive for influenza.

- **Severity Surveillance:**
  - **Influenza hospitalisations.** The Influenza Complications Network (FluCAN) collects detailed clinical information on all hospitalised cases of influenza and pneumonia from a sample of four sentinel hospitals across Australia. Overall, the majority of admissions have been with influenza A, with 15% of cases due to influenza B. Around 45% of the cases are aged 65 years and over (median age 61 years) and 75% of all cases have known medical co-morbidities.

  - **Queensland public hospital admissions (EpiLog).** EpiLog is a web based application developed by Queensland Health. This surveillance system generates admission records for confirmed influenza cases through interfaces with the inpatient information and public laboratory databases. Records are also able to be generated manually. Admissions data reported are based on date of reported onset. Up to 2 September 2012, there have been 1472 admissions of confirmed influenza this year, including 137 to intensive care units. The age distribution of confirmed influenza admissions in 2012 shows a bimodal distribution peaking in the 0-9 and also the 70 years and over age groups.

- **Australian Paediatric Surveillance.** This surveillance system reports on hospital admissions of children aged 15 years and under to intensive care units (ICUs) around Australia following complications due to influenza infection, and was initiated at the start of June 2009 through the Australian Paediatric Surveillance Unit (APSU). Details of admissions are reported weekly. From 1 July to 31 August 2012, there have been 28 hospitalisations associated with severe influenza complications in children, including 8 ICU admissions. The majority of these hospitalisations were associated with influenza A infections. More than one third of the cases had an underlying chronic condition reported.

- **Death associated with influenza and pneumonia.** Nationally reported influenza deaths are notified by jurisdictions to the NNDSS. As of 31 August 2012, 43 influenza-related deaths have been notified to this system with a median age of 80 years. Almost all cases were reported as having influenza A(unsubtyped) or A(H3N2), with the A(unsubtyped) infections also likely to be attributable to A(H3N2). The number of influenza associated deaths reported the NNDSS are reliant on the follow up of cases to determine the outcome of their infection and most likely do not represent the true mortality impact associated with this disease.

- **Death certificate survey.** The registered death certificates from the births, deaths and marriages office in New South Wales were collected for influenza and pneumonia deaths. Death registration data show that until the week ending 10 August 2012, there were 1.67 pneumonia- or influenza-associated deaths per 100,000 population in NSW, which is below the seasonal threshold of 1.73 per 100,000 NSW population for this period.

(Abridged from the Australian Influenza Surveillance Report 2012, No.7, Department of Health and Ageing, Australia and a report by Dr. Ian Barr, WHO Collaborating Centre for Influenza, Melbourne.)

1.3 Influenza activity in South Africa, March to September 2012

Influenza surveillance in South Africa has been expanded significantly during 2012 and includes three main active surveillance programmes and one passive surveillance system.

- **Viral watch programme** – A total of 246 doctors and primary health care nurses have been recruited across the country to participate in the ILI sentinel surveillance programme from all nine provinces. This programme focuses on mild infections seen mainly by GPs as well as a few paediatricians and primary health care clinics across the country.

- **Enhanced viral watch programme** – This programme was established following the emergence of the influenza A(H1N1)pdm09 with the aim of expanding the "viral watch" to include hospitalised patients. This programme includes 11 hospitals covering all nine provinces and focuses on hospitalised patients with severe acute respiratory-tract infection (SARI) across the country.

- **SARI surveillance programme** - The SARI surveillance programme was established in 2009 and monitors cases of more severe disease in hospitalised patients. Detailed epidemiologic data are collected on all patients. This programme currently includes 5 hospitals as 4 sentinel sites covering 4 provinces: Chris Hani Baragwanath Hospital (CHBH), an urban setting hospital situated in Gauteng Province with a well-defined population (Soweto); Edendale

Hospital (EH) a semi-urban setting hospital situated in KwaZulu-Natal Province, Klerksdorp and Tshepong Hospitals (KH) situated in a semi-urban setting in the Northwest Province and Mapulaneng and Matikwana Hospitals (MMHs), rural setting hospitals in Mpumalanga Province. In addition the respiratory consultations and hospitalisations surveillance system collects anonymous influenza- and pneumonia-associated outpatient consultations and hospitalisations data from one private hospital group in 7 provinces (Gauteng, North West, Free State, Mpumalanga, Eastern and Western Cape and KwaZulu-Natal). These data on the number of consultations and hospitalisations are compared to the influenza season as described by the viral watch and SARI programmes.

- **Passive surveillance system**: Apart from these active surveillance sites, the National Institute for Communicable Diseases (NICD) also offers support to National Health Laboratory Service laboratories that routinely test for respiratory virus disease across the country.

In 2012, a total of 6516 suspected influenza specimens were processed up to week 36. Of which, 1037 influenza viruses were detected. This gave an overall detection rate of 15.9% compared with 23% in 2011. Among all detected influenza viruses, influenza A was detected in 612 (59%, 612/1037) and influenza B in 425 (41%, 425/1037). Among all influenza A viruses, influenza A(H3N2) was the predominant strain (98.5%, 603/612) compared with the A(H1N1)pdm09 strain (0.8%, 5/612). Among all influenza B viruses (425), B/Victoria lineage viruses (32%, 136/425) outnumbered B/Yamagata lineage viruses (14.4%, 61/425).

A total of 60 seasonal influenza A(H3N2) viruses were sequenced and they were clustered genetically with the A/Victoria/208/2009 clade. A total of 26 A(H3N2) virus isolates could be characterised antigenically by hemagglutination inhibition assay (HIA) and almost all showed normal reactivity to the A/Perth/16/2009 reference antiserum. The NA genes of the 142 seasonal influenza A(H3N2) viruses were sequenced and no resistance causing mutations were identified.

In the 2012 season only five influenza A viruses were subtyped as A(H1N1)pdm09 and no virus isolates were recovered in cell cultures. The HA gene could be sequenced from one and further sequencing of the rest of the viruses is in progress. The M gene was sequenced from 3 clinical samples and all 3 viruses are resistant to amantadine as it carries the S31N mutation.

Thirty three influenza B viruses were characterized for reactivity to reference antisera raised against vaccine or other reference antigens using the hemagglutination inhibition assay. Twenty six isolates reacted to the B/Brisbane/60/2008-like reference antisera and showed low antigenic reactivity to reference antisera. For the seven B/Yamagata-like isolates, all except one of the B/Yamagata-like virus isolates showed low reactivity with antisera raised against the B/Wisconsin/1/2010 strain. Phylogenetic analysis was done for the 45 B/Victoria/lineage-like viruses and showed that the majority of the viruses are B/Brisbane/60/2008-like (or genetic clade 1). Phylogenetic analysis was done for 21 B/Yamagata lineage viruses. Fourteen of the 21 B/Yamagata lineage-like viruses fall in clade 3 and 7 fall in clade 2.

No neuraminidase inhibitor resistant influenza viruses have been detected for 20 tested viruses by using phenotypic assay.

(Abridged from a report by Dr. Florette Treurnicht, National Institute for Communicable Diseases, South Africa.)

2. INFLUENZA ACTIVITY IN NEW ZEALAND IN 2012

The national influenza surveillance system in New Zealand is an essential public health tool for assessing and implementing strategies to control influenza. The surveillance system includes community-based surveillance (ESR's sentinel general practitioners (GP) surveillance, HealthStat GP surveillance), hospital-based surveillance (SHIVERS, ICD-based hospitalisation and non-sentinel laboratory surveillance), and event-based surveillance (telephone health advice service – Healthline).

Influenza activity during the 2012 New Zealand winter was at a medium level compared to that of the past 21 years of surveillance. When the 2012 sentinel ILI consultation data were compared to the 1992-2012 data, the 2012 peak consultation rate of 154.1 per 100 000 was the 11th highest.

The 2012 influenza activity remained below the baseline in May and June. The ILI rate first crossed the baseline level in week 26 (25 June – 1 July 2012) and reached the peak in week 31 (30 July – 5 August 2012). As in previous years, the influenza activity in 2012 had uneven geographical distribution.

ILI disease burden was higher in children (0-5 years) compared to other age groups. SARI disease burden was higher in both young children (0-5 years) and elderly (65+) compared to other age groups. SARI disease burden was also higher in Pacific peoples and Maori ethnic groups than Europeans and Asians.

Influenza A(H3N2) was the predominant strain among all influenza viruses in most of the regions in the 2012 New Zealand winter. It represented 67.8% (1356/2000) of all viruses including 243 of A/Perth/16/2009 viruses. The influenza strain predominance had regional and temporal variation. For example, in the Auckland region during May-July, influenza A(H1N1)pdm09 predominated. However, this was replaced by influenza A(H3N2) predominance in August. Most of A(H3N2) viruses reacted well with sheep/rabbit antisera raised against A/Perth/16/2009 vaccine strain. The sequenced viruses showed that they fell into the genetic group 3 within the A/Victoria/316/2011 genetic clade.

Influenza A(H1N1)pdm09 and influenza B viruses co-circulated with A(H3N2) viruses. Influenza A(H1N1)pdm09 viruses represented 11.9% (237/2000) of all viruses, including 70 of A/California/7/2009 viruses. Influenza B viruses represented 8.9% (178/2000) of all viruses, including 39 of B/Wisconsin/1/2010 viruses and 11 of B/Brisbane/60/2008 viruses.

All circulating influenza viruses tested (except one) were sensitive to oseltamivir. The first oseltamivir resistant influenza A(H1N1)pdm09 was detected from a 26 year old male who was hospitalised with acute upper respiratory infection within 7 days after returning to New Zealand from India. This virus is genetically closer to the Indian A(H1N1)pdm09 viruses than the New Zealand A(H1N1)pdm09 viruses.

2.1 Community-based surveillance

2.1.1 ESR's sentinel GP-based surveillance

The New Zealand sentinel GP surveillance system was established in 1991 as part of the World Health Organization (WHO) global program for influenza surveillance. The system is operated nationally by the Institute of Environmental Science and Research (ESR) and locally by

surveillance coordinators in the public health units of the country's 20 District Health Boards (DHB). Surveillance is conducted during May–September (the southern hemisphere winter) by volunteer sentinel GP's distributed across New Zealand.

The sentinel system defines a case of ILI as *an acute respiratory tract infection characterized by an abrupt onset of at least two of the following: fever, chills, headache, and myalgia*. Each participating GP records the daily number of patients consulted for ILI, along with the patient's age. These data are collected by local district coordinators each week. Total crude national ILI consultation rates are calculated weekly using the sum of the GP patient populations as the denominator. As age group–specific GP patient population data are not provided by the participating practitioners, the denominator for age group–specific ILI consultation rates is based on New Zealand census data with the assumption that the age group distribution for GP patient populations is the same as the distribution for the entire New Zealand population.

Each participating GP also collects three respiratory samples (nasopharyngeal or throat swab) each week from the first ILI patients examined on Monday, Tuesday, and Wednesday. The GP's forward these samples to the WHO National Influenza Centre at ESR or to hospital virology laboratories in Auckland, Waikato, or Christchurch for virus characterization. Laboratory identification methods include molecular detection by polymerase chain reaction, isolation of the virus, or direct detection of viral antigen. Influenza viruses are typed and subtyped as influenza A, B, seasonal A (H1N1), seasonal A (H3N2), or pandemic (H1N1) 2009. The virus identification data are forwarded by hospital laboratories to ESR each week. ESR compiles and reports national epidemiologic and virologic data on influenza to WHO and also publishes these data on the ESR website (http://www.esr.cri.nz/virology/virology_weekly_report.php)

In 2012, 84 sentinel practices were recruited from 19 of 20 DHBs under ESR's sentinel GP-based surveillance. Some sentinel practices did not report every week. The average number of practices participating per week was 81, with an average patient population roll of 375 676 (approximately 8.5% of the New Zealand population). From week 18 (the week ending 6 May 2011) through week 34 (the week ending 26 August 2012), a total of 3571 consultations for ILI were reported from the 19 DHBs. It is estimated that ILI resulting in a visit to a general practitioner affected over 41 873 New Zealanders (0.95% of total population). The cumulative incidence of ILI consultation during this period was 950.6 per 100 000 population. The average weekly ILI consultation rate during this period was 57.2 per 100 000 population.

Weekly national ILI consultation rates for the study period were compared with the same period in 2007 and 2011. From week 18 (ending 6 May 2012) through week 26 (ending 1 July 2012), the weekly ILI consultation rate remained below the baseline level of 50 consultations per 100 000 patient population (Figure 1). The ILI rate first crossed the baseline level in week 27 (2–8 July 2012) and increased to the peak in week 31 (30 July – 5 August 2012) at 154.1 per 100 000 patient population. This was slightly higher than the peak rate of 151.6 consultations recorded in 2010 but lower than the peak of 284.0 consultations in 2009. The peak ILI rate in 2012 was in the middle range (11th highest) during 1992-2012 (Figure 2). Since week 31, influenza activity has been declining.

Figure 1. Weekly Consultation Rates for Influenza-like Illness in New Zealand, 2007-2012

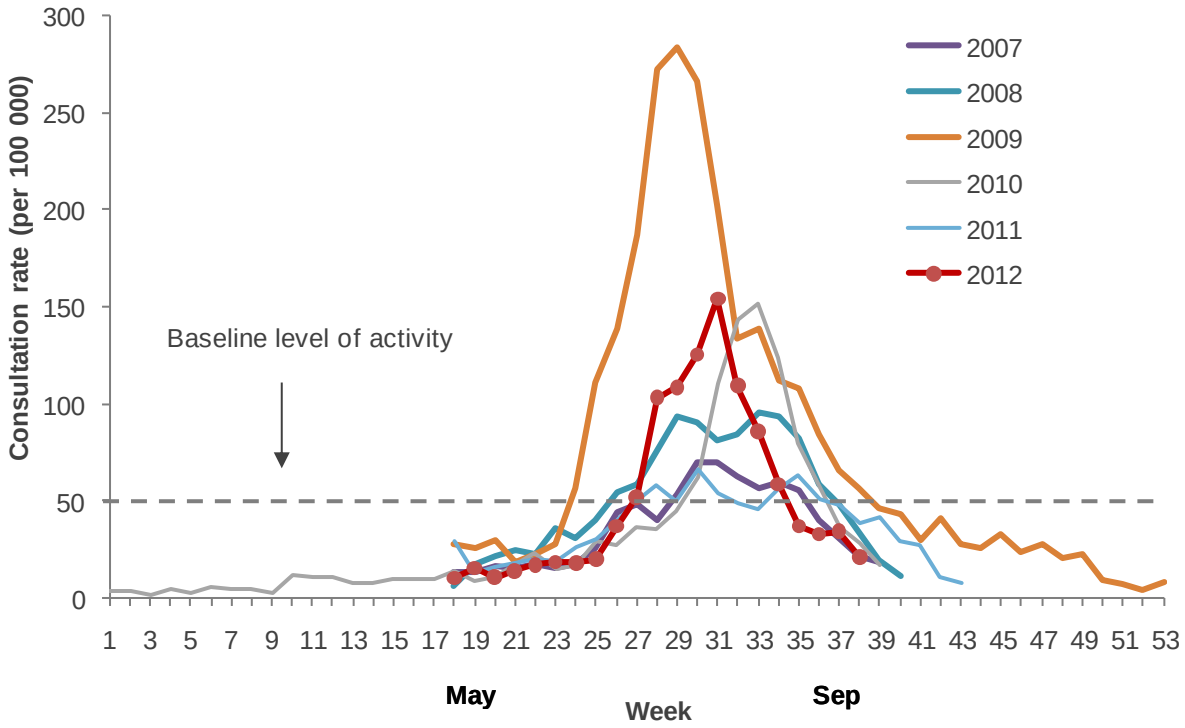
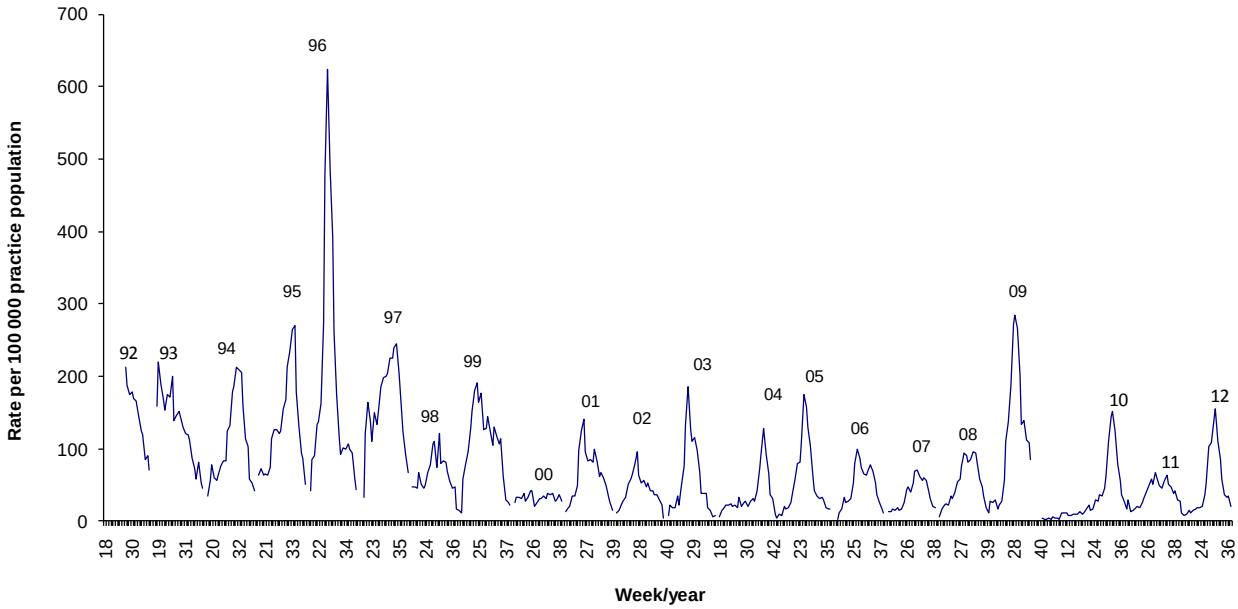


Figure 2. Weekly Consultation Rates for Influenza-like Illness in New Zealand, 1992-2012



As in previous years, 2012 consultation rates for ILI varied greatly among DHBs (Figure 3). From week 18 (the week ending 6 May 2011) through week 34 (the week ending 26 August 2012), Waitemata DHB had the highest consultation rate (153.8 per 100 000), followed by South Canterbury (20.5 per 100 000) and Auckland (81.0 per 100 000).

Figure 3. Average weekly consultation rate for influenza-like illness by District Health Board, 2012

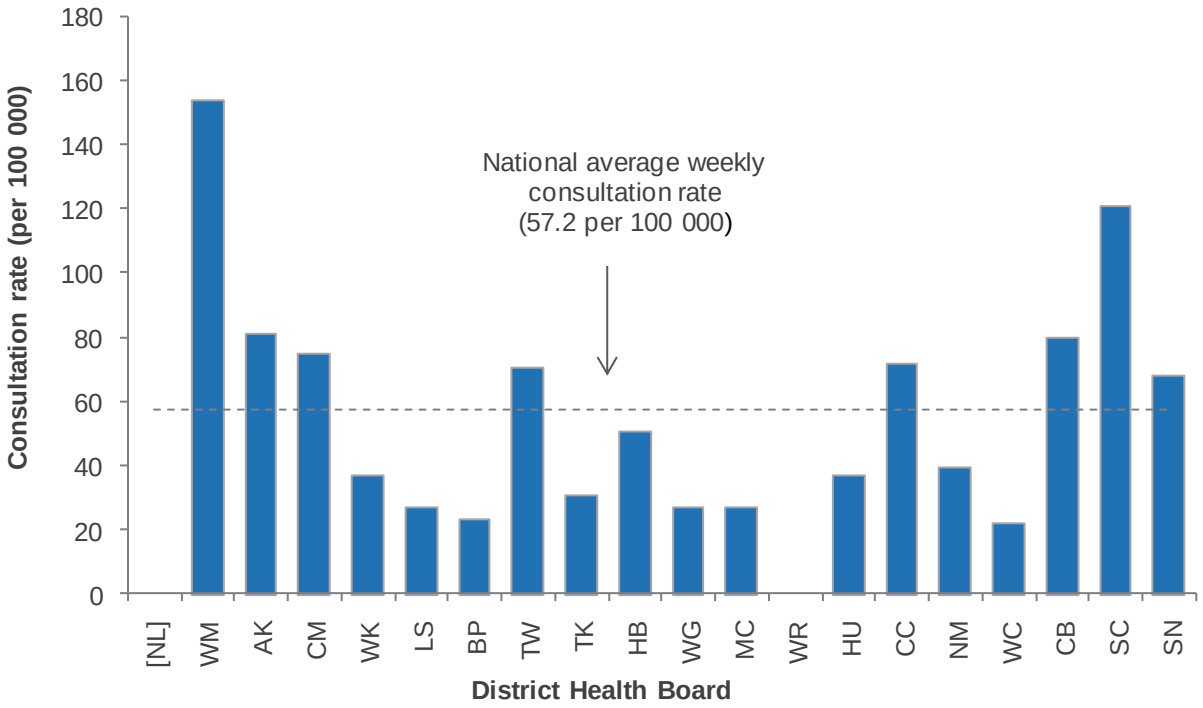
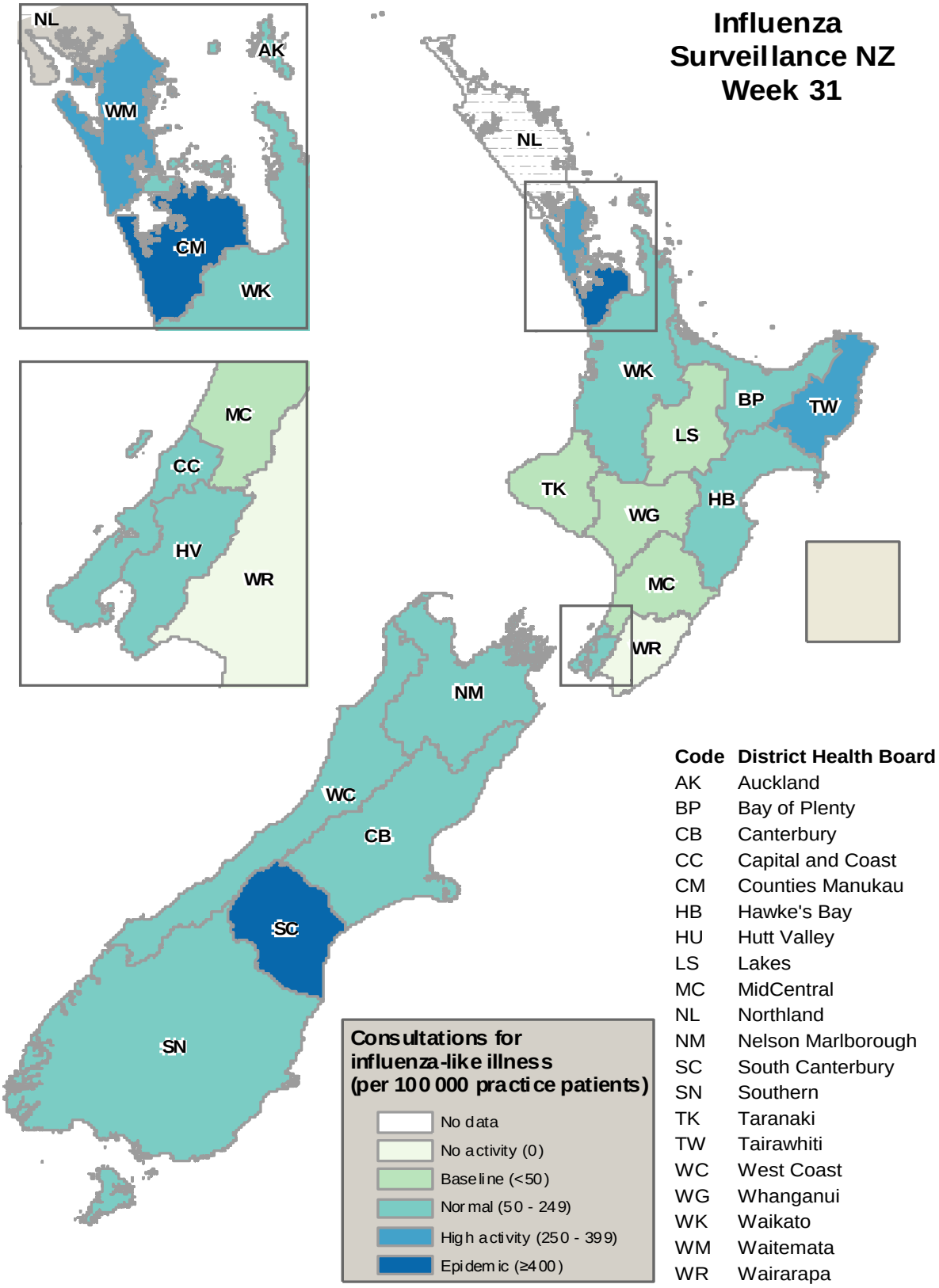


Figure 4 shows ILI consultations among DHBs during the peak week 31 (30 July – 5 August 2012). South Canterbury DHB had the highest consultation rate (594.9 per 100 000, 31 cases) followed by Counties Manukau (424.1 per 100 000, 5 cases). The following DHBs also had rates above the national average of 152.0 per 100 000: Tairawhiti (373.4 per 100 000, 12 cases), Waitemata (268.3 per 100 000, 26 cases), Capital and Coast (245.0 per 100 000, 54 cases), Southern (238.9 per 100 000, 137 cases), Hawke's Bay (233.8 per 100 000, 45 cases), Auckland (218.2 per 100 000, 48 cases), and Canterbury (155.1 per 100 000, 110 cases).

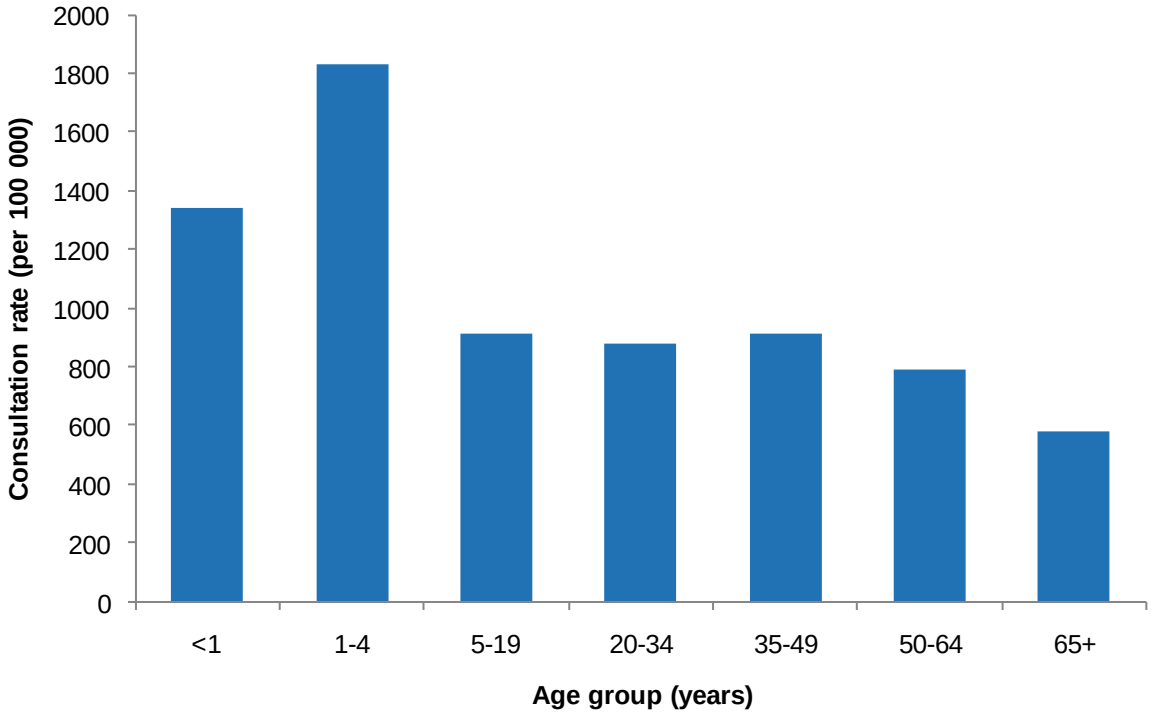
Figure 4. ILI consultation rates by District Health Board for the peak week 31 (30 July – 5 August 2012)



A weekly rate <50 ILI consultations per 100 000 patient population is considered baseline activity. A rate of 50–249 is considered indicative of normal seasonal influenza activity, and a rate of 250–399 indicative of higher than expected influenza activity. A rate ≥400 ILI consultations per 100 000 patient population indicates an epidemic level of influenza activity.

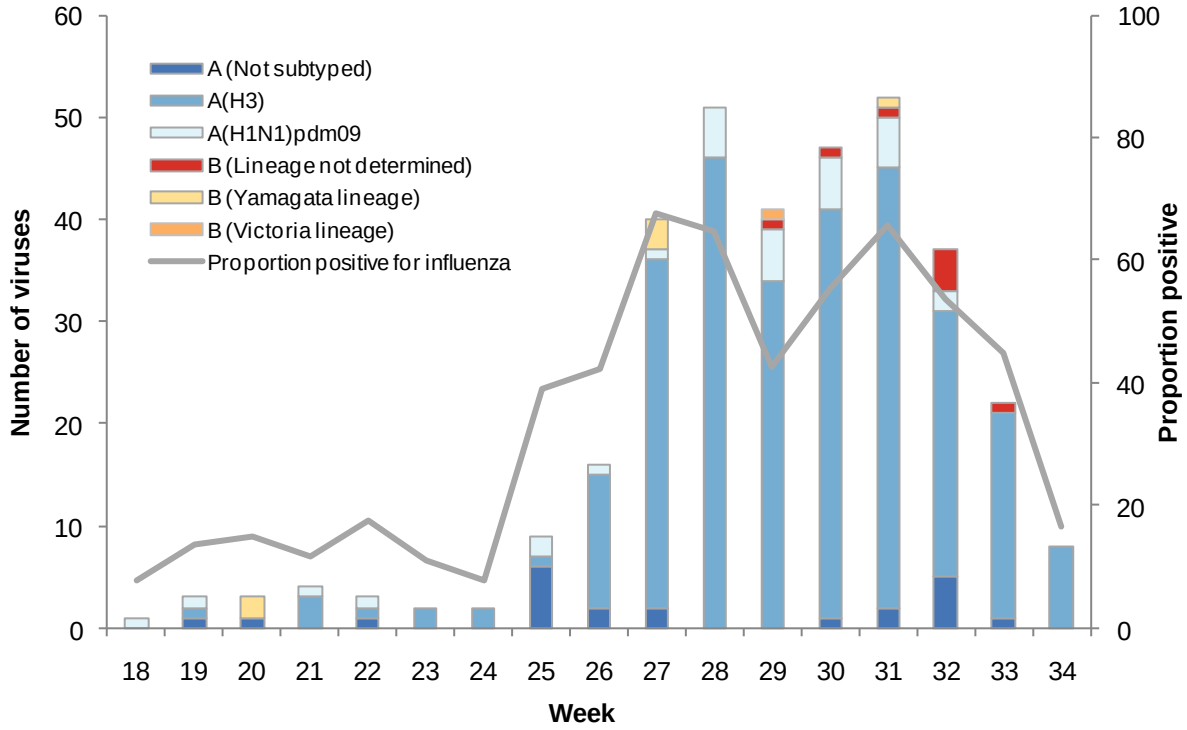
From week 18 (the week ending 6 May 2011) through week 34 (the week ending 26 August 2012), the highest cumulative ILI consultation rates were recorded among children and aged 1-4 years (1832.0 per 100 000 age group population) and those aged <1 year (1337.9 per 100 000) (Figure 5). The lowest rates were in the ≥65 years (580.6 per 100 000) and those in the 50-64 years (792.5 per 100 000).

Figure 5. Sentinel Average Cumulative Consultation Rates for ILI by Age Group, 2012



A total of 775 swabs were sent to virology laboratories from sentinel GPs during week 18 (ending 6 May 2011) through week 34 (ending 26 August 2012). From these swabs, 341 influenza viruses were identified. This gave an overall detection rate of 44.0%. The predominant strain was influenza A(H3N2) (274) including 102 A/Perth/16/2009 (H3N2) -like viruses, 30 A(H1N1)pdm09 including 18 A/California/7/2009 (H1N1)-like viruses, B (15) including one of B/Brisbane/60/2008-like (belonging to the B/Victoria lineage) and six B/Wisconsin/1/2010-like viruses (belonging to the B/Yamagata lineage), and A (not sub-typed) (22) (Figure 6). Influenza A(H3N2) strain has been the predominant strain for the most of the winter season in 2012.

Figure 6. Number of influenza viruses reported by type and week from sentinel surveillance



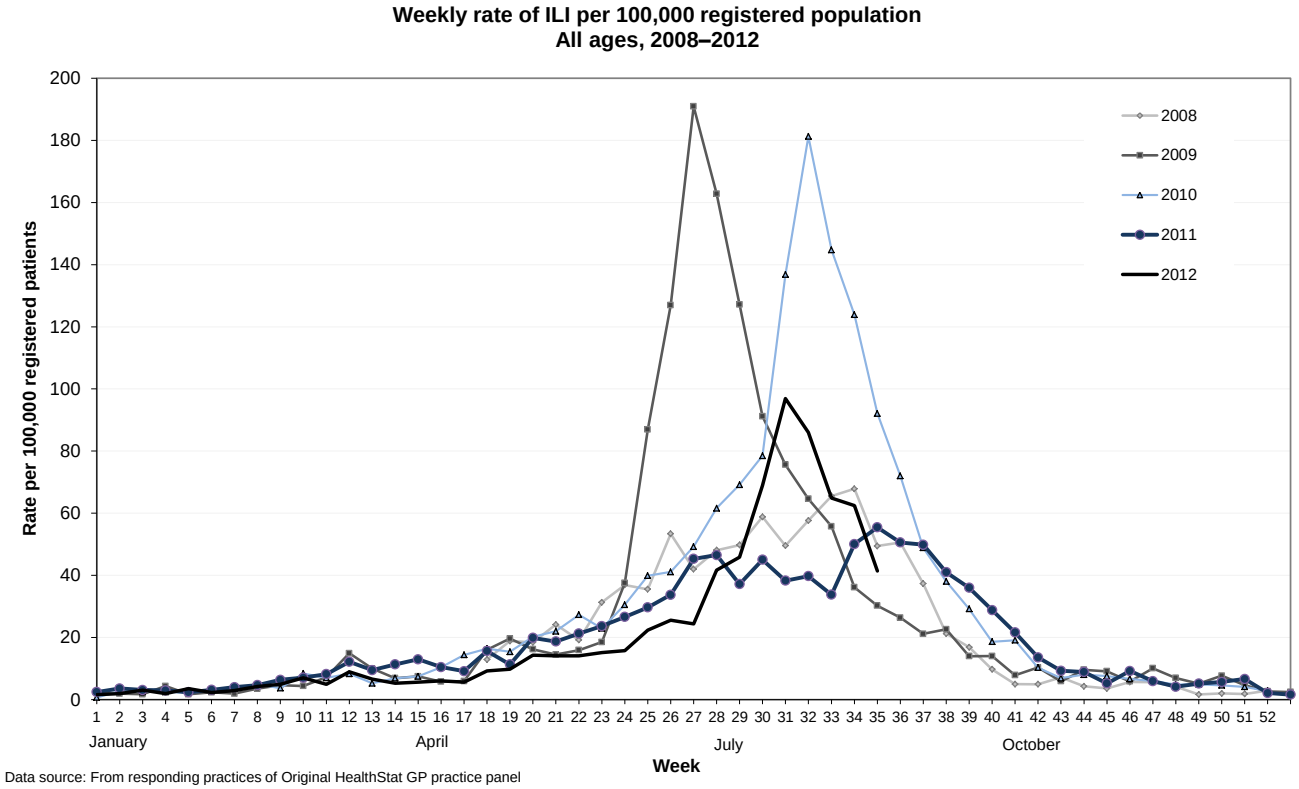
2.1.2 HealthStat GP-based surveillance

HealthStat is a computer-based routine surveillance system of a nationally representative random sample of approximately 100 general practices that code for influenza-like-illness (ILI). The case definition used for ILI by HealthStat is: "acute URTI, with abrupt onset of 2+ symptoms from chills, fever, headache and myalgia". This surveillance system monitors the number of people who have primary care (GP) consultations. HealthStat is based on the automated downloads from GP practice management computer systems. This service is provided to ESR by CBG Health Research Ltd. HealthStat GP-based surveillance does not contain a component of the virological surveillance.

Analysis is frequency based with alarms raised by identifying statistical deviations (aberations) from previous counts. The analysis of the ILI count is based on the cumulative summation (CUSUM) algorithm implemented in Early Aberration Reporting System (EARS) application developed by the Centres for Disease Control and Prevention (CDC), Atlanta, United States. EARS has three sensitivity thresholds (high, medium and low). If the daily call count exceeds a threshold a flag is signalled.

Figure 7 below shows the weekly rate of ILI per 100 000 registered population, 2008-2012. The 2009 and 2010 data shows major difference compared to other surveillance systems, probably reflecting low sensitivity of the coding practices in 2009. It appears that the coding practices have been improved since 2010.

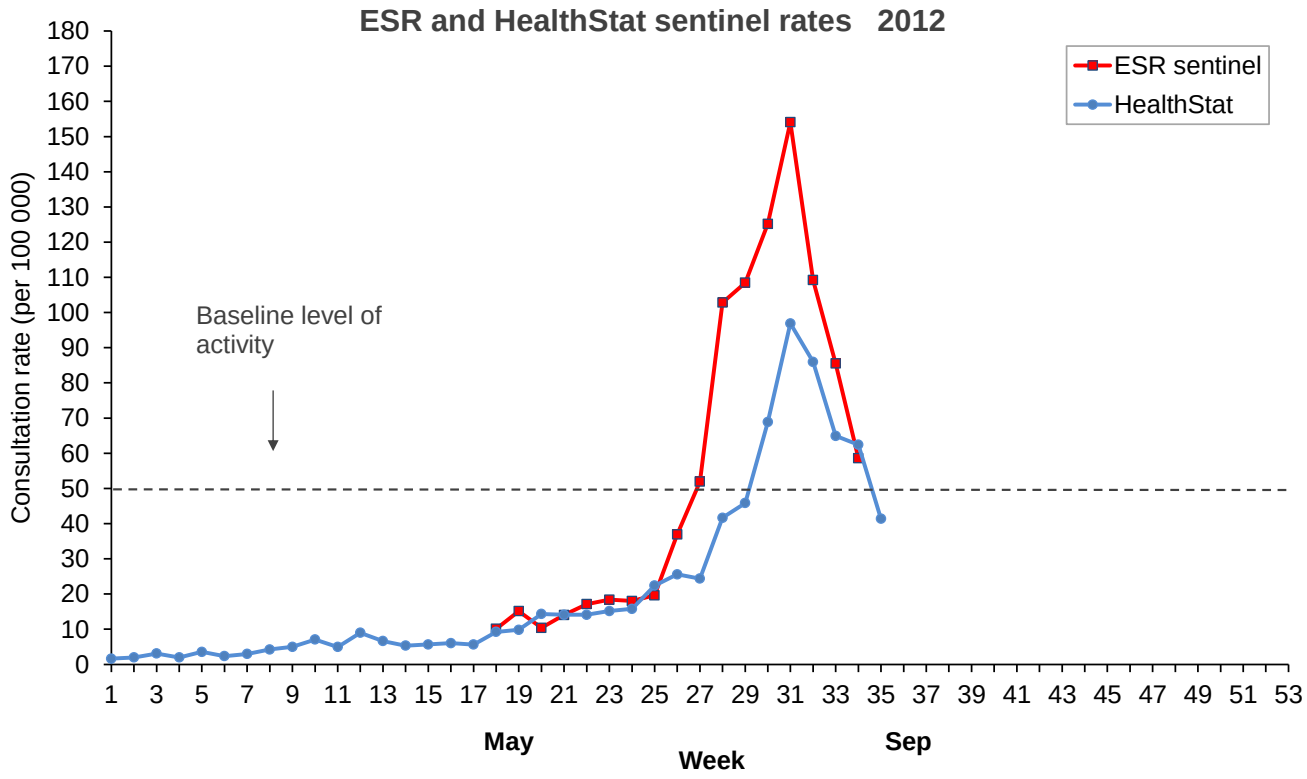
Figure 7. HealthStat ILI consultation rates by week, 2008-2012



Data source: From responding practices of Original HealthStat GP practice panel

Overall, the trend of the 2012 data is similar to ESR's sentinel GP surveillance but with overall lower ILI rates (Figure 8 below). HealthStat recorded the peak (96.9 per 100 000) in week 31 which was lower than the peak (154.1 per 100 000 in week 31) recorded by ESR's sentinel surveillance.

Figure 8. ESR and HealthStat sentinel GP-based ILI rates comparison, 2012



2.2 Hospital-based surveillance

2.2.1 Southern hemisphere influenza and vaccine effectiveness research and surveillance (SHIVERS)

Recent global experience with pandemic influenza A(H1N1)pdm09 highlights the importance of monitoring severe respiratory disease. Hospital surveillance for severe acute respiratory infections (SARI) provides evidence to inform public health and clinical practice to reduce the impact of influenza virus infection and other important respiratory pathogens and support pandemic preparedness. Enhanced, active, year-round, population-based surveillance has been established for SARI cases admitted to hospitals in the Auckland region with a population of 838,000 people, covering Auckland District Health Board (ADHB) and Counties Manukau District Health Board (CMDHB). The aims of SARI surveillance are:

- To measure the burden of severe disease caused by influenza and other respiratory pathogens;
- To monitor trends in severe disease caused by influenza and other respiratory pathogens;
- To identify high risk groups that should be prioritized for prevention and treatment;
- To monitor antigenic, genetic and antiviral characteristics of influenza viruses associated with severe disease.
- To provide a study base to estimate the effectiveness of influenza vaccine.

Any inpatient with suspected respiratory infections admitted overnight to each of the four DHB hospitals are to be screened by research nurses daily. Overnight admission is defined as: *"A patient who is admitted under a medical team, and to a hospital ward or assessment unit"*. Suspected respiratory infections include acute infections and acute exacerbations of chronic respiratory conditions. The scope is covered by the following broad conditions:

- Suspected acute upper respiratory tract infection (including coryza, pharyngitis)
- Suspected croup
- Suspected bronchiolitis (in children)
- Suspected pneumonia
- Exacerbations of asthma
- Exacerbations of childhood chronic lung disease (including bronchiectasis, cystic fibrosis)
- Exacerbations of adult chronic lung disease (including COPD, emphysema, bronchitis)
- Respiratory failure
- Other suspected acute respiratory infections
- Febrile illness with respiratory symptoms (including shortness of breath)
- Other suspected acute respiratory infection

All patients with suspected respiratory infections are ascertained to see whether they meet the WHO SARI case definition: An acute respiratory illness with:

- a history of fever or measured fever of ≥38°C, **AND**
- cough**, AND**
- onset within the past 7 days**, AND**
- requiring inpatient hospitalization

If a patient with suspected respiratory infection who meet SARI case definition, a respiratory sample is collected for testing influenza and other respiratory pathogens. In addition, the patient information is captured via a case report form contains the following data elements:

- Patient demographics
- History of presenting illness
- Co-morbidities

- Disease course and outcome, including major treatments, ICU admission and SARI-related mortality
- Additional questions designed to ascertain more detailed information regarding possible epidemiologic risk factors for SARI, environmental factors and health conditions (vaccination and smoking etc)
- Laboratory results

This report summarises data obtained from SARI surveillance from 30 April (week 18) to 9 September (week 36) in 2012. This includes incidence, demographic characteristics, clinical outcomes and aetiologies for SARI cases and preliminary analysis for vaccine effectiveness.

SEVERE ACUTE RESPIRATORY INFECTION (SARI)

From 30 April 2012 to 9 September 2012, there were 50449 acute admissions to ADHB and CMDHB hospitals. A total of 3896 patients with suspected respiratory infections were assessed in these hospitals. Of these, 1804 (46.3%) patients met the SARI case definition. Among these SARI patients, 307 (17%) had influenza viruses detected. Table 1 shows the admission diagnoses/syndromes of the suspected respiratory infections and SARI cases since start of the SARI surveillance and in week 36.

Table 1. Admission diagnoses/syndromes of suspected respiratory infections and SARI cases

	Week 36, ending 9 September 2012			Cumulative since 30 April 2012		
Admission diagnoses/syndrome	Overall (%)	SARI cases	Prop SARI (%)	Overall (%)	SARI cases	Prop SARI (%)
Suspected acute upper respiratory infection (including coryza, pharyngitis)	10 (4.4)	4	40.0	201 (5.2)	118	58.7
Suspected croup	0 (0)	0	0.0	20 (0.5)	10	50.0
Suspected bronchiolitis (in children)	34 (15)	8	23.5	604 (15.5)	328	54.3
Suspected pneumonia	72 (31.9)	44	61.1	982 (25.2)	631	64.3
Exacerbation of adult chronic lung disease (including COPD, emphysema, bronchitis)	30 (13.3)	10	33.3	469 (12)	125	26.7
Exacerbation of asthma	21 (9.3)	6	28.6	352 (9)	116	33.0
Exacerbations of bronchiectasis	0 (0)	0	0.0	20 (0.5)	7	35.0
Respiratory failure	3 (1.3)	0	0.0	37 (0.9)	11	29.7
Febrile illness with respiratory symptoms (including shortness of breath)	31 (13.7)	23	74.2	294 (7.5)	196	66.7
Other suspected acute respiratory infection	22 (9.7)	8	36.4	789 (20.3)	232	29.4
Not provided	3 (1.3)	0	0.0	128 (3.3)	30	23.4
Total	**226 (100)**	**103**	**45.6**	**3896 (100)**	**1804**	**46.3**

Table 2 shows the cumulative data on the demographic features of the influenza cases, SARI cases, suspected respiratory infections, and acute hospital admissions. From 30 April 2012 (week 18) to 9 September (week 36) 2012, the proportion of SARI cases among acute hospitalisations was 35.8 per 1000 hospitalisations. Among the 1804 SARI cases, 1508 were residents of ADHB and CMDHB, giving a cumulative SARI incidence of 180 per 100 000 population. 69 SARI cases were admitted to ICU; nine SARI cases were reported to have died during this period.

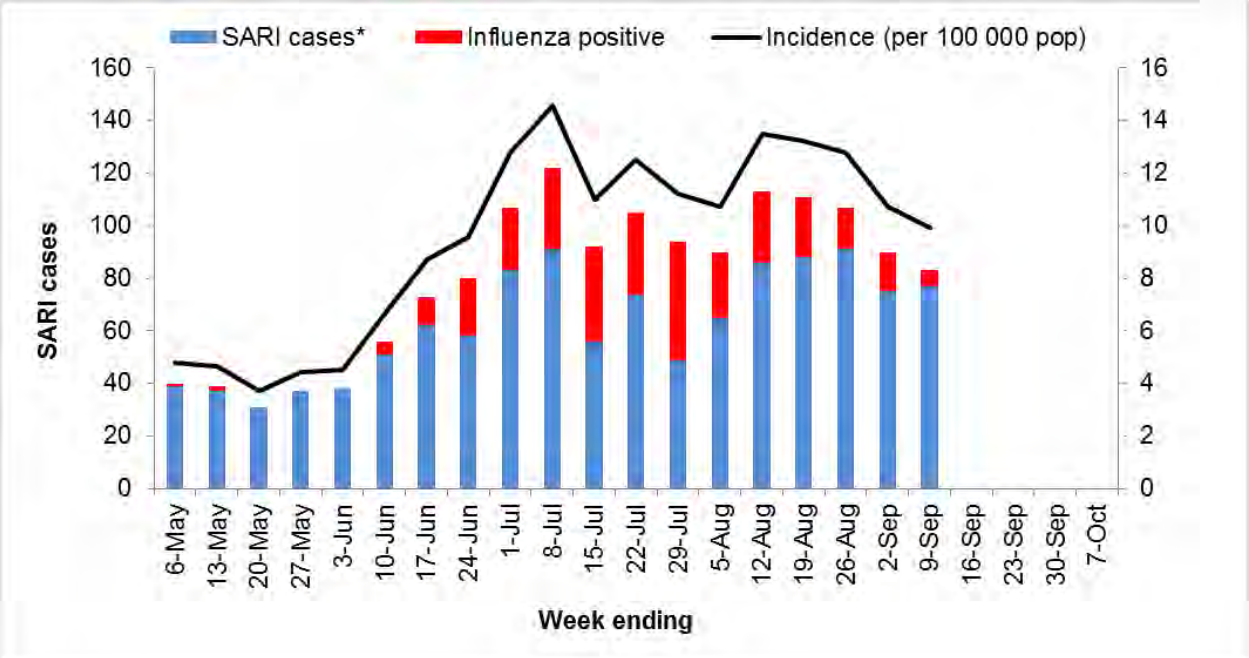
Figure 9 shows the weekly incidence of SARI cases per 100 000 population for ADHB and CMDHB residents as well as the numbers of SARI and influenza positive cases.

Table 2. Demographic characteristics of SARI and influenza cases, Weeks 18-36

Characteristics	Cumulative since 30 April 2012					
	Admissions	Assessed	Cases (%)	Cases per 1000 hospitalisations	Population[1] incidence (per 100 000)	Influenza positive (%)
Overall	**50449**	**3896**	**1804 (46.3)**	**35.8**	**180**	**307 (17)**
Age group (years)						
< 1	2393		331	138.3	2279.7	37 (11.2)
1 to 4	4151		235	56.6	412.8	33 (14)
5 to 19	6197		92	14.8	40.0	22 (23.9)
20 to 34	8856		147	16.6	69.1	32 (21.8)
35 to 49	7818		147	18.8	71.2	33 (22.4)
50 to 64	8021		228	28.4	179.7	51 (22.4)
65 to 79	7582		258	34	442.5	47 (18.2)
80 and over	5431		154	28.4	727.3	29 (18.8)
Unknown		2297	212			
Ethnicity						
Maori	6984		295	42.2	277.1	46 (15.6)
Pacific Peoples	11180		503	45	374.4	114 (22.7)
Asians	6838		150	21.9	87.4	30 (20)
European and others	25109		618	24.6	134.8	89 (14.4)
Unknown	338	2323	238			
Hospitals						
ADHB	27959	1567	995 (63.5)	35.6	208.4	142 (14.3)
CMDHB	22490	1509	735 (48.7)	32.7	151.7	160 (21.8)
Sex						
Female	26492		808	30.5	173.7	149 (18.4)
Male	23957		811	33.9	183.0	138 (17)
Unknown	0	2269	185			

[1]Includes only SARI cases residing in the study area, ADHB and CMDHB; cumulative incidence calculated for the period between week 18 and week 36 using census 2006 population. Incidence calculated on less than 5 cases should be interpreted with caution.

Figure 9. Weekly incidence of SARI, numbers and cases per 100 000 population



RESPIRATORY PATHOGEN SURVEILLANCE

From 30 April 2012 to 9 September 2012, 1475 SARI specimens have been tested and 319 (21.6%) were positive for influenza viruses: A (not subtyped) (106), A(H1N1)pdm09 (72) including 17 A/California/7/2009(H1N1) viruses, A(H3N2) (74) including 23 A/Perth/16/2009(H3N2), and B (68) including 13 B/Wisconsin/1/2010-like virus (belonging to the B/Yamagata lineage) and one B/Brisbane/60/2008. 42 SARI specimens had co-detection of influenza and non-influenza viruses.

From 30 April 2012 to 9 September 2012, 851 SARI specimens were tested for non-influenza respiratory viruses (Table 5). Of these, 387 (45.5%) were positive with the following viruses: respiratory syncytial virus (192), parainfluenza virus type 1 (21), parainfluenza virus type 3 (25), rhinovirus (155), adenovirus (25), and human metapneumovirus (24). 339 SARI specimens had single virus detection and 48 had multiple virus detection.

Table 3. Influenza and non-influenza respiratory viruses among SARI cases, 30 April 2012 to 26 August 2012

SARI cases virology	Cumulative since 30 April 2012		
	Cases	ICU	Deaths
Influenza viruses			
No. of specimens tested	1475	87	
No. of positive specimens (%)	319 (21.6)	16 (18.4)	
Influenza A			
A (not subtyped)	106	5	
A (H1N1)pdm09	72	6	
A (H3N2)	74	2	
Influenza B			
B (lineage not determined)	54	2	
B (Yamagata)	13	1	
B (Victoria)	1	-	
Influenza and non-influenza co-detection (% +ve)	42 (13.2)	1	
Non-influenza respiratory viruses			
No. of specimens tested	851	21	
No. of positive specimens (%)[1]	387 (45.5)	13 (61.9)	
Respiratory syncytial virus (RSV)	192	7	
Parainfluenza 1 (PIV1)	21	-	
Parainfluenza 2 (PIV2)	0	-	
Parainfluenza 3 (PIV3)	25	1	
Rhinovirus (RV)	155	6	
Adenovirus (AdV)	25	1	
Human metapneumovirus (hMPV)	24	1	
Single virus detection (% of positives)	339 (87.6)	10	
Multiple virus detection (% of positives)	48 (12.4)	3	

The temporal distribution of the number and proportion of the influenza viruses and non-influenza respiratory viruses is shown in Figures 10 & 11. Influenza A(H1N1)pdm09 was the predominant strain over A(H3N2) from week 23 (ending 10 June) to week 29 (ending 22 July). Since week 30 (ending 29 July), A(H3N2) became the predominant strain.

Figure 10. Temporal distribution of the number and proportion of influenza viruses from SARI specimens by type and week[1]

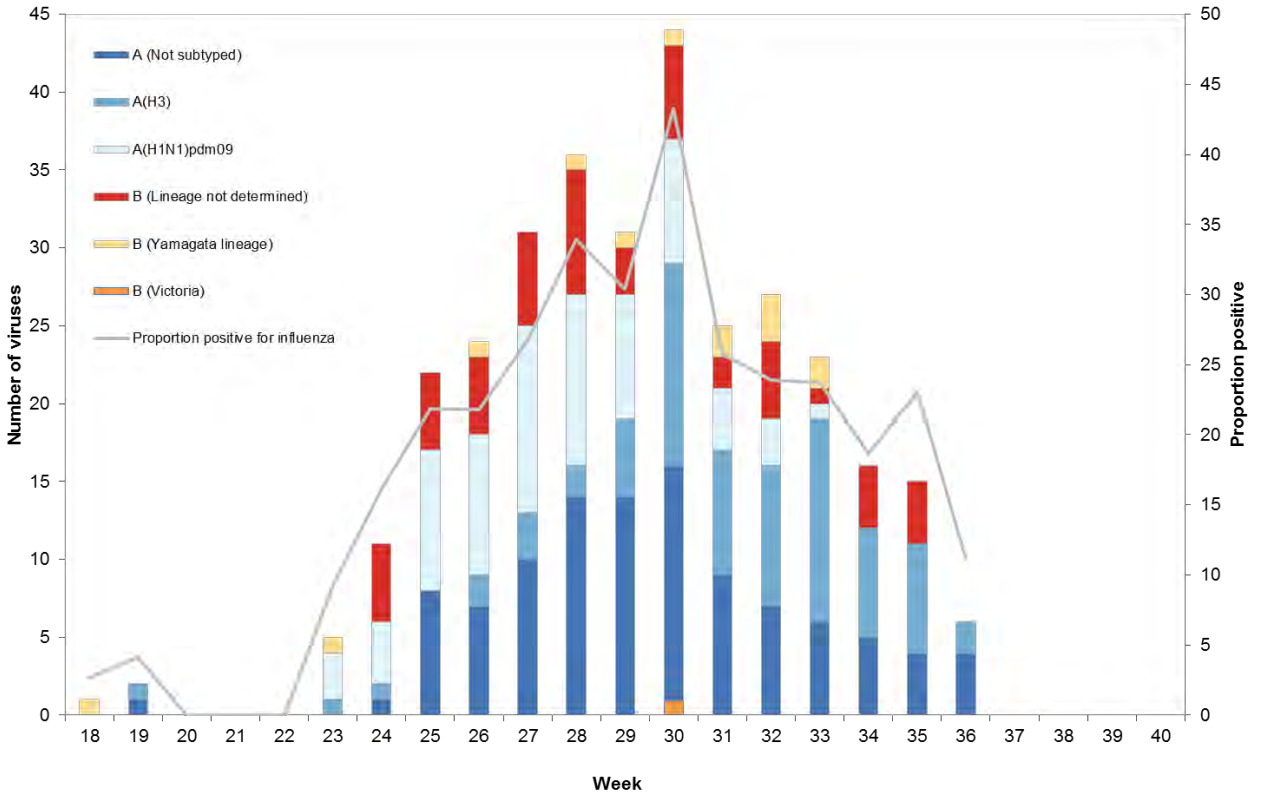
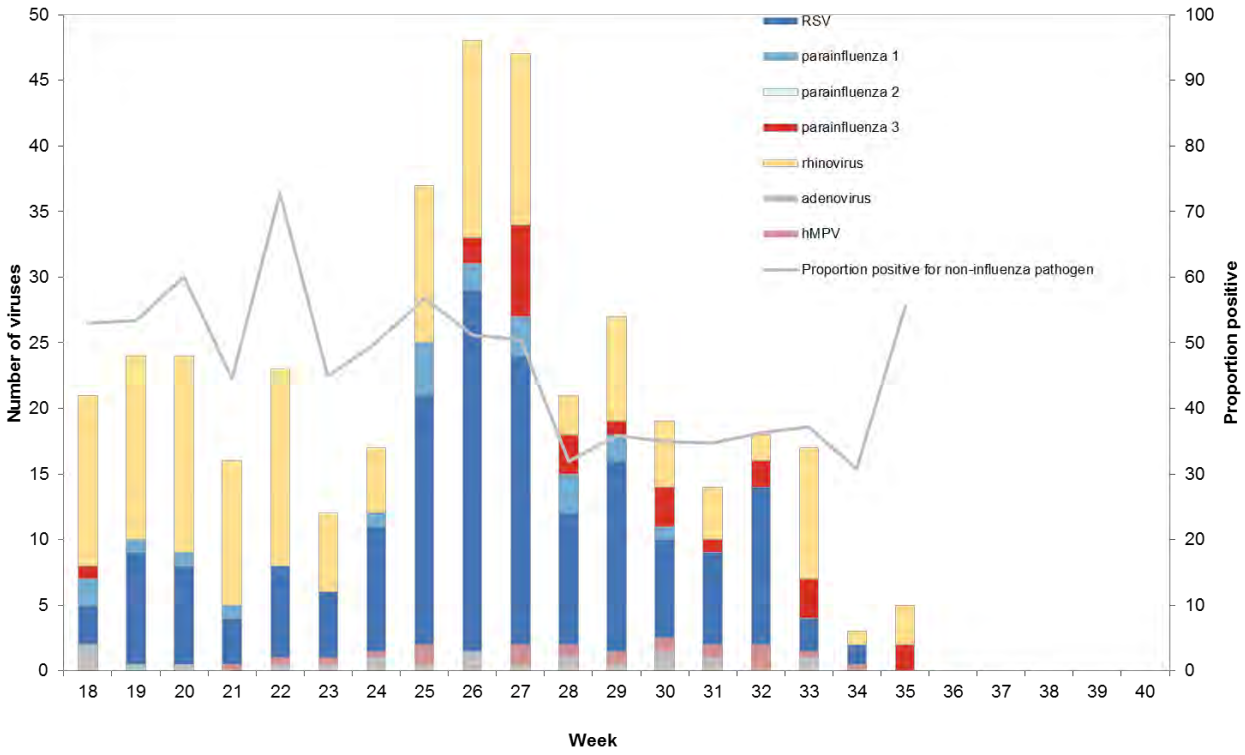


Figure 11. Temporal distribution of the number and proportion of non-influenza viruses from SARI specimens by type and week[1]



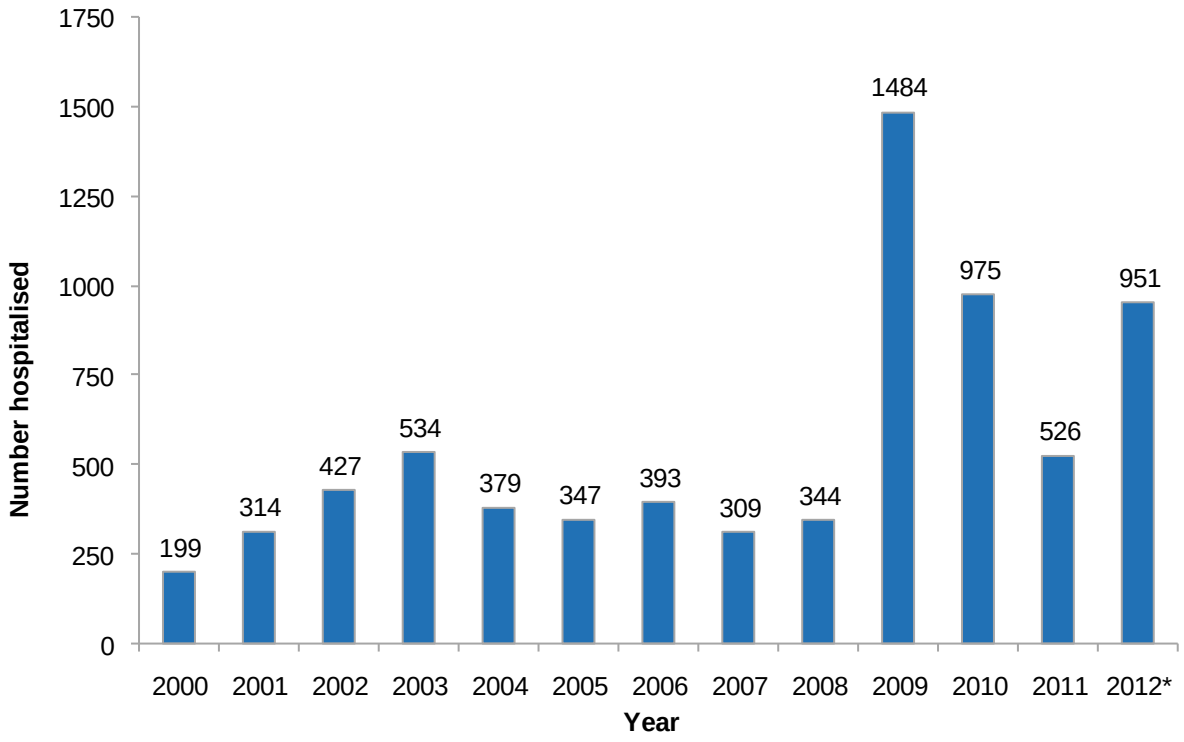
[1]Figures for recent weeks will be underestimates due to time lag in receiving laboratory test results.

2.2.2 ICD code based hospitalisation surveillance

Hospitalisation data for influenza (ICD-10AM-VI code I (J09-J11) for 2012 which correlate with previous versions of ICD-10AM codes J10-J11, were extracted from the New Zealand Ministry of Health's NMDS (by discharge date). In this dataset, people who received less than 1 day of hospital treatment in hospital emergency departments were excluded from any time series analysis of influenza hospitalisations during 2000–2012. Influenza-related hospitalisations were conservatively taken to include only those cases where influenza was the principal diagnosis. Repeat admissions were included, as infections with another influenza A subtype or B virus are possible.

From 1 January to 21 September 2012, there were a total of 951 hospitalisations for influenza (Figure 12). The number of influenza hospitalisations in 2012 ranked the third highest during the period from 2000 to 2012.

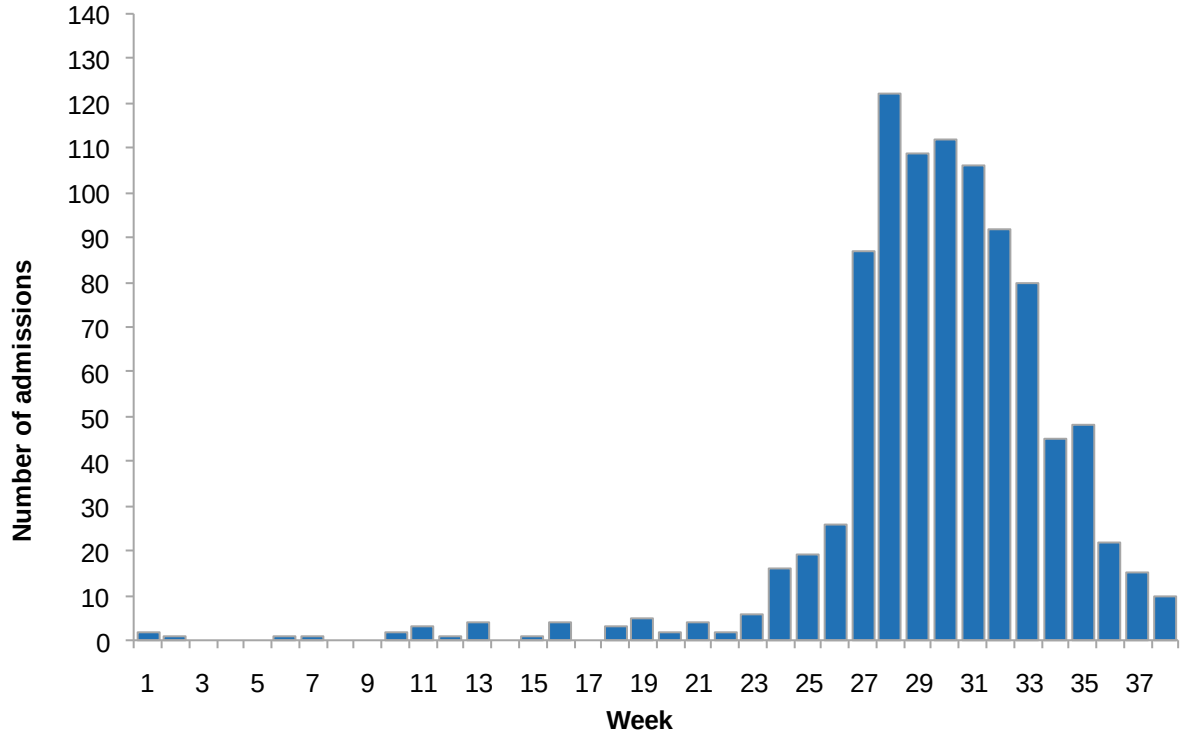
Figure 12. Influenza Hospitalisations, 2000–2012*



*Data from 1 Jan to 21 September 2012 only

Figure 13 shows influenza hospitalisations by week discharged. The high number of hospitalisations occurred in July (478) (weeks 26-30). Hospitalisations peaked in week 28.

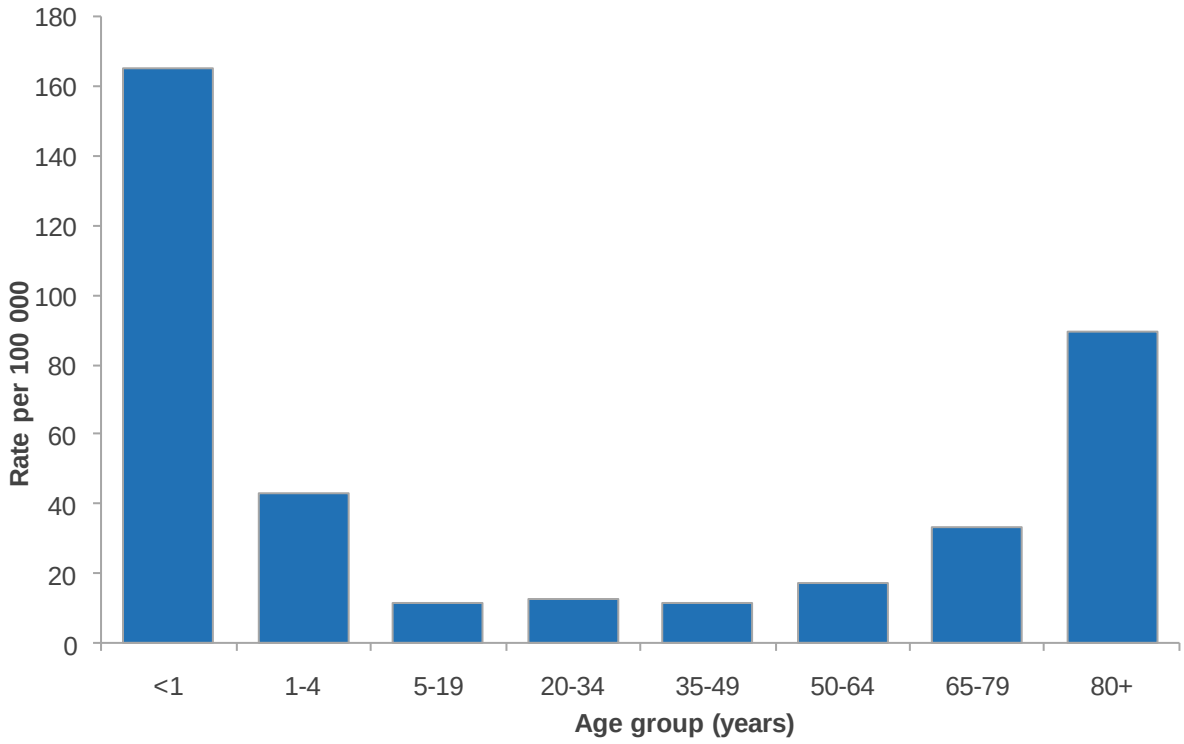
Figure 13. Influenza Hospitalisations by Week Discharged, 2012



*Data from 1 Jan to 21 September 2012 only

From 1 January to 21 September 2012, the highest influenza hospitalisation rates were recorded among young infants aged less than one year old (Figure 14), with rates of 165.1 per 100 000 age group population. This was followed by the elderly 80+ years (89.3 per 100 000).

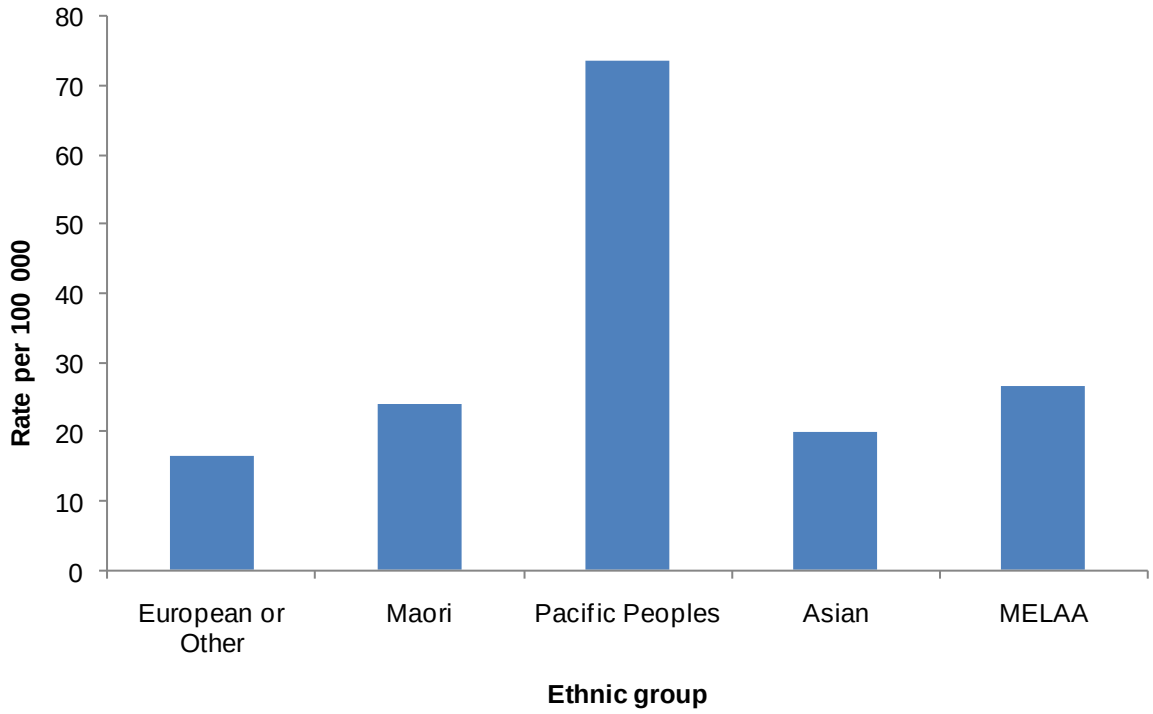
Figure 14. Influenza Hospitalisation Rates by Age Group, 2012*



*Data from 1 Jan to 21 September 2012 only

The ethnic distribution of influenza hospitalisations in 2012 is shown in Figure 15. Pacific Peoples had the highest hospitalisation rate (73.6 per 100 000), followed by MELAA (26.5), Maori (24.0), Asian (19.9), and European or Other (16.5).

Figure 15. Hospitalisation Rates by prioritised Ethnic group, 2012*



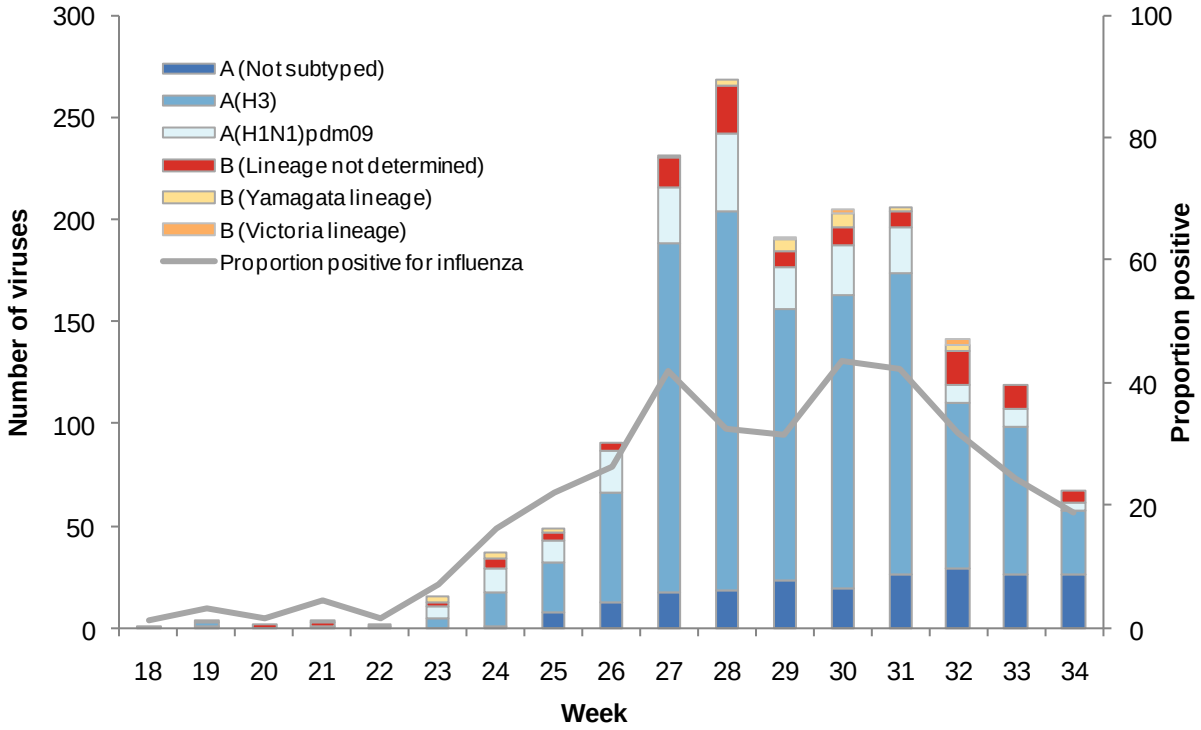
*Data from 1 Jan to 21 September 2012 only

2.2.3 Non-sentinel laboratory surveillance

Non-sentinel laboratory surveillance is conducted by the New Zealand virus laboratory network consisting of the National Influenza Centre at ESR and four hospital virology laboratories in Auckland, Waikato, Wellington, and Christchurch. ESR collates year-round national laboratory data on influenza from mainly hospital in-patient and outpatients during routine viral diagnosis.

A total of 5781 non-sentinel swabs were received during 1 January to 26 August 2012. Among them, 1659 influenza viruses were identified. This gave an overall detection rate of 28.7%. The predominant strain was influenza A(H3N2) (1082) including 141 A/Perth/16/2009 (H3N2)-like viruses, 207 A(H1N1)pdm09 including 52 A/California/7/2009 (H1N1)-like viruses, B (163) including 10 of B/Brisbane/60/2008-like (belonging to the B/Victoria lineage) and 33 B/Wisconsin/1/2010-like viruses (belonging to the B/Yamagata lineage), and A (not sub-typed) (207) (Figure 16). Influenza A(H3N2) strain has been the predominant strain for the most of the winter season.

Figure 16. Number of influenza viruses reported by type and week from non-sentinel surveillance



*data is only shown from week 18.

2.3 Event-based surveillance (telephone health advice service – Healthline)

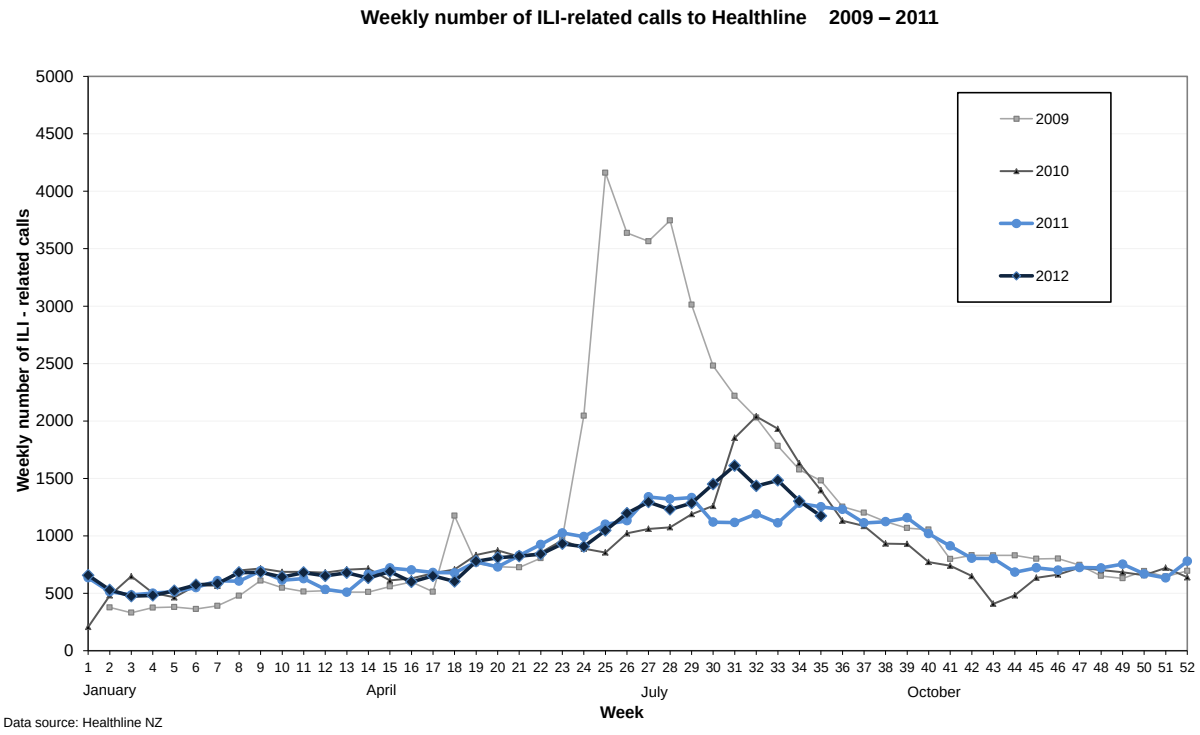
Healthline is the free national 0800 24 hour telephone health advice service funded by the Ministry of Health. Calls made to Healthline are triaged using electronic clinical decision support software. Data collected are daily counts of all symptomatic calls made to Healthline and those triaged for Influenza-Like-Illness (ILI). Note that about 70% of all calls to Healthline are symptomatic (other calls not part of this analysis include queries for information etc).

Analysis is frequency based with alarms raised by identifying statistical deviations (aberations) from previous calls. Data are reported for all ages and in five age bands (0–4, 5–14, 15–44, 45–64, 65+ years). The analysis of the call frequency is based on the cumulative summation (CUSUM) algorithm implemented in Early Aberration Reporting System (EARS) application developed by the Centres for Disease Control and Prevention (CDC), Atlanta, United States. EARS has three sensitivity thresholds (high, medium and low). If the daily call count exceeds a threshold a flag is signalled.

Cases of ILI are defined as those that are recorded in the Healthline database as having one of the following 18 guidelines: adult fever; breathing problems; breathing difficulty – severe (paediatric); colds (paediatric); cough (paediatric); cough – adult; fever (paediatric); flu-like symptoms or known/suspected influenza; flu like symptoms pregnant; influenza (paediatric); headache; headache (paediatric); muscle ache/pain; sore throat (paediatric); sore throat/hoarseness; sore throat/hoarseness pregnant; upper respiratory tract infections/colds; upper respiratory tract infections/colds – pregnant.

Figure 17 shows the weekly number of calls to Healthline for ILI during 2009-2012. Healthline calls in 2012 were higher than 2011, lower than 2009-2010. In 2012, Healthline calls had the peak in week 31, correlated with the peak from the sentinel GP surveillance in week 31.

Figure 17. Weekly number of ILI-related calls to Healthline, 2009-2012



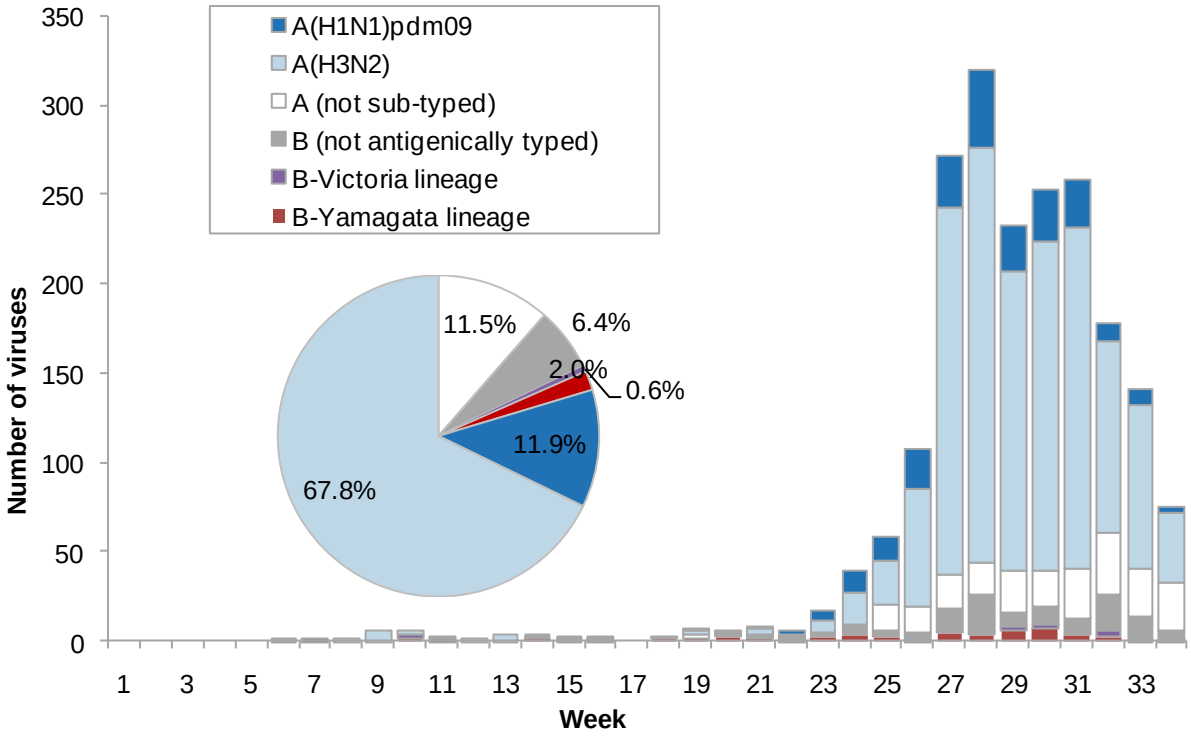
Data source: Healthline NZ

3. NEW ZEALAND STRAIN CHARACTERISATIONS

3.1 Circulating strains in 2012

A total of 2000 influenza viruses were detected from sentinel and non-sentinel surveillance in 2012 from week 1 (2-8 January 2012) to week 34 (20-26 August 2012) (Figure 18). The predominant strain was A(H3N2) (1356) including 243 A/Perth/16/2009 (H3N2)-like viruses, A(H1N1)pdm09 (237) including 70 A/California/7/2009 (H1N1)-like virus, and A (Not subtyped) (229), and B (178) including 11 of B/Brisbane/60/2008-like (belonging to the B/Victoria lineage) and 39 B/Wisconsin/1/2010-like viruses (belonging to the B/Yamagata lineage).

Figure 18. Total influenza viruses by type and week specimen taken, 2012



The influenza virus detections by type and subtype for weeks 1 to 34, 2012 is shown in Table 4.

Table 4. Influenza viruses by type and subtype, 2012

Viruses	All viruses (%)	Antigenically typed/sub-typed (%)
Influenza A	**229 (11.5)**	
A (not sub-typed)	229 (11.5)	
Influenza A(H1N1)pdm09	**237 (11.9)**	
A(H1N1)pdm09 by PCR	167 (8.4)	
A/California/7/2009 (H1N1) – like	70 (3.5)	70 (19.3)
Influenza A(H3N2)	**1356 (67.8)**	
A(H3N2) by PCR	1113 (55.7)	
A/Perth/16/2009 (H3N2) – like	243 (12.2)	243 (66.9)
Influenza B	**178 (8.9)**	
B by PCR	128 (6.4)	
B/Victoria lineage	11 (0.6)	11 (3.0)
B/Yamagata lineage	39 (2.0)	39 (10.7)
Total	**2000 (100)**	**363 (100)**

Overall, influenza A(H3N2) was the predominant strain among all influenza viruses. It represented 67.8% (1356/2000) of all viruses. A/Perth/16/2009 (H3N2)-like viruses represented 66.9% (243/363) of all antigenically typed and subtyped viruses.

Influenza A(H1N1)pdm09 viruses (237) were detected, 11.9% (237/2000) of all viruses. A/California/7/2009 (H1N1)-like viruses represented 19.3% (70/363) of all antigenically typed and subtyped viruses.

Influenza B viruses (178) represented 12.2% (178/2000) of all viruses. B/Victoria lineage viruses (B/Brisbane/60/2008-like strain) represented 3% (11/363) of all antigenically typed and subtyped viruses. B/Yamagata lineage viruses (B/Wisconsin/1/2011-like strain) represented 10.7% (39/363) of all antigenically typed and subtyped viruses.

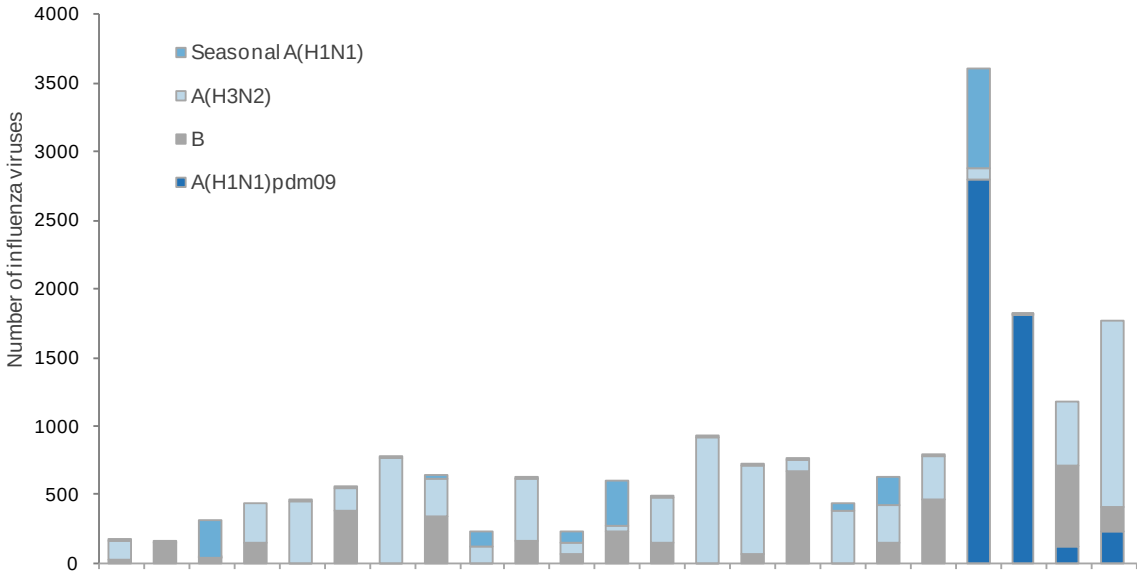
3.2 Predominant strains during 1990-2012

Overall, the patterns of the predominant strains during 1990-2012 are described below:

- Influenza A(H1N1)pdm09 strain has become the predominant strain in 2010 and 2009.
- Seasonal influenza A(H1N1) strain predominated in three seasons (1992, 2000 and 2001) with associated relatively low hospitalisations (193 in 1992, 228 in 2000 and 379 in 2001). It has not been detected in New Zealand since 2010.
- Seasonal influenza A(H3N2) strain predominated for 12 seasons (1990, 1993, 1994, 1996, 1998, 1999, 2002, 2003, 2004, 2006, 2007 and 2012). A/Fujian/411/02 (H3N2)-like strain predominated in 2003 with the highest recorded hospitalisations during 1990-2008. A/Wuhan/359/95 (H3N2)-like strain predominated in 1996 with associated 94 deaths (93 of these deaths were in people aged ≥65 years).
- Influenza B strains predominated for six seasons (1991, 1995, 1997, 2005, 2008, and 2011). In 2005, the disease burden was high in children aged 5-19 years with associated deaths in 3 children.
- Since the introduction of the B-Victoria lineage viruses into New Zealand in 2002, this strain predominated over the B/Yamagata lineage viruses in every three years in New Zealand (2002, 2005, 2008 and 2011).

Figure 19 shows the number and percentage of typed and subtyped (not including A not subtyped) influenza viruses from 1990 to 2012.

Figure 19. Influenza viruses by type and subtypes, 1990-2012

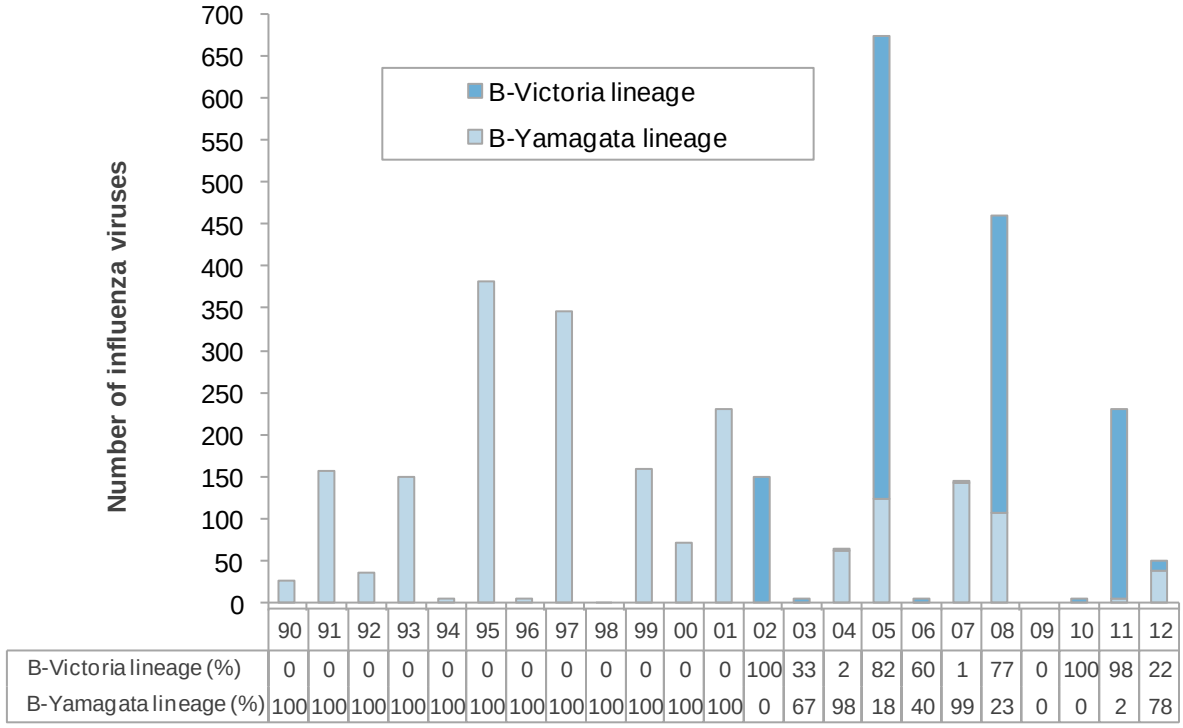


	90	91	92	93	94	95	96	97	98	99	00	01	02	03	04	05	06	07	08	09	10	11	12
Seasonal A(H1N1)(%)	0.6	7.7	85.7	0.0	0.2	1.1	0.3	3.6	47.4	0.3	36.0	54.4	0.4	0.1	0.1	2.3	12.6	32.1	0.8	20.1	0.0	0.0	0.0
A(H3N2)(%)	83.2	0.0	2.8	65.7	98.7	30.1	99.1	43.0	51.7	73.7	32.9	7.9	68.0	99.6	91.3	10.7	86.3	45.0	41.0	2.2	0.7	39.6	76.6
B(%)	16.2	92.3	11.5	34.3	1.1	68.8	0.7	53.5	0.9	26.0	31.1	37.8	31.6	0.3	8.6	87.0	1.1	23.0	58.3	0.0	0.5	50.3	10.1
A(H1N1)pdm09(%)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	77.7	98.8	10.0	13.4

*2009-2011 A(H1N1) is influenza A(H1N1)pdm09

Figure 20 shows the number and percentage of all antigenically typed B viruses from 1990 to 2012. Since the introduction of the B-Victoria lineage viruses into New Zealand in 2002, this strain predominated over the B/Yamagata lineage viruses in every three years in New Zealand in 2002, 2005, 2008 and 2011.

Figure 20. Influenza B antigenic types, 1990-2012



	90	91	92	93	94	95	96	97	98	99	00	01	02	03	04	05	06	07	08	09	10	11	12
B-Victoria lineage (%)	0	0	0	0	0	0	0	0	0	0	0	0	100	33	2	82	60	1	77	0	100	98	22
B-Yamagata lineage (%)	100	100	100	100	100	100	100	100	100	100	100	100	0	67	98	18	40	99	23	0	0	2	78

3.3 Influenza A(H1N1)pdm09

Representative of influenza A(H1N1)pdm09 isolates (70) were antigenically subtyped at the WHO National Influenza Centre at ESR using sheep/rabbit antisera supplied by the WHO Collaborating Centre (WHOCC) in Melbourne. Some of these isolates were also sent to WHOCC-Melbourne. Results indicated that New Zealand isolates were antigenically closely related to the A(H1N1)pdm09 reference strain A/California/7/2009 (H1N1)pdm09. The results of the genetic analysis of the hemagglutinatin (HA) gene and neuraminidase (NA) of the representative viruses are shown in Figures 21 & 22.

3.4 Seasonal influenza A(H3N2)

Representative seasonal influenza A(H3N2) isolates (243) were antigenically subtyped at the WHO National Influenza Centre at ESR using HAI typing kit supplied by the WHO Collaborating Centre (WHOCC) in Melbourne. Some of these isolates were also sent to WHOCC-Melbourne. Results indicated that New Zealand isolates were reacted well antigenically to the reference strain A/Perth/16/2009 (H3N2) with small number of low reactor identified. Genetically, A(H3N2) viruses have drifted away from A/Perth/16/2009 strain. The sequenced viruses showed that they fell into the genetic group 3C within the A/Victoria/316/2011 genetic clade. The results of the genetic analysis of the hemagglutinatin (HA) gene of the representative viruses are shown in Figure 23.

3.5 Influenza B

Representative seasonal influenza B/Victoria lineage isolates (B/Brisbane/60/2008 – like) (11) and B/Yamagata lineage isolates (B/Wisconsin/1/2010-like) (39) isolates were antigenically typed at the WHO National Influenza Centre at ESR using HAI typing kit supplied by the WHO Collaborating Centre (WHOCC) in Melbourne. Some of these isolates were also sent to WHOCC-Melbourne. Results indicated that New Zealand isolates were antigenically related to the reference strain B/Brisbane/60/2008, and B/Wisconsin/1/2010–like viruses. The results of the genetic analysis of the hemagglutinatin (HA) gene of the representative viruses are shown in Figures 24 & 25.

Figure 21. Phylogenetic analysis of HA gene sequence of A(H1N1)pdm09 viruses

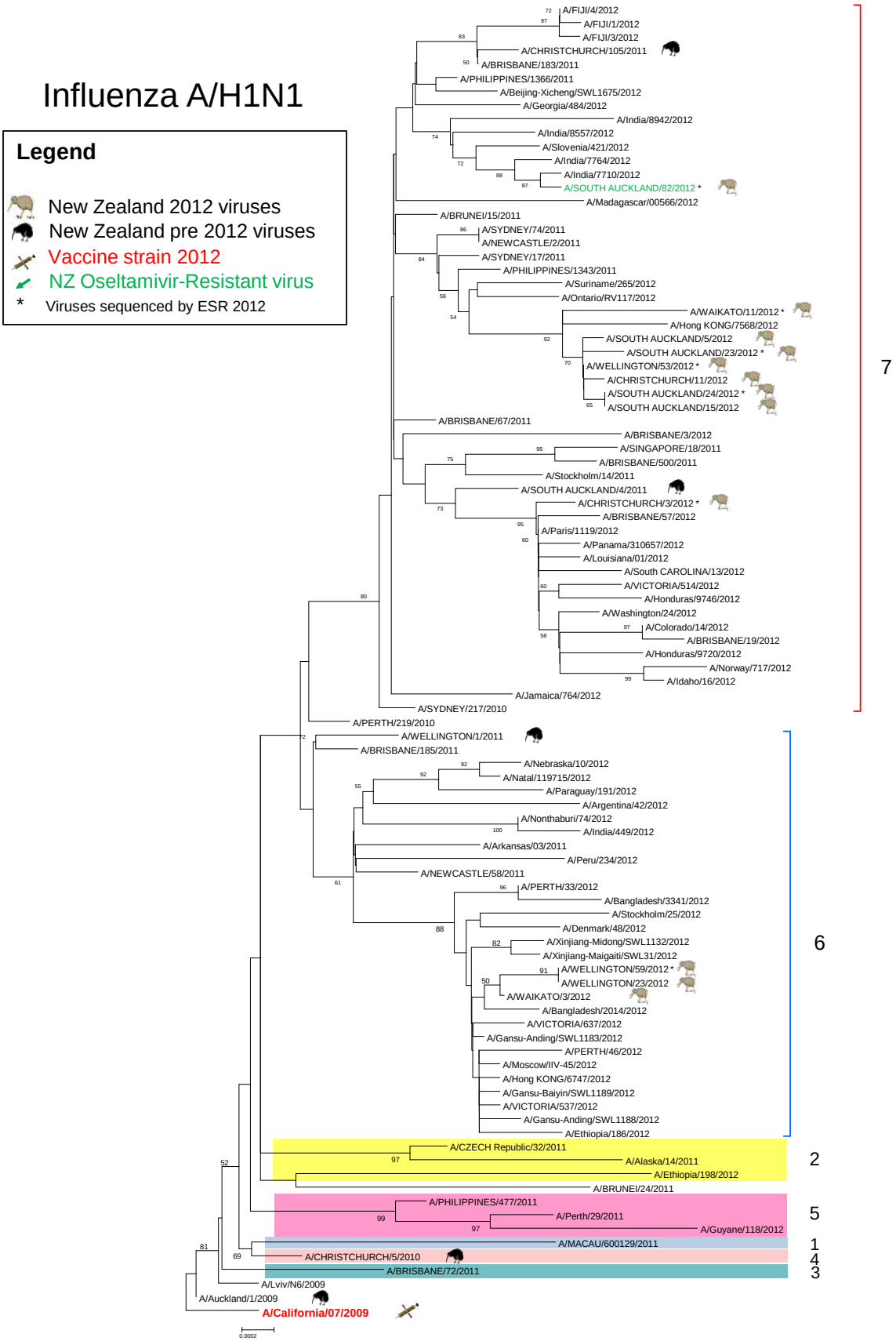


Figure 22. Phylogenetic analysis of NA gene sequence of A(H1N1)pdm09 viruses

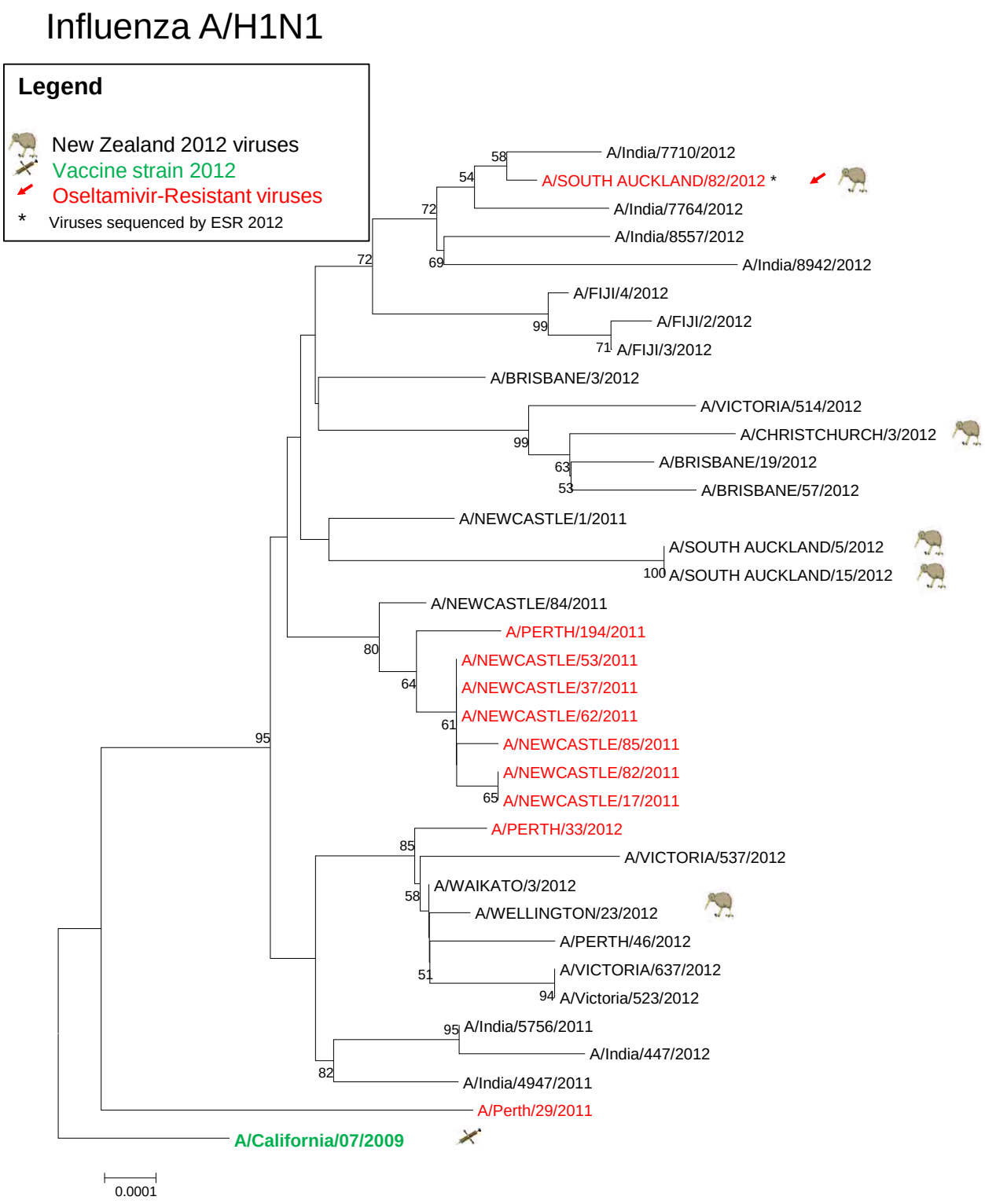


Figure 23. Phylogenetic analysis of HA gene sequence of A(H3N2) viruses

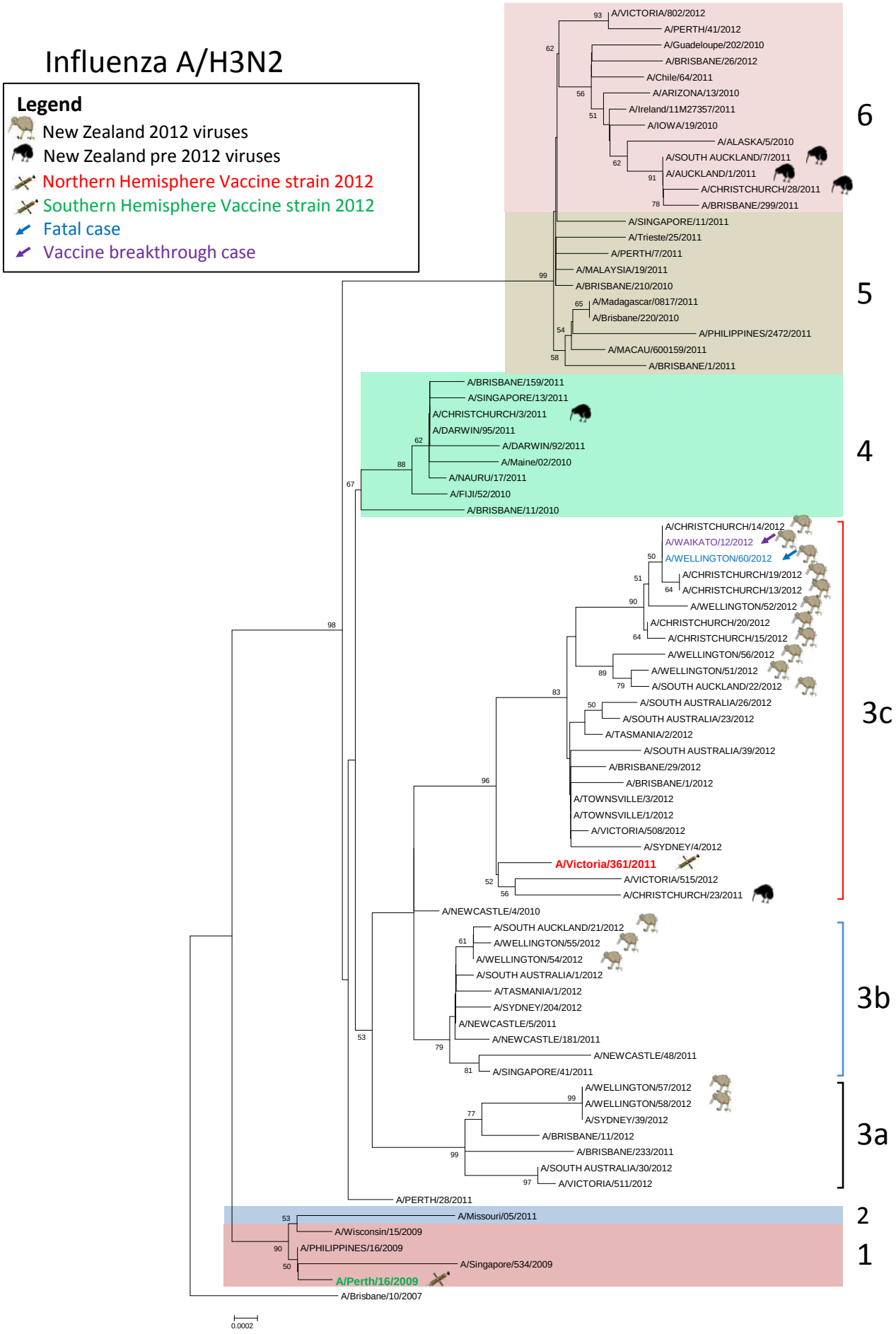


Figure 24. Phylogenetic analysis of HA gene sequence of B/Yamagata lineage viruses

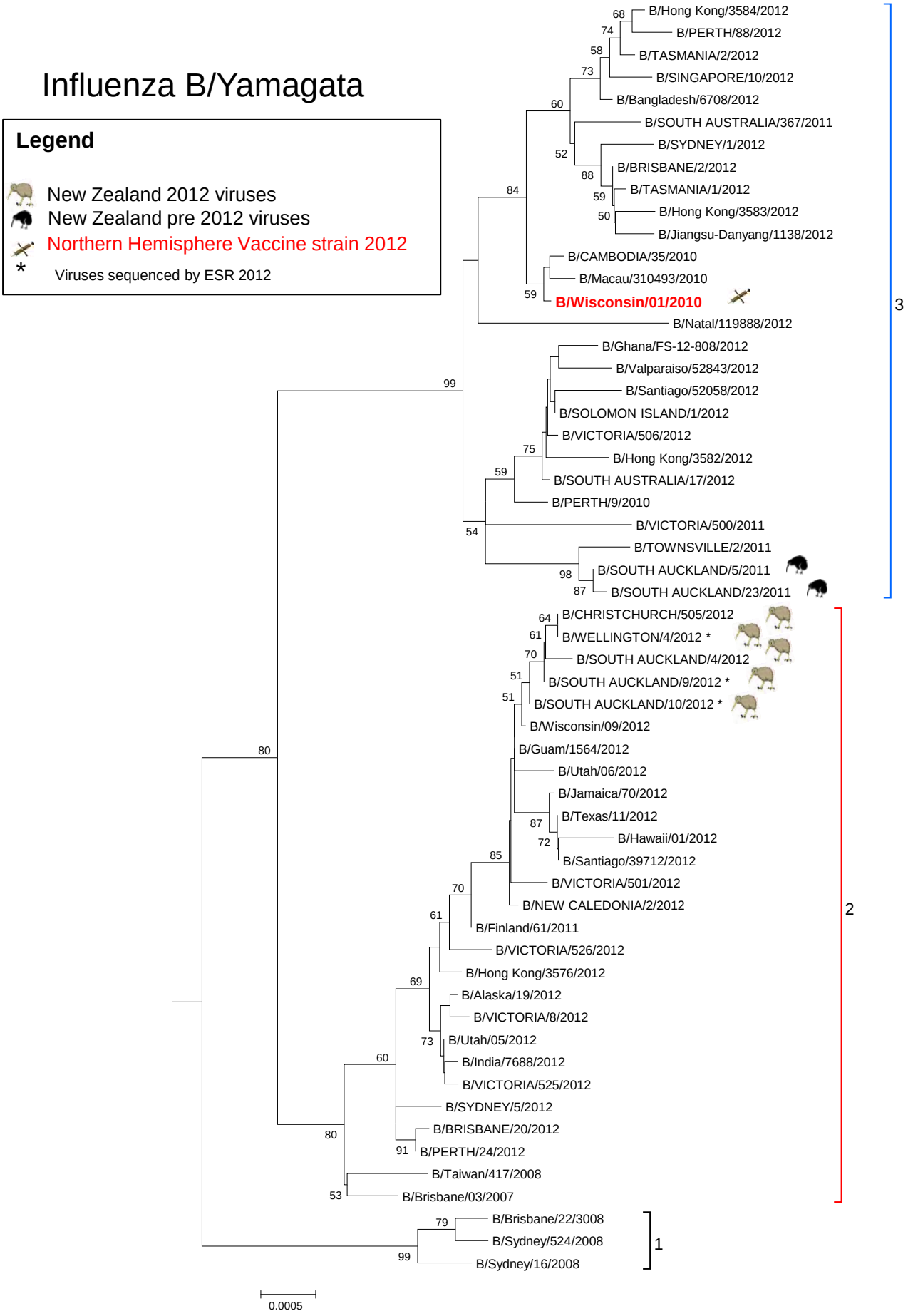
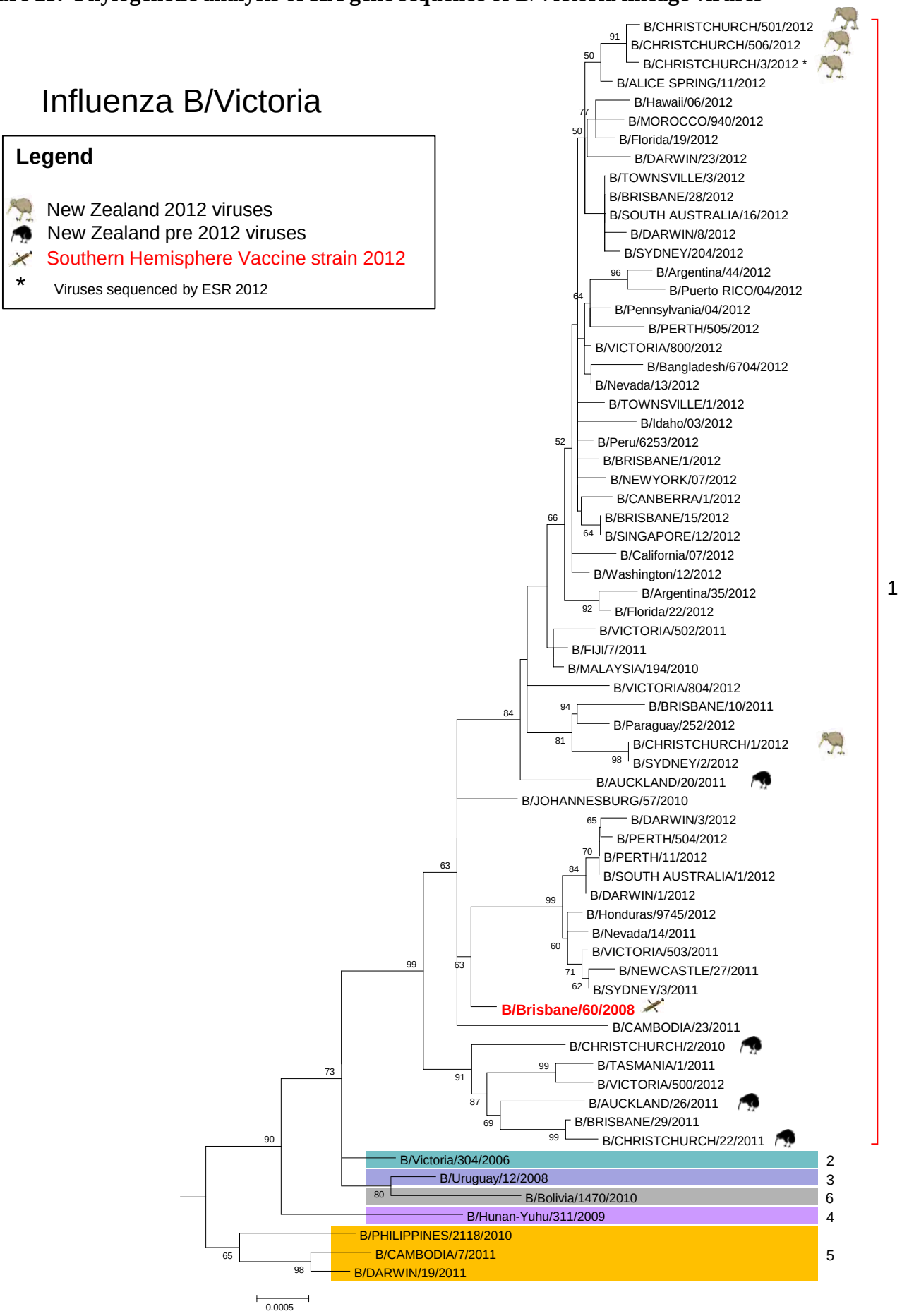


Figure 25. Phylogenetic analysis of HA gene sequence of B/Victoria lineage viruses



3.6 Oseltamivir resistance

The WHO National Influenza Centre at ESR employed a phenotypic method (fluorometric neuraminidase inhibition assay) for the surveillance of anti-viral drug resistance in influenza viruses. In addition, NIC at ESR employed a molecular method (PCR and sequencing) to monitor the H275Y mutation (histidine-to-tyrosine mutation at the codon of 275 in N1 numbering) which is known to confer resistance to oseltamivir.

In 2012, fluorometric neuraminidase inhibition assay was used to test a total of 417 influenza viruses. All viruses (except one A(H1N1)pdm09) were sensitive to oseltamivir with mean IC50 values for A(H1N1)pdm09 at 0.32 nM, A(H3N2) at 0.41 nM and B at 11.2 nM (Table 5). The first oseltamivir resistant influenza A(H1N1)pdm09 was detected from a 26 year old male who was hospitalised with acute upper respiratory infection within 7 days after returning New Zealand from India. The results of the fluorometric neuraminidase inhibition assay indicated that the virus had highly reduced sensitivity to oseltamivir with IC50 value of 271 nM, 847 fold higher than the mean of IC50 value (0.32 nM) for the 81 tested influenza A(H1N1)pdm09 viruses. The sequencing analysis of the neuraminidase gene confirmed that the virus had the H275Y mutation (histidine-to-tyrosine at codon 275 in N1 nomenclature), conferring resistance to oseltamivir. In addition, this virus is genetically closer to the Indian A(H1N1)pdm09 viruses than the New Zealand A(H1N1)pdm09 viruses.

During 2006-2007, all influenza A(H1N1) viruses tested were sensitive to oseltamivir. In 2008, six seasonal A(H1N1) viruses (0.8%) were detected, of which, only four were available for antiviral susceptibility testing and were all resistant to oseltamivir. The results of the fluorometric neuraminidase inhibition assay indicated that the four viruses had highly reduced sensitivity to oseltamivir with IC50 values in the range of 500-1700 nM, typical of the recently global emerging oseltamivir-resistant A(H1N1) viruses. Genetic analysis of the neuraminidase gene confirmed that the four viruses had the H275Y mutation (histidine-to-tyrosine at codon 275 in N1 nomenclature), conferring resistance to oseltamivir. None of the patients or their close contacts had received Tamiflu prior to sample collection. In 2009, 25 seasonal A(H1N1) virus were phenotypically tested and all were resistant to oseltamivir. However, all pandemic A(H1N1) tested between 2009-2012 were sensitive to oseltamivir.

Table 5. Antiviral susceptibility to oseltamivir for influenza viruses, 2006-2012

Influenza type/sub-type	2006	2007	2008	2009	2010	2011**	2012**
Influenza B							
Number of isolates tested	1	132	306	-	1	179	64
Mean IC50 (nM)	-	37.5	26.5	-	-	31.9	11.2
Standard Deviation (nM)	-	22.5	16.9	-	-	15.3	5.8
Minimum IC50 (nM)	-	0.9	0.22	-	-	4.12	4.8
Maximum IC50 (nM)	-	97.4	87.8	-	-	71.3	31.8
Influenza A(H3N2)							
Number of isolates tested	189	45	120	-	1	70	271
Mean IC50 (nM)	0.7	0.38	0.28	-	-	0.46	0.41
Standard Deviation (nM)	0.27	0.26	0.17	-	-	0.27	0.19
Minimum IC50 (nM)	0.06	0.07	0.01	-	-	0.06	0.08
Maximum IC50 (nM)	1.4	1.13	1.08	-	-	1.5	1.22
Seasonal influenza A(H1N1)							
Number of isolates tested	18	136	4	25	-	-	-
Mean IC50 (nM)	1.26	0.81	768	1385	-	-	-
Standard Deviation (nM)	0.89	0.64	287	1996	-	-	-
Minimum IC50 (nM)	0.2	0.05	573	305	-	-	-
Maximum IC50 (nM)	3	2.7	1184	7912	-	-	-
Influenza A(H1N1)pdm09							
Number of isolates tested	-	-	-	483	334	12	82
Mean IC50 (nM)	-	-	-	0.4	0.68	0.54	0.32
Standard Deviation (nM)	-	-	-	0.24	0.41	0.24	0.2
Minimum IC50 (nM)	-	-	-	0.09	0.01	0.19	0.11
Maximum IC50 (nM)	-	-	-	1.4	2.05	0.965	271

*IC50; inhibitory concentration of the drug at which a 50% reduction in enzymatic activity is observed.
** Mean and standard deviation calculated for 2011 and 2012 excludes 3 outliers deemed to be resistant to oseltamivir (having IC50 values >10-fold higher than the overall mean for a given subtype recorded for all years). Outliers excluded were one pandemic influenza A/H1N1 viruses in 2012 and two influenza B viruses in 2011.)

4. RECENT STRAIN CHARACTERISATION FOR SOUTHERN HEMISPHERE VIRUSES AND LIKELY VACCINE CANDIDATES

4.1 Influenza A(H1N1)pdm09

The influenza A(H1N1)pdm09 virus was first detected in April 2009 in the United States and was responsible for outbreaks in Mexico in March and April 2009. Outbreaks subsequently occurred in all regions of the world and, by July 2009, influenza A(H1N1)pdm09 was the predominant influenza virus circulating in many countries in the Americas, Asia, Europe and Oceania.

During the 2012 influenza season, 20 A(H1N1)pdm09 viruses were received at the Melbourne WHOCC from 3 countries with most coming from Australia and New Zealand. The virology laboratories in New Zealand use the kit supplied by the Melbourne WHOCC to analyse influenza A(H1N1)pdm09 strains. The antiserum used for antigenic typing was the rabbit/sheep antisera raised against A/California/7/2009-like strain. A total of 237 influenza A(H1N1)pdm09 viruses were detected in New Zealand in 2012, of which, 70 had undergone antigenic typing and they were all antigenically closely related to the A/California/7/2009-like strain.

Among all of the influenza A(H1N1)pdm09 viruses analysed at the Melbourne WHOCC, most of the viruses reacted well with ferret sera to A/California/7/2009, with 13.7% of A(H1N1)pdm09 viruses being classified as low reactors (≥8-fold reduction compared with the homologous titre) (Tables 3.3 and 3.4 in Appendix 3). Many of these low reactors had changes in the HA gene in the 153-158 amino acid region which has been shown to reduce reactivity in HI assays but as these changes were mostly not in the original clinical samples, these mutations appear to be artefacts caused by isolation in MDCK cells or in eggs. In addition, a total of 24 influenza A(H1N1)pdm09 viruses were sequenced in the HA gene. The sequence analysis indicated that there was genetic diversity evident in most of the viruses isolated during 2012 with two major sub-clades designated group 7 and group 6 (CDC designations, Figure 3.2 in Appendix 3). The NA (N1) genes of the A(H1N1)pdm09 viruses were also sequenced, resulting in groups similar to their HA grouping (Figure 3.3 in Appendix 3). Furthermore, vaccines containing influenza A/California/7/2009-like antigen stimulated anti-HA antibodies of similar geometric mean HI titres to the vaccine virus and recent influenza A(H1N1)pdm09 isolates. (WER 86(42), and Tables 3.7 & 3.8 in Appendix 3).

In summary, influenza A(H1N1)pdm09 viruses have replaced seasonal A(H1N1) viruses since 2009. HI tests showed that most isolates were antigenically similar to A/California/7/2009-like strain. Current vaccines containing the A/California/7/2009 antigen stimulated anti-HA antibodies of similar geometric mean HI titres to the vaccine virus and recent A(H1N1) influenza isolates. Based on all of the epidemiological, antigenic, genetic and serological data, the WHO consultation recommended vaccines containing a A/California/7/2009 (H1N1)-like strain. The AIVC accepted this recommendation.

4.2 Seasonal influenza A(H3N2)

Influenza A(H3N2) has frequently been associated with severe disease and excess mortality in high-risk groups. This subtype has also shown the greatest tendency for antigenic drift as illustrated by the frequency of vaccine formulation changes recommended by the WHO and AIVC (Table 1).

The Melbourne WHOCC analysed 1076 A(H3N2) isolates from eight countries during this period. These viruses made up 68.5% of all viruses analysed at the Melbourne WHOCC. Virtually all of the influenza A(H3N2) viruses were recognised by ferret sera raised against cell propagated A/Victoria/361/2011-like viruses, with no viruses showing reduced reactivity (Tables 4.2,4.3 and

4.4 in Appendix 4). This was not the case for ferret sera raised to egg grown A/Victoria/361/2011 which generally showed marked reductions compared to the homologous titre for recent cell propagated viruses. In addition, HA gene phylogenetic analysis of the influenza A(H3N2) viruses (173) sequenced showed that most viruses were A/Victoria/208/2009-like. Most of the recent viruses fell into group 3 with only a few viruses in groups 5 & 6 (CDC designations, Figure 4.2 in Appendix 4). Within group 3, viruses were further divided into 3 subgroups (3A, 3B, 3C) with the majority falling into group 3C. Group 3 had an A198S, V223I and N312S changes with additional S45N and T48I changes in 3C. Sequence analysis of the N2 NA gene analysed in 2012 showed that the most recent viruses grouped in a similar manner as their HA genes (Figure 4.3 in Appendix 4). Furthermore, vaccines containing influenza A/Perth/16/2009 (H3N2)-like antigens stimulated anti-HA antibodies of similar geometric mean HI titres to the vaccine virus and to recent A(H3N2) isolates. Similar results were obtained in microneutralisation tests for a subset of sera and viruses (WER 86(42), and Tables 4.10 and 4.11 in Appendix 4).

In summary, influenza A(H3N2) viruses were associated with widespread outbreaks in many southern hemisphere countries. Most isolates were antigenically similar to A/Perth/16/2009-like strain. Current vaccines containing the A/Victoria/361/2011 antigen stimulated anti-HA antibodies of similar geometric mean HI titres to the vaccine virus, when measured against cell-propagated A/Victoria/361/2011 and to recent A(H3N2) isolates. Based on all of the epidemiological, antigenic, genetic and serological data, the WHO Consultative Group recommended the H3 component of the vaccines containing an A/Victoria/361/2011 (H3N2)-like strain. AIVC accepted this recommendation.

4.3 Influenza B

Two distinct lines of influenza B have co-circulated in many countries during recent years. This dates from the late 1980s when the B/Panama/45/90 variant of influenza B was first observed. This strain and its further variants of the Yamagata/16/88 lineage (most recently representative strain-B/Florida/4/2006) spread worldwide, whereas strains of the previous B/Victoria/2/87-like viruses continued to circulate in Asia and subsequently underwent independent evolution as an antigenically distinct lineage (most recent representative strain-B/Brisbane/60/2008). For reasons not wholly understood, these remained geographically restricted to Asia until 2001. In 2002 the B/Victoria/2/87 lineage viruses were the predominant viruses worldwide.

Both recent B/Victoria-like strains (B/Brisbane/60/2008 is the current reference strain) and B/Yamagata-like strains (B/Wisconsin/1/2010 is the current reference strain) continued to be isolated worldwide in 2012. The proportion of B/Yamagata/16/88 lineage viruses increased in many parts of the world but B/Victoria/2/87 lineage viruses predominated in some countries. A total of 178 influenza B viruses were detected in New Zealand in 2012. Among all antigenically typed B viruses, 39 were as the B/Yamagata lineage and 11 as the B/Victoria lineage.

476 influenza B isolates were received in 2012 by the Melbourne WHOCC from nine countries (30.3% of total isolates). The majority of isolates (77.9%) were typed as B/Victoria lineage. When B/Victoria-lineage viruses were reacted with ferret sera raised against egg grown B/Brisbane/60/2008-like virus, about 42% of viruses showed reduced reactivity (≥8-fold reduction compared with the homologous titre). However, when ferret serum raised to cell propagated virus was used only a small percentage of viruses were low reactors in HI assays. The remaining 22.1% of B viruses were of the B/Yamagata lineage and these viruses were generally reacted well with ferret sera to egg derived B//Wisconsin/1/2010 with only 9% of viruses showing reduced reactivity ((≥8-fold reduction); HI assays in Tables 5.2, 5.3, 5.4 and 5.5 (Appendix 5) were performed at the Melbourne WHOCC. In addition, sequence analysis of the HA1 gene of recent isolates showed that recent isolates fell into one of the two major lineages of B viruses (B/Victoria/2/87 or

B/Yamagata/16/88) consistent with their antigenic typing. The B/Victoria lineage viruses mostly grouped in the B/Brisbane/60/2008 group with signature amino acid changes at S172P, N75K, N165K with no viruses grouping with the older B/Malaysia/2506/2004-like viruses with a T37I substitution. B/Yamagata lineage fell into two clades represented by B/Wisconsin/1/2010-like virus (group 3) and B/Brisbane/3/2007-like virus group (Group 2), with increasing number of viruses falling in group 2. Group 2 viruses have several amino acid changes including P48K, P108A, and T182A compared to group 3 viruses (Figures 5.5, and 5.7, in Appendix 5). The NA sequence analysis from viruses with a B/Brisbane/60/2008-like HA showed some heterogeneity with some viruses having similar groups as their HA and others having HA's from different HA groupings. This reasserting of NA genes is often seen with influenza B viruses (Figure 5.6 in Appendix 5). B/Yamagata lineage virus NA genes matched the HA genes falling into the same group 2 or groups 3 pattern as their HA did (Figure 5.8 in Appendix 5). Furthermore, vaccines containing influenza B/Brisbane/60/2008-like antigens stimulated anti-HA antibodies of similar geometric mean HI titres to the vaccine virus and to recent B/Victoria-lineage isolates. Vaccines containing influenza B/Wisconsin/1/2010-like antigens stimulated anti-HA antibodies of similar geometric mean HI titres to the vaccine virus and the majority of representative recent B/Yamagata/16/88 lineage viruses. (WER 86(42), Tables 5.9, 5.10, 5.11 and 5.12 in Appendix 5).

In summary, influenza B outbreaks were reported in southern hemisphere countries. The proportion of B/Yamagata/16/88 lineage viruses increased in many parts of the world but B/Victoria/2/87 lineage viruses predominated in some countries. The majority of recent B/Victoria/2/87 lineage viruses were antigenically and genetically closely related to B/Brisbane/60/2008. Most recently isolated B/Yamagata/16/88 lineage viruses were antigenically closely related to B/Wisconsin/1/2010-like viruses. Current vaccines containing B/Brisbane/60/2008 antigen stimulated HA antibodies that were similar in titre to recently isolated B/Brisbane/60/2008-like viruses. However, titres were lower to recent viruses of the B/Yamagata/16/88 lineage. Vaccines containing B/Wisconsin/1/2010 antigen stimulated HA antibodies that were similar in titre to recently isolated B/Yamagata/16/88 lineage but titres were lower to recent viruses of the B/Victoria/2/87 lineage. In light of the increase in the proportion of B/Yamagata/16/88 lineage viruses relative to B/Victoria/2/87 lineage viruses over the last 2 months, a B/Yamagata/16/88 lineage virus is recommended for the 2013 southern hemisphere season trivalent vaccine. The AIVC accepted this recommendation.

5. SUMMARY OF VACCINE COMPOSITION RECOMMENDATION

It is recommended that the influenza vaccine formulation for New Zealand for 2013 is:

- A(H1N1) an A/California/7/2009 (H1N1)pdm09 - like virus
- A(H3N2) an A/Victoria/361/2011 (H3N2) - like virus
- B a B/Wisconsin/1/2010 - like virus

5.1 Explanation of "like" strains suitable for inclusion in vaccine

In the past, some strains of influenza recommended for inclusion in the vaccine formulation have been unsuitable vaccine candidates due to their poor growth potential with resulting low yields or poor serological responses in vaccinees. Under the "like" strain concession in the vaccine recommendation, an antigenically similar strain can be substituted which has the qualities that are lacking in the prototype strain.

The AIVC considered the information about international surveillance by WHO, recent data from Australia, New Zealand, South Africa and Argentina on influenza epidemiology and virus strain characterisation, and the recommendations of the WHO annual consultation on the composition of influenza vaccine for the southern hemisphere, held in Geneva on 26-28 September 2011.

The AIVC agreed to adopt the September 2011 WHO recommendations. The influenza vaccine components for year 2012 season should contain the following:

A (H1N1):	an A/California/7/2009 (H1N1)-like strain,	15 μg HA per dose
A (H3N2):	an A/Victoria/361/2011 (H3N2)-like strain,	15 μg HA per dose
B:	a B/Wisconsin/1/2010-like strain,	15 μg HA per dose

The following available reassortants or viruses are recommended as suitable vaccine strains:

- A(H1N1)pdm09:
  - NYMC X-179A egg or cell, NYMC X-181, NYMC X-181A, NIBRG-121, NIBRG-121xp reassortants derived from A/California/7/2009.
  - NIBRG-122 reassortant derived from A/England/195/2009.
  - IVR-158 reassortant derived from A/Brisbane/10/2010.
  - A reassortant of A/Christchurch/16/2010 NIB-74 has also been produced by NIBSC and is being used by a European manufacturer.

- A(H3N2):
  - A/Victoria/361/2011 viruses have been made and distributed by CSL (IVR-165). Most companies are using IVR-165 due to high yields.
  - NYMC (X-217 and X-217A)
  - NIBSC (NIB-79)

- B:
  - B/Wisconsin/1/2010 and B/Sichuan-Anyue/139/2011 but these generally grow poorly.
  - Reassortants of B/Wisconsin/1/2010 and B/Sichuan-Anyue/139/2011have been produced, NYMC-BX-39 (B/Hubei-Wujiagang/158/2009) and NYMC-BX-41A (B/Wisconsin/1/2010), and both appear to have much improved yields compared to their wild type virus counterparts.

APPENDIX 1 - Composition of the Australian Influenza Vaccine Committee 2012

AIVC Members and Observers 2012

Committee Members (Voting and Non-voting NV):

1. Dr Gary Grohmann, OLSS, TGA NV
2. Dr Ian Barr, WHOCC NV
3. Professor Robert Booy
4. Dr Mike Catton, VIDRL
5. Prof Dominic Dwyer, ICPMR
6. Prof Ian Gust, University of Melbourne
7. Dr Alan Hampson, Interflu Pty Ltd
8. Dr Sue Huang, CDI, ESR, NZ NV
9. Assoc Prof Heath Kelly, VIDRL
10. Prof Anne Kelso, WHOCC NV
11. Ms Rhonda Owen, DoHA NV
12. Dr David Smith, UWA
13. Emeritus Prof Greg Tannock, Macfarlane Burnet Institute
14. Assoc Prof Helen Marshall
15. Dr Tania Dalla Pozza, OLSS, TGA (Secretary) NV

*Dr Florette Treurnicht, NICD, SA NV (TC)

Observers:

1. Mr Tony Wilson-Williams, Abbott
2. Ms Justine Japp, CSL Ltd
3. Mr Peter Schoofs, CSL Ltd
4. Dr David Crump, GlaxoSmithKline Australia Pty Ltd
5. Ms Louise Carter, GlaxoSmithKline Australia Pty Ltd
6. Ms Alicia Ham, Sanofi Pasteur
7. Dr Nadim Naser, Sanofi Pasteur
8. Mr Mathieu Miele Novartis
9. Mr John Fox Novartis (TC)

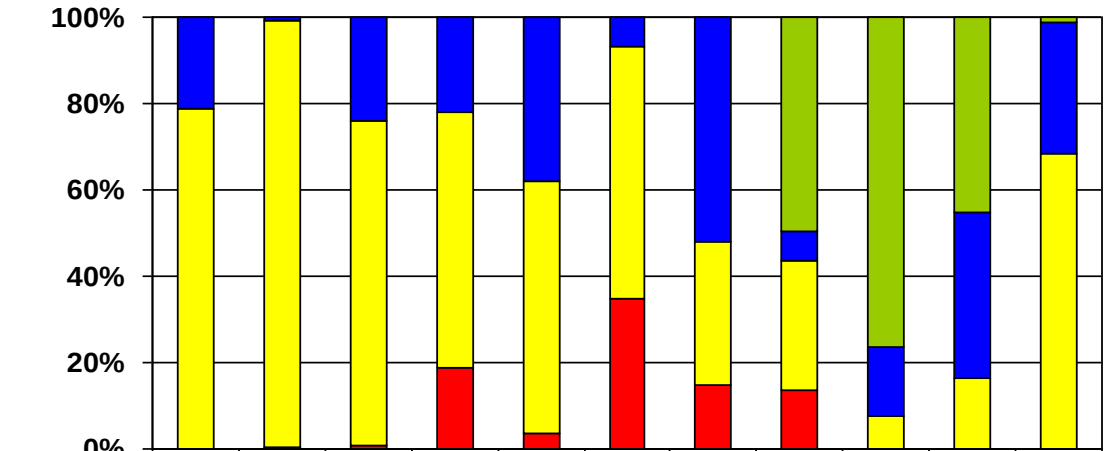
*Participating by teleconference

APPENDIX 2 - Isolates Received For Analysis at the Australian WHO Collaborating Centre

Table 3.7 Influenza Viruses Analysed at the Melbourne WHO CC
1 March – 12 September 2012

Country	A(H1N1) pdm09	A(H3N2)	B	Mixed	TOTAL
Australia	16	875	406	0	1297
Fiji	0	2	0	0	2
Malaysia	0	0	2	0	2
New Zealand	3	115	28	0	146
New Caledonia	0	3	3	0	6
Papua New Guinea	0	7	0	0	7
Philippines	0	15	2	0	17
Singapore	0	13	14	0	27
Thailand	1	1	9	0	11
Vietnam	0	1	0	0	1
Macau, China	0	10	0	0	10
Solomon Islands	0	0	3	0	3
Cambodia	0	34	9	0	43
Total	**20**	**1076**	**476**	**0**	**1572**
%	1.3	68.5	30.3	0	

Figure 2.1
Influenza isolates by type/subtype received and analysed at the Melbourne WHO CC
2002-12



	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
A(H1)pdm								47.3	76.2	45.1	1.3
B	21.3	0.6	24.1	21.9	37.9	6.9	52	6.8	16.3	38.5	30.3
A(H3)	78.6	99.2	75	59.4	58.6	58.1	33.3	28.5	7.5	16.4	68.5
A(H1)	0.1	0.2	0.9	18.7	3.5	34.4	14.7	13	0	0	0

APPENDIX 3 – Influenza A(H1N1)pdm09

TABLE 3.3 – (H1N1)pdm09 viruses

	Date: August 29, 2012	Haemagglutination Inhibition Assay - WHO Influenza Centre, Melbourne												
	Turkey no. 91	Reference Antisera												
	Sequenced	A	B	C	D	E	F	F	G	H	I	J		
		F1656-13D	FS5	F1614-143D	F1620-13D	F1686-13D	F1704-14D	F1860-13D	F1857-13D	F1903-13D	MAB 175	Human	Passage	Sample
		E4		C2,MDCK1	MDCK4	E2	E2	E3	MDCK1	E4		Sera	Details	Date
	Reference Antigens	CAL/7	AUCK/1	ILLINOIS/9	BAY/69	BRIS/10	CHCH/16	PERTH/198	VIC/918	BRIS/70		Pool		
A	A/CALIFORNIA/7/2009	**1280**	320	320	640	1280	1280	640	1280	2560	5120	640	E5	
B	A/AUCKLAND/1/2009	5120	**640**	640	1280	2560	2560	2560	>5120	>5120	>10240	640	E4	
C	A/ILLINOIS/9/2007	2560	640	**1280**	320	640	640	1280	2560	2560	5120	160	C2,MDCK2	
D	A/BAYERN/69/2009	<80	<40	<40	**640**	160	40	80	<40	160	2560	320	MDCK7	
E	A/BRISBANE/10/2010	640	160	320	640	**2560**	1280	640	640	640	2560	640	E3	
F	A/CHRISTCHURCH/16/2010	2560	320	640	1280	5120	**2560**	2560	1280	2560	5120	640	E3	
G	A/PERTH/198/2010	1280	320	640	320	1280	640	**1280**	1280	1280	2560	320	E4	
H	A/VICTORIA/918/2010	5120	1280	1280	1280	2560	2560	>5120	**>5120**	>5120	>10240	640	MDCK2	
I	A/BRISBANE/70/2011	2560	640	1280	1280	1280	1280	2560	1280	**2560**	5120	640	E4	
	Test Antigens													
1	A/SOUTH AUCKLAND/15/2012	2560	640	640	640	2560	1280	2560	2560	2560	5120	640	SIAT,MDCK2	26/06/2012
2	A/WELLINGTON/10/2012	2560	640	640	640	1280	640	1280	2560	2560	2560	160	MDCK,MDCK1	20/06/2012
3	A/SOUTH AUCKLAND/12/2012	1280	320	320	640	640	640	1280	1280	1280	320	80	MDCKX,MDCK3	17/06/2012
4	A/SINGAPORE/2/2012	1280	320	640	320	640	640	1280	1280	1280	5120	160	MDCK2	16/03/2012
5	A/SINGAPORE/7/2012	1280	160	160	320	640	640	640	1280	1280	2560	160	MDCK0,MDCK1	01/06/2012
6	A/SINGAPORE/12/2012	1280	320	320	320	640	320	1280	2560	1280	5120	160	MDCK0,MDCK1	22/06/2012
7	A/SINGAPORE/8/2012	1280	320	320	320	640	640	1280	1280	1280	2560	320	MDCK0,MDCK2	06/06/2012
8	A/SINGAPORE/5/2012	1280	320	320	320	640	640	1280	1280	1280	2560	160	MDCK0,MDCK2	19/03/2012
9	A/SINGAPORE/6/2012	1280	640	320	640	1280	640	1280	1280	1280	2560	320	MDCK0,MDCK2	01/06/2012
10	A/VICTORIA/378/2012	1280	320	320	320	640	640	640	1280	1280	2560	320	MDCK3	17/07/2012
11	A/FIJI/4/2012	1280	160	320	320	320	320	640	640	1280	5120	160	MDCK2	
12	A/SRI LANKA/19/2012	1280	320	320	320	640	640	1280	2560	1280	2560	160	MDCK2	
13	A/SOUTH AUCKLAND/20/2012	1280	320	320	640	1280	640	1280	2560	1280	2560	320	SIAT,MDCK1	24/06/2012
14	A/CHRISTCHURCH/11/2012	1280	640	640	1280	1280	1280	2560	2560	2560	5120	320	SIAT,MDCK1	24/06/2012
15	A/SINGAPORE/1/2012	640	160	320	320	640	320	1280	1280	1280	2560	160	MDCK0, MDCK1	20/02/2012
16	A/SINGAPORE/4/2012	640	320	320	320	640	640	1280	1280	1280	2560	160	MDCK0,MDCK2	14/03/2012
17	A/SINGAPORE/3/2012	640	160	640	640	1280	640	1280	2560	2560	5120	320	MDCK3	09/02/2012
18	A/VICTORIA/637/2012	640	320	320	320	640	320	1280	2560	1280	2560	320	MDCK2	17/07/2012
19	A/PHILIPPINES/6/2012	640	320	320	320	640	320	640	1280	1280	5120	160	MDCK3	31/01/2012
20	A/PHILIPPINES/1/2012	640	320	320	320	640	640	1280	1280	1280	5120	160	MDCK2	12/01/2012
21	A/SRI LANKA/22/2012	640	320	320	640	1280	640	1280	1280	1280	2560	320	MDCK2	
22	A/WELLINGTON/23/2012	640	320	160	640	640	640	1280	1280	1280	1280	160	SIAT,MDCK1	06/07/2012
23	A/WAIKATO/2/2012	640	320	160	>5120	640	640	1280	1280	1280	1280	80	MDCK,MDCK1	28/06/2012
24	A/WAIKATO/3/2012	640	320	320	320	640	640	1280	1280	1280	2560	160	SIAT,MDCK1	41088
25	A/SINGAPORE/13/2012	160	80	<40	640	320	160	320	320	640	2560	320	MDCK0,MDCK1	13/06/2012
26	A/SINGAPORE/9/2012	160	80	<40	1280	320	160	320	160	640	1280	320	MDCK0,MDCK2	07/06/2012
27	A/SINGAPORE/11/2012	160	40	<40	320	160	1280	1280	1280	640	640	160	MDCK0,MDCK2	15/06/2012
28	A/VICTORIA/523/2012	160	80	80	320	160	80	160	320	640	2560	160	E5	41071

TABLE 3.4 – (H1N1)pdm09 viruses

	Date: June 21, 2012	Haemagglutination Inhibition Assay - WHO Influenza Centre, Melbourne												
	Turkey no. 85	Reference Antisera												
	Sequenced	A	C	D	E	F	F	G	H	I	J	K	L	
		F1656-14D	FS5	F2260-13D	F1614-14D	F2255-13D	F1620-13D	F1686-13D	F1704-14D	F1860-13D	F1857-13D	F1903-13D	Passage	Sample
		E4			C2,MDCK1	C2,MDCK5	MDCK4	E2	E2	E3	MDCK1	E4	Details	Date
	Reference Antigens	CAL/7	AUCK/1	AUCK/1	ILLINOIS/9	ILLINOIS/9	BAY/69	BRIS/10	CHCH/16	PERTH/198	VIC/918	BRIS/70		
A	A/CALIFORNIA/7/2009	**2560**	320	2560	320	2560	640	1280	640	1280	2560	2560	E5	
B	A/AUCKLAND/1/2009	2560	640	>5120	640	2560	1280	2560	1280	2560	>5120	2560	E4	
C	A/ILLINOIS/9/2007	2560	**640**	2560	640	>5120	640	1280	640	1280	2560	1280	C2/MDCK2	
D	A/BAYERN/69/2009	<80	40	**80**	<40	<40	320	160	80	80	<40	160	MDCK7	
E	A/BRISBANE/10/2010	640	160	640	**160**	640	640	1280	2560	640	640	640	E2	
F	A/CHRISTCHURCH/16/2010	2560	320	2560	320	**1280**	1280	5120	2560	1280	2560	2560	E3	
G	A/PERTH/198/2010	1280	160	2560	320	1280	**640**	640	640	1280	1280	1280	E4	
H	A/VICTORIA/918/2010	2560	320	>5120	640	2560	640	**1280**	640	1280	2560	2560	MDCK2	
I	A/BRISBANE/70/2011	2560	320	>5120	640	2560	640	**1280**	1280	1280	2560	2560	E4	
	Test Antigens													
1	A/VICTORIA/514/2012	2560	320	2560	640	2560	640	1280	1280	1280	2560	2560	MDCK2	28/05/2012
2	ASONG KHLA/40/2012	1280	320	2560	640	2560	640	1280	1280	1280	2560	2560	mdckx,mdck1	06/03/2012
3	A/PERTH/42/2012	1280	320	2560	320	1280	320	640	640	640	1280	1280	MDCKX, MDCK2	10/04/2012
4	A/PERTH/47/2012	1280	320	2560	320	1280	320	640	640	640	1280	1280	MDCKX, MDCK2	13/04/2012
5	A/VICTORIA/4/2012	1280	320	2560	320	1280	320	640	640	640	1280	1280	MDCK2	07/05/2012
6	A/VICTORIA/6/2012	1280	320	2560	320	2560	320	640	1280	1280	2560	1280	MDCK4	15/05/2012
7	A/GOROKA/7/2011	1280	320	2560	320	1280	320	640	640	1280	1280	1280	MDCK2	08/01/2011
8	A/GOROKA/9/2011	1280	160	2560	320	1280	320	640	640	640	1280	1280	MDCK2	08/02/2011
9	A/GOROKA/14/2011	1280	320	2560	320	1280	320	640	1280	640	1280	1280	MDCK2	08/04/2011
10	A/GOROKA/16/2011	1280	320	2560	320	1280	320	640	1280	1280	1280	1280	MDCK2	08/09/2011
11	A/GOROKA/20/2011	1280	320	2560	320	1280	320	640	640	640	1280	1280	MDCK2	
12	A/SOUTH AUSTRALIA/42/2012	1280	320	2560	320	2560	320	640	640	1280	1280	1280	MDCK2	31/05/2012
13	A/PERTH/501/2012	640	160	2560	160	640	320	640	640	640	1280	1280	MDCK2	02/03/2012
14	A/PERTH/46/2012	320	80	320	<40	40	640	160	320	320	160	320	MDCKX, MDCK2	13/04/2012
15	A/GOROKA/15/2011	320	160	1280	80	320	320	320	640	640	640	640	MDCK2	08/05/2011

FIGURE 3.2
Phylogenetic relationships among influenza A(H1N1)pdm09 HA genes

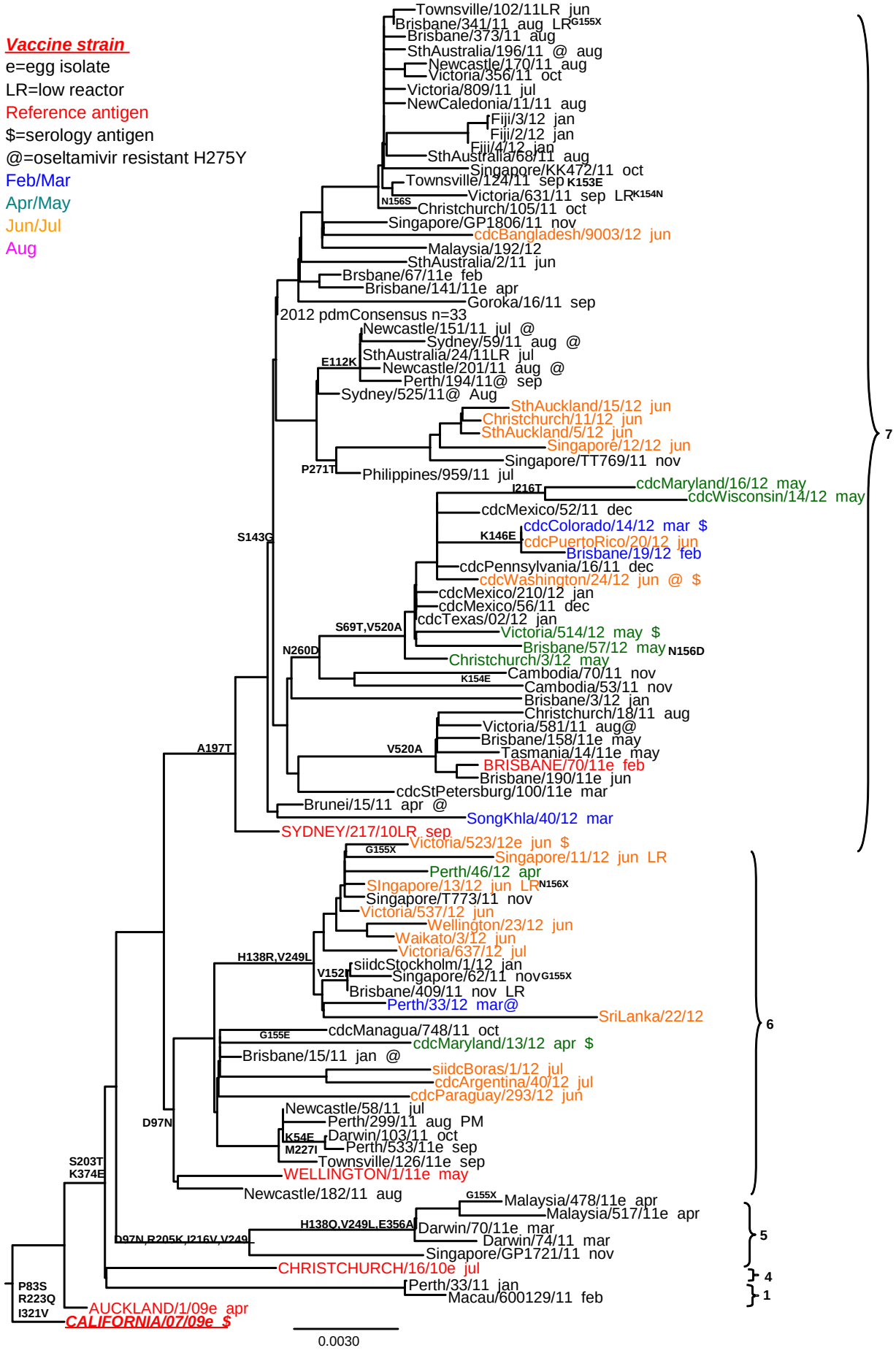


FIGURE 3.3
Phylogenetic relationships among influenza A(H1N1)pdm09 N1 neuraminidase genes

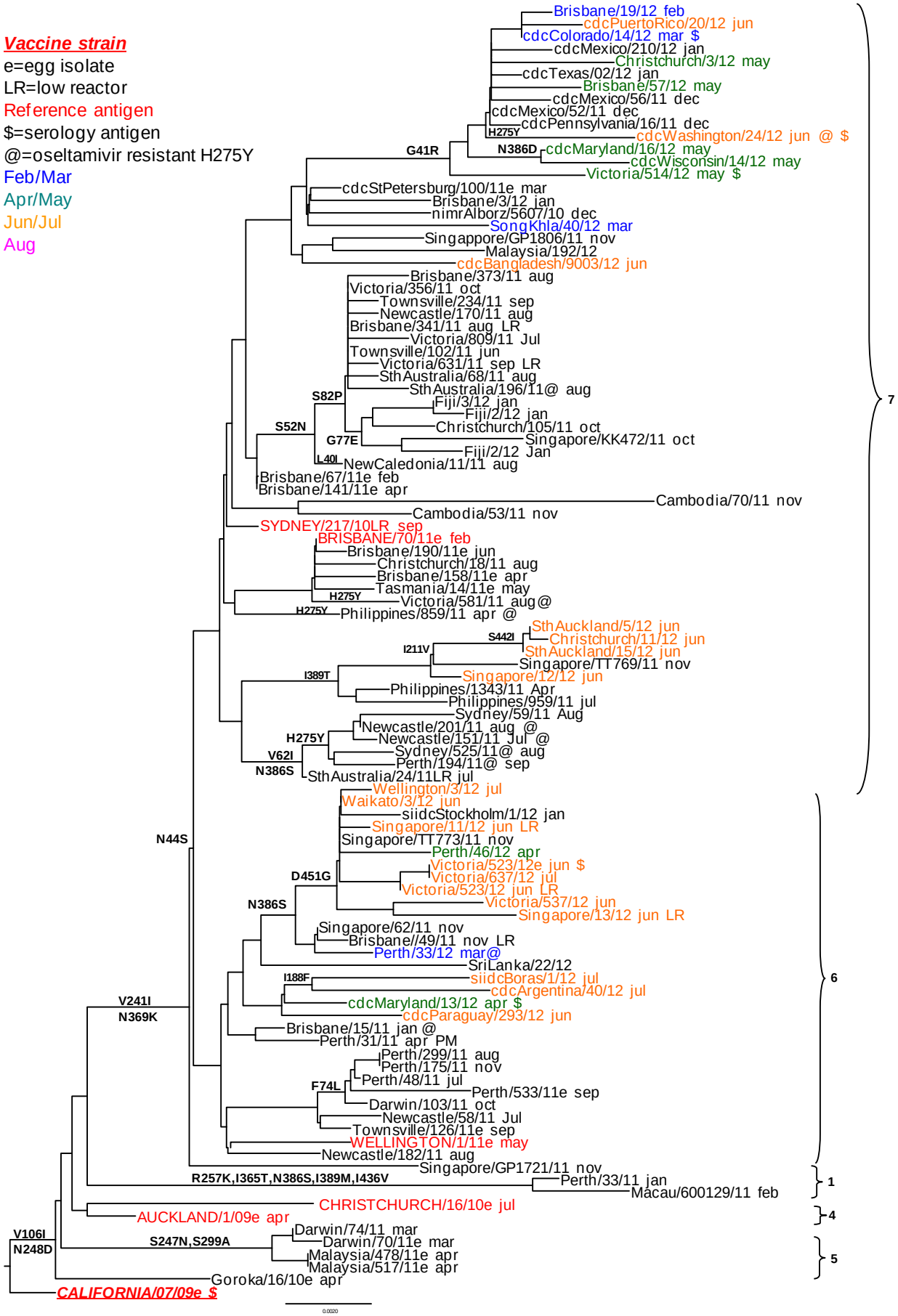


TABLE 3.7
Haemagglutination inhibition antibody titres
Influenza type A(H1N1)pdm09 viruses – Young Adults

	Antigen	Pop	N	Passage History	% Rise	GMT		%>/=40		%>/=160	
						Pre	Post	Pre	Post	Pre	Post
A(H1N1)pdm	A/California/7/2009*	Aus	20	E5	60.0	20.0	117.1	45.0	95.0	15.0	65.0
		Japan	30	E5	33.3	11.0	24.1	20.0	56.7	6.7	13.3
		Eur	24	E5	75.0	11.9	151.0	16.7	87.5	12.5	66.7
A(H1N1)pdm	A/Victoria/537/2012	Aus	20	E4	60.0	12.3	52.8	30.0	80.0	5.0	15.0
		Japan	30	E4	6.8	6.8	11.2	6.7	20.0	0.0	0.0
		Eur	24	E4	50.0	6.6	40.0	8.3	58.3	0.0	37.5
A(H1N1)pdm	A/Norway/418/2012	Aus	20	MDCK2/MDCK3	60.0	10.4	42.9	30.0	80.0	0.0	10.0
		Japan	30	MDCK2/MDCK3	23.3	7.2	13.2	6.7	20.0	0.0	0.0
		Eur	24	MDCK2/MDCK3	75.0	6.3	46.2	4.2	58.3	0.0	33.3

***Vaccine strain**

TABLE 3.8
Haemagglutination inhibition antibody titres
Influenza type A(H1N1)pdm09 viruses – Older Adults

	Antigen	Pop	N	Passage History	% Rise	GMT		%>/=40		%>/=160	
						Pre	Post	Pre	Post	Pre	Post
A(H1N1)pdm	A/California/7/2009*	Aus	20	E5	40.0	8.1	34.8	5.0	50.0	0.0	20.0
		Japan	30	E5	30.0	9.1	18.2	16.7	33.3	0.0	16.7
		Eur	24	E5	62.5	9.2	47.6	12.5	66.7	8.3	33.3
A(H1N1)pdm	A/Victoria/537/2012	Aus	20	E4	40.0	5.5	18.7	0.0	35.0	0.0	20.0
		Japan	30	E4	16.7	7.9	12.3	13.3	23.3	0.0	6.7
		Eur	24	E4	50.0	7.9	29.6	12.5	45.8	8.3	25.0
A(H1N1)pdm	A/Norway/418/2012	Aus	20	MDCK2/MDCK3	35.0	7.6	20.7	0.0	40.0	0.0	15.0
		Japan	30	MDCK2/MDCK3	30.0	8.7	16.6	13.3	30.0	0.0	10.0
		Eur	24	MDCK2/MDCK3	41.7	6.9	24.5	8.3	37.5	0.0	25.0

***Vaccine strain**

APPENDIX 4 - Influenza A (H3N2)

TABLE 4.2 – A(H3) viruses

	Date: August 30, 2012	Haemagglutination Inhibition Assay - WHO Influenza Centre, Melbourne													
	Part A, B, C, D	Reference Antisera													
	Sequenced	**A**	**B**	**C**	**D**	**E**	**F**	**F**	**G**	**H**	**I**	**J**			
	Guinea Pig RBC's	**F1886-13D**	**F2243-13D**	**F2182-13D**	**F2180-13D**	**F1756-13D**	**F1887-13D**	**F2018-15D**	**F2178-13D**	**F2179-13D**	**F2202-14D**	**F2240-14D**		**Passage**	**Sample**
		E4	MDCK	E4	E3	MDCK	MDCK6	MDCK3	E5	MDCK	E3	MDCK2	Mab	**History**	**Date**
	Phylogenetic clade	1	1	-	5	5	5	3C	6	6	3C	3C			
	Reference Antigens	PERTH/16	PERTH/16	VIC/208	PERTH/10	PERTH/10	T'VILLE 87	STH AUST 3	BRIS/299	BRIS/299	VIC/361	VIC/361	189		
A	A/PERTH/16/2009	**640**	320	160	160	320	160	640	320	160	20	160	>10240	E7	
B	A/PERTH/16/2009	1280	**>2560**	320	320	640	640	1280	640	320	160	640	5120	MDCKX, MDCK2	
C	A/VICTORIA/208/2009	1280	>2560	**2560**	>2560	>2560	>2560	>2560	>2560	>2560	>2560	1280	>10240	E4	
D	A/PERTH/10/2010	160	80	160	**160**	640	320	640	320	160	80	160	2560	E3	
E	A/PERTH/10/2010	160	160	80	80	**320**	320	320	320	160	80	160	<80	MDCKX, MDCK3	
F	A/TOWNSVILLE/87/2010	160	160	80	80	320	**320**	320	320	160	80	320	<80	MDCK4	
G	A/SOUTH AUSTRALIA/3/2011	320	160	80	80	320	320	**320**	320	160	80	320	<80	MDCK3	
H	A/BRISBANE/299/2011	320	160	160	320	1280	640	1280	**1280**	320	80	320	>10240	E5	
I	A/BRISBANE/299/2011	160	80	80	80	160	160	160	160	**160**	80	160	<80	MDCK4	
J	A/VICTORIA/361/2011	80	160	320	80	640	320	640	160	320	**>2560**	160	5120	E3	
K	A/VICTORIA/361/2011	160	80	80	80	320	320	160	320	160	80	**160**	<80	MDCK3	
	Test Antigens														
1	A/SYDNEY/99/2012	640	640	320	640	1280	1280	>2560	640	640	320	640	2560	MDCK,MDCK1	08/06/2012
2	A/PHILIPPINES/22/2012	320	320	160	160	320	640	1280	640	320	320	640	80	MDCK2	19/07/2012
3	A/SOUTH AUCKLAND/18/2012	320	320	160	160	640	640	1280	320	320	320	640	320	SIAT,MDCK1	21/06/2012
4	A/VICTORIA/686/2012	640	640	320	320	640	1280	1280	640	320	320	640	640	MDCK2	28/07/2012
5	A/WELLINGTON/33/2012	320	320	160	160	320	640	1280	640	320	160	640	2560	SIAT,MDCK1	16/07/2012
6	A/SYDNEY/95/2012	320	320	160	160	640	640	1280	320	320	160	320	2560	MDCK,MDCK1	04/06/2012
7	A/SYDNEY/102/2012	320	640	160	160	320	320	640	320	320	160	320	2560	MDCK,MDCK1	12/06/2012
8	A/SOUTH AUSTRALIA/143/2012	160	320	80	160	320	320	640	320	160	160	320	2560	MDCK1	16/08/2012
9	A/PHILIPPINES/27/2012	320	320	160	160	320	320	640	320	320	160	320	640	MDCK2	24/07/2012
10	A/WELLINGTON/17/2012	320	320	160	160	320	320	320	320	160	160	320	<80	SIAT,MDCK1	02/07/2012
11	A/CHRISTCHURCH/22/2012	320	320	160	160	320	320	640	320	320	160	320	640	SIAT,MDCK1	01/07/2012
12	A/VICTORIA/721/2012	320	320	160	160	320	320	640	320	160	160	320	80	MDCK2	07/08/2012
13	A/CAMBODIA/20/2012	320	320	160	160	320	320	640	320	160	160	320	160	MDCK1	30/06/2012
14	A/TASMANIA/59/2012	320	320	160	160	320	320	640	320	320	160	320	80	MDCK2	17/07/2012
15	A/PERTH/119/2012	320	320	160	160	320	320	320	320	160	160	320	80	MDCK2	26/06/2012
16	A/CAMBODIA/13/2012	160	160	80	80	320	320	320	320	160	80	320	80	MDCK1	30/07/2012
17	A/VICTORIA/657/2012	160	160	80	80	160	160	160	160	160	80	320	80	MDCK2	23/07/2012
18	A/PERTH/91/2012	160	160	80	80	320	320	20	320	160	80	320	80	MDCKX,MDCK2	12/06/2012
19	A/VICTORIA/692/2012	320	320	160	160	320	320	320	320	320	80	320	80	MDCK2	01/08/2012
20	A/WELLINGTON/30/2012	160	160	160	160	320	320	640	320	160	160	160	2560	MDCK,MDCK1	10/07/2012
21	A/SYDNEY/96/2012	160	160	160	160	320	320	640	320	160	160	160	640	MDCK,MDCK1	05/06/2012
22	A/SOUTH AUSTRALIA/130/2012	160	160	80	160	640	320	640	320	160	160	160	2560	MDCK1	20/08/2012
23	A/VICTORIA/683/2012	160	160	160	160	320	320	320	320	160	160	160	80	MDCK2	28/07/2012
24	A/CHRISTCHURCH/24/2012	160	160	80	80	320	320	640	320	160	80	160	640	SIAT,MDCK1	02/07/2012
25	A/WELLINGTON/24/2012	160	160	80	80	320	320	320	320	160	80	160	160	SIAT,MDCK1	06/07/2012
26	A/WELLINGTON/26/2012	160	160	80	160	160	320	160	160	160	80	160	640	SIAT,MDCK1	09/07/2012
27	A/SYDNEY/211/2012	160	80	80	80	320	320	320	160	160	80	160	1280	MDCK,MDCK1	06/06/2012
28	A/PHILIPPINES/18/2012	160	80	40	80	160	160	160	160	160	80	160	80	MDCK2	31/07/2012
29	A/PHILIPPINES/23/2012	80	80	40	80	160	160	160	160	160	80	160	<80	MDCK2	31/07/2012
30	A/PHILIPPINES/25/2012	80	80	80	80	160	160	320	160	160	80	160	80	MDCK2	31/07/2012
31	A/VICTORIA/720/2012	160	160	80	80	320	320	320	320	160	80	160	80	MDCK2	07/08/2012
32	A/SOUTH AUCKLAND/16/2012	160	160	80	80	320	320	320	320	160	80	160	<80	MDCK,MDCK1	16/06/2012
33	A/CHRISTCHURCH/23/2012	160	160	80	80	320	320	320	320	160	80	160	640	SIAT,MDCK1	01/07/2012
34	A/PERTH/229/2012	80	80	80	80	160	160	160	160	160	80	160	640	MDCK1	08/08/2012
35	A/CAMBODIA/21/2012	160	160	80	80	160	160	160	160	160	80	160	320	MDCK1	10/07/2012
36	A/CAMBODIA/27/2012	160	160	80	80	160	160	160	160	160	80	160	80	MDCK1	20/06/2012
37	A/TASMANIA/29/2012	160	160	80	160	320	320	320	320	160	80	160	80	MDCK2	08/07/2012
38	A/VICTORIA/134/2012	160	160	160	160	320	320	320	320	320	80	160	80	MDCK2	23/07/2012

TABLE 4.3 – A(H3) viruses

	Date: August 28, 2012	Haemagglutination Inhibition Assay - WHO Influenza Centre, Melbourne													
	Part A & B	Reference Antisera													
	Sequenced	A	B	C	D	E	F	F	G	H	I	J			
	Guinea Pig RBC's # 2	F1886-13D	F2243-13D	F2182-13D	F2180-13D	F1756-13D	F1887-13D	F2018-15D	F2178-13D	F2179-13D	F2202-14D	F2240-14D		Passage	Sample
		E4	MDCK	E4	E3	MDCK	MDCK6	MDCK3	E5	MDCK	E3	MDCK2	Mab	History	Date
	Phylogenetic clade	1	1	-	5	5	5	3C	6	6	3C	3C			
	Reference Antigens	PERTH/16	PERTH/16	VIC/208	PERTH/10	PERTH/10	T'VILLE 87	STH AUST 3	BRIS/299	BRIS/299	VIC/361	VIC/361	189		
A	A/PERTH/16/2009	**640**	320	160	160	320	160	640	320	160	40	160	>10240	E4	
B	A/PERTH/16/2009	1280	**1280**	160	320	640	640	640	640	320	160	640	5120	MDCKX, MDCK3	
C	A/VICTORIA/208/2009	1280	1280	**>2560**	>2560	>2560	>2560	>2560	>2560	>2560	>2560	1280	>10240	E4	
D	A/PERTH/10/2010	160	80	160	**160**	640	320	640	320	160	80	160	5120	E5	
E	A/PERTH/10/2010	160	160	80	80	**320**	320	320	320	160	80	160	80	MDCKX, MDCK3	
F	A/TOWNSVILLE/87/2010	160	160	80	160	320	**320**	320	320	320	160	160	80	MDCK7	
G	A/SOUTH AUSTRALIA/3/2011	320	160	80	160	320	320	**320**	320	160	160	320	<80	MDCK3	
H	A/BRISBANE/299/2011	640	160	320	320	>2560	1280	>2560	**>2560**	640	160	640	>10240	E5	
I	A/BRISBANE/299/2011	320	320	160	160	320	320	320	320	**320**	160	320	80	MDCK5	
J	A/VICTORIA/361/2011	160	160	320	160	640	320	640	160	320	**>2560**	160	>10240	E3	
K	A/VICTORIA/361/2011	160	160	80	80	320	320	320	320	160	80	**320**	<80	MDCK3	
	Test Antigens														
1	A/CHRISTCHURCH/25/2012	1280	640	320	320	1280	1280	>2560	1280	640	640	1280	>10240	SIAT,MDCK1	25/07/2012
2	A/SYDNEY/207/2012	640	320	320	320	1280	1280	1280	640	640	320	640	>10240	MDCK,MDCK1	17/06/2012
3	A/SYDNEY/208/2012	640	640	320	320	>2560	1280	>2560	640	640	320	640	5120	MDCK,MDCK1	17/06/2012
4	A/NEWCASTLE/57/2012	320	320	160	160	320	320	1280	640	320	160	640	5120	MDCK1	13/07/2012
5	A/CAMBODIA/29/2012	640	320	160	160	640	640	1280	320	320	160	640	5120	MDCK2	27/06/2012
6	A/CAMBODIA/33/2012	640	640	320	320	640	640	1280	640	320	160	640	5120	MDCK2	28/06/2012
7	A/CHRISTCHURCH/17/2012	320	320	160	160	320	640	640	320	320	160	640	640	SIAT,MDCK1	29/06/2012
8	A/WELLINGTON/36/2012	320	320	160	160	320	640	1280	640	160	160	640	80	SIAT,MDCK1	16/07/2012
9	A/VICTORIA/858/2012	640	640	320	320	1280	1280	>2560	640	640	320	640	2560	MDCK1	09/08/2012
10	A/VICTORIA/866/2012	320	320	320	320	640	640	1280	640	320	320	640	2560	MDCK1	13/08/2012
11	A/SYDNEY/110/2012	320	320	160	320	640	640	1280	320	320	160	320	5120	MDCK,MDCK1	12/06/2012
12	A/CAMBODIA/30/2012	320	160	160	160	640	640	640	320	320	160	320	5120	MDCK2	27/06/2012
13	A/CAMBODIA/34/2012	320	320	160	160	640	320	640	320	320	80	320	5120	MDCK2	28/06/2012
14	A/WELLINGTON/22/2012	160	160	160	160	640	640	640	320	320	160	320	2560	SIAT,MDCK1	04/07/2012
15	A/CAMBODIA/17/2012	160	160	80	160	320	320	640	320	320	80	320	5120	MDCK2	22/06/2012
16	A/WELLINGTON/18/2012	160	160	80	80	320	320	640	320	320	80	320	1280	SIAT,MDCK1	04/07/2012
17	A/WELLINGTON/19/2012	320	160	160	160	640	640	1280	320	320	160	320	2560	SIAT,MDCK1	02/07/2012
18	A/WELLINGTON/41/2012	160	320	160	160	320	320	640	320	160	80	320	320	SIAT,MDCK1	23/07/2012
19	A/CHRISTCHURCH/26/2012	320	320	160	160	640	640	1280	320	320	160	320	2560	SIAT,MDCK1	25/07/2012
20	A/VICTORIA/867/2012	320	320	160	160	320	640	1280	640	320	160	320	<80	MDCK1	14/08/2012
21	A/VICTORIA/869/2012	320	160	80	160	320	320	640	320	320	80	320	2560	MDCK1	16/08/2012
22	A/VICTORIA/873/2012	320	320	160	160	320	320	640	320	160	160	320	80	MDCK1	16/08/2012
23	A/SYDNEY/205/2012	80	80	40	80	160	160	160	160	160	40	160	1280	MDCK,MDCK1	28/05/2012
24	A/SYDNEY/107/2012	160	160	80	80	320	320	320	160	160	80	160	2560	MDCK,MDCK1	08/06/2012
25	A/SYDNEY/229/2012	160	160	160	160	320	320	320	320	320	80	160	2560	MDCK,MDCK1	20/07/2012
26	A/SYDNEY/232/2012	160	160	160	160	320	320	640	320	320	160	160	1280	MDCK,MDCK1	16/07/2012
27	A/SYDNEY/233/2012	160	160	80	80	320	320	320	160	160	80	160	1280	MDCK,MDCK1	25/07/2012
28	A/CAMBODIA/31/2012	160	160	80	80	320	320	320	320	160	80	160	2560	MDCK2	27/06/2012
29	A/WELLINGTON/12/2012	160	160	80	80	320	320	320	160	160	80	160	160	SIAT,MDCK1	25/06/2012
30	A/CHRISTCHURCH/12/2012	160	160	80	160	320	320	320	160	160	80	160	160	SIAT,MDCK1	29/06/2012
31	A/WELLINGTON/21/2012	160	160	80	160	320	320	320	320	160	80	160	1280	SIAT,MDCK1	02/07/2012
32	A/CAMBODIA/24/2012	160	160	160	160	640	640	640	320	320	80	160	5120	MDCK2	06/06/2012
33	A/CAMBODIA/25/2012	160	160	160	160	320	320	640	320	160	80	160	5120	MDCK2	13/06/2012
34	A/WELLINGTON/37/2012	160	80	80	80	160	160	160	160	160	80	160	80	SIAT,MDCK1	17/07/2012
35	A/WAIKATO/6/2012	160	80	80	80	160	160	160	160	160	80	160	<80	SIAT,MDCK1	24/07/2012
36	A/CHRISTCHURCH/27/2012	160	160	80	160	320	320	320	320	160	80	160	5120	SIAT,MDCK1	25/07/2012
37	A/CHRISTCHURCH/28/2012	320	160	160	80	320	320	640	320	320	80	160	5120	SIAT,MDCK1	25/07/2012

TABLE 4.4 – A(H3) viruses

	August 23, 2012		Plaque Reduction Assay - WHO Influenza Centre, Melbourne					
	Assay tested by: Rob		Reference Antisera					
	Data entered by: Rob	1	2	3	4	5		
		F1466-14D	F1886-13D	F2182-13D	F2202-14D	F2240-14D	Passage	Sample
			E4	E4	E3	MDCK2	History	Date
	Reference Antigens	Bris/10	PERTH/16	VIC/208	VIC/361	VIC/361		
1	A/BRISBANE/10/2007	**1280**	640	640	640	640	E5	
2	A/PERTH/16/2009	640	**1280**	2560	1280	640	E7	
3	A/VICTORIA/208/2009	160	640	**1280**	640	640	E4	
4	A/VICTORIA/361/2011	640	1280	1280	**2560**	1280	E3	
5	A/VICTORIA/361/2011	320	1280	2560	1280	**1280**	MDCK3	
	Test Ag							
	A/VICTORIA/92/2012	320	1280	2560	2560	2560	MDCKX,MDCK1	12/07/2012
	A/VICTORIA/131/2012	320	640	1280	1280	1280	MDCKX,MDCK1	19/07/2012
	A/VICTORIA/130/2012	640	1280	2560	2560	1280	MDCKX,MDCK1	19/07/2012
	A/MACAU/600142/2012	320	1280	2560	2560	1280	MDCKX,MDCK1	01/03/2012
	A/MACAU/600193/2012	320	640	1280	640	640	MDCKX,MDCK1	15/03/2012
	A/MACAU/200446/2012	320	640	1280	640	640	MDCK1	15/03/2012
	A/MACAU/600628/2011	160	320	1280	320	320	MDCK1	19/08/2011

FIGURE 4.2
Phylogenetic relationships among influenza A(H3) HA genes

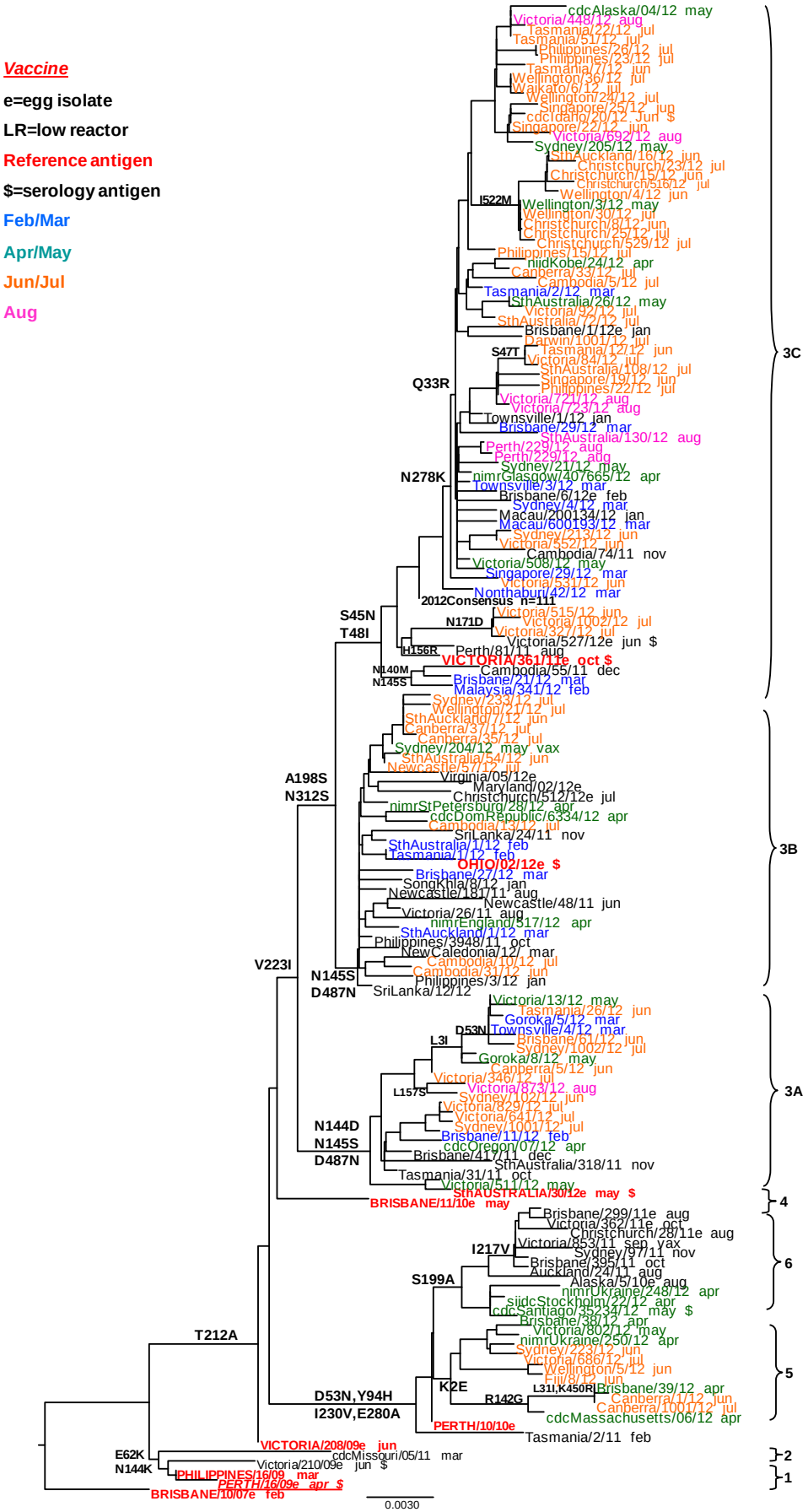


FIGURE 4.3
Phylogenetic relationships among influenza N2 Neuraminidase genes

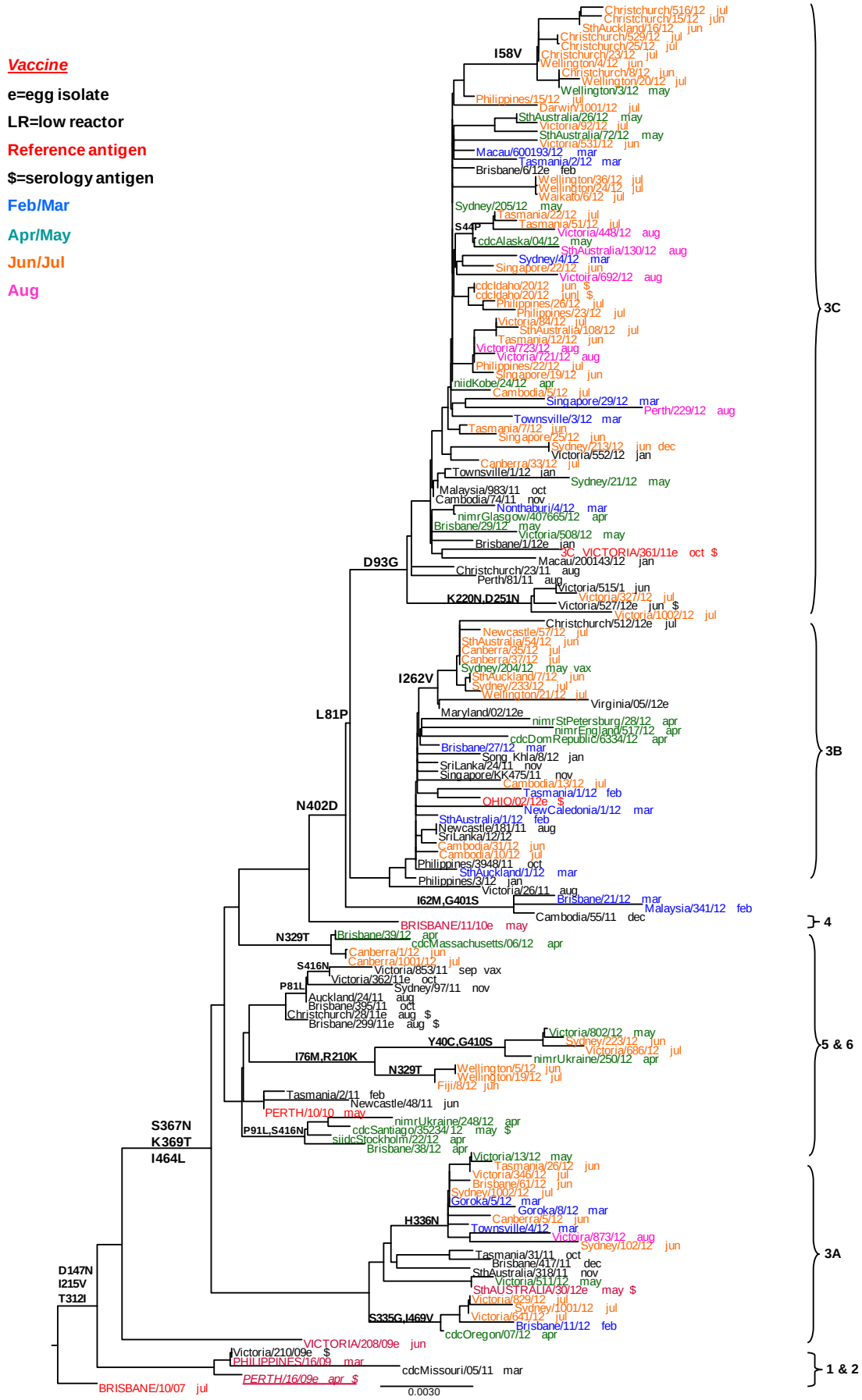


TABLE 4.10
Haemagglutination inhibition antibody titres
Influenza type A(H3N2) viruses – Young Adults

	Antigen	Pop	N	Passage History	% Rise	GMT		%>/=40		%>/=160	
						Pre	Post	Pre	Post	Pre	Post
H3N2	A/Perth/16/2009*	Aus	20	E5	70.0	16.2	98.5	40.0	95.0	0.0	40.0
		Japan	30	E5	30.0	10.5	20.5	16.7	33.3	3.3	6.7
		Eur	24	E5	79.2	7.3	87.2	4.2	83.3	0.0	62.5
H3N2	A/Victoria/361/2011	Aus	20	MDCK3	45.0	11.5	26.4	10.0	50.0	0.0	0.0
		Japan	30	MDCK3	6.7	13.5	17.4	20.0	26.7	0.0	0.0
		Eur	24	MDCK3	66.7	12.2	43.6	8.3	87.5	0.0	0.0
H3N2	A/Ohio/2/2012	Aus	20	E4	65.0	12.7	72.1	25.0	90.0	5.0	35.0
		Japan	30	E4	16.7	8.5	13.5	16.7	26.7	3.3	3.3
		Eur	24	E4	66.7	5.1	43.6	0.0	62.5	0.0	33.3
H3N2	A/Victoria/361/2011**	Aus	20	E3	55.0	21.4	98.5	35.0	90.0	10.0	50.0
		Japan	30	E3	36.7	11.8	27.6	20.0	56.7	3.3	13.3
		Eur	24	E3	100.0	10.6	160.0	20.8	100.0	4.2	62.5
H3N2	A/Victoria/527/2012	Aus	20	MDCK3	10.0	28.3	45.9	50.0	85.0	5.0	5.0
		Japan	30	MDCK3	0.0	19.1	25.8	33.3	46.7	0.0	0.0
		Eur	24	MDCK3	50.0	18.9	56.6	41.7	95.8	0.0	4.2

***Vaccine strain**

TABLE 4.11
Haemagglutination inhibition antibody titres
Influenza type A(H3N2) viruses – Older Adults

	Antigen	Pop	N	Passage History	% Rise	GMT		%>/=40		%>/=160	
						Pre	Post	Pre	Post	Pre	Post
H3N2	A/Perth/16/2009*	Aus	20	E5	65.0	13.7	95.1	35.0	85.0	5.0	35.0
		Japan	30	E5	36.7	10.7	26.4	13.3	50.0	0.0	6.7
		Eur	24	E5	62.5	11.9	71.3	20.8	66.7	12.5	45.8
H3N2	A/Victoria/361/2011	Aus	20	MDCK3	30.0	13.2	27.3	15.0	55.0	0.0	0.0
		Japan	30	MDCK3	10.0	10.7	15.5	3.3	23.3	0.0	0.0
		Eur	24	MDCK3	58.3	13.7	38.9	16.7	70.8	0.0	8.3
H3N2	A/Ohio/2/2012	Aus	20	E4	65.0	8.4	54.6	15.0	75.0	0.0	15.0
		Japan	30	E4	26.7	6.9	13.8	6.7	26.7	0.0	6.7
		Eur	24	E4	47.8	9.2	40.0	17.4	60.9	4.3	26.1
H3N2	A/Victoria/361/2011**	Aus	20	E3	50.0	12.3	56.6	20.0	75.0	5.0	30.0
		Japan	30	E3	26.7	9.8	19.5	13.3	30.0	0.0	6.7
		Eur	24	E3	70.8	16.8	106.8	29.2	95.8	8.3	37.5
H3N2	A/Victoria/527/2012	Aus	20	MDCK3	10.0	31.4	44.4	55.0	80.0	0.0	0.0
		Japan	30	MDCK3	6.7	15.5	20.9	23.3	33.3	0.0	0.0
		Eur	24	MDCK3	45.8	21.8	56.6	45.8	87.5	0.0	12.5

***Vaccine strain for Aus/Japan **Vaccine strain for Eur**

APPENDIX 5 - Influenza B

TABLE 5.2 – B viruses (B/Victoria lineage)

Date: August 7, 2012 Part A & B		Haemagglutination Inhibition Assay – WHO Influenza Centre, Melbourne Reference Antisera													
	Sequenced	**A**	**B**	**C**	**D**	**E**	**F**	**G**	**H**	**I**	**J**	**K**			
	Turkey number 72	**F1175-21D**	**F1640-21D**	**F1901-21D**	**F1904-21D**	**F1233-19D**	**F1236-21D**	**F1880-21D**	**F1364-21D**	**F1900-21D**	**F2314-21D**	**F2315-21D**	**F1687-21D**		
		E4	**MDCK3**	**MDCK**	**E3**	**MDCKX,MDCK1**	**E4**	**E3**	**E3**	**E2**	**MDCK1**	**MDCK1**	**E4**	**Passage**	**Date**
		MAL/2506	PHIL/6363	SING/616	CAMB/30	BRIS/60	BRIS/60	BRIS/33	HK/90	SYD/508	SA/11	DAR/40	WISC/1	History	
	Reference Antigens														
A	B/MALAYSIA/2506/2004	**1280**	1280	1280	1280	20	320	640	320	640	40	<20	<20	E5	
B	B/PHILIPPINES/6363/2009	320	**640**	320	320	<20	80	160	160	160	<20	<20	<20	MDCK3	
C	B/SINGAPORE/616/2008	320	640	**640**	640	<20	160	320	320	160	<20	<20	<20	MDCK5	
D	B/CAMBODIA/30/2011	640	1280	1280	**1280**	20	320	640	320	320	40	20	<20	E3	
E	B/BRISBANE/60/2008	<20	160	20	40	**160**	160	320	320	160	320	640	<20	MDCKX,MDCK4	
F	B/BRISBANE/60/2008	320	640	640	640	160	**1280**	>2560	1280	>2560	160	640	<20	E6	
G	B/BRISBANE/33/2008	320	1280	320	1280	160	1280	**>2560**	>2560	>2560	320	640	<20	E4	
H	B/HONG KONG/90/2008	320	640	640	640	160	1280	1280	**>2560**	1280	160	320	<20	E5	
I	B/SYDNEY/508/2010	320	640	640	1280	160	1280	1280	1280	**>2560**	160	640	<20	E2	
J	B/SOUTH AUSTRALIA/11/2012	<20	80	<20	40	160	160	320	320	160	**320**	1280	<20	MDCK2	
K	B/DARWIN/40/2012	<20	160	<20	40	320	160	320	320	160	320	**1280**	<20	MDCK2	
L	B/WISCONSIN/1/2010	80	20	<20	40	<20	40	<20	20	20	<20	<20	**640**	E4	
	Test antigens														
1	B/SOUTH AUSTRALIA/21/2012	<20	160	<20	40	320	320	320	320	320	320	640	<20	MDCK1	25/06/2012
2	B/DARWIN/42/2012	<20	160	<20	40	160	160	320	320	160	320	1280	<20	MDCK1	27/06/2012
3	B/DARWIN/45/2012	<20	160	<20	40	320	160	320	320	320	320	1280	<20	MDCK1	04/07/2012
4	B/DARWIN/46/2012	<20	160	<20	40	320	160	320	320	160	320	1280	<20	MDCK1	04/07/2012
5	B/VICTORIA/806/2012	<20	160	<20	40	320	160	320	320	160	320	1280	<20	MDCK1	04/07/2012
6	B/VICTORIA/314/2011	<20	160	<20	40	320	160	320	320	160	320	1280	<20	MDCK1	06/07/2012
7	B/ALICE SPRINGS/11/2012	<20	160	<20	40	320	160	320	640	320	320	1280	<20	MDCK1	05/07/2012
8	B/SOUTH AUSTRALIA/22/2012	<20	80	<20	40	160	160	320	320	320	320	1280	<20	MDCK!	06/07/2012
9	B/CHRISTCHURCH/501/2012	<20	160	<20	20	320	160	320	320	320	320	1280	<20	mdck1	09/07/2012
10	B/CHRISTCHURCH/1/2012	<20	160	<20	40	320	160	320	320	320	320	640	<20	MDCKX,MDCK1	15/06/2012
11	B/SOUTH AUCKLAND/1/2012	<20	160	<20	40	160	160	320	320	160	320	1280	<20	MDCKX,MDCK1	09/03/2012
12	B/VICTORIA/316/2012	<20	160	<20	20	160	160	320	320	160	320	640	<20	MDCK1	17/07/2012
13	B/BRISBANE/32/2012	<20	80	<20	20	160	160	320	320	160	320	1280	<20	mdck2	08/06/2012
14	B/TOWNSVILLE/20/2012	<20	160	<20	40	320	320	320	320	320	320	1280	<20	mdck2	09/06/2012
15	B/BRISBANE/35/2012	<20	160	<20	40	320	320	320	640	320	640	1280	<20	mdck2	11/06/2012
16	B/TOWNSVILLE/21/2012	<20	80	<20	20	320	160	320	320	320	320	1280	<20	mdck2	14/06/2012
17	B/TOWNSVILLE/22/2012	<20	160	<20	40	320	320	320	640	320	640	640	<20	mdck2	13/06/2012
18	B/TOWNSVILLE/23/2012	<20	80	<20	20	160	160	320	320	160	320	640	<20	mdck2	12/06/2012
19	B/TOWNSVILLE/25/2012	<20	80	<20	20	160	160	320	320	160	320	1280	<20	mdck3	06/06/2012
20	B/BRISBANE/37/2012	<20	160	<20	40	160	160	320	320	320	320	1280	<20	mdck2	14/06/2012
21	B/BRISBANE/38/2012	<20	160	<20	40	320	320	320	320	320	320	1280	<20	mdck2	18/06/2012
22	B/BRISBANE/39/2012	<20	160	<20	40	320	160	320	640	320	640	1280	<20	mdck2	18/06/2012
23	B/TOWNSVILLE/27/2012	<20	80	<20	20	160	160	320	320	160	320	1280	<20	mdck2	07/06/2012
24	B/SYDNEY/204/2012	<20	160	<20	40	160	160	320	320	320	320	1280	<20	mdckx,mdck1	21/06/2012
25	B/VICTORIA/517/2012	<20	160	<20	40	320	320	320	640	320	640	1280	<20	MDCK1	01/07/2012
26	B/BRISBANE/33/2012	<20	80	<20	20	160	160	320	320	160	320	640	<20	mdck2	07/06/2012
27	B/TOWNSVILLE/19/2012	<20	160	<20	40	320	320	320	320	320	640	1280	<20	mdck2	06/06/2012
28	B/BRISBANE/34/2012	<20	160	<20	40	320	160	320	320	320	320	1280	<20	mdck2	09/06/2012
31	B/TASMANIA/4/2012	<20	80	<20	20	160	160	320	320	160	320	640	<20	MDCK1	09/07/2012
32	B/DARWIN/48/2012	<20	80	<20	40	160	160	320	320	160	320	640	<20	mdck1	09/07/2012
33	B/VICTORIA/516/2012	<20	160	<20	40	320	160	320	320	160	320	1280	<20	MDCK1	27/06/2012
34	B/SINGAPORE/1/2012	<20	80	<20	<20	160	160	320	320	160	320	640	<20	MDCK0, MDCK1	02/02/2012
35	B/SINGAPORE/2/2012	<20	80	<20	<20	160	160	320	320	160	160	320	<20	MDCK0, MDCK1	07/02/2012
36	B/SINGAPORE/12/2012	<20	80	<20	<20	160	160	320	320	160	320	640	<20	MDCK0, MDCK1	13/06/2012
37	B/SINGAPORE/13/2012	<20	80	<20	<20	160	160	320	320	160	320	640	<20	MDCK0, MDCK1	13/06/2012
38	B/SINGAPORE/18/2012	<20	80	<20	<20	160	160	320	320	160	320	640	<20	MDCK0, MDCK1	23/02/2012
39	B/SINGAPORE/20/2012	<20	80	<20	<20	160	160	320	320	160	320	640	<20	MDCK0, MDCK1	20/03/2012
40	B/MACAU/200200/2012	<20	160	<20	20	160	80	160	160	160	160	640	<20	MDCK,MDCK1	13/02/2012

TABLE 5.3 – B viruses (B/Victoria lineage)

	Date: August 16, 2012	Haemagglutination Inhibition Assay - WHO Influenza Centre, Melbourne												
	Turkey no. 82	Reference Antisera												
	Sequenced	A	B	C	D	E	F	F	G	H	I	J		
		F1175-21D	F1640-21D	F1901-21D	F1904-21D	F1233-19D	F1236-21D	F1880-21D	F1364-21D	F1900-21D	F1687-21D	Mab 172		
		E4	MDCK3	MDCK	E3	MDCKX,MDCK1	E4	E3	E3	E2	E4		Passage	Date
	Reference Antigens	MAL/2506	PHIL/6363	SING/616	CAMB/30	BRIS/60	BRIS/60	BRIS/33	HK/90	SYD/508	WISC/1		History	
A	B/MALAYSIA/2506/2004	**1280**	1280	1280	1280	20	320	640	640	640	<20	<80	E5	
B	B/PHILIPPINES/6363/2009	160	**1280**	160	320	20	80	160	160	160	<20	<80	MDCK3	
C	B/SINGAPORE/616/2008	320	640	**640**	640	20	320	320	320	320	<20	<80	MDCK5	
D	B/CAMBODIA/30/2011	640	1280	1280	**1280**	40	320	640	640	640	<20	<80	E3	
E	B/BRISBANE/60/2008	20	160	<20	80	**160**	160	320	320	320	<20	1280	MDCKX,MDCK4	
F	B/BRISBANE/60/2008	320	640	320	640	160	**1280**	1280	1280	1280	<20	1280	E6	
G	B/BRISBANE/33/2008	320	640	320	1280	160	1280	**>2560**	1280	>2560	<20	1280	E4	
H	B/HONG KONG/90/2008	320	640	640	640	80	640	1280	**1280**	1280	<20	1280	E5	
I	B/SYDNEY/508/2010	160	640	320	1280	160	1280	1280	1280	**>2560**	<20	1280	E2	
J	B/WISCONSIN/1/2010	80	<20	<20	20	<20	<20	<20	20	<20	**640**	<80	E4	
	Test Antigens													
1	B/CHRISTCHURCH/504/2012	<20	160	<20	40	640	320	640	640	320	<20	2560	MDCK1	23/07/2012
2	B/SRI LANKA/3/2012	<20	80	<20	20	640	160	320	320	320	<20	1280	X,MDCK1	
3	B/SINGAPORE/19/2012	<20	80	<20	<20	320	160	320	320	320	<20	1280	MDCK2	28/03/2012
4	B/PERTH/75/2012	<20	160	<20	40	320	160	320	320	320	<20	2560	MDCKX,MDCK1	30/05/2012
5	B/PERTH/79/2012	<20	160	<20	40	320	160	320	320	320	<20	2560	MDCKX,MDCK1	03/06/2012
6	B/PERTH/86/2012	<20	160	<20	40	320	320	320	640	320	<20	2560	MDCKX,MDCK1	07/06/2012
7	B/PERTH/89/2012	<20	160	<20	40	320	160	320	320	320	<20	2560	MDCKX,MDCK1	05/06/2012
8	B/PERTH/113/2012	<20	160	<20	40	320	160	320	320	320	<20	1280	MDCKX,MDCK1	25/06/2012
9	B/PERTH/116/2012	<20	160	<20	<20	320	320	320	640	320	<20	2560	MDCKX,MDCK1	25/06/2012
10	B/VICTORIA/523/2012	<20	160	<20	40	320	160	320	320	320	<20	2560	MDCK1	17/07/2012
11	B/PERTH/64/2012	<20	80	<20	40	320	320	320	320	320	<20	1280	MDCKX,MDCK1	09/05/2012
12	B/PERTH/71/2012	<20	160	<20	20	320	160	320	320	320	<20	1280	MDCKX,MDCK1	23/05/2012
13	B/PERTH/72/2012	<20	80	<20	40	320	160	320	320	320	<20	1280	MDCKX,MDCK1	28/05/2012
14	B/CHRISTCHURCH/502/2012	<20	160	<20	40	320	160	320	320	320	<20	1280	MDCK1	17/07/2012
15	B/CHRISTCHURCH/503/2012	<20	160	<20	80	320	320	640	640	320	<20	2560	MDCK1	21/07/2012
16	B/CHRISTCHURCH/506/2012	<20	160	<20	40	320	320	640	640	320	<20	1280	MDCK1	24/07/2012
17	B/SRI LANKA/1/2012	<20	160	<20	40	320	320	640	640	320	<20	1280	X,MDCK1	
18	B/SRI LANKA/4/2012	<20	160	<20	20	320	160	320	640	320	<20	1280	X,MDCK1	
19	B/SINGAPORE/21/2012	<20	80	<20	<20	160	160	320	320	320	<20	640	MDCK2	30/03/2012
20	B/TASMANIA/3/2012	<20	80	<20	<20	160	160	320	320	160	<20	1280	MDCK1	21/07/2012
21	B/PERTH/69/2012	<20	80	<20	<20	160	160	320	320	160	<20	640	MDCKX,MDCK1	15/05/2012
22	B/PERTH/85/2012	<20	80	<20	40	160	160	320	320	320	<20	640	MDCKX,MDCK1	06/06/2012
23	B/TASMANIA/6/2012	<20	80	<20	<20	160	160	320	320	320	<20	2560	MDCK1	01/08/2012
24	B/PERTH/76/2012	<20	80	<20	20	160	160	320	320	160	<20	640	MDCKX,MDCK1	31/05/2012
25	B/SRI LANKA/2/2012	<20	40	<20	<20	160	<20	160	160	40	<20	<80	X,MDCK1	
26	B/PERTH/58/2012	20	40	20	<20	<20	<20	<20	40	20	<20	<80	MDCKX,MDCK1	03/05/2012

TABLE 5.4 – B viruses (B/Yamagata lineage)

Date: August 2, 2012		Haemagglutination Inhibition Assay - WHO Influenza Centre, Melbourne													
		Reference Antisera													
	Sequenced	**A**	**B**	**C**	**D**	**E**	**F**	**G**	**H**	**I**	**J**	**K**			
	Turkey number 65	**F982-21D**	**F997-21D**	**F1145-21D**	**F1151-19D**	**F1323-19D**	**F1149-19D**	**F1687-21D**	**F1654-21D**	**F2313-21D**	**F2313-21D**	**F1880-21D**	**Mab 184**		
		E2	E4	mdckx,mdck1	E5	E3	CELL	E4	E4	MDCK1	MDCKX,MDCK1	E3		Passage	Date
	Reference Antigens	BRIS/3	FLORID/4	STH AUST/5	BANG/3333	INDI/1	BRIS/9	WISC/1	HBEI/158	STH AUS/17	MAL/412	BRIS/33	1/40	History	
A	B/BRISBANE/3/2007	**1280**	1280	80	1280	640	1280	160	640	160	160	<20	160	E3	
B	B/FLORIDA/4/2006	>2560	**>2560**	80	640	640	>2560	160	1280	160	320	<20	160	E4	
C	B/SOUTH AUSTRALIA/5/2008	160	160	**640**	320	320	160	160	160	320	40	<20	320	MDCKX.MDCK2	
D	B/BANGLADESH/3333/2007	640	1280	320	**1280**	1280	640	320	640	320	20	<20	320	E6	
E	B/INDIANA/1/2008	640	640	160	1280	**640**	640	320	320	160	<20	<20	160	E3	
F	B/BRISBANE/9/2008	80	160	640	160	320	**80**	80	80	320	20	<20	160	MDCKX, MDCK4	
G	B/WISCONSIN/1/2010	640	640	320	640	320	640	**320**	640	320	20	<20	160	E4	
H	B/HUBEI WUJIAGANG/158/2009	320	320	160	160	160	320	80	**320**	80	<20	<20	320	E7	
I	B/SOUTH AUSTRALIA/17/2012	80	80	320	160	160	80	80	80	**320**	<20	<20	160	MDCK2	
J	B/MALAYSIA/412/2012	320	320	160	160	160	320	80	80	160	**320**	<20	160	MDCKX,MCDK2	
K	B/BRISBANE/33/2008 (Victoria)	<20	<20	<20	<20	<20	<20	<20	<20	<20	<20	**1280**	<40	E4	
	Test Antigens														
1	B/WAIKATO/1/2012	320	320	320	160	320	640	160	160	320	320	<20	80	SIATX,MDCK1	23/05/2012
2	B/VICTORIA/3/2012	160	160	80	80	160	160	80	40	160	320	<20	160	MDCK1	20/06/2012
3	B/NEW CALEDONIA/2/2012	320	320	80	160	320	640	80	160	160	320	<20	320	MDCK1	19/06/2012
4	B/SOUTH AUCKLAND/4/2012	160	160	80	80	160	160	80	40	80	160	<20	80	MDCKX,MDCK1	05/06/2012
5	B/VICTORIA/6/2012	80	160	640	160	160	80	80	80	320	40	<20	640	mdck1	30/06/2012
6	B/SOUTH AUCKLAND/3/2012	160	160	80	80	160	160	80	80	160	320	<20	160	MDCKX,MDCK1	05/05/2012
7	B/VICTORIA/7/2012	160	160	160	80	160	160	80	40	160	320	<20	320	mdck1	02/07/2012
8	B/MACAU/60079/2012	80	80	320	80	160	80	80	80	320	40	<20	320	MDCK,MDCK1	07/02/2012
9	B/MACAU/200162/2012	160	160	80	80	160	320	80	80	160	320	<20	320	MDCK,MDCK1	07/02/2012
10	B/BRISBANE/36/2012	160	80	160	80	160	320	80	80	320	320	<20	160	mdck2	13/06/2012
11	A/WELLINGTON/9/2012	160	160	80	40	160	160	80	40	160	320	<20	160	mdckx,MDCK1	22/06/2012
12	B/VICTORIA/4/2012	160	160	80	40	160	160	40	40	160	320	<20	320	MDCK1	25/06/2012
13	B/VICTORIA/8/2012	160	80	80	40	80	160	40	40	80	160	<20	160	mdck1	04/07/2012

TABLE 5.5 – B viruses (B/Yamagata lineage)

	Compilation: August 14, 2012	Haemagglutination Inhibition Assay - WHO Influenza Centre, Melbourne													
		Reference Antisera													
	Sequenced	1	2	3	4	5	6	7	8	9	10	11			
	Turkey number 85	F982-21D	F997-21D	F1145-21D	F1151-19D	F1323-21D	F1149-19D	F1687-21D	F1654-21D	F2313-21D	F2313-21D	F1880-21D	Mab 184		
		E2	E4	mdckx,mdck1	E5	E3	CELL	E4	E4	MDCK1	MDCKX,MDCK1	E3		Passage	Date
	Reference Antigens	BRIS/3	FLORID/4	STH AUST/5	BANG/3333	INDI/1	BRIS/9	WISC/1	HBEI/158	STHAUS/17	MAL/412	BRIS/33	1/40	History	
A	B/BRISBANE/3/2007	1280	1280	80	640	640	1280	160	320	80	160	<20	160	E5	
B	B/FLORIDA/4/2006	**1280**	1280	80	640	640	1280	160	640	160	320	<20	160	E4	
C	B/SOUTH AUSTRALIA/5/2008	160	**160**	640	320	320	160	160	160	320	<20	<20	320	MDCKX.MDCK2	
D	B/BANGLADESH/3333/2007	640	640	**320**	1280	640	640	320	640	320	<20	<20	320	E6	
E	B/INDIANA/1/2008	640	640	160	**1280**	640	640	320	320	160	<20	<20	320	E3	
F	B/BRISBANE/9/2008	80	160	640	320	**320**	80	80	160	320	<20	<20	320	MDCKX, MDCK4	
G	B/WISCONSIN/1/2010	640	640	320	640	640	**640**	320	640	320	<20	<20	320	E4	
H	B/HUBEI WUJIAGANG/158/2009	320	320	80	160	160	320	**80**	320	80	<20	<20	320	E7	
I	B/BRISBANE/33/2008 (Victoria)	<20	<20	<20	<20	<20	<20	<20	**<20**	<20	<20	>2560	<40	E4	
J	B/SOUTH AUSTRALIA/17/2012	160	160	640	320	320	160	160	160	**320**	<20	<20	320	MDCK2	
K	B/MALAYSIA/412/2012	640	320	320	160	160	320	80	160	160	**640**	<20	320	MDCKX,MCDK2	
	Test Antigens														
1	B/SOUTH AUCKLAND/5/2012	1280	640	640	320	320	1280	320	640	640	640	<20	320	MDCKX,MDCK1	16/06/2012
2	B/SOUTH AUCKLAND/6/2012	640	640	320	320	320	640	320	320	640	640	<20	320	MDCKX,MDCK1	17/06/2012
3	B/SINGAPORE/10/2012	640	640	1280	640	320	640	320	640	640	320	<20	320	MDCK0, MDCK1	09/06/2012
4	B/SINGAPORE/4/2012	160	160	640	320	160	160	160	160	320	<20	<20	320	MDCK0, MDCK1	07/03/2012
5	B/SINGAPORE/5/2012	320	320	1280	320	320	160	160	320	640	80	<20	320	MDCK2	14/02/2012
6	B/SINGAPORE/6/2012	160	160	640	320	160	160	160	160	320	<20	<20	320	MDCK0, MDCK1	20/02/2012
7	B/SINGAPORE/7/2012	320	320	1280	320	320	320	160	320	640	<20	<20	320	MDCK0, MDCK1	05/06/2012
8	B/SINGAPORE/8/2012	320	320	640	320	320	160	160	320	320	<20	<20	320	MDCK0, MDCK1	08/06/2012
9	B/SINGAPORE/9/2012	160	160	1280	320	320	160	160	320	640	<20	<20	320	MDCK0, MDCK1	08/06/2012
10	B/SINGAPORE/11/2012	160	160	640	320	320	160	160	160	320	<20	<20	320	MDCK0, MDCK1	12/06/2012
11	B/SINGAPORE/15/2012	320	320	640	320	320	160	160	320	320	<20	<20	320	MDCK0, MDCK1	31/05/2012
12	B/SINGAPORE/17/2012	320	320	640	320	320	160	160	320	640	<20	<20	320	MDCK0, MDCK1	16/02/2012
13	B/VICTORIA/320/2012	160	160	640	320	160	160	160	160	320	<20	<20	320	MDCK1	27/07/2012
14	B/PERTH/53/2012	160	160	640	320	320	160	160	160	320	<20	<20	320	MDCKX,MDCK1	26/04/2012
15	B/PERTH/68/2012	320	320	640	320	320	320	160	320	640	80	<20	160	MDCKX,MDCK1	15/05/2012
16	B/PERTH/84/2012	160	160	640	320	320	160	160	160	320	<20	<20	320	MDCKX,MDCK1	06/06/2012
17	B/PERTH/114/2012	160	160	640	320	160	160	160	160	640	<20	<20	320	MDCKX,MDCK1	24/06/2012
18	B/PERTH/115/2012	160	160	640	320	320	160	160	160	320	<20	<20	320	MDCKX,MDCK1	24/06/2012
19	B/CHRISTCHURCH/505/2012	320	160	320	320	320	320	160	80	320	320	<20	160	MDCK1	23/07/2012
20	B/PERTH/54/2012	80	160	640	160	320	80	80	80	320	<20	<20	160	MDCKX,MDCK1	02/05/2012
21	B/PERTH/88/2012	80	80	640	320	160	80	80	160	320	<20	<20	320	MDCKX,MDCK1	06/06/2012
22	B/VICTORIA/526/2012	320	160	320	160	320	320	80	80	160	640	<20	320	MDCK1	27/07/2012
23	B/VICTORIA/524/2012	160	160	80	80	160	160	80	80	160	320	<20	160	MDCK1	20/07/2012
24	B/PERTH/50/2012	80	80	640	320	320	80	80	80	320	<20	<20	320	MDCKX,MDCK1	14/04/2012
25	B/PERTH/63/2012	80	80	640	160	320	80	80	80	320	<20	<20	160	MDCKX,MDCK1	08/05/2012
26	B/VICTORIA/809/2012	160	160	320	160	160	160	80	40	320	640	<20	320	MDCK1	02/08/2012
27	B/VICTORIA/525/2012	160	160	80	80	160	160	40	80	160	320	<20	160	MDCK1	23/07/2012

FIGURE 5.5
Phylogenetic relationships among influenza B HA genes
B/Victoria Lineage

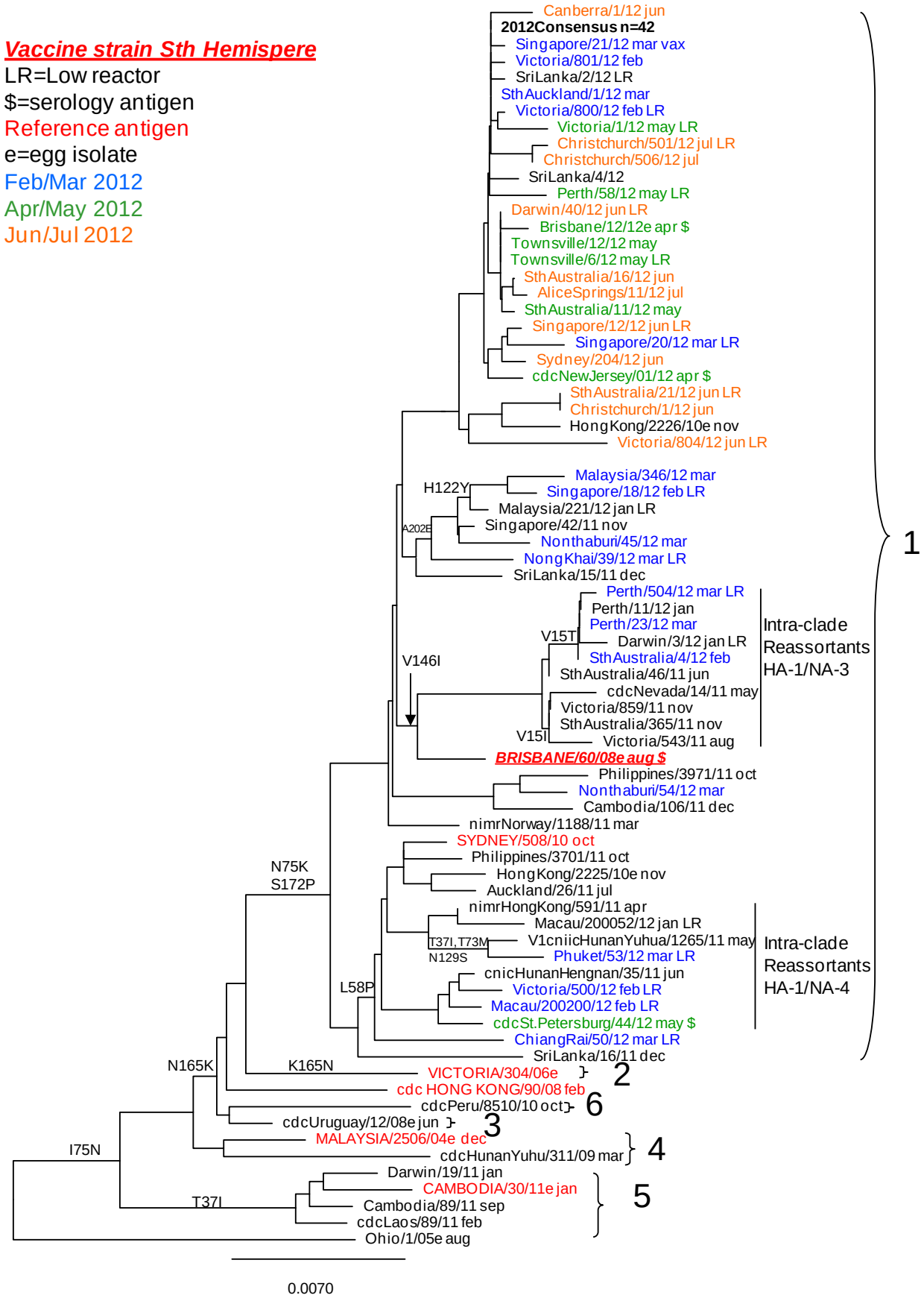


FIGURE 5.6
Phylogenetic relationships among influenza B neuraminidase genes
B/Victoria Lineage

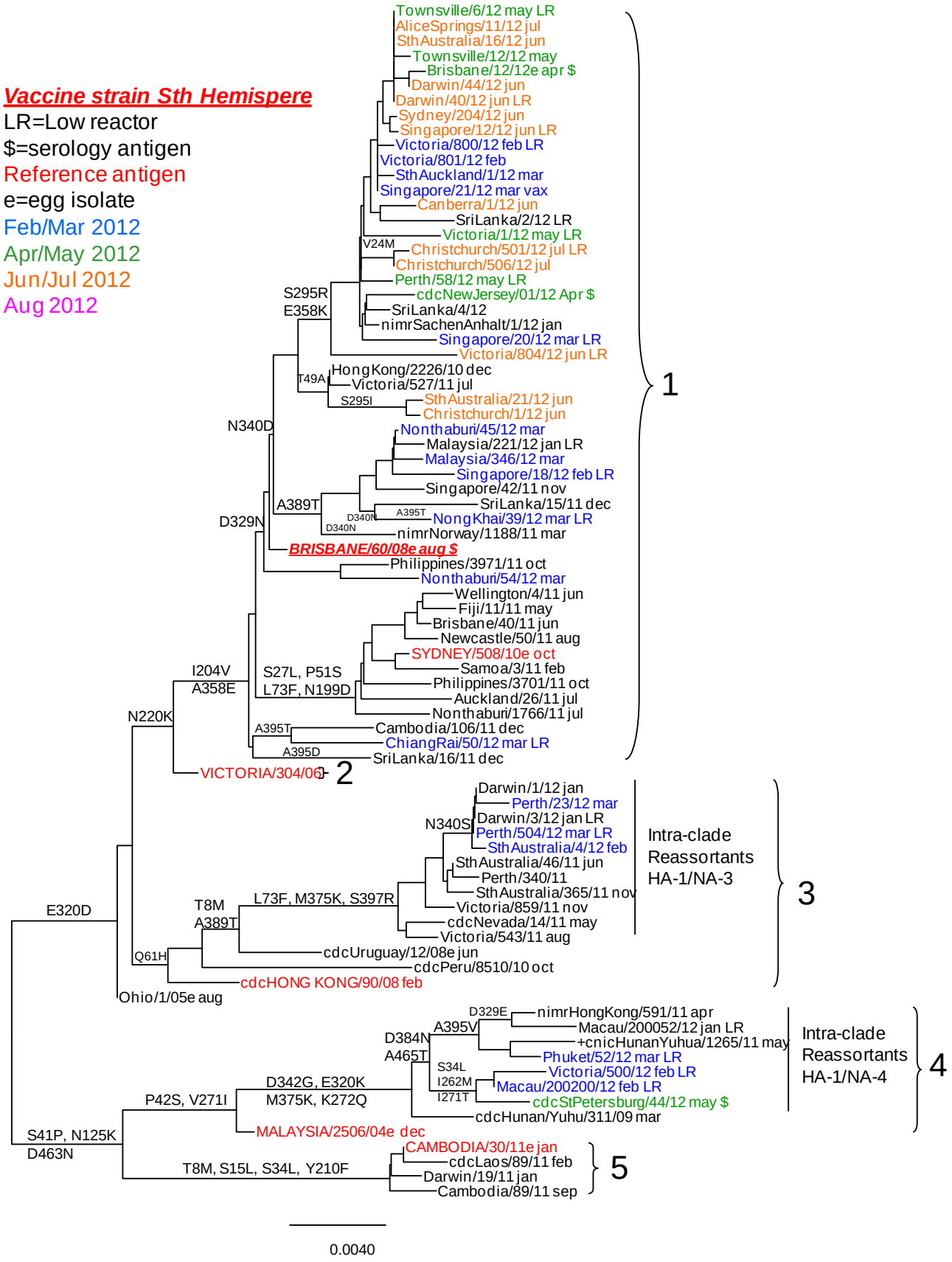


FIGURE 5.7
Phylogenetic relationships among influenza B HA genes
B/Yamagata Lineage

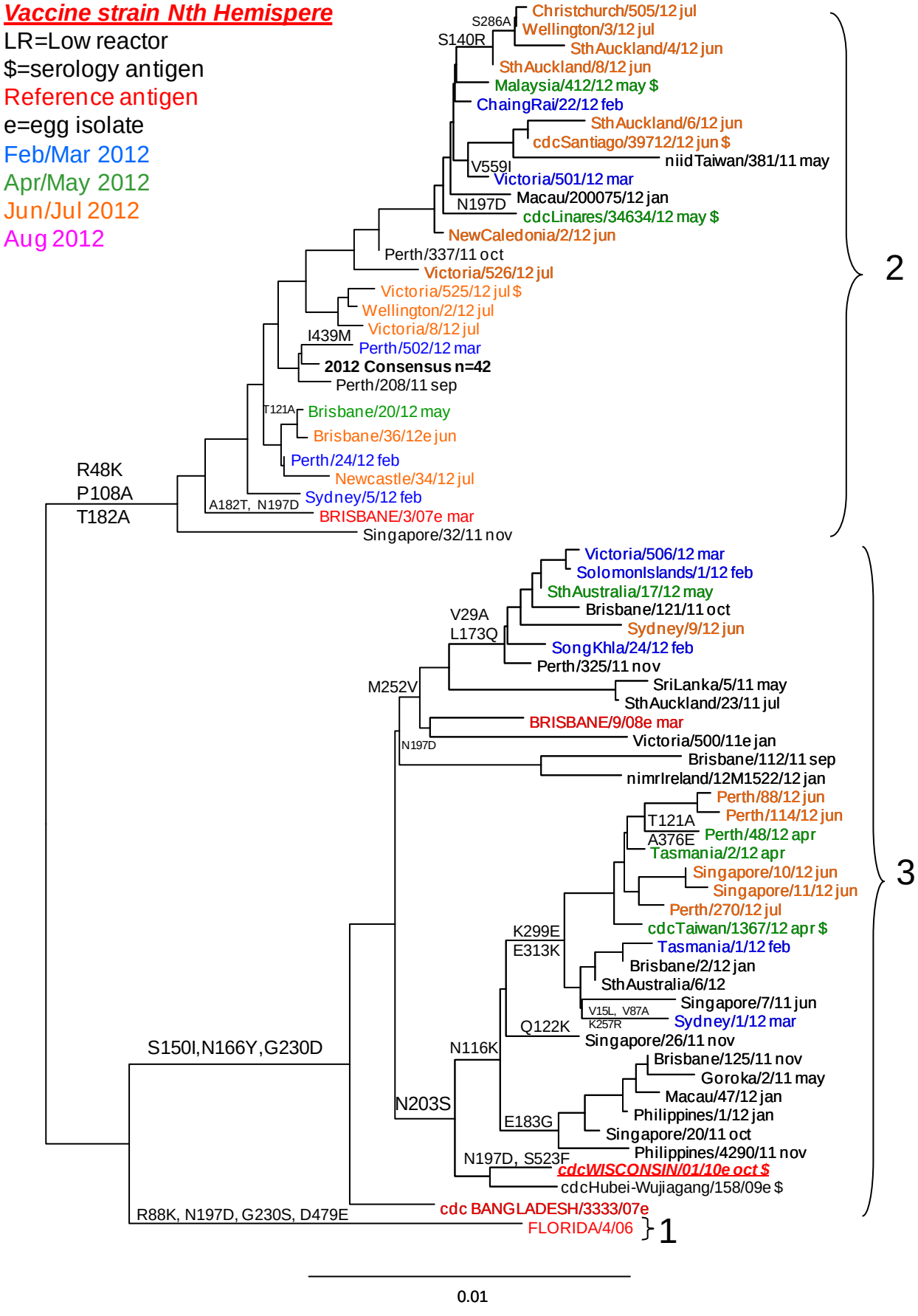


FIGURE 5.8
Phylogenetic relationships among influenza B neuraminidase genes
B/Yamagata Lineage

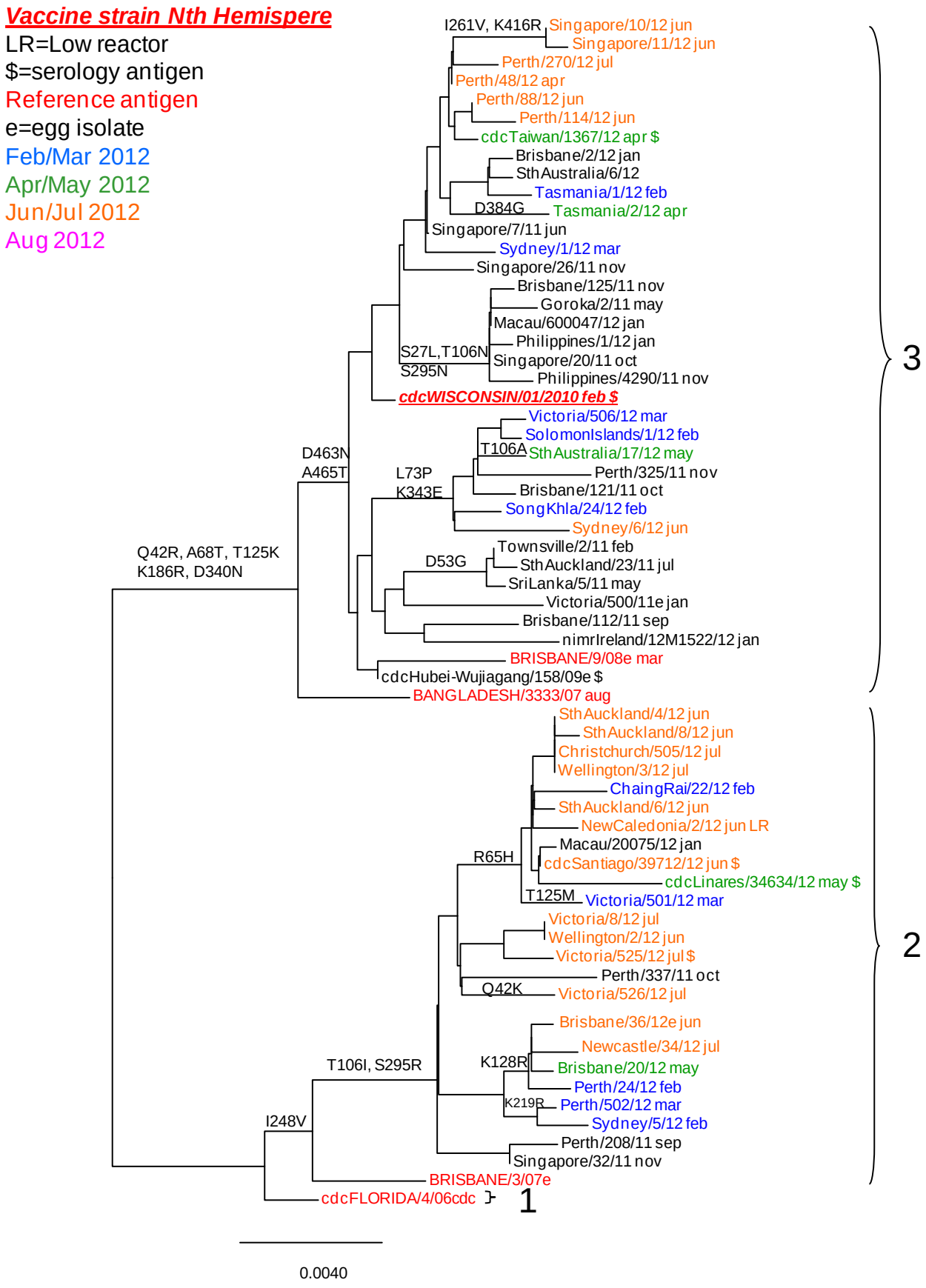


TABLE 5.9
HI serology assays of influenza type B/Victoria viruses – Young Adults

	Antigen	Pop	N	Passage History	% Rise	GMT		%>/=40		%>/=160	
						Pre	Post	Pre	Post	Pre	Post
B Vic	B/Brisbane/60/2008*	Aus	20	E6	35.0	27.3	98.5	50.0	80.0	25.0	55.0
		Japan	30	E6	6.7	40.9	69.6	66.7	86.7	20.0	33.3
B Vic	B/Brisbane/12/2012	Aus	20	E3	50.0	24.6	117.1	45.0	90.0	20.0	50.0
		Japan	30	E3	10.0	18.7	30.3	26.7	63.3	0.0	3.3
		Eur	24	E3	37.5	10.9	32.7	16.7	58.3	8.3	20.8

TABLE 5.10
HI serology assays of influenza type B/Victoria viruses – Older Adults

	Antigen	Pop	N	Passage History	% Rise	GMT		%>/=40		%>/=160	
						Pre	Post	Pre	Post	Pre	Post
B Vic	B/Brisbane/60/2008*	Aus	20	E6	35.0	12.3	40.0	30.0	65.0	0.0	15.0
		Japan	30	E6	13.3	18.7	34.8	36.7	53.3	16.7	33.3
B Vic	B/Brisbane/12/2012	Aus	20	E3	30.0	13.7	44.4	35.0	70.0	0.0	15.0
		Japan	30	E3	23.3	14.1	29.6	23.3	53.3	3.3	16.7
		Eur	24	E3	25.0	6.9	12.6	8.3	25.0	0.0	4.2

TABLE 5.11
HI serology assays of influenza type B/Yamagata viruses – Young Adults

	Antigen	Pop	N	Passage History	% Rise	GMT		%>/=40		%>/=160	
						Pre	Post	Pre	Post	Pre	Post
B Yam	B/Wisconsin/12010**	Aus	20	E5	30.0	41.4	85.7	60.0	70.0	45.0	50.0
		Japan	30	E5	3.3	52.8	69.6	66.7	83.3	26.7	33.3
		Eur	24	E5	87.5	13.3	195.8	25.0	87.5	8.3	70.8
B Yam	B/Victoria/525/2012	Aus	20	MDCK2	15.0	26.4	41.4	55.0	65.0	20.0	20.0
		Japan	30	MDCK2	3.3	34.0	40.9	53.3	53.3	26.7	26.7
		Eur	24	MDCK2	87.5	19.4	195.8	45.8	95.8	12.5	62.5
B Yam	B/Massachusetts/2/2012	Aus	20	E3	15.0	37.3	72.1	60.0	65.0	30.0	50.0
		Japan	30	E3	6.7	69.6	85.7	76.7	83.3	43.3	40.0
		Eur	24	E3	79.2	23.8	239.7	45.8	91.7	8.3	70.8
B Yam	B/Taiwan/1367/2012	Eur	24	MDCK3	87.5	10.6	123.4	20.8	87.5	4.2	54.2
B Yam	B/Hubei-Wujiagang/158/2009	Eur	24	E6	75.0	12.2	179.6	25.0	83.3	8.3	66.7

TABLE 5.12
HI serology assays of influenza type B/Yamagata viruses - Older Adults

	Antigen	Pop	N	Passage History	% Rise	GMT		%>/=40		%>/=160	
						Pre	Post	Pre	Post	Pre	Post
B Yam	B/Wisconsin/12010**	Aus	20	E5	25.0	23.0	44.4	50.0	70.0	10.0	20.0
		Japan	30	E5	6.7	18.2	24.1	43.3	46.7	6.7	16.7
		Eur	24	E5	79.2	12.6	103.7	20.8	83.3	8.3	50.0
B Yam	B/Victoria/525/2012	Aus	20	MDCK2	25.0	15.7	28.3	40.0	60.0	5.0	10.0
		Japan	30	MDCK2	3.3	9.5	11.0	16.7	23.3	3.3	3.3
		Eur	24	MDCK2	79.2	12.6	106.8	25.0	87.5	0.0	50.0
B Yam	B/Massachusetts/2/2012	Aus	20	E3	30.0	23.8	38.6	50.0	65.0	15.0	15.0
		Japan	30	E3	6.7	20.9	27.0	40.0	50.0	10.0	20.0
		Eur	24	E3	75.0	12.6	80.0	29.2	79.2	4.2	41.7
B Yam	B/Taiwan/1367/2012	Eur	24	MDCK3	83.3	7.1	67.3	8.1	75.0	0	29.17
B Yam	B/Hubei-Wujiagang/158/2009	Eur	24	E6	70.8	11.9	95.1	25.0	79.2	8.3	50.0

***Vaccine strain for Aus/Japan **Vaccine strain for Eur**