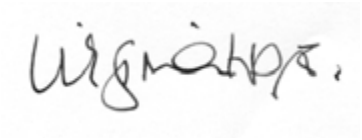
RECOMMENDATION FOR SEASONAL INFLUENZA VACCINE COMPOSITION FOR NEW ZEALAND 2011



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RECOMMENDATION FOR SEASONAL INFLUENZA VACCINE COMPOSITION FOR NEW ZEALAND 2011

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by

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- The Therapeutic Goods Administration, DOHA for hosting the Australian Influenza Vaccine Committee.

Recommendations

The Australian Influenza Vaccine Committee (AIVC) met with New Zealand representatives (Appendix 1) in Canberra on 6 October 2010 to consult on the influenza vaccine composition for 2011 for New Zealand, Australia and South Africa. The recommended composition was:

- A(H1N1) an A/California/7/2009 (H1N1) - like virus*
- A(H3N2) an A/Perth/16/2009 (H3N2) - like virus
- B a B/Brisbane/60/2008 - like virus

* Note: A/California/7/2009 is a pandemic A(H1N1) virus, also known as pandemic (H1N1) 09 virus.

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It is known that influenza viruses frequently go through antigenic changes in their two surface proteins, the haemagglutinin (HA) and neuraminidase (NA). It is known that protection by vaccines is dependent on achieving a good match between vaccine strains and the circulating viruses, particularly for the haemagglutinin 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 neutralization tests provide complementary data. Antigenic cartography is used as an additional analytical tool to visualize and integrate antigenic data. Phylogenetic analyses of haemagglutinin and neuraminidase 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 in February for the northern hemisphere winter and another in September for the southern hemisphere winter. This recommendation is published in 8 October issue of the *Weekly Epidemiological Record, 2010 85(41):401-412 (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 standardization.

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 Australian Influenza Vaccine Committee met with New Zealand representatives (Appendix 1) on 6 October 2010 to consult on the seasonal influenza vaccine composition for New Zealand, Australia and South Africa for 2011. The recommended composition (Table 1) was:

- A(H1N1) an A/California/7/2009 (H1N1) - like virus*
- A(H3N2) an A/Perth/16/2009 (H3N2) - like virus
- B a B/Brisbane/60/2008 - like virus

* Note: A/California/7/2009 is a pandemic A(H1N1) virus, also known as pandemic (H1N1) 09 virus.

TABLE 1. Influenza Vaccine Recommendations for New Zealand, 1991-2011

Formulation Recommendations		Vaccine used for	A H3N2	A H1N1	B
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, March-September 2010

Between February and September 2010, influenza activity was reported in Africa, the Americas, Asia, Europe and Oceania. In many countries influenza activity was low compared with the same period in 2009; it was due to the pandemic A(H1N1)[1], seasonal A(H3N2) and B viruses. In general, outbreaks due to pandemic A(H1N1) viruses decreased during this period, leading to the declaration of the post-pandemic phase by WHO on 10 August 2010.

In the southern hemisphere, influenza activity was variable among the different regions. Pandemic A(H1N1) viruses predominated in some countries, such as Australia, Colombia and New Zealand. In general, activity increased from July and had declined in most countries by September.

In the northern hemisphere, influenza activity generally declined from February and was very low in Europe and North America compared with the same period in the previous year. In Asia, widespread outbreaks of pandemic A(H1N1) occurred in India; regional pandemic A(H1N1) activity was reported in Bhutan, Cambodia, China and Malaysia, and localised activity was reported in Nepal. Seasonal influenza A(H3N2) or B viruses predominated in some African and South American countries, and regional activity of A(H3N2) and B viruses was experienced in China. Confirmed cases of seasonal A(H1N1) viruses were rare.

In tropical areas, many countries experienced outbreaks of varying intensity of pandemic A(H1N1), A(H3N2) and B.

From 17 February 2010 to 26 September 2010, 27 human cases of A(H5N1), 12 of which were fatal, were confirmed and reported by Cambodia, China, Egypt, Indonesia and Viet Nam, where highly pathogenic avian influenza A(H5N1) is present in poultry. Since December 2003, a total of 505 cases with 300 deaths have been confirmed in 15 countries. To date there has been no evidence of sustained human-to-human transmission.

No human cases of influenza A(H9N2) were reported during the period from February to September 2010.
(Abridged from the Weekly Epidemiological Record, 2010 85(41):401-412)

The WHO Collaborating Centre for Reference and Research on Influenza in Melbourne, Australia (Melbourne WHOCC) analysed influenza isolates received from 1 March to 30 September 2010. Pandemic A(H1N1) virus was the predominant strain which accounted for 72.1% (1216/1687) of isolates while 7% (119/1687) were seasonal influenza A(H3N2) and 15.4% (260/1687) of isolates were influenza B (Figures 2.1 and 2.2 in Appendix 2).

[1] For the consistency of the virus nomenclature, pandemic (H1N1) 09 virus is termed as pandemic A(H1N1) virus in this report.

1.2 Influenza activity in Australia, March-September 2010

Influenza activity in Australia in 2010 was low with some regional variations regarding influenza activities and types/subtypes.

There are nine forms of influenza surveillance system in Australia:

- **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. In 2010, confirmed pandemic A(H1N1) cases are still being received from all jurisdictions through the NNDSS. As of 8 October 2010, there were 9084 confirmed cases of influenza of all types. Of these, 5386 (59%) have been subtyped as pandemic A(H1N1), 2827 (31%) as influenza A (untyped), 162 (2%) as seasonal influenza A(H3N2) and 10 (<1%) as type A&B. A further 552 (6%) have been characterised as influenza type B and 147 (2%) were untyped. Overall, the 2010 notification data are lower than the confirmed cases of pandemic A(H1N1) in 2009 (43 022).

- **Laboratory Surveillance.** This is conducted by the Melbourne WHOCC. A total of 907 influenza isolates from Australia were received for analysis at the Melbourne WHOCC (Appendix 2) from 1 March to 30 September 2010. Seven hundred and seventy-seven pandemic A(H1N1) viruses (86%, 777/907) were isolated and antigenically closely related to A/California/7/2009 (H1N1)-like strain. Thirty-nine (4%, 39/907) of the isolates were A(H3N2) viruses with the majority relating antigenically to the A/Perth/16/2009-like strain. Forty-two (5%, 42/907) influenza B viruses were isolated with most of them belonging to the B/Brisbane/60/2008 lineage. Regarding oseltamivir-resistant viruses, between 1 January to 10 October 2010, no isolates (out of 749 tested) showed resistance to oseltamivir or zanamivir by enzyme inhibition assay and two pandemic A(H1N1) isolates (out of 41 tested) showed the H275Y mutation known to confer resistance to oseltamivir.

- **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 and Western Australia. As jurisdictions joined ASPREN at different times and the number of GPs reporting has changed over time, the representativeness of ASPREN data in 2010 may be different from that of previous years. Overall, ILI presentations to GPs were the lowest compared with the 2007–2009 data.

- **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 2010 was lower than that of 2007–2009.

- **Absenteeism Survey.** Australia Post conducts an absenteeism survey that consists of national employer of more than 30 000 people in all jurisdictions except the Northern Territories. The absenteeism data are supplied weekly per jurisdiction. The percentage of sick leave for three days or more continuously is reported. These data are not influenza- or ILI- specific, and absenteeism may be a result of other illnesses.

Unfortunately, the absenteeism data have not been updated since July 2010 due to system changes.

- **Influenza hospitalisations.** The Influenza Complications Network (FluCAN) collects detailed clinical information on all hospitalised cases of influenza and pneumonia from a sample of 15 sentinel hospitals across Australia. From 1 March to 8 October 2010, FluCAN has reported a total of 258 influenza associated hospitalisations. Of these, 211 were associated with pandemic A(H1N1) viruses, including 57 with intensive care unit (ICU) admissions.

- **Australian Paediatric Surveillance.** This surveillance system reports on hospital admissions of children aged 15 years and under to 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 on a weekly basis. Since 1 July 2010, 30 hospitalisations have been reported, 13 of which were associated with pandemic A(H1N1) viruses. Five of these cases were admitted to ICU. Nine cases were associated with influenza A (not further subtyped), and one case was associated with influenza B. Four of the cases associated with pandemic A(H1N1) viruses had an underlying chronic condition.

- **Death associated with influenza and pneumonia.** Nationally reported pandemic A(H1N1) deaths are notified by jurisdictions to the Commonwealth Department of Health and Ageing as they occur. As of 8 October 2010, 20 pandemic influenza related deaths have been notified to this system. The deaths occurred in late May, July, August and September, and the median age of death was 52 years. Sixteen of the deaths were reported as having underlying risk factors.

- **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 8 October 2010, there were 124 pneumonia or influenza associated deaths per 1,000 deaths in NSW, which is below the seasonal threshold for this period of 143 per 1,000 deaths

(Abridged from the Australian Influenza Surveillance Report 2010, No.40, 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-September 2010

Influenza surveillance in South Africa has been expanded significantly during 2010 and includes three main active surveillance programmes:

- **Viral watch programme** – A total of 246 doctors and primary health care nurses have been recruited across the country to participate in the influenza like Illness (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 pandemic influenza A(H1N1) 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 which monitors cases of more severe disease in hospitalised patients. Detailed epidemiologic data are collected on all patients. This programme currently includes three hospitals, 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 and Mapulaneng and Matikwana Hospitals (MMHs), rural setting hospitals in Mpumalanga Province. Apart from these active surveillance sites, the National Institute of Communicable Diseases (NICD) also offers routine testing for respiratory virus disease to clinicians across the country. This service has become particularly active after the emergence of pandemic influenza A(H1N1) and served as the initial diagnostic service for the country and later as diagnostic facility for severe cases and confirmation of fatal cases. Apart from these surveillance and diagnostic services the NICD has also participated in an influenza vaccine efficacy trail in HIV positive patients.

In 2010, a total of 5349 suspected influenza specimens were processed. Influenza A was detected in 955 specimens and influenza B in 618 specimens with an isolation rate of 29.5%. In South Africa, influenza B was the predominant strain (39.3%, 618/1573) compared with the seasonal A(H3N2) (19.1%, 301/1573) and pandemic A(H1N1) (11.3%, 177/1573) strains.

Most of the influenza B strains belonged to the B/Victoria/2/87 lineage with only a small proportion (3.5%, 4/116) of influenza B viruses belonging to the B/Yamagata/16/88 lineage. Most of the B/Victoria-like lineage viruses were antigenically similar to the B/Brisbane/60/2008-like viruses.

A total of 32 seasonal influenza A(H3N2) viruses were sequenced and they were clustered genetically with the A/Perth/16/2009-like virus. Only five seasonal influenza A(H3N2) viruses haemagglutinated red blood cells and they were antigenically similar to the vaccine strain A/Perth/16/2009. The neuraminidase genes of the eight seasonal influenza A(H3N2) viruses were sequenced and all had the wild type E119 amino acid with no resistance causing mutations being identified.

A total of 26 pandemic A(H1N1) viruses were sequenced. They grouped separately from the 2009 South African strains and they were clustered with the 2010 strains from northern hemisphere such as Victoria, California, New York and Singapore. The neuraminidase genes of the 12 pandemic A(H1N1) viruses were sequenced and none had the H274Y mutation, indicating they were sensitive to oseltamivir.

(Abridged from a report by Professor Barry Schoub, National Institute for Communicable Diseases, South Africa.)

2. INFLUENZA ACTIVITY IN NEW ZEALAND IN 2010

2.1 Summary

Influenza activity during the 2010 New Zealand winter was in a range of low to medium compared with that of the past 19 years of surveillance. When the 2010 sentinel ILI consultation data were compared to the 1992-2009 data, the 2010 cumulative incidence rate of 946.6 per 100 000 was the seventh lowest (or 13th highest) during 1992-2010. The 2010 peak consultation rate of 152 per 100 000 was the ninth lowest (or 11th highest) during 1992-2010. In addition, the 2010 influenza hospitalisations (594, 13.8 per 100 000) were the third highest recorded over the period 1990-2010. The 2010 influenza mortality rate (11, 0.25 per 100 000) was the sixth lowest during 1990-2010.

The 2010 influenza activity started late in the winter season. It peaked in week 33 (16-22 August 2010) and the intense activity lasted about one month. Again, the influenza activity in 2010 had an uneven geographical distribution. Some regions (mainly small urban and rural areas) that experienced relatively low ILI activity or hospitalisations in 2009 experienced higher levels of influenza activity in 2010. Children (0-19 years) and young adults (20-29 years) had a higher disease burden compared with other age groups.

Pandemic influenza A(H1N1) virus was the predominant strain detected in New Zealand. This strain represented 83.9% (1590/1896) of all influenza viruses. The pandemic A(H1N1) viruses tested were antigenically and genetically closely related to the pandemic vaccine candidate strain A/California/7/2009 (H1N1). All pandemic A(H1N1)viruses (280) tested were sensitive to oseltamivir.

A small number of seasonal influenza A(H3N2) (4) viruses were detected. This strain represented 0.2% (4/1896) of all influenza viruses. The seasonal influenza A(H3N2) viruses from New Zealand were antigenically related to the reference strain A/Perth/16/2009 (H3N2) with a low reactor identified. In addition, a small number of influenza B viruses (6) were detected, representing 0.3% (6/1896) of all influenza viruses. Two out of six influenza B viruses were available for antigenic typing. They were B/Brisbane/60/2008-like strains, belonging to the B/Victoria/2/87 lineage. No seasonal influenza A(H1N1) virus was detected.

2.2 The 2010 New Zealand influenza season

The national influenza surveillance system in New Zealand is an essential public health component for assessing and implementing strategies to control influenza. The surveillance system includes notifiable disease surveillance, sentinel general practitioners (GP) surveillance and non-sentinel laboratory surveillance.

2.2.1 Notifiable disease surveillance

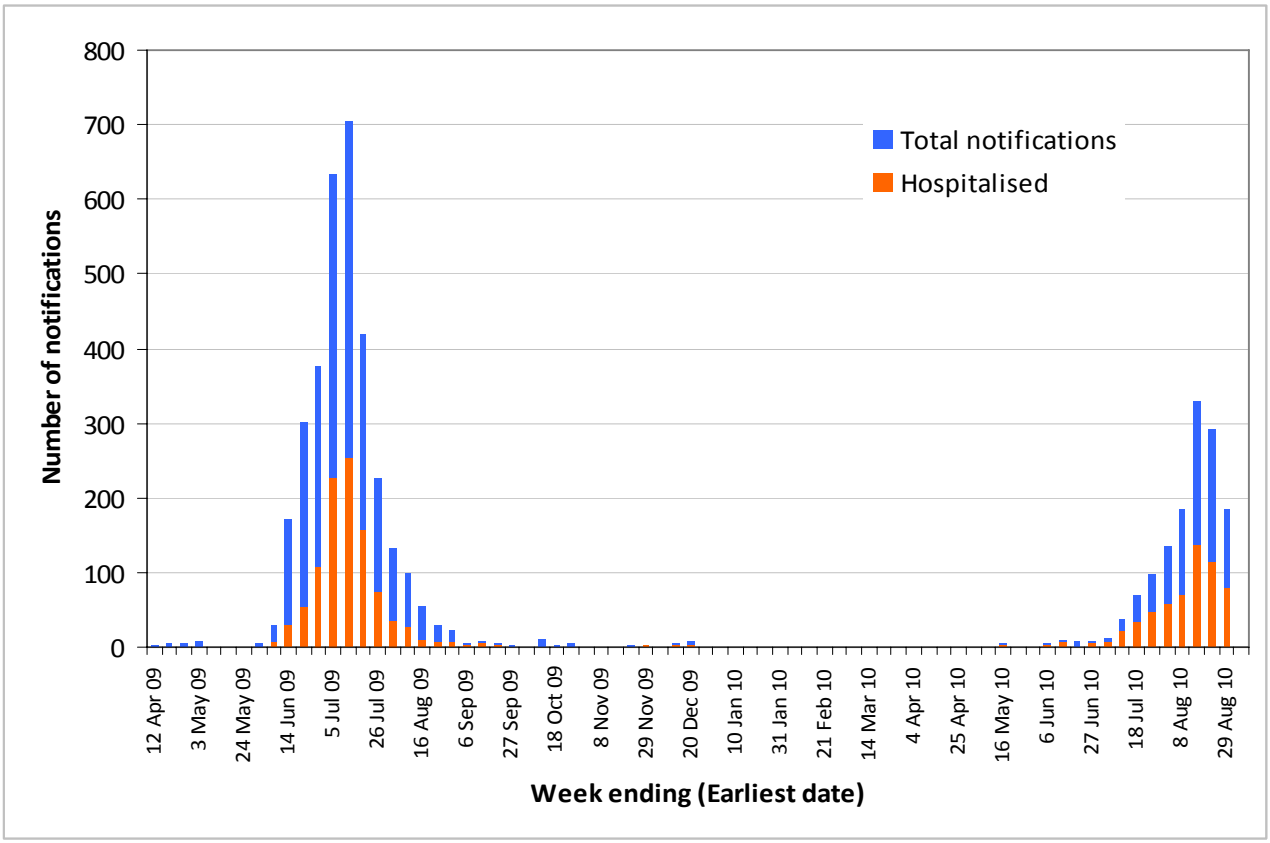
Seasonal influenza is not a notifiable disease in New Zealand. Pandemic influenza A(H1N1) was made a notifiable and quarantineable disease on 30 April 2009. Data are entered into a web-based database (EpiSurv) held at the Institute of Environmental Science and Research (ESR) and available for immediate analysis. This system also records hospitalized and fatal cases. Since only confirmed cases are being notified and only a small proportion of suspected cases are investigated, notifications while useful for trend analysis do not give an accurate picture of the true extent of the current situation.

During the first wave of infection from 1 April to 31 December 2009, a total of 3211 confirmed cases of pandemic influenza A(H1N1) had been notified, including 1122 hospitalisations and 35 deaths. The highest notification rates were seen in the less than one year age group, and high notification and hospitalisation rates were seen among Pacific Peoples and Māori ethnic groups.

2.2.1.1 Temporal distribution

During the period of 26 December 2009 to 29 August 2010, a total of 1384 hospitalised and non-hospitalised cases of pandemic influenza A(H1N1) had been notified in EpiSurv, including 1360 confirmed and 24 probable cases. The epidemic curves for 2009 and 2010 (to date) are shown in Figure 1. These epidemic curves were constructed using the earliest date that pandemic A(H1N1) was recorded in EpiSurv (onset, hospitalised or report date) and are expressed as cases per week since 6 April 2009. Confirmed and probable cases were combined for this purpose.

Figure 1. Notified cases and hospitalisations of pandemic influenza A(H1N1) April 2009 to August 2010



2.2.1.2 Age and ethnic distribution

Notification rates in 2010 across different age groups are shown in Figure 2 and Table 2. The under one year age group had the highest overall notification rate (106.1 per 100 000 population) followed by the 20-29 year old age group (48.1 per 100 000 population). The 20-29 year old age group had the highest number of cases (274). The rate for all reported cases was 32.4 per 100 000 (using 2008 mid-year population estimates), although the actual rate is likely to be much higher as only a small proportion of people with symptoms are being tested.

Figure 2. Cumulative rate of pandemic A(H1N1) cases by age, 2010

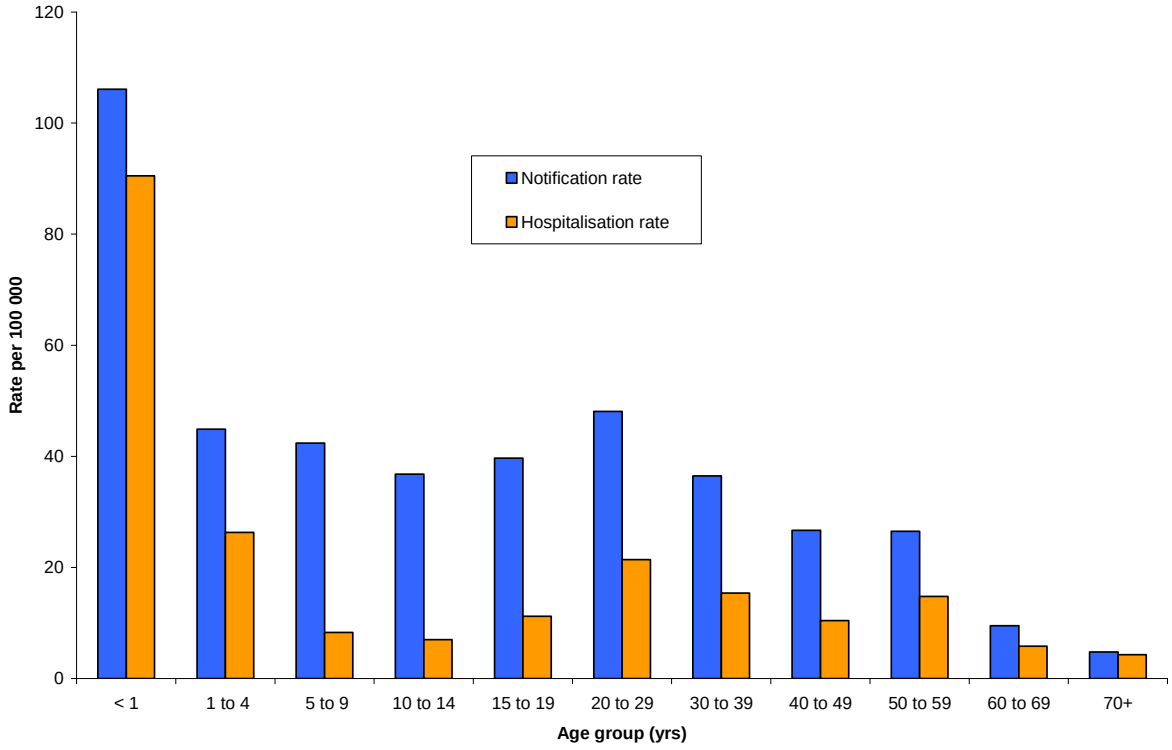


Table 2. Age distribution of pandemic influenza A(H1N1) cases and hospitalisations, 2010

Age group (years)	Cumulative cases*		Cumulative cases hospitalised	
	Number	Rate^	Number	Rate^
< 1	68	106.1	58	90.5
1 to 4	106	44.9	62	26.3
5 to 9	122	42.4	24	8.3
10 to 14	111	36.8	21	7.0
15 to 19	128	39.7	36	11.2
20 to 29	274	48.1	122	21.4
30 to 39	213	36.5	90	15.4
40 to 49	169	26.7	66	10.4
50 to 59	138	26.5	77	14.8
60 to 69	36	9.5	22	5.8
70+	18	4.8	16	4.3
Unknown	1	-	0	-
Total	**1384**	**32.4**	**594**	**13.9**

* All cases notified with a report date between 26/12/09 and 29/08/2010 inclusive.
^ Rate per 100 000 population, calculated using 2008 mid-year population estimates.

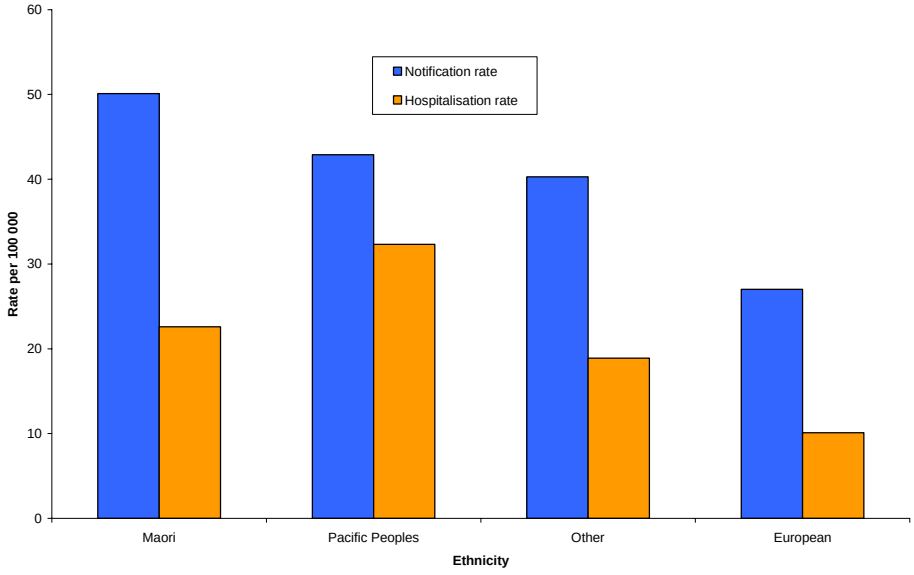
Notification rates among ethnic groups are shown in Table 3 and Figure 3. Māori had the highest notification rate, followed by Pacific Peoples and Other ethnic groups, though the total number of cases was higher among Europeans (726) and Māori (283). Pacific Peoples had the highest reported rate of hospitalisations (32.3 per 100 000 population) followed by Māori ethnic group (22.6 per 100 000). The age-adjusted notification rates were 43.1 per 100 000 for Māori, 39.3 per 100 000 for Pacific Peoples, 36.7 per 100 000 for Other ethnic groups, and 29.0 per 100 000 for Europeans (Figure 3).

Table 3. Ethnic (prioritised) distribution of pandemic influenza A(H1N1) cases and hospitalisations, 2010

Ethnicity (prioritised)	Cumulative cases*		Cumulative cases hospitalised	
	Number	Rate^	Number	Rate^
Maori	283	50.1	128	22.6
Pacific Peoples	97	42.9	73	32.3
Other	151	40.3	71	18.9
European	726	27.0	271	10.1
Unknown	127	-	51	-
Total	**1384**	**34.4**	**594**	**14.7**

* All cases notified with a report date between 26/12/09 and 29/08/2010 inclusive.
^ Rate per 100 000 population, calculated using the 2006 Census figures.

Figure 3. Pandemic Influenza A(H1N1) notification and hospitalisation rates by ethnicity in 2010



2.2.1.3 Geographic distribution

The geographic distribution of the notified cases and hospitalisations is shown in Fig. 4a and Table 4. The District Health Boards (DHBs) reporting the highest overall rates were Lakes (89.7 per 100 000 population), followed by Bay of Plenty (77.4 per 100 000 population), and South Canterbury (63.3 per 100 000 population) DHBs. The highest cumulative rate of hospitalisations was reported from Bay of Plenty (35.1 per 100 000) and Counties Manukau (23.4 per 100 000).

Figure 4a. Pandemic A(H1N1) notification and hospitalisation rates by DHB, 2010

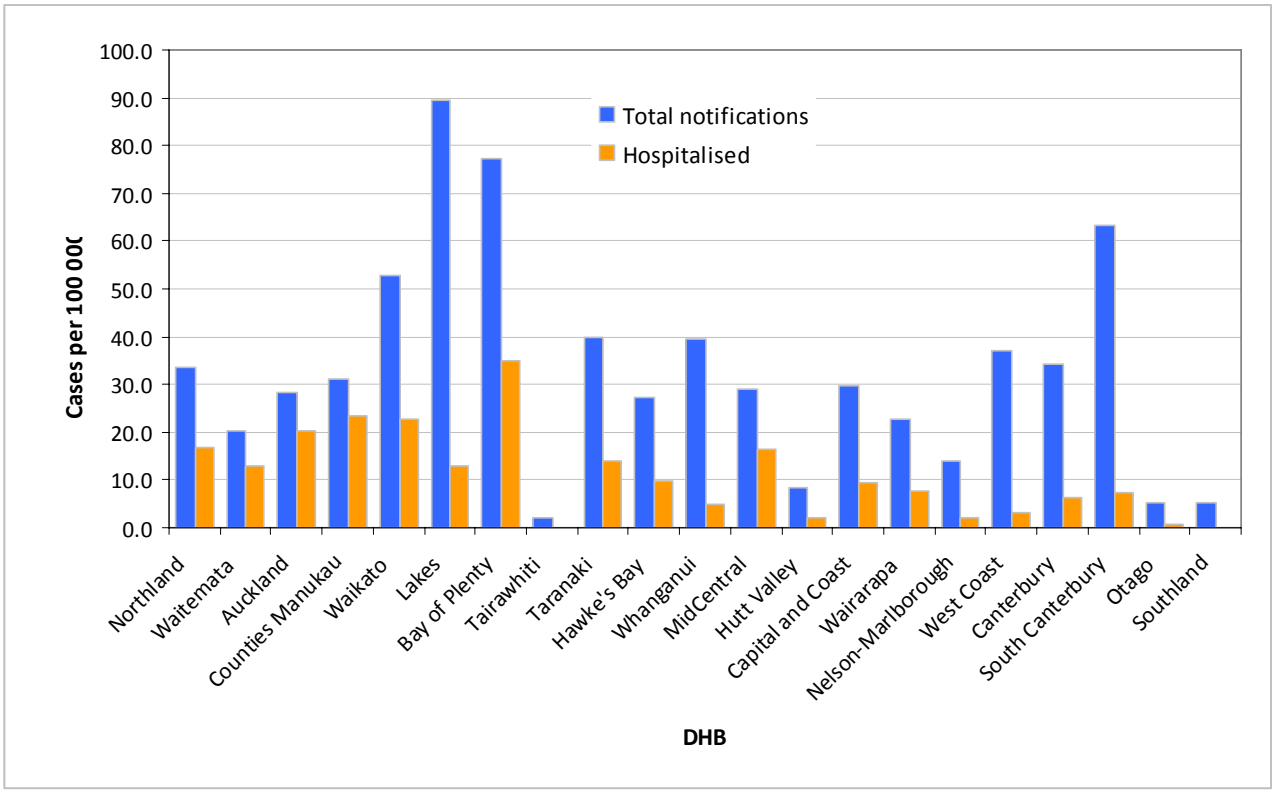


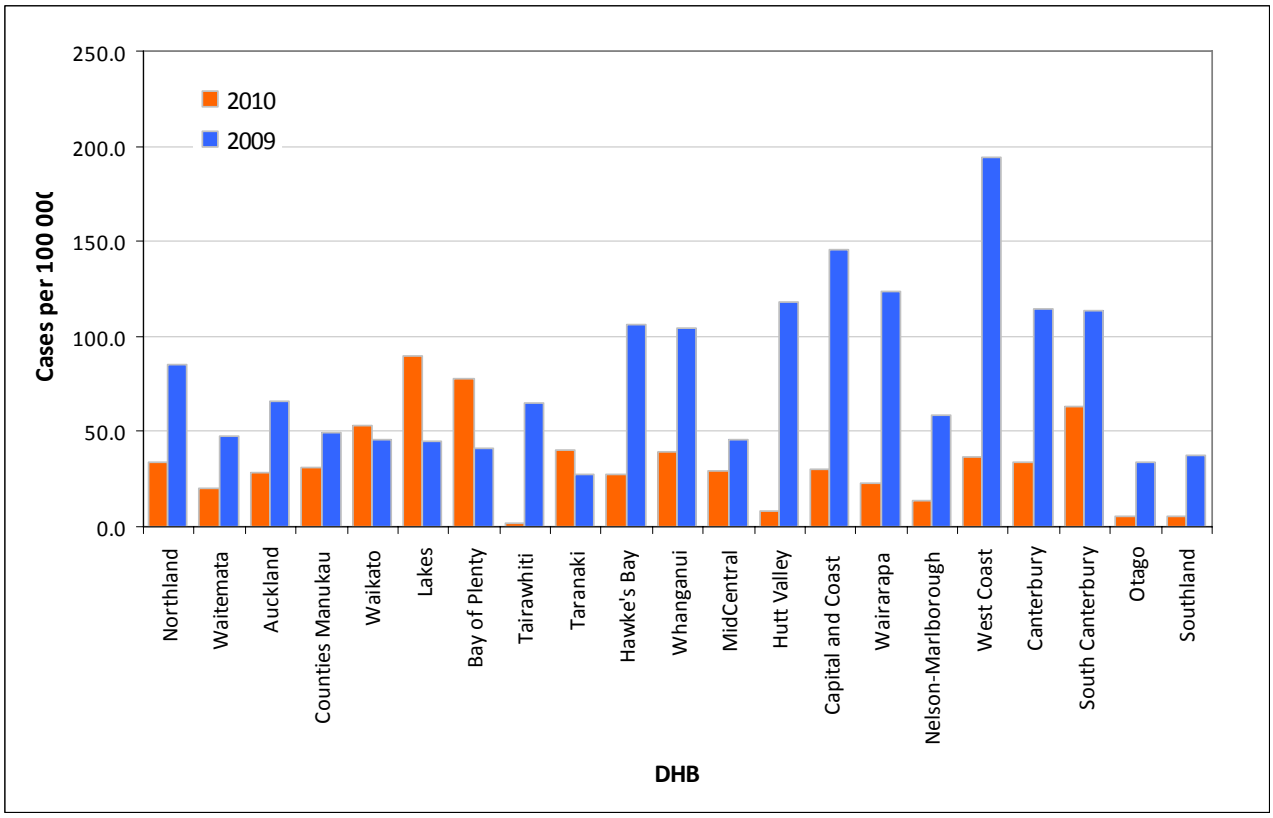
Table 4. Distribution of pandemic influenza (H1N1) 09 cases and hospitalisations by DHB, 2010

DHB	Cumulative cases*		Cumulative cases hospitalised	
	Number	Rate^	Number	Rate^
Northland	52	33.6	26	16.8
Waitemata	105	20.2	68	13.1
Auckland	124	28.3	89	20.3
Counties Manukau	148	31.3	111	23.4
Waikato	188	52.8	81	22.7
Lakes	91	89.7	13	12.8
Bay of Plenty	159	77.4	72	35.1
Tairawhiti	1	2.2	0	-
Taranaki	43	39.9	15	13.9
Hawke's Bay	42	27.4	15	9.8
Whanganui	25	39.5	3	4.7
MidCentral	48	29.1	27	16.4
Hutt Valley	12	8.5	3	2.1
Capital and Coast	85	29.9	27	9.5
Wairarapa	9	22.6	3	7.5
Nelson-Marlborough	19	14.0	3	2.2
West Coast	12	37.1	1	3.1
Canterbury	170	34.3	32	6.5
South Canterbury	35	63.3	4	7.2
Otago	10	5.3	1	0.5
Southland	6	5.4		-
New Zealand	1384	32.4	594	13.9

* All cases notified with a report date between 26/12/09 and 29/08/2010 inclusive.
^ Rate per 100 000 population, calculated using 2008 mid-year population estimates.

The geographic distribution of the pandemic cases by DHBs in 2010 was compared with that of 2009 (Figure 4b). A number of DHBs (Waikato, Lakes, Bay of Plenty, Taranaki) that had relatively low rates during the first wave of infection have experienced much higher rates in 2010.

Figure 4b. Cumulative rates of the pandemic influenza A(H1N1) cases by DHB in 2010 and 2009

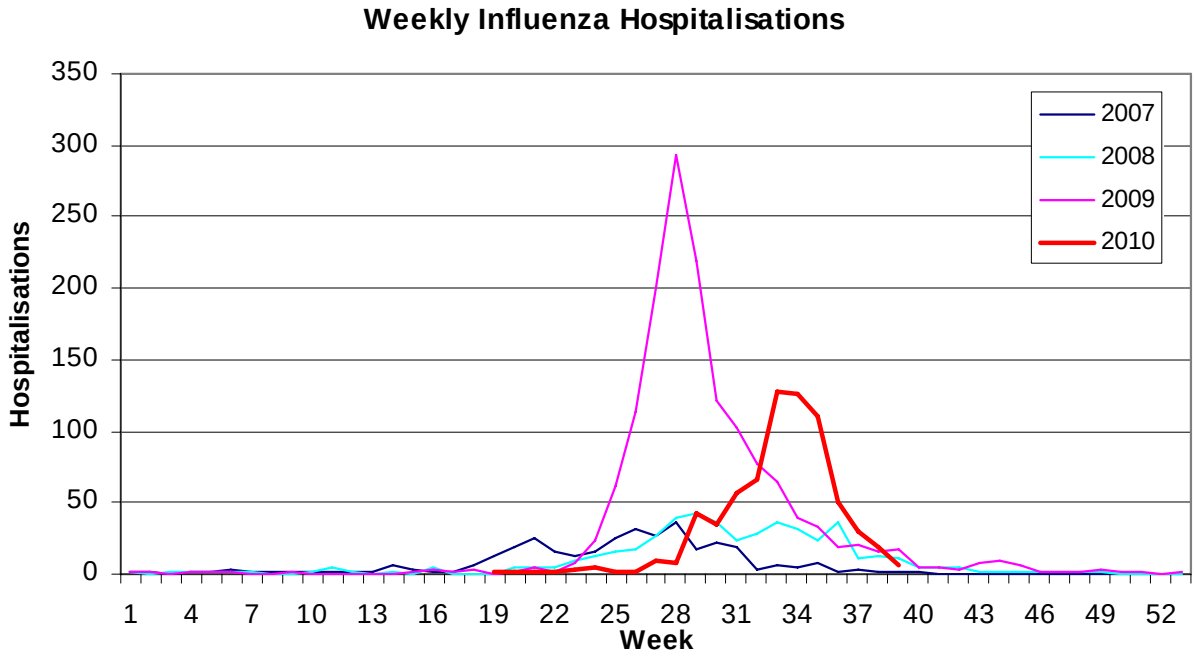


2.2.1.4 Hospitalisations

A total of 594 hospitalisations have been reported in EpiSurv up to the end of August 2010. This was just over half (53%) of the hospitalisations in 2009 (1122) and gave a hospitalisation rate of 13.8 per 100 000. This was the third highest recorded over the period of 1990-2010. A total of 91 ICU admissions were recorded which was 76% of 2009 ICU admissions (119). Of the 78 cases that occurred in pregnant women, 52 were hospitalised.

Figure 5 compares weekly hospitalisations for the years 2007, 2008, 2009 and 2010 (week 39). The 2010 data are for laboratory-confirmed pandemic influenza A(H1N1) cases. In 2010, the epidemic commenced two months later than in 2009 and the numbers are significantly lower. We have however seen regional and local epidemics, occurring at different times since June 2010. Each of these epidemics spread rapidly, and the peaks occurred at differing times. When these regional/local curves are put together to produce a national curve it looks like the epidemic in 2010 has spread more slowly.

Figure 5. Weekly influenza hospitalisations 2007-2009 plus lab-confirmed pandemic influenza A (H1N1) hospitalisations for 2010



Notes – Data is as reported in EpiSurv and may change in past weeks as reports are received. Data for 2007-2009 are any influenza hospitalisations, data for 2010 are lab-confirmed pandemic A(H1N1) hospitalisations only.

2.2.1.5 Deaths

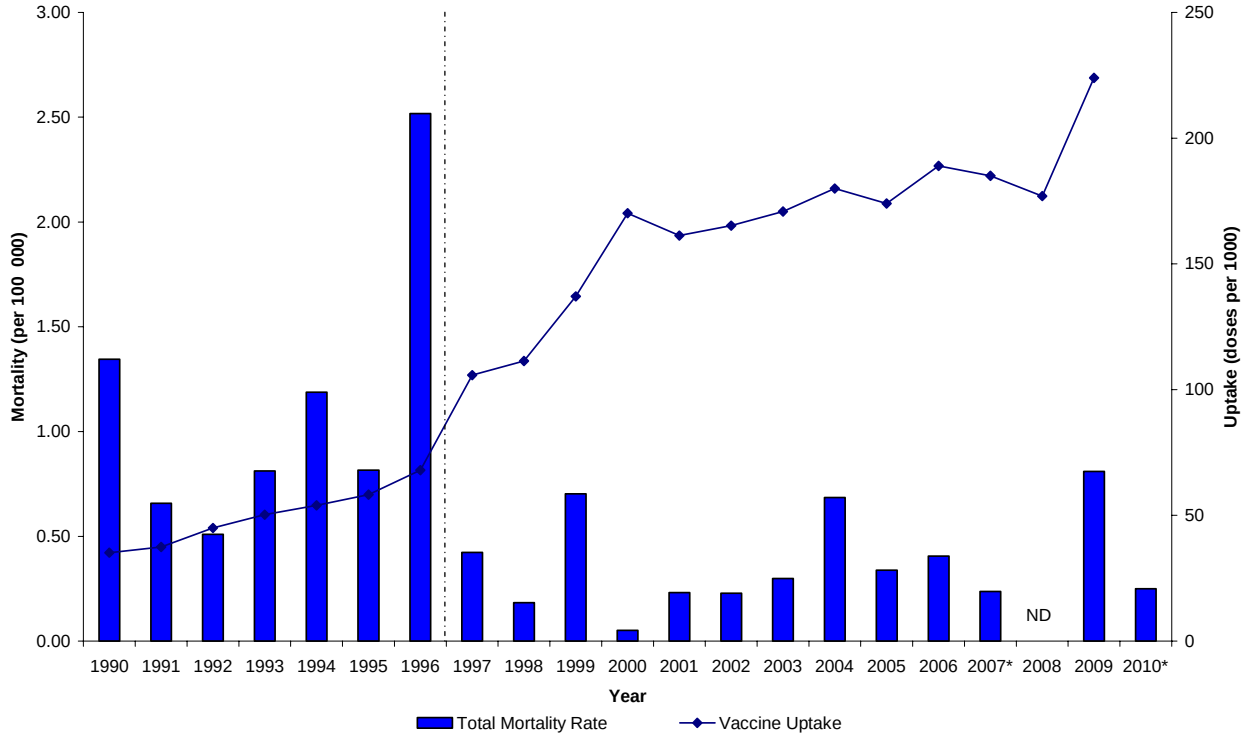
*A pandemic influenza A(H1N1) – associated death is defined as:
A person with confirmed pandemic influenza A(H1N1) infection determined from ante-mortem or post-mortem specimens, and who died from a clinically compatible illness or complications attributable to that infection. There should be no period of complete recovery between illness and death, and no alternative agreed upon cause of death.

The Ministry of Health (MoH) collates data from deaths reported through the standard processes for death certification and case notification, and deaths referred to the Coroner. In addition, a Pandemic Influenza Mortality Review Committee was established to review all possible deaths linked to the pandemic A(H1N1) virus.

As at the end of August 2010, 17 deaths had been reported in EpiSurv among pandemic influenza A(H1N1) cases in New Zealand. Of these, 11 were Europeans, two Māori, two Pacific Peoples, and one was in the Other ethnic groups. Ethnicity was not recordedfor one death. Most deaths occurred in the adults age groups including 50-59 years (7 cases), 20-29 and 30-49 years (3 cases each), and 10-19 and 70+ years (2 cases each). Of the 17 deaths, pandemic influenza A(H1N1) was recorded in EpiSurv as being the primary cause of death in 11 cases. This gave rise to a mortality rate of 0.25 per 100 000 for 2010. Current information on deaths can be found in the Ministry of Health website http://www.moh.govt.nz/moh.nsf/indexmh/influenza-a-h1n1-news-media.

The 2010 influenza mortality rate was compared with that of 1990-2010 (Figure 6). The 2010 mortality rate was lower than that of the 1990-1996 pre-vaccination period. The 2010 mortality rate was the 6th lowest when compared with that of the 1997-2003 vaccination period. The first (0.81 per 100 000) and second (0.7 per 100 000) highest mortality rates during the vaccination period were recorded in 2009 and 1999 respectively.

Figure 6. Influenza mortality rates and vaccine uptake, 1990-2010



(Note: In 1997, the Ministry of Health made influenza vaccination available free to persons aged 65 years and older. In 1999, this policy was extended to risk groups less than 65 years. Data on influenza vaccination uptake for 2010 are not yet available). 2010 mortality data are only up to August 2010.

2.2.2 Sentinel GP 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 (PCR), 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 A(H1N1). 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)

As a direct response to the pandemic, sentinel GP surveillance was extended beyond the 2009 winter season. In 2010, a total of 91 sentinel GPs participated in the sentinel surveillance, representing all of the country's 20 DHBs and with a combined patient population of 409 687, approximately 9.5% of the New Zealand population. From week 1 (the week ending 4 January 2010) through week 36 (the week ending 12 September 2010), a total of 3878 consultations for ILI were reported from the 20 District Health Boards (DHBs). It is estimated that ILI resulting in a visit to a GP affected over 40 852 New Zealanders (0.96% of total population). The cumulative incidence of ILI consultation during this period was 946.6 per 100 000 population. The average weekly ILI consultation rate during this period was 32.1 per 100 000 population.

As in previous years, 2010 consultation rates for ILI varied greatly among DHBs during the study period. The ILI rates by DHB in 2010 were compared with that of 2009 (Figure 7). Hawke's Bay DHB had the highest consultation rate (52.9 per 100 000), followed by Bay of Plenty (51.4 per 100 000) and Lakes (50.7 per100 000). It appears that some regions (mainly small urban and rural areas) that had relatively low ILI activity experienced higher level of influenza activity during the second wave in 2010.

Figure 7. Average weekly consultation rate for influenza-like illness by District Health Board, 2009 and 2010* in sentinel practices

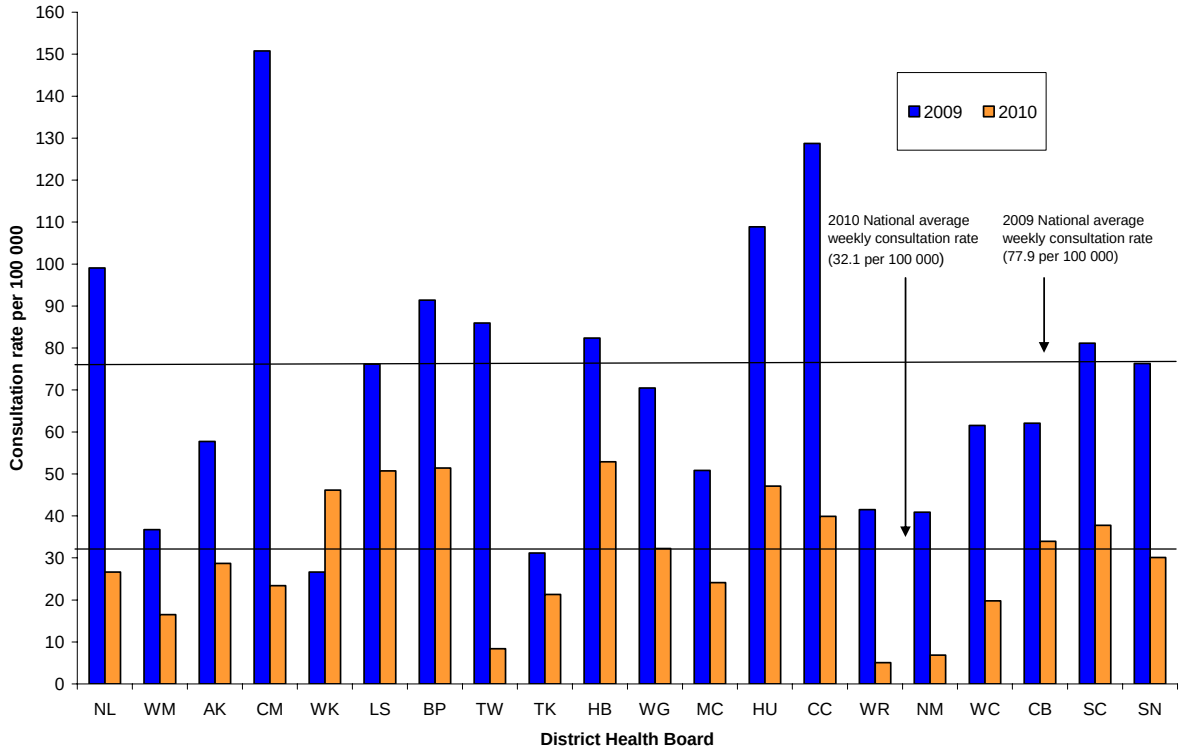
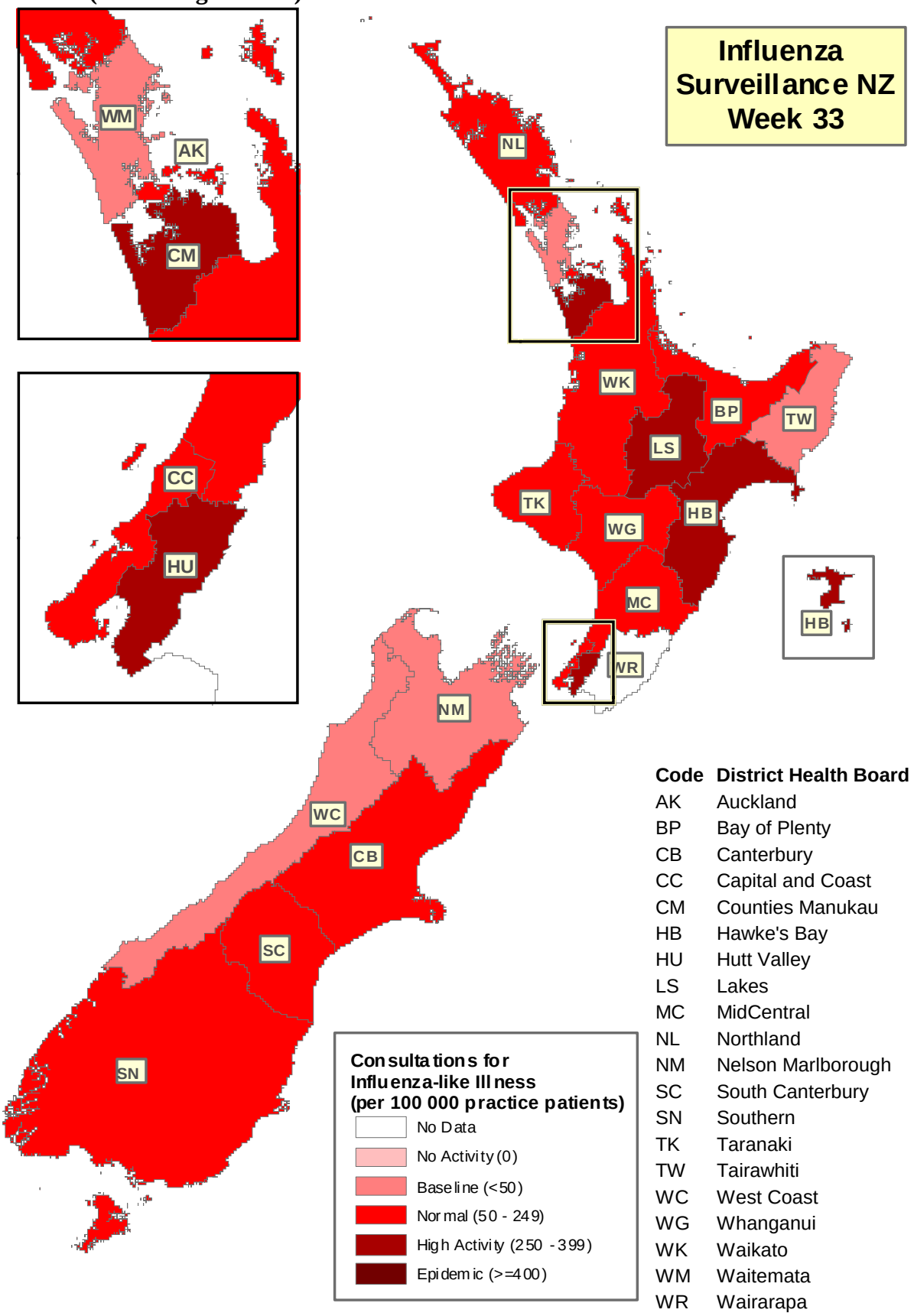


Figure 8 shows ILI consultations among DHBs during the peak week 33 (16–22 August 2010). Hawke's Bay DHB had the highest consultation rate (354.6 per 100 000, 72 cases), followed by Hutt Valley (303.9 per 100 000, 105 cases) and Lakes (283.8 per 100 000, 10 cases).

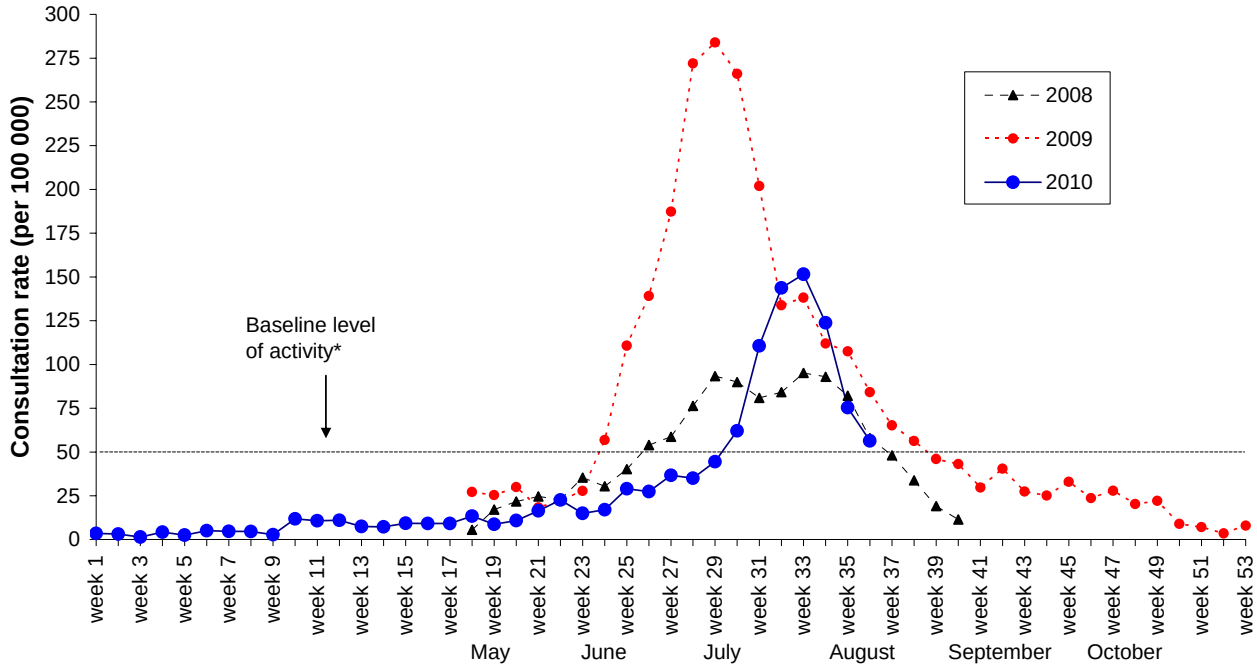
Figure 8. ILI consultation rates by District Health Board for the peak week 33 (16–22 August 2010)



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

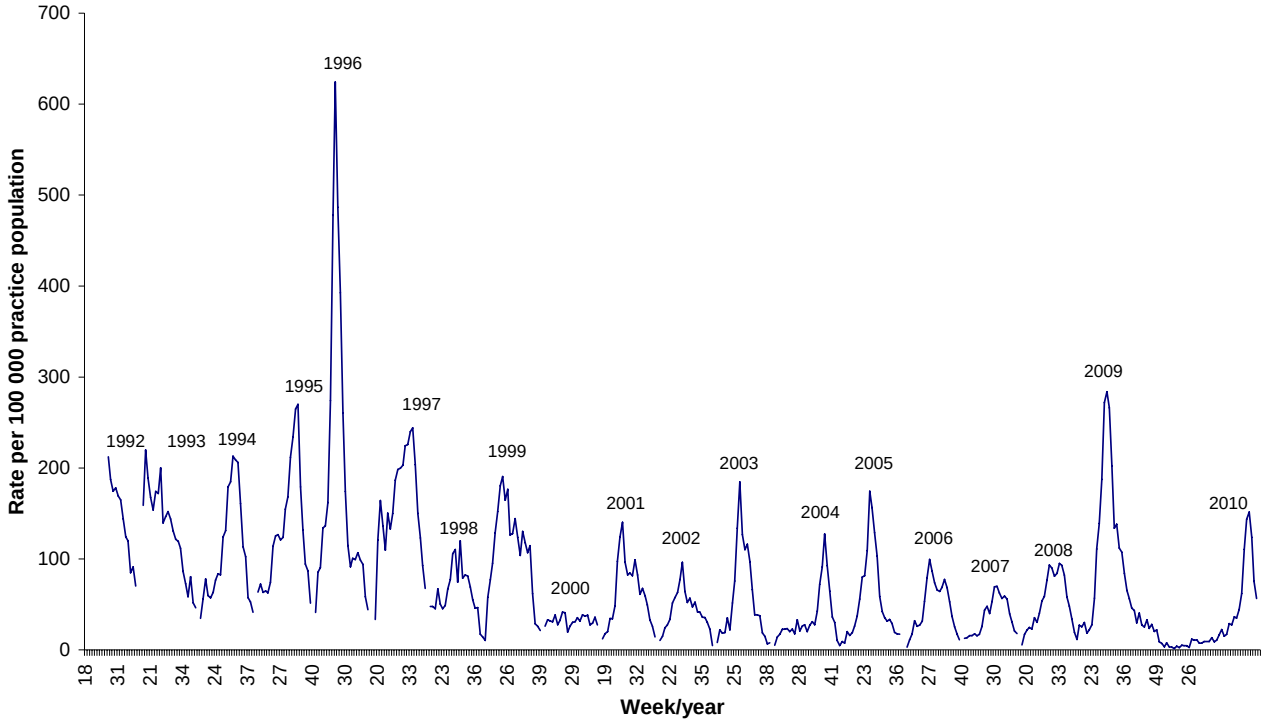
Weekly national ILI consultation rates for the study period were compared with the same period in 2008 and 2009. From week 18 (the week ending 9 May 2010) through week 29 (19–25 July 2010), the weekly ILI consultation rate remained below the baseline level of 50 consultations per 100 000 patient population (Figure 9). The ILI rate first crossed the baseline level in week 30 (26 July to 1 August 2010) and increased sharply from week 31 (2-8 August 2010) to week 32 (9-15 August 2010). The ILI consultation rate peaked at 152 consultations per 100 000 patient population in week 33 (16–22 August 2010).This was lower than the peak rate of 284 consultations per 100 000 patient population recorded in 2009 but higher than the peak of 95 consultations per 100 000 patient population in 2008. The peak ILI rate in 2010 was in the middle range (the 11th highest) during 1992-2010 (Figure 10). Since week 34 (23–29 August 2010), influenza activity has been declining.

Figure 9. Weekly Consultation Rates for Influenza-like Illness in New Zealand, 2008, 2009, 2010



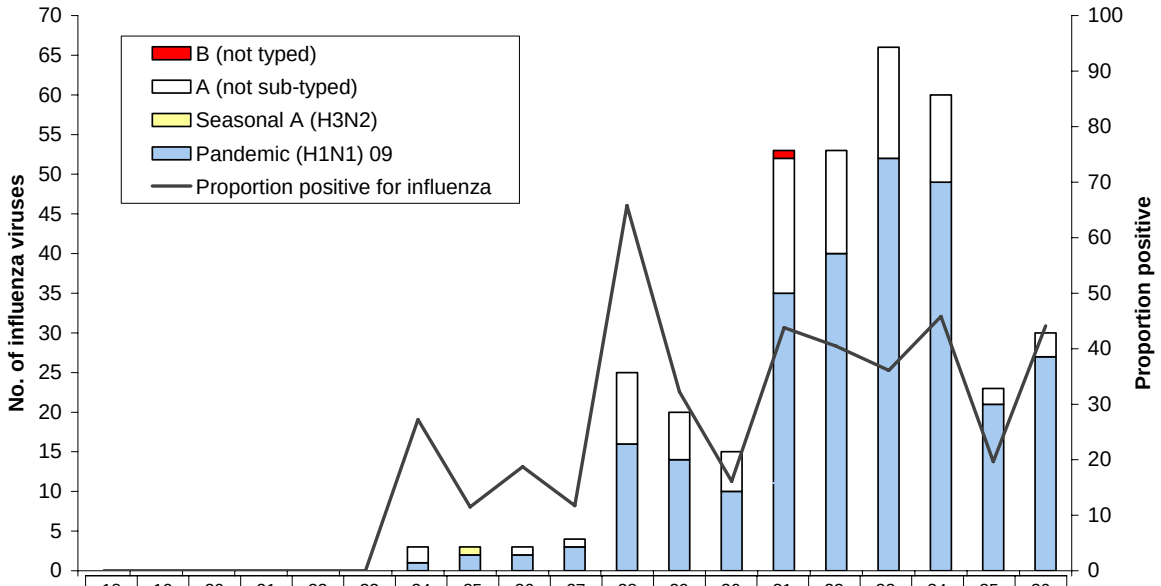
In 2010, the highest cumulative ILI consultation rates were recorded among children and youths aged <19 years. Children aged 1–4 years had the highest ILI consultation rate (1998.4 per 100 000 age group population), followed by infants aged <1 year (1840.3 consultations per 100 000 patient population), and persons aged 5–19 years (1018.8 consultations per 100 000 patient population), 20–34 years (993.2 consultations per 100 000 patient population), 35–49 years (854.8 consultations per 100 000 patient population), 50–64 years (634.9 consultations per 100 000 patient population) and >65 years (287.6 consultations per 100 000 patient population).

Figure 10. Weekly Consultation Rates for Influenza-like Illness in New Zealand, 1992-2010



A total of 1119 swabs were sent to virology laboratories from sentinel GPs during January to September 2010. From these swabs, 358 influenza viruses were identified. This gave an overall detection rate of 32%. The predominant strain was pandemic A(H1N1) (272) including 118 of pandemic influenza A/California/7/2009 (H1N1)-like strains, followed by influenza A not subtyped (84), seasonal influenza A (H3N2) (1), and influenza B (1) (Figure 11a). The pandemic virus has been the predominant strain for the most of the winter season (weeks 25-36).

Figure 11a. Number of influenza viruses reported by type and week from sentinel surveillance



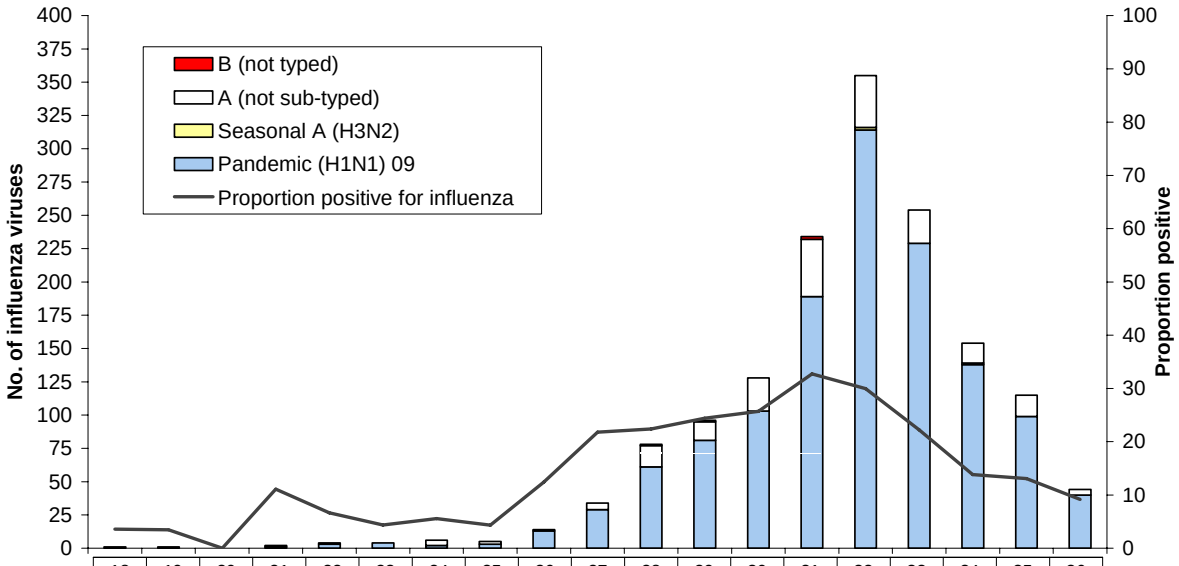
	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36
B (not typed)	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	2%	0%	0%	0%	0%	0%
A (not sub-typed)	0%	0%	0%	0%	0%	0%	67%	0%	33%	25%	36%	30%	33%	32%	25%	21%	18%	9%	10%
Seasonal A (H3N2)	0%	0%	0%	0%	0%	0%	0%	33%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
Pandemic (H1N1) 09	0%	0%	0%	0%	0%	0%	33%	67%	67%	75%	64%	70%	67%	66%	75%	79%	82%	91%	90%

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 nationally mainly from hospital in-patients and outpatients during routine viral diagnosis.

A total of 7620 non-sentinel swabs were received during January to September 2010 and 1538 influenza viruses were identified. giving an overall detection rate of 20%. The predominant strain was pandemic A(H1N1) (1318) including 148 of pandemic influenza A/California/7/2009 (H1N1)-like strains, followed influenza A not subtyped (212), influenza B (5) including B/Brisbane/60/2008-like strains (2), and seasonal influenza A (H3N2) (3) including A/Perth/16/2009 (H3N2)-like strains (2) (Figure 11b). The pandemic virus has been the predominant strain for the most of the winter season (weeks 25-36).

Figure 11b. Number of influenza viruses reported by type and week from non-sentinel surveillance



	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36
B (not typed)	0%	0%	0%	0%	0%	0%	0%	0%	7%	0%	1%	1%	0%	1%	0%	0%	0%	0%	0%
A (not sub-typed)	0%	100%	0%	50%	25%	0%	67%	40%	0%	15%	21%	15%	20%	18%	11%	10%	10%	14%	9%
Seasonal A (H3N2)	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	1%	0%	1%	0%	0%
Pandemic (H1N1) 09	100%	0%	0%	50%	75%	100%	33%	60%	93%	85%	78%	84%	80%	81%	88%	90%	90%	86%	91%

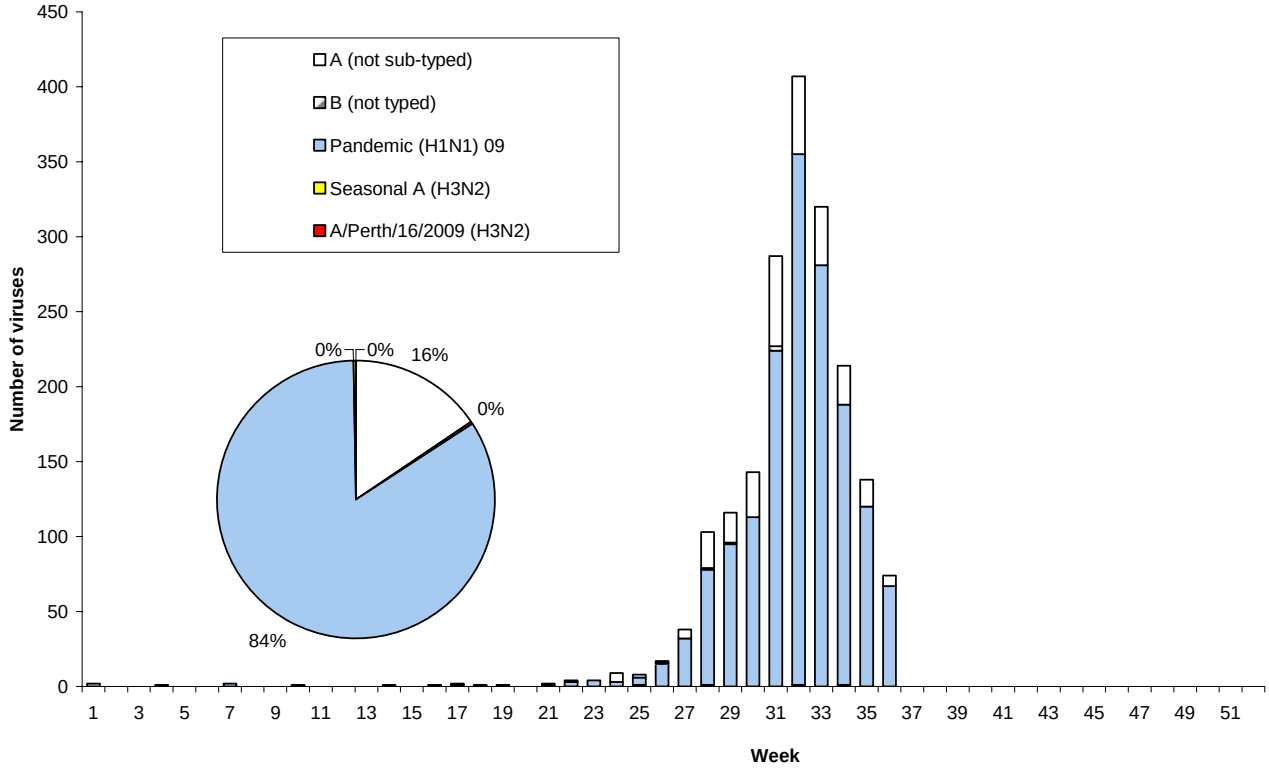
* data are only shown from week 18.

2.3 Recent strain characterisations

2.3.1 Circulating strains in 2010 in New Zealand

A total of 1896 influenza viruses were detected from sentinel and non-sentinel surveillance in 2010 from week 1 (the week ending 4 January 2009) to week 36 (6-12 September) (Figure 12). The predominant strain was pandemic A(H1N1) (1590) including 266 of pandemic influenza A/California/7/2009 (H1N1)-like strains, followed by influenza A not yet subtyped (296), influenza B (6) including B/Brisbane/60/2008-like strains (2), and seasonal influenza A (H3N2) (4) including A/Perth/16/2009 (H3N2)-like strains (2),.

Figure 12. Total influenza viruses by type and week specimen taken, 2010



The influenza virus detections by type and subtype for weeks 1 to 36, 2010 are shown in Table 5.

Table 5. Influenza viruses by type and subtype for weeks 1-36, 2010

Virus	**All viruses** n=1896 (%)	**Typed/Subtyped** n= 1600 (%)
Influenza A		
Influenza A (not sub-typed) by PCR	296 (15.6)	
Pandemic A(H1N1)		
Pandemic A(H1N1) by PCR	1324 (69.8)	1324 (82.8)
A/California/7/2009 (H1N1)-like	266 (14.0)	266 (16.6)
Subtotal pandemic A(H1N1)	**1590 (83.9)**	**1590 (99.4)**
Seasonal influenza A(H3N2)		
Influenza A subtype H3N2 by PCR	2 (01)	2 (0.1)
A/Perth/16/2009 (H3N2) - like	2 (0.1)	2 (0.1)
Subtotal seasonal A(H3N2)	**4 (0.2)**	**4 (0.3)**
Influenza B		
Influenza B by PCR	4 (0.2)	4 (0.2)
B/Brisbane/60/2008	2 (0.1)	2 (0.1)
Subtotal B	**6 (0.3)**	**6 (0.3)**
Total	**1896 (100)**	**1600 (100)**

Overall, pandemic A(H1N1) was the predominant strain among all influenza viruses. The pandemic A(H1N1) strain represented 83.9% (1590/1896) of all viruses and 99.4% (1590/1600) of all typed and subtyped viruses.

A very small number of seasonal influenza A(H3N2) viruses (4) were detected. The seasonal A(H3N2) strain represented 0.2% (4/1896) of all influenza viruses, 0.3% (4/1600) of all typed and subtyped viruses.

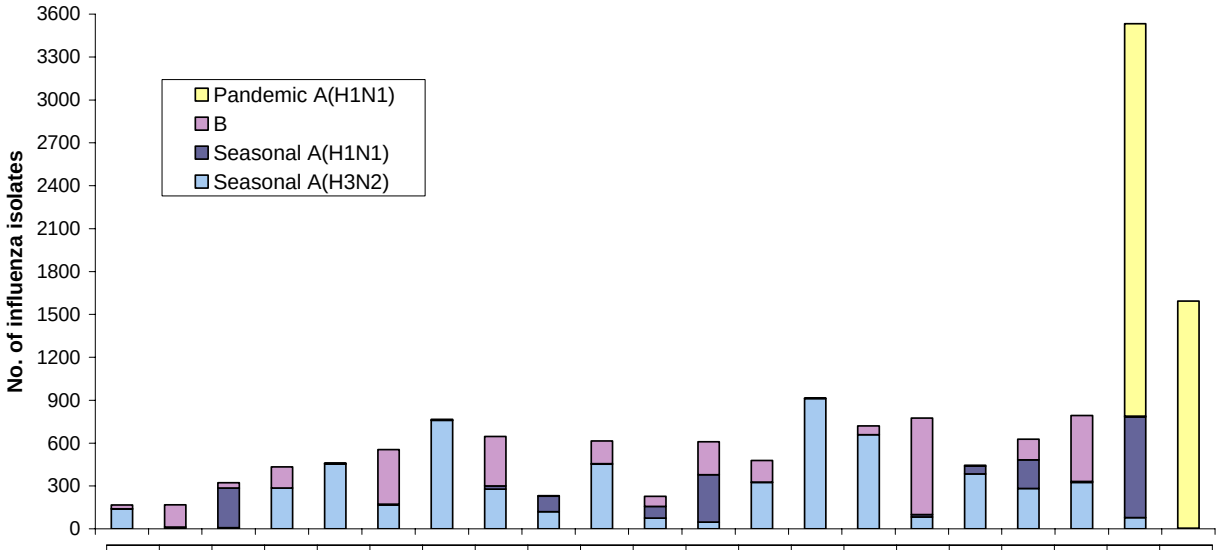
A very small number of influenza B viruses (6) were detected. The influenza B strain represented 0.3% (6/1896) of all influenza viruses, 0.4% (6/1600) of all typed and subtyped viruses.

2.3.2 Predominant strains during 1990-2010 in New Zealand

Figure 13 shows the number and percentage of typed and subtyped (not total) influenza viruses from 1990 to 2010. The noticeable changes in terms of predominant patterns are described below:

- Pandemic A(H1N1) 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).
- Seasonal influenza A(H3N2) strain predominated for 11 seasons (1990, 1993, 1994, 1996, 1998, 1999, 2002, 2003, 2004, 2006, and 2007). A/Fujian/411/02 (H3N2)-like strain predominated in 2003 with the highest recorded hospitalistaions 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 five seasons (1991, 1995, 1997, 2005 and 2008). B/HongKong/330/2001-like strain (B-Victoria lineage) predominated in 2005 and the disease burden was high in children aged 5-19 years with associated deaths in three children.

Figure 13. Influenza viruses by type, 1990-2010



	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010
Seasonal A(H1N1)	1%	8%	86%	0%	0%	1%	0%	4%	47%	0%	36%	54%	0%	0%	0%	2%	13%	32%	1%	20%	0%
Seasonal A(H3N2)	83%	0%	3%	66%	99%	30%	99%	43%	52%	74%	33%	8%	68%	100%	91%	11%	86%	45%	41%	2%	0%
B	16%	92%	11%	34%	1%	69%	1%	53%	1%	26%	31%	38%	32%	0%	9%	87%	1%	23%	58%	0%	0%
Pandemic A(H1N1)	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	78%	100%

2.3.3 Pandemic influenza A(H1N1)

Representative pandemic influenza A(H1N1) isolates (266) 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 pandemic A(H1N1) reference strain A/California/7/2009 (H1N1).

Genetic analysis of the haemagglutinatin (HA) gene of the representative pandemic A(H1N1) isolates was also performed. It showed that the New Zealand isolates were closely related to the reference virus A/California/7/2009 (H1N1) (Figure 14). Genetic analysis of the neuraminidase (NA) gene of the representative pandemic viruses showed that the New Zealand isolates were also closely related to the reference virus (Figure 15). No H275Y mutations were detected, suggesting these viruses were sensitive to oseltamivir.

Figure 14. Phylogenetic analysis of HA gene sequence of pandemic A(H1N1) viruses

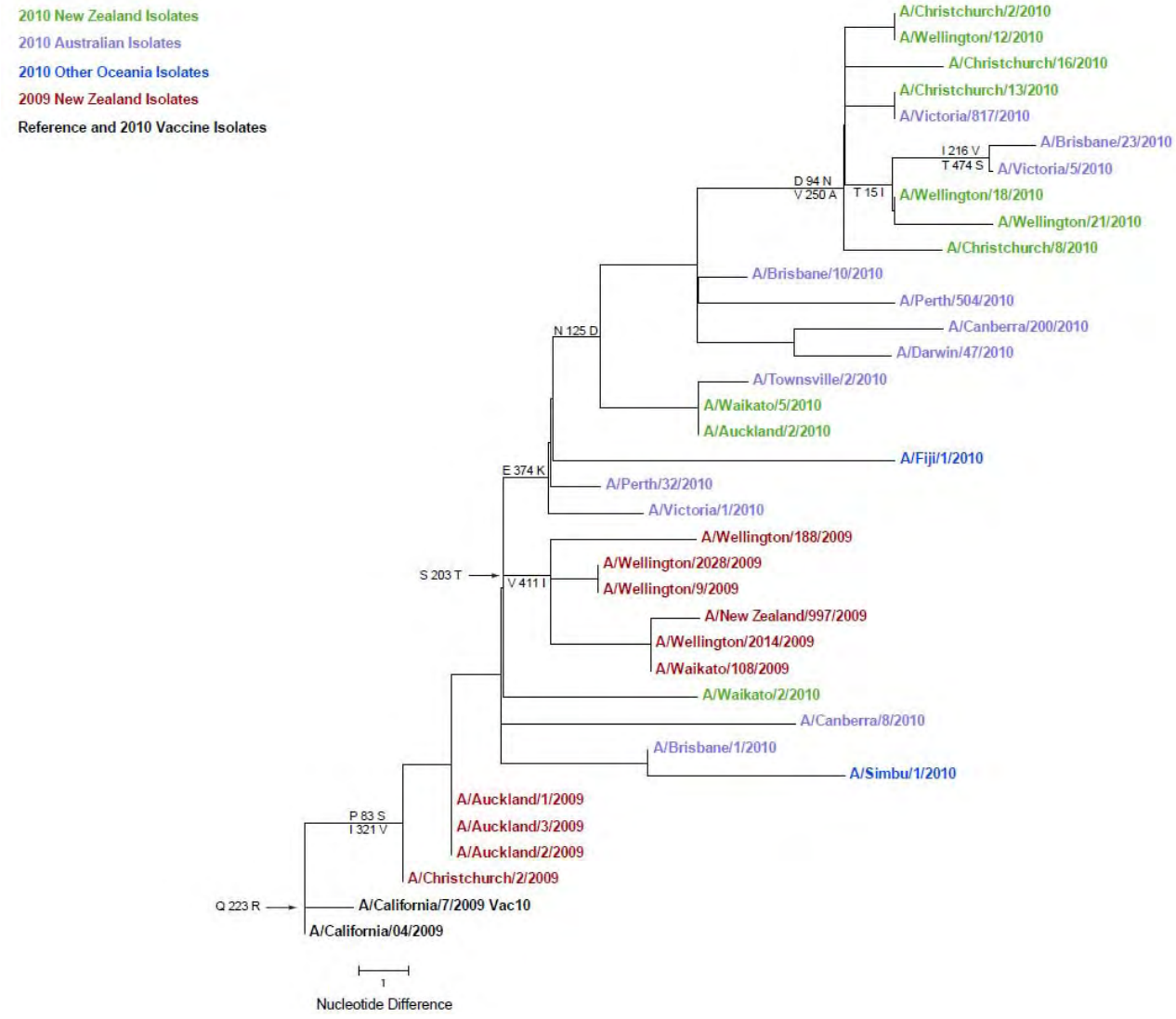
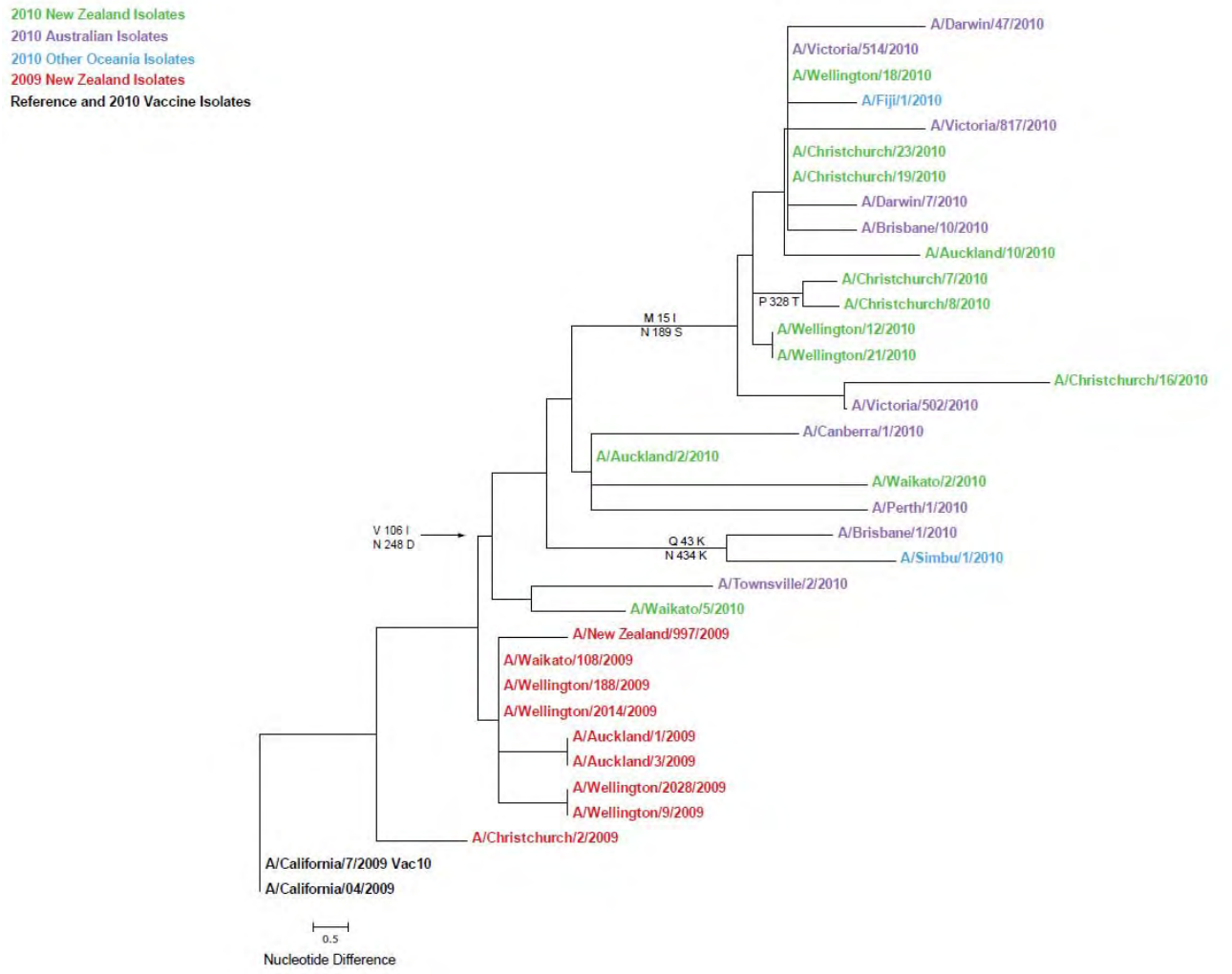


Figure 15. Phylogenetic analysis of NA gene sequence of pandemic A(H1N1) viruses



Note: The evolutionary history was inferred using the Neighbor-Joining method [1]. The bootstrap consensus tree inferred from 1000 replicates [2] is taken to represent the evolutionary history of the taxa analysed [2]. Branches corresponding to partitions reproduced in less than 50% bootstrap replicates are collapsed. The percentage of replicate trees in which the associated taxa clustered together in the bootstrap test (1000 replicates) is shown next to the branches [2]. The tree is drawn to scale, with branch lengths in the same units as those of the evolutionary distances used to infer the phylogenetic tree. Codon positions included were 1st+2nd+3rd+Noncoding. All positions containing gaps and missing data were eliminated from the dataset (Complete deletion option). There were a total of 1681 positions in the final dataset. Phylogenetic analyses were conducted in MEGA4 [3].

1. Saitou N & Nei M (**1987**) The neighbor-joining method: A new method for reconstructing phylogenetic trees. *Molecular Biology and Evolution* **4**:406-425.
2. Felsenstein J (**1985**) Confidence limits on phylogenies: An approach using the bootstrap. *Evolution* **39**:783-791.
3. Tamura K, Dudley J, Nei M & Kumar S (**2007**) MEGA4: Molecular Evolutionary Genetics Analysis (MEGA) software version 4.0. Molecular Biology and Evolution **24**:1596-1599.

2.3.4 Seasonal influenza A(H1N1)

No seasonal influenza A(H1N1) was detected in 2010.

2.3.5 Seasonal influenza A(H3N2)

Two representative seasonal influenza A(H3N2) isolates 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 antigenically related to the reference strain A/Perth/16/2009 (H3N2) with low reactor identified.

2.3.6 Influenza B

Two representative seasonal influenza B isolates were antigenically subtyped at the WHO National Influenza Centre at ESR using HAI typing kit supplied by the WHO Collaborating Centre (WHOCC) in Melbourne. Results indicated that New Zealand isolates were antigenically related to the reference strain B/Brisbane/60/2008, belonging to the B/Victoria/2/87 lineage.

2.3.7 Oseltamivir resistance

The WHO National Influenza Centre at ESR has established a phenotypic method (fluorometric NA inhibition assay) for the surveillance of anti-viral drug resistance in influenza viruses. In addition, the WHO National Influenza Centre at ESR has developed 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 2010, fluorometric NA inhibition assay was used to test a total of 280 pandemic A(H1N1) viruses. All viruses were sensitive to oseltamivir with IC50 values in the range of 0.01-2.9 nM (Table 6).

During 2006-2007, all influenza A(H1N1) viruses tested were sensitive to oseltamivir. In 2008, only 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 NA 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 global emerging oseltamivir-resistant seasonal 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) viruses were phenotypically tested and all were resistant to oseltamivir while 486 pandemic (H1N1) 09 viruses were phenotypically tested and all were sensitive to oseltamivir. The WHO National Influenza Centre at ESR has reported the findings to the WHO.

Table 6. Antiviral susceptibility to oseltamivir for influenza A(H1N1) viruses in New Zealand, 2006-2010

Influenza type/subtype	*Seasonal A (H1N1)*				*Pandemic A(H1N1)*	
Year	**2006**	**2007**	**2008**	**2009**	**2009**	**2010**
Number of viruses	17	138	4	25	486	280
Mean IC50*	1.84	0.83	728	1399	0.396	0.616
Std. dev.	0.71	0.63	136	1990	0.234	0.379
Min IC50	0.25	0.01	547	305	0.092	0.01
Max IC50	3.099	4.219	870	7912	1.402	2.864

3. RECENT STRAIN CHARACTERISATION AND LIKELY VACCINE CANDIDATES

3.1 Pandemic influenza A(H1N1)

The pandemic influenza A(H1N1) 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, pandemic A(H1N1) was the predominant influenza virus circulating in many countries in the Americas, Asia, Europe and Oceania.

During the 2010 influenza season, 1216 pandemic influenza A(H1N1) isolates were received at the Melbourne WHOCC from 16 countries from Australia, New Zealand, South Africa, Asia and Pacific Island countries. The virology laboratories in New Zealand use the kit supplied by the Melbourne WHOCC to analyse pandemic influenza A(H1N1) strains. The antiserum used for antigenica typing was the ferret antisera raised against A/California/7/2009-like strain. A total of 1590 pandemic influenza A(H1N1) viruses were detected in New Zealand in 2009, of which 266 had undergone antigenic typing and they were all antigenically closely related to A/California/7/2009-like strain.

Among all pandemic A(H1N1) viruses analysed at the Melbourne WHOCC, most of viruses reacted well with ferret sera to A/California/7/2009 with less than 1% classified as low reactors (≥8 fold reduction compared to the homologous titre). The Centers for Disease Control and Prevention in Atlanta reported that 99% of their viruses were A/California/7/2009-like with only 4/401 (<1%) being classified as low reactors (Tables 3.1, 3.3, 3.4 and 3.5 in Appendix 3). In addition, a total of 107 pandemic A(H1N1) viruses were sequenced in the HA-1 region of the haemagglutinin. The sequence analysis indicated that viruses was increasing genetic drift which was evident in the viruses isolated from Australia, New Zealand and Singapore during 2010 with two major subclades both with E374K and N125D amino acid changes from previously circulating viruses. One of these subclades had viruses with further amino acid substitutions (Figure 3.2 in Appendix 3). Low reactors in the HI assay were mainly found in both of these new subclades. The neuraminidase (N1) genes of the pandemic viruses were also sequenced, resulting in groups similar to their HA grouping. For example, viruses with HA E374K and N125D changes had amino acid changes at M15I and N189S in the N1 gene and fell into a separate group (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 pandemic A(H1N1) isolates. For a small number of pandemic A(H1N1) viruses, the geometric mean HI titres of human post-vaccination sera were lower than titres to the vaccine virus (average reduction: adults, 68%; elderly adults, 55%) (WER 85(41), and Tables 3.9 & 3.10 in Appendix 3).

In summary, pandemic influenza A(H1N1) viruses became the predominant circulating strain in southern hemisphere countries. HI tests showed that most isolates were antigenically similar to A/California/7/2009-like strain. Current vaccines containing 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.

3.2 Seasonal influenza A(H1N1)

Very few seasonal influenza A(H1N1) viruses were reported (mainly from China). Of these, the majority were antigenically and genetically similar to the previous vaccine virus A/Brisbane/59/2007. It is expected that seasonal influenza A(H1N1) will not co-circulate in the 2011 southern hemisphere influenza season. Thus no vaccine strain is selected for seasonal influenza A(H1N1).

3.3 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 has analysed 119 A(H3N2) isolates from nine countries since January 2009. These viruses made up 7% of all viruses analysed at the Melbourne WHOCC. Most (76.4%) of the influenza A(H3N2) viruses reacted well with ferret sera raised against A/Perth/16/2009-like viruses. However, a number of viruses showed reactivity. Tables 5.1, 5.3 and 5.4 (Appendix 4) show the HI titres obtained with the isolates using ferret sera against A/Perth/16/2009. In addition, HA gene phylogenetic analysis of the 2009 influenza A(H3N2) viruses sequenced showed that most viruses were A/Victoria/208/2009-like. Viruses in this group had acid changes at K158N, N189K and T212A compared with the pre-2009 circulating viruses. A number of recent viruses from the USA, Australia, New Zealand and Cambodia fell into a sub-clade of the A/Victoria/208/2009 and this group had additional signature amino acid changes at D53N, Y94H, I230V and E280A. A small number of recent viruses fell into the A/Perth/16/2009-like clade with changes at K158N, N189K, E62K and N144K. Sequence analysis of the N2 NA gene analysed in 2010 showed that the most recent viruses grouped in a similar manner as their HA genes with the majority falling into A/Victoria/208/2009 group. The viruses in the emerging A/Victoria/208/2009 subgroup also groupsed together based on their NA genes (Figures 5.2 and 5.3 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 (WER 85(41), and Tables 5.12 and 5.13 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/Perth/16/2009 antigen stimulated anti-HA antibodies of similar geometric mean HI titres to the vaccine virus 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/Perth/16/2009 (H3N2)-like strain. AIVC accepted this recommendation.

3.4 Influenza B

Two distinct lines of influenza B have co-circulated in many countries during recent years. This dates from the late 1980's when the B/Panama/45/90 variant of influenza B was first observed. This strain and its further variants of the Yamagata 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/Florida/4/2006 is the current reference strain) continued to be isolated worldwide in 2010. Varying proportions of the two lineages were seen in many countries with mainly B/Victoria-like lineage strains circulating in southern hemisphere countries. Only 6 influenza B viruses were detected in New Zealand in 2010 with two antigenically typed as B/Brisbane/60/2008 –like viruses.

Two hundred and sixty influenza B isolates were received in 2010 by the Melbourne WHOCC from 13 countries (15.4% of total isolates). The majority of isolates (95.2%) were typed as B/Victoria lineage with the majority reacting well with ferret sera raised against egg grown B viruses of this lineage. Only 4.8% of B viruses were of the B/Yamagata lineage and were generally poorly reactive with ferret sera to egg derived B/Florida/4/2006 virus; they reacted somewhat better with ferret antisera against B/Bangladesh/3333/2007 virus. HI assays in Tables 6.1, 6.3, 6.4 and 6.5 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 either in the B/Brisbane/60/2008 group with signature amino acid changes at S172P, N75K, N165K and V146I. A smaller number of viruses, mainly from the Philippines, grouped with the older B/Malaysia/2506/2004-like viruses with a T37I substitution. Very few viruses were available for sequencing from the B/Yamagata lineage and most fell into B/Bangladesh/3333/2007-like group (Group 3) with a S150I change along with more recent reference viruses such as B/Wisconsin/1/2010 (Figures 6.3, 6.4 and 6.5 in Appendix 5). All of the B viruses analysed in 2009 had NA sequences that were of the B/Yamagata lineage but can still be sub-divided into two groups that were similar to either the B/Florida/4/2006 and B/Bangladesh/3333/2007, or to the B/Malaysia/2506/2004 and B/Brisbane/60/2008 groups. Both groups showed low levels of genetic drift. 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. However, geometric mean HI titres were somewhat lower to recent B/Yamagata/16/88 lineage viruses than to the vaccine virus (average reductions: adults, 37%; elderly adults, 27%). (WER 85(41), Tables 5.7 to 5.8 in Appendix 5).

In summary, influenza B outbreaks were reported in southern hemisphere countries. Most recent isolates were antigenically and genetically similar to B/Brisbane/60/2008 (B/Victoria/2/87 lineage). 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. Based on all of epidemiological, antigenic, genetic and serological data, the WHO consultation recommended the B component of the vaccines containing a B/Brisbane/60/2008–like strain. The AIVC accepted this recommendation.

4. SUMMARY OF VACCINE COMPOSITION RECOMMENDATION

It is recommended that the influenza vaccine formulation for New Zealand for 2011 is:

- A(H1N1) an A/California/7/2009 (H1N1) - like virus*
- A(H3N2) an A/Perth/16/2009 (H3N2) - like virus
- B a B/Brisbane/60/2008 - like virus

* Note: A/California/7/2009 is a pandemic A(H1N1) virus.

4.1 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 2010.

The AIVC agreed to adopt the September 2010 WHO recommendations. The influenza vaccine components for year 2011 season should contain the following:

A (H1N1):	an A/California/7/2009 (H1N1) - like strain,	15 µg HA per dose
A (H3N2):	an A/Perth/16/2009 (H3N2) - like strain,	15 µg HA per dose
B:	a B/Brisbane/60/2008 - like strain,	15 µg HA per dose

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

- A(H1N1):
  - 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(H3N2):
  - A/Wisconsin/15/2009 and A/Victoria/210/2009 (these are A/Perth/16/2009-like viruses)
  - NYMC X-183 reassortant derived from A/Wisconsin/15/2009;
  - NYMC X-187, NIB-65, IVR-155 reassortants derived from A/Victoria/210/2009
- B:
  - B/Brisbane/60/2008; NYMC BX-31, NYMC BX-35, NIB-65 reassortants derived from B/Brisbane/60/2008;
  - B/Brisbane/33/2008.

APPENDIX 1 - Composition of the Australian Influenza Vaccine Committee 2010

Australian Influenza Vaccine Committee 2010

The Australia Influenza Vaccine Committee (AIVC) meeting was convened at 3:00 pm on 6 October 2010 in Conference Room 1, TGA, Symonston, Canberra, when overseas participants in the teleconference were connected by Telstra. The New Zealand representatives attended the meeting by face-to-face meeting and teleconference.

Chairperson: Dr Gary Grohmann, TGAL, TGA
Secretary: Ms Thérèse Marengo, TGAL, TGA

Committee Members:
Ass Prof Gary Grohmann, OLSS, TGA (Chairperson)
Prof Anne Kelso, Melbourne WHOCC
Dr Ian Barr, Melbourne WHOCC
Dr Mike Catton, VIDRL
Dr Heath Kelly, VIDRL
Dr Dominic Dwyer, ICPMR
Dr David Smith, UWA
Emeritus Prof Greg Tannock, Macfarlane Burnet Institute
Dr Ruth Lopert, PMA, TGA
Dr Grahame Dickson, OPM, TGA
Dr Alan Hampson, Interflu Pty Ltd
*Dr Sue Huang, CDI, ESR, NZ
*Prof Barry Schoub, NICD, SA
Dr Andrea Forde, OHP, DoHA
Dr Tania Dalla Pozza, OLSS, TGA (Secretary)

Observers:
Dr Don Bandaranayake, ESR, NZ
Ms Rhonda Owen, OHP, DoHA
Ms Kate Robinson, OHP, DoHA
Mr Peter Schoofs, CSL Ltd
Mr William Cracknell, CSL Ltd
Ms Sarah Payton, CSL Ltd
Ms Nicole Schaefer, CSL Ltd
Mr Peter Schoofs CSL Ltd
Ms Christine Wadey CSL Ltd
Mr Jonah Smith CSL Ltd
Ms Alicia Ham, Sanofi Pasteur
Dr Glen Mason, Sanofi Pasteur
Ms Reshma Ajinka, GlaxoSmithKline Australia Pty Ltd
Dr Cheryl Keech, GlaxoSmithKline Australia Pty Ltd
Ms Louise Carter, GlaxoSmithKline Australia Pty Ltd
Ms Rema Sakr, GlaxoSmithKline Australia Pty Ltd
Dr Mandy Cooke, GlaxoSmithKline Australia Pty Ltd
Mr Tony Wilson-Williams, Solvay Biosciences Pty Ltd
Ms Alina Danaila, Solvay Biosciences Pty Ltd
Dr Christine Apostopoulos, Novartis Vaccines and Diagnostic Pty Ltd
*Mr Tony Colgate, Novartis Vaccines and Diagnostic Pty Ltd
Mr Lionel Cornu, Baxter Healthcare Pty Ltd
Mr Tony Shelton, Baxter Healthcare Pty Ltd
Ms Elizabeth de Somer, Medicines Australia

Mr Sam Shirley, Medicines Australia
Ms Pearl Bamford, OLSS, TGA
Dr Peter Christian, OLSS, TGA
Dr Peter Bird, OLSS, TGA

*Participating by teleconference

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

FIGURE 2.1 Influenza viruses received and analysed at the Melbourne WHO CC

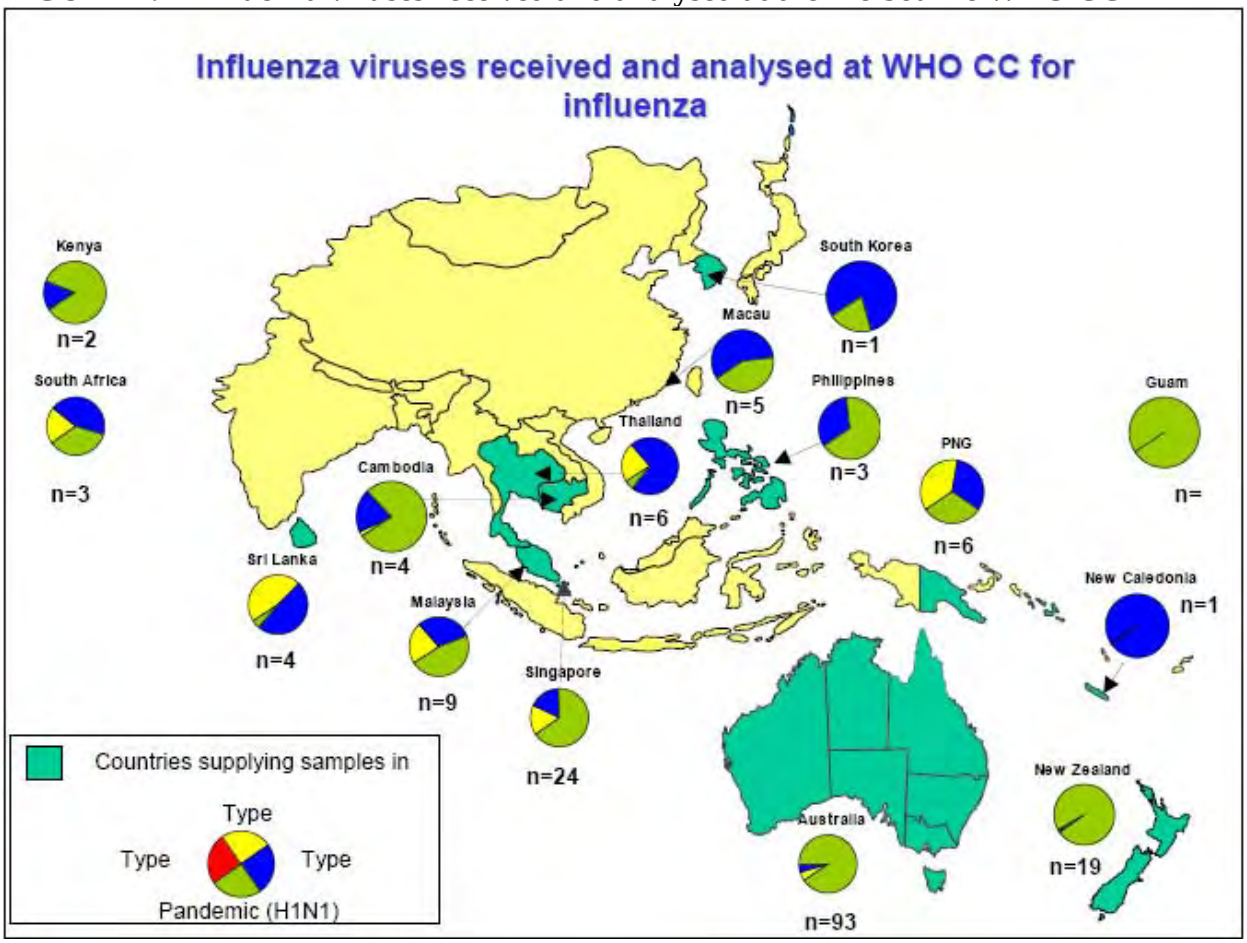
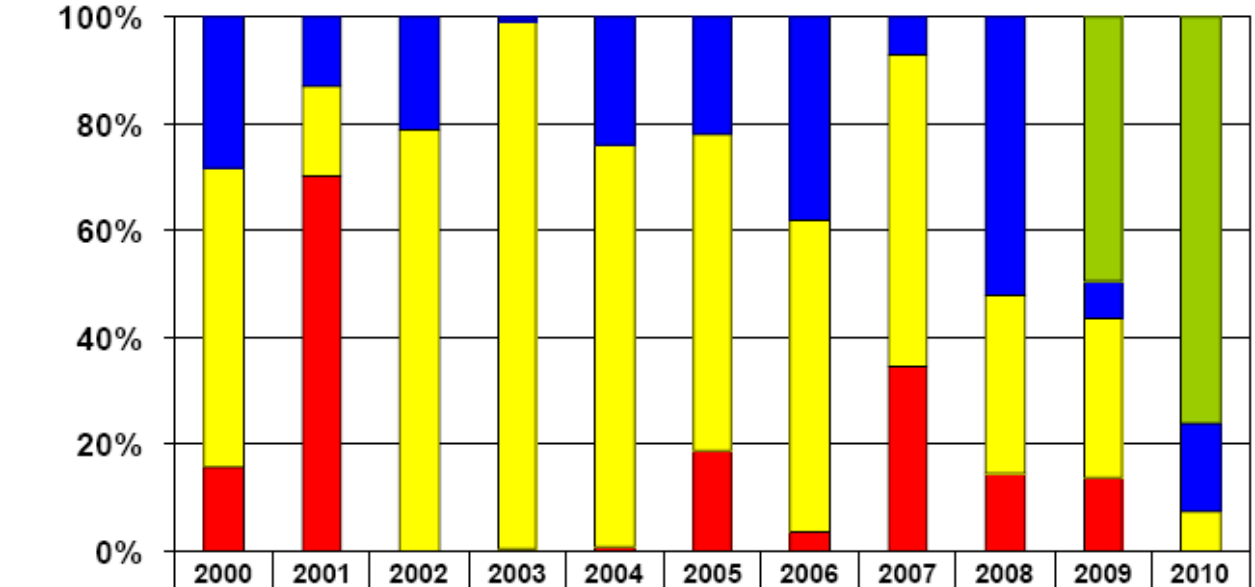


FIGURE 2.2 Influenza isolates by type/subtype received and analysed at the Melbourne WHO CC 2000-10



	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010
A(H1)pdm										47.3	76.2
B	28.2	12.8	21.3	0.6	24.1	21.9	37.9	6.9	52	6.8	16.3
A(H3)	56.3	17.1	78.6	99.2	75	59.4	58.6	58.1	33.3	28.5	7.5
A(H1)	15.5	70.1	0.1	0.2	0.9	18.7	3.5	34.4	14.7	13	0

APPENDIX 3 - Influenza A (H1N1)

TABLE 3.1 Summary – Antigenic Characterisation of Influenza A(H1N1)pdm at Melbourne WHO CC

	Australia, New Zealand	Pacific	SE Asia	Africa	East Asia	South Asia	Total (%)
March - September 2009							
A/California/7/2009-like	588	33	89	1	1	0	712 (94.7%)
A/ California/7/2009 (low)*	36	0	4	0	0	0	40 (5.3%)
Total	624	33	93	1	1	0	752
October 2009 – February 2010							
A/California/7/2009-like	183	28	122	21	0	2	356 (91.5%)
A/ California/7/2009 (low)*	5	0	27	0	0	1	33 (8.5%)
Total	188	28	149	21	0	3	389
March - September 2010							
A/California/7/2009-like	599	20	131	7	23	0	780 (99.2%)
A/ California/7/2009 (low)*	5	0	1	0	0	0	6 (0.8%)
Total	604	20	132	7	23	0	786

TABLE 3.2 Summary – Antigenic Characterisation of Influenza A(H1N1)pdm at CDC

	U.S.A.	North America	Europe	Asia	Cent/So America	Africa, Australia, New Zealand	Total (%)
March 2009 – August 2009							
A/California/07/2009-like*	974	70	9	71	523	116	1763 (96%)
A/California/07/2009-like **	33		1	2	29	1	66 (4%)
A/California/07/2009 (low)***	1		3	1			5 (<1%)
						Total	1834
September 2009 – February 2010							
A/California/07/2009-like*	1663	20	54	110	88	95	2030 (95%)
A/California/07/2009-like **	68	2	6	6	7	3	92 (4%)
A/California/07/2009 (low)***	6		3			1	10 (<1%)
						Total	2132
March 2010 – August 2010							
A/California/07/2009-like*	189	24	8	27	90	52	390 (97%)
A/California/07/2009-like **	6				1		7 (2%)
A/California/07/2009 (low)***	4						4 (1%)
						Total	401
Total	2944	116	84	217	738	268	4367

* ≤ 2-fold low to vaccine strain Preliminary Data 09/17/2010
** = 4-fold low to vaccine strain
*** ≥ 8-fold low to vaccine strain (Most or all of the isolates low to A/California/07/2009 have acquired at least one amino change at positions 153-157 in the HA which have been associated with reductions in titers compared with the homologous titer of the A/California/7/09 vaccine strain.)

TABLE 3.3 Haemagglutination Inhibition Assay - WHO Influenza Centre, Melbourne

	Compilation: 15 & 16 September 2010	Haemagglutination Inhibition Assay - WHO Influenza Centre, Melbourne													
		Reference Antisera													
	Sequenced	A	B	C	D	E	F	G	H	I	J		Human Serum Pool	Passage History	Sample Date
	Turkey RBC	F1656	FS5	F1616	F1614	F1615	F1620	F1623	F1684	F1686	F1704	MAB			
	Reference Antigens	CAL/7	AUCK/1	PHIL/344	ILLIN/9	BRI/2013	BAY/69	LVIV/N6	SING/548	BRIS/10	CHCH/16	175			
A	A/CALIFORNIA/7/2009	**2560**	320	320	640	1280	640	640	1280	1280	1280	1280	320	E5	
B	A/AUCKLAND/1/2009	2560	**640**	320	1280	2560	1280	1280	2560	2560	2560	2560	640	E3	
C	A/PHILIPPINES/344/2004	2560	320	**640**	640	1280	320	640	1280	1280	640	<80	320	MDCK7	
D	A/ILLINOIS/9/2007	1280	320	320	**1280**	1280	320	640	1280	640	640	5120	160	C2/MDCK2	
E	A/BRISBANE/2013/2009	2560	320	320	640	**1280**	640	1280	2560	1280	1280	5120	640	MDCK3	
F	A/BAYERN/69/2009	<80	<40	<40	<40	40	**320**	80	80	80	80	2560	160	MDCK7	
G	A/LVIV/N6/2009	160	40	<40	<40	160	1280	**640**	320	320	320	1280	320	MDCK6	
H	A/SINGAPORE/548/2010	1280	160	160	320	640	640	640	**5120**	2560	2560	1280	160	MDCKX,MDCK2	
I	A/BRISBANE/10/2010	1280	160	160	320	640	640	640	5120	**5120**	2560	1280	160	E2	
J	A/CHRISTCHURCH/16/2010	1280	320	320	640	1280	1280	1280	5120	5120	**5120**	1280	160	E3	
	Test Antigens														
1	A/PERTH/52/2010	5120	640	640	1280	2560	1280	1280	>10240	5120	5120	1280	320	MDCKX,MDCK1	09/08/2010
2	A/VICTORIA/839/2010	2560	320	320	640	1280	640	640	5120	5120	2560	2560	320	mdck1	27/08/2010
3	A/SYDNEY/15/2010	2560	640	320	640	2560	1280	2560	5120	5120	5120	2560	320	mdckx,mdck1	25/08/2010
4	A/SYDNEY/16/2010	2560	320	320	640	1280	1280	2560	5120	5120	2560	1280	320	mdckx,mdck1	25/08/2010
5	A/SOUTH AUCKLAND/18/2010	2560	320	320	640	1280	1280	1280	5120	5120	5120	2560	160	mdckx,mdck1	20/07/2010
6	A/SOUTH AUCKLAND/19/2010	2560	320	160	320	1280	1280	1280	2560	2560	2560	1280	160	MDCK-SIATX,mdck1	19/07/2010
7	A/VICTORIA/850/2010	2560	640	320	1280	1280	2560	1280	5120	5120	5120	1280	320	mdck1	03/09/2010
8	A/PHILIPPINES/2203/2010	1280	320	320	640	640	1280	1280	5120	5120	5120	1280	160	MDCK2	31/05/2010
9	A/SOUTH AUSTRALIA/62/2010	1280	320	160	640	640	640	640	1280	1280	640	5120	320	MDCK1	18/08/2010
10	A/SOUTH AUSTRALIA/65/2010	1280	320	160	640	640	640	640	1280	640	640	5120	320	MDCK1	19/08/2010
11	A/VICTORIA/836/2010	1280	320	160	320	640	640	640	5120	2560	2560	1280	160	mdck1	26/08/2010
12	A/VICTORIA/838/2010	1280	160	160	320	640	320	320	640	640	640	2560	320	mdck1	27/08/2010
13	A/DARWIN/57/2010	1280	160	160	320	640	640	320	2560	2560	2560	1280	160	MDCK1	27/08/2010
14	A/DARWIN/60/2010	1280	160	160	320	640	640	320	5120	2560	2560	1280	160	MDCK1	29/08/2010
15	A/VICTORIA/843/2010	1280	160	160	320	640	640	640	2560	2560	1280	1280	160	MDCK1	30/08/2010
16	A/PERTH/51/2010	1280	160	160	640	1280	640	640	2560	2560	2560	1280	160	MDCKX,MDCK1	04/08/2010
17	A/PERTH/53/2010	1280	160	160	320	640	640	640	5120	2560	2560	1280	160	MDCKX,MDCK1	09/08/2010
18	A/VICTORIA/848/2010	1280	320	160	640	1280	1280	1280	5120	5120	5120	1280	160	MDCK1	31/08/2010
19	A/VICTORIA/576/2010	1280	320	320	640	1280	1280	1280	5120	5120	5120	2560	320	mdck1	01/09/2010
20	A/VICTORIA/580/2010	1280	320	320	640	1280	1280	1280	5120	5120	5120	1280	320	mdck1	02/09/2010
21	A/VICTORIA/583/2010	1280	320	320	640	1280	1280	1280	5120	5120	5120	1280	160	mdck1	02/09/2010
22	A/SOUTH AUSTRALIA/67/2010	640	160	160	320	640	640	320	2560	2560	2560	2560	160	MDCK1	19/08/2010
23	A/VICTORIA/571/2010	320	80	80	160	320	320	160	1280	1280	1280	1280	80	mdck1	01/09/2010
24	A/BRISBANE/76/2010	320	80	160	160	640	640	320	2560	2560	2560	2560	320	MDCK1,MDCK2	11/08/2010

TABLE 3.4 Haemagglutination Inhibition Assay - WHO Influenza Centre, Melbourne

	Compilation: 3 September & 31 August 2010	Haemagglutination Inhibition Assay - WHO Influenza Centre, Melbourne													
		Reference Antisera													
	Sequenced	A	B	C	D	E	F	G	H	I	J		Human		
	Turkey RBC	F1656	FS5	F1616	F1614	F1615	F1620	F1623	F1684	F1686	F1704	MAB	Serum	Passage History	Sample Date
	Reference Antigens	CAL/7	AUCK/1	PHIL/344	ILLIN/9	BRIS/2013	BAY/69	LVIV/N6	SING/548	BRIS/10	CHCH/16	175	Pool		
A	A/CALIFORNIA/7/2009	**1280**	160	160	640	1280	640	640	640	640	640	1280	160	E5	
B	A/AUCKLAND/1/2009	1280	**320**	320	640	1280	640	640	1280	1280	1280	2560	320	E3	
C	A/PHILIPPINES/344/2004	2560	320	**640**	1280	1280	320	640	1280	1280	1280	<40	320	MDCK7	
D	A/ILLINOIS/9/2007	1280	320	320	**640**	1280	320	640	1280	1280	640	1280	160	C2/MDCK2	
E	A/BRISBANE/2013/2009	1280	160	80	320	**640**	320	320	640	640	640	2560	160	MDCK3	
F	A/BAYERN/69/2009	<80	<40	<40	<40	40	**320**	80	<80	80	80	1280	160	MDCK7	
G	A/LVIV/N6/2009	160	<40	<40	<40	80	1280	**640**	160	320	320	1280	320	MDCK6	
H	A/SINGAPORE/548/2010	640	80	80	160	640	640	320	**1280**	2560	1280	1280	160	MDCKX,MDCK2	
I	A/BRISBANE/10/2010	320	80	40	160	320	320	160	1280	**2560**	1280	1280	80	E2	
J	A/CHRISTCHURCH/16/2010	2560	320	160	640	1280	1280	1280	5120	5120	**5120**	1280	160	E2	
	Test Antigens														
1	A/PERTH/35/2010	2560	160	160	320	1280	640	640	2560	2560	2560	640	160	MDCKX,MDCK1	22/07/2010
2	A/CHRISTCHURCH/7/2010	1280	160	40	320	640	640	640	2560	2560	1280	640	80	E1	08/07/2010
3	A/VICTORIA/819/2010	1280	320	160	320	1280	640	640	2560	2560	2560	1280	160	MDCK1	19/08/2010
4	A/PERTH/34/2010	1280	160	80	320	1280	640	640	2560	2560	2560	640	80	MDCKX,MDCK1	22/07/2010
5	A/PERTH/39/2010	1280	320	160	640	1280	640	640	2560	2560	2560	1280	160	MDCKX,MDCK1	29/07/2010
6	A/VICTORIA/523/2010	1280	160	160	640	640	640	640	2560	2560	2560			MDCK1	13/08/2010
7	A/VICTORIA/526/2010	1280	320	160	640	1280	1280	1280	5120	5120	2560			MDCK1	13/08/2010
8	A/VICTORIA/527/2010	1280	160	160	640	1280	1280	640	2560	2560	2560			MDCK1	17/08/2010
9	A/DARWIN/51A/2010	1280	320	320	640	1280	1280	1280	5120	5120	5120			MDCK1	26/07/2010
10	A/DARWIN/53/2010	1280	320	320	640	1280	1280	1280	5120	5120	5120			MDCK1	27/07/2010
11	A/TOWNSVILLE/1/2010	1280	320	160	640	1280	1280	1280	5120	2560	5120			mdck2	27/07/2010
12	A/BRISBANE/44/2010	1280	160	80	320	1280	640	640	2560	2560	2560			mdck2	28/07/2010
13	A/BRISBANE/45/2010	1280	320	160	640	1280	640	640	1280	1280	1280			mdck2	26/07/2010
14	A/GRAFTON/1/2010	1280	160	80	320	640	640	640	2560	2560	2560			mdck2	17/08/2010
15	A/CHRISTCHURCH/5/2010	640	160	80	320	640	640	640	2560	2560	2560	1280	80	E1	06/07/2010
16	A/DAEGU/1374/2010	640	160	80	160	640	320	320	640	320	320	1280	80	MDCK-P3	09/04/2010
17	A/INCHEON/1862/2010	640	160	<40	80	640	320	320	320	640	640	80	40	MDCK-P4	12/04/2010
18	A/PERTH/32/2010	640	160	80	320	640	320	320	640	320	320	1280	160	MDCKX,MDCK1	15/07/2010
19	A/VICTORIA/534/2010	640	80	80	160	320	320	320	1280	1280	1280	1280	80	MDCK1	17/08/2010
20	A/VICTORIA/539/2010	640	160	80	160	640	160	320	320	320	320	640	160	MDCK1	19/08/2010
21	A/PHILIPPINES/2019/2010	640	80	40	160	640	640	320	1280	1280	1280	640	80	MDCK3	11/08/2010
22	A/VICTORIA/528/2010	640	320	160	320	640	640	640	2560	2560	2560			MDCK1	17/08/2010
23	A/DARWIN/51B/2010	640	160	80	320	640	640	640	2560	2560	2560			MDCK1	26/07/2010
24	A/BRISBANE/41/2010	640	160	80	320	640	640	640	1280	1280	1280			mdck2	22/07/2010
25	A/BRISBANE/43/2010	640	160	80	320	640	640	640	2560	2560	2560			mdck2	30/07/2010
26	A/TOWNSVILLE/2/2010	640	80	80	160	640	640	320	1280	1280	1280			mdck2	11/08/2010
27	A/BRISBANE/51/2010	640	160	80	320	640	640	320	2560	2560	2560			mdck2	12/08/2010
28	A/VICTORIA/524/2010	320	80	40	320	320	320	320	1280	1280	1280			MDCK1	30/07/2010
29	A/BRISBANE/50/2010	320	80	40	160	320	320	160	1280	1280	1280			mdck2	30/07/2010

TABLE 3.5 Haemagglutination Inhibition Assay - WHO Influenza Centre, Melbourne

	Date: 24 August 2010	Haemagglutination Inhibition Assay - WHO Influenza Centre, Melbourne													
		Reference Antisera													
	Sequenced	A	B	C	D	E	F	G	H	I	J	K			
	Turkey RBC	F1656	FS5	F1616	F1613	F1614	F1615	F1620	F1623	F1684	F1686	F1689	Human Serum Pool	Passage History	Sample Date
	Reference Antigens	CAL/7	AUCK/1	PHIL/344	IOWA/2006	ILLIN/9	BRIS/2013	BAY/69	LVIV/N6	SING/548	BRIS/10	BRIS/12			
A	A/CALIFORNIA/7/2009	**2560**	320	320	1280	320	1280	640	1280	1280	1280	640	160	E5	
B	A/AUCKLAND/1/2009	2560	**320**	320	1280	640	1280	640	1280	1280	1280	1280	320	E3	
C	A/PHILIPPINES/344/2004	5120	320	**1280**	2560	1280	2560	320	2560	2560	1280	1280	320	MDCK7	
D	A/SWINE/IOWA/2006	<80	<40	40	**160**	<40	40	40	80	<80	<80	<80	160	C1/C1,MDCK2	
E	A/ILLINOIS/9/2007	2560	320	640	2560	**640**	2560	640	2560	2560	1280	1280	160	C2/MDCK2	
F	A/BRISBANE/2013/2009	2560	320	320	1280	640	**1280**	1280	2560	2560	2560	2560	640	MDCK3	
G	A/BAYERN/69/2009	<80	<40	<40	<40	<40	80	**640**	320	80	160	160	160	MDCK7	
H	A/LVIV/N6/2009	80	<40	<40	<40	<40	160	640	**640**	160	160	160	320	MDCK6	
I	A/SINGAPORE/548/2010	2560	320	160	640	320	1280	640	1280	**5120**	5120	1280	160	MDCKX,MDCK1	
J	A/BRISBANE/10/2010	1280	160	160	640	320	640	640	1280	2560	**2560**	2560	160	E2	
K	A/BRISBANE/12/2010	5120	320	640	2560	640	2560	2560	5120	5120	5120	**5120**	160	E2	
	Test Antigens														
1	A/SOUTH AUCKLAND/5/2010	2560	320	640	1280	640	2560	1280	2560	5120	5120	5120	160	mdckx,mdck1	07/07/2010
2	A/SOUTH AUCKLAND/7/2010	2560	320	640	1280	640	1280	1280	2560	5120	5120	5120	320	mdckx,mdck1	07/07/2010
3	A/SOUTH AUCKLAND/10/2010	2560	320	320	1280	640	1280	1280	1280	5120	5120	5120	160	MDCK-SIAT1,mdck1	10/07/2010
4	A/SOUTH AUCKLAND/12/2010	2560	320	640	1280	640	1280	1280	2560	5120	5120	5120	160	MDCK-SIAT1,mdck1	11/07/2010
5	A/CAMBODIA/7/2010	2560	320	320	640	640	1280	320	1280	1280	1280	1280	160	MDCK0,MDCK1	19/07/2010
6	A/WELLINGTON/22/2010	1280	160	320	640	320	640	640	1280	2560	2560	2560	80	MDCK-SIAT1,mdck1	26/07/2010
7	A/CAMBODIA/17/2010	1280	320	320	640	320	1280	320	1280	1280	1280	1280	160	MDCK0,MDCK1	16/03/2010
8	A/CAMBODIA/25/2010	1280	320	320	640	320	640	640	1280	640	1280	1280	320	MDCK3	03/06/2010
9	A/CAMBODIA/29/2010	1280	320	320	640	320	640	640	1280	2560	2560	2560	160	MDCK0,MDCK1	02/07/2010
10	A/CAMBODIA/30/2010	1280	160	320	640	320	640	640	1280	5120	5120	5120	160	MDCK0,MDCK1	03/07/2010
11	A/CAMBODIA/31/2010	1280	320	320	1280	320	1280	640	1280	1280	1280	1280	320	MDCK0,MDCK1	05/07/2010
12	A/WELLINGTON/12/2010	1280	160	160	640	320	1280	640	640	2560	2560	2560	160	MDCK-SIAT1,mdck1	12/07/2010
13	A/FIJI/1/2010	1280	160	160	640	320	640	320	640	640	640	640	160	MDCK1	12/05/2010
14	A/CAMBODIA/8/2010	1280	320	320	1280	320	1280	320	1280	1280	1280	1280	160	MDCK0,MDCK1	14/07/2010
15	A/CHRISTCHURCH/16/2010	1280	320	320	1280	320	1280	1280	2560	2560	5120	2560	160	E2	12/07/2010
16	A/CAMBODIA/9/2010	1280	320	320	640	320	1280	640	1280	1280	1280	1280	160	MDCK0,MDCK1	14/07/2010
17	A/CAMBODIA/10/2010	1280	160	160	640	320	640	320	640	640	640	640	160	MDCK0,MDCK1	16/07/2010
18	A/WAIKATO/5/2010	640	80	160	320	160	320	320	320	1280	1280	1280	160	mdckx,mdck1	08/07/2010

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

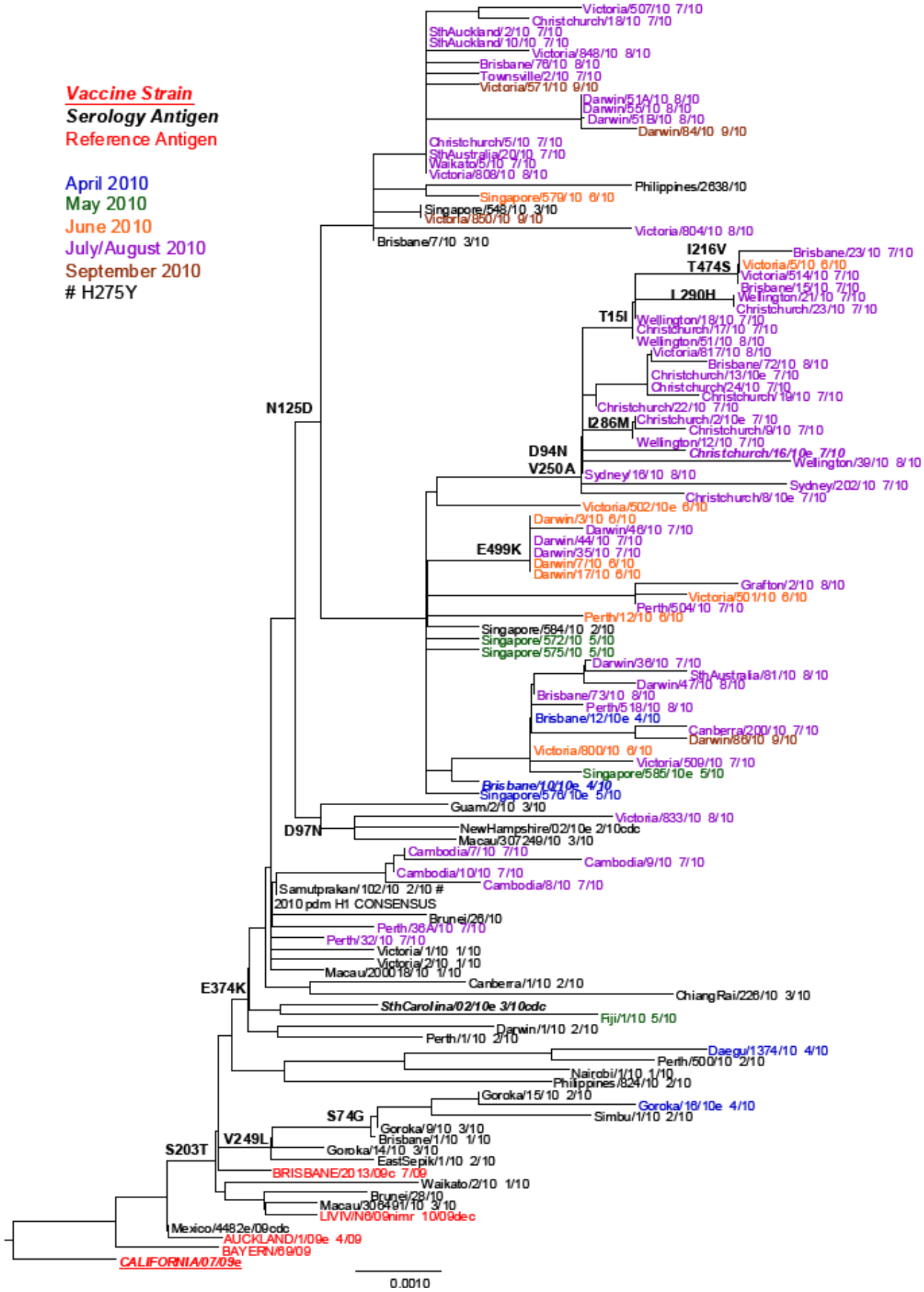


FIGURE 3.3 Phylogenetic relationships among influenza A(H1N1)pdm neuraminidase genes

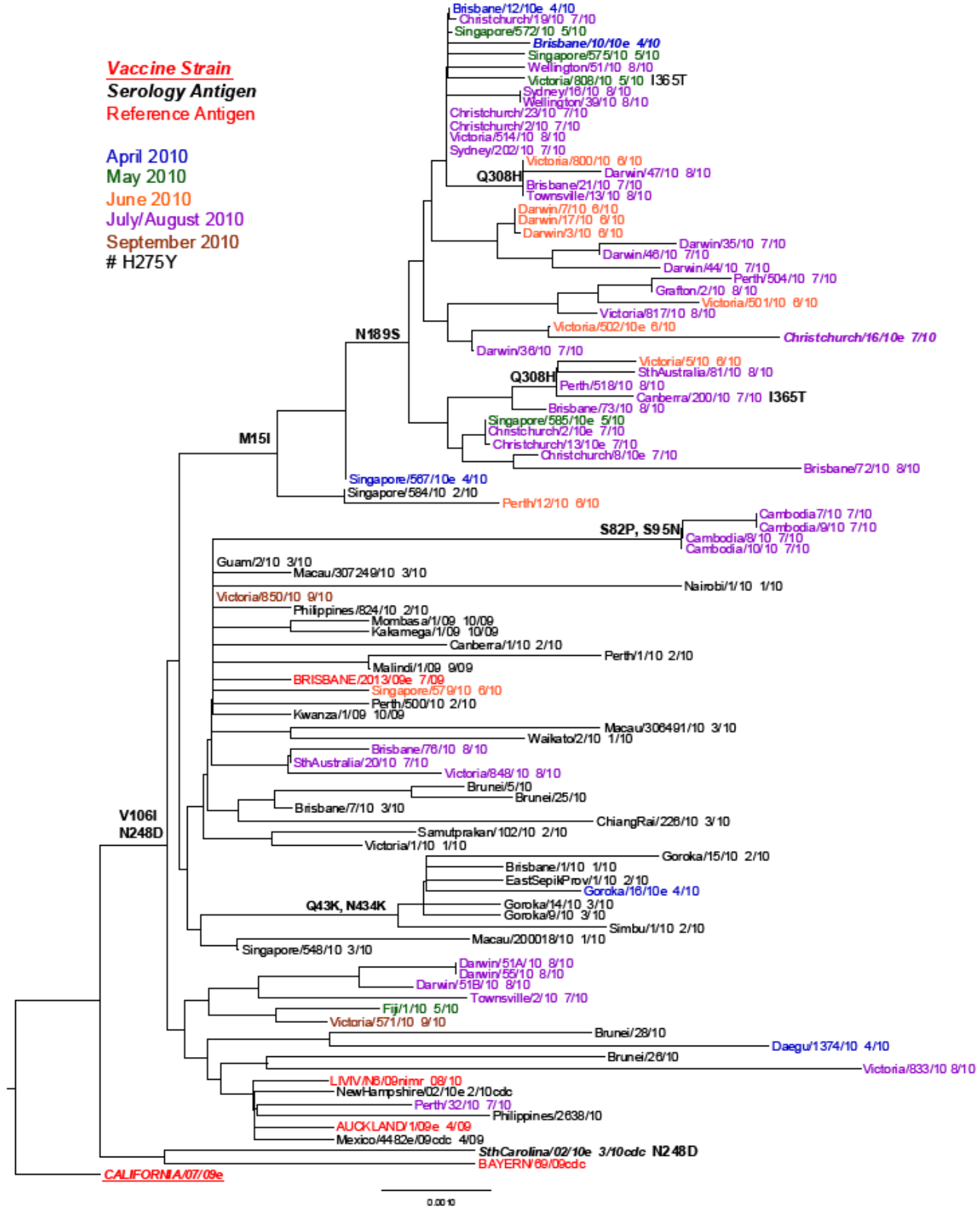


TABLE 3.9 Haemagglutination inhibition antibody responses Influenza type A(H1N1)pdm vaccine component Young Adults

Population	N	Antigen	Passage History	% Rise	GMT		%>/=40		%>/=160	
					Pre	Post	Pre	Post	Pre	Post
Australian Younger Adults	24	A/California/7/2009 X179A*	IZP	58	13.3	82.3	25	88	8	33
		A/California/7/2009 WT	E5	58	17.3	80.0	25	83	8	38
		A/Brisbane/10/2010	E2	54	13.3	49.0	33	71	8	25
		A/South Carolina/2/2010	E4	58	17.3	80.0	42	71	4	42
		A/Christchurch/16/2010	E3	58	16.8	61.7	42	67	8	42
		A/Victoria/583/2010	MDCK2	42	8.9	23.8	17	50	0	13
		A/Wellington/53/2010	MDCK-SIATX, MDCK2	38	10.6	29.1	25	54	0	13
European Younger Adults	24	A/California/7/2009 X179A*	IZP							
		A/California/7/2009 WT	E5							
		A/Brisbane/10/2010	E2	83	5.8	65.3	4	71	0	38
		A/South Carolina/2/2010	E4	83	5.8	84.7	4	79	0	50
		A/Christchurch/16/2010	E3	88	6.9	103.7	8	83	0	58
		A/Victoria/583/2010	MDCK2	58	5.0	27.5	0	54	0	17
		A/Wellington/53/2010	MDCK-SIATX, MDCK2	58	5.5	32.7	0	58	0	21

TABLE 3.10 Haemagglutination inhibition antibody titres Influenza type A(H1N1)pdm vaccine component Older Adults

Population	N	Antigen	Passage History	% Rise	GMT		%>/=40		%>/=160	
					Pre	Post	Pre	Post	Pre	Post
Australian Older Adults	24	A/California/7/2009 X179A*	IZP	38	25.9	71.3	54	88	8	42
		A/California/7/2009 WT	E5	25	30.0	65.3	54	83	13	29
		A/Brisbane/10/2010	E2	46	14.1	40.0	25	67	4	21
		A/South Carolina/2/2010	E4	38	22.4	63.5	42	79	13	33
		A/Christchurch/16/2010	E3	42	20.6	56.6	38	75	8	38
		A/Victoria/583/2010	MDCK2	50	10.0	25.9	21	58	4	8
		A/Wellington/53/2010	MDCK-SIATX, MDCK2	50	10.3	26.7	21	58	4	13
European Older Adults	24	A/California/7/2009 X179A*	IZP							
		A/California/7/2009 WT	E5	58	5.6	49.0	4	63	0	38
		A/Brisbane/10/2010	E2	50	5.3	27.5	0	50	0	25
		A/South Carolina/2/2010	E4	54	5.6	37.7	4	58	0	25
		A/Christchurch/16/2010	E3	63	5.3	40.0	0	58	0	3
		A/Victoria/583/2010	MDCK2	42	5.0	18.9	0	38	0	21
		A/Wellington/53/2010	MDCK-SIATX, MDCK2	42	5.0	18.9	0	38	0	21

*Vaccine strain

APPENDIX 4 - Influenza A (H3N2)

TABLE 5.1 Summary – Antigenic Characterisation of Influenza A(H3N2) from Melbourne WHO CC

	Australia New Zealand	Pacific	SE Asia	Africa	East Asia	South Asia	Total (%)
October 2006 – February 2007							
A/Wisconsin/67/2005-like	87	1	19	0	3	0	110 (35.3%)
A/Wisconsin/67/2005 (low)*	86	1	11	0	4	0	202 (64.7%)
Total	173	2	130	0	7	0	312
March – September 2007							
A/Wisconsin/67/2005-like	66	0	13	0	16	0	95 (22.4%)
A/Wisconsin/67/2005 (low)*	157	0	121	13	37	2	330 (77.6%)
Total	223	0	134	13	53	2	425
October 2007 – February 2008							
A/Brisbane/10/2007-like	145	0	38	0	50	0	233 (80.1%)
A/Brisbane/10/2007 (low)*	30	0	23	0	5	0	58 (19.8%)
Total	175	0	61	0	55	0	291
March - September 2008							
A/Brisbane/10/2007-like	246	0	128	4	17	11	406 (80.2%)
A/Brisbane/10/2007 (low)*	49	0	38	0	10	3	100 (19.8%)
Total	295	0	166	4	27	14	506
October 2008 – February 2009							
A/Brisbane/10/2007-like	130	0	28	0	4	0	162 (94.7%)
A/Brisbane/10/2007 (low)*	6	0	3	0	0	0	9 (5.3%)
Total	136	0	31	0	4	0	171
March - September 2009							
A/Brisbane/10/2007-like	28	1	64	2	0	0	95 (23.3%)
A/Brisbane/10/2007 (low)*	134	6	109	31	33	0	313 (76.7%)
Total	162	7	173	33	33	0	408
October 2009 – February 2010							
A/Perth/16/2009-like	15	2	67	0	0	4	88 (61.9%)
A/Perth/16/2009 (low)*	4	19	30	0	0	1	54 (38.1%)
Total	19	21	97	0	0	5	142
March - September 2010							
A/Perth/16/2009-like	21	0	32	1	0	1	55 (76.4%)
A/Perth/16/2009 (low)*	7	0	8	0	0	2	17 (23.6%)
Total	28	0	40	1	0	3	72

* $\geq$ 8 fold lower in HI assays

TABLE 5.3 Haemagglutination Inhibition Assay - WHO Influenza Centre, Melbourne

	21 September 2010	Haemagglutination Inhibition Assay - WHO Influenza Centre, Melbourne												
		Reference Antisera												
	Sequenced	A	B	C	D	E	F	G	H	I	J	K		
	Guinea Pig RBC	F1465	F1154	F1646	F1391	F1393	F1413	F1474	F1468	CDC	F1708	F1707	Passage History	Sample Date
	Reference Antigens	NY/55	WISC/67	BRIS/10	PHIL/16	ST/72	PER/16	SING/37	VIC/208	RHO. IS	VIC/8	PER/519		
A	A/NEW YORK/55/2004	**640**	160	80	<20	80	<20	<20	<20	<20	<20	<20	SPFCK3,E4	
B	A/WISCONSIN/67/2005	320	**320**	160	<20	80	<20	<20	<20	<20	<20	<20	SPFCK3,E5	
C	A/BRISBANE/10/2007	320	320	**320**	<20	640	20	<20	40	40	80	80	E3	
D	A/PHILIPPINES/16/2009	20	20	80	**320**	40	160	160	160	80	160	80	MDCK4	
E	A/SURAT THANI/72/2009	40	<20	40	40	**80**	40	<20	40	40	40	40	MDCK4	
F	A/PERTH/16/2009	<20	<20	<20	160	<20	**160**	160	80	160	80	160	E4	
G	A/SINGAPORE/37/2009	<20	<20	<20	160	<20	160	**160**	80	160	160	160	E3	
H	A/VICTORIA/208/2009	<20	80	80	1280	40	320	1280	**1280**	640	1280	>2560	E3	
I	A/RHODE ISLAND/1/2010	<20	20	<20	80	<20	320	80	320	**320**	320	320	E5	
J	A/VICTORIA/8/2010	<20	40	40	640	80	320	320	640	1280	**>2560**	640	E3	
K	A/PERTH/519/2010	20	40	40	80	80	160	80	160	80	160	**80**	MDCK2	
	Test Ag.													
1	A/PERTH/38/2010	<20	40	80	160	80	160	160	160	160	160	160	MDCKX,MDCK1	29/07/2010
2	A/JOHANNESBURG/59/2010	<20	40	40	80	80	160	80	160	160	320	160	mdck3	15/07/2010
3	A/SONG KHLA/442/2010	<20	40	80	160	80	160	160	160	160	320	80	MDCK3	02/08/2010
4	A/PERTH/10/2010	<20	40	80	160	80	160	160	320	160	160	160	MDCKX,mdck1	25/05/2010
5	A/PERTH/49/2010	<20	40	80	160	80	160	160	320	160	320	160	MDCKX,MDCK1	04/08/2010
6	A/PERTH/21/2010	<20	20	40	80	40	80	80	160	80	160	80	MDCKX,MDCK2	29/06/2010
7	A/PERTH/54/2010	<20	20	40	80	40	80	80	80	80	160	80	MDCKX,MDCK2	09/08/2010
8	A/PERTH/56/2010	<20	20	40	40	40	80	40	80	80	160	80	MDCKX,MDCK2	09/08/2010
9	A/SYDNEY/13/2010	<20	20	40	80	40	80	40	80	80	80	80	mdckx,mdck1	12/08/2010
10	A/VICTORIA/563/2010	<20	20	40	80	80	80	40	80	80	160	80	mdck1	30/08/2010
11	A/TRAT/410/2010	<20	20	40	80	40	80	40	80	80	160	80	MDCK2	03/08/2010
12	A/SUPHANBURI/452/2010	<20	20	40	80	40	80	80	160	160	320	80	MDCK3	12/08/2010
13	A/BANGKOK/480/2010	<20	40	40	80	40	80	80	160	160	320	160	MDCK3	10/08/2010

TABLE 5.4 Haemagglutination Inhibition Assay - WHO Influenza Centre, Melbourne

		Haemagglutination Inhibition Assay - WHO Influenza Centre, Melbourne													
		Reference Antisera													
	Sequenced	A	B	C	D	E	F	G	H	I	J	K	L		
	Guinea Pig RBC	F1154	F1464	F1466	F1082	F1391	F1393	F1413	F1474	F1467	CDC	F1707	F1708	Passage History	Sample Date
	Reference Antigens	WIS/67	BRIS/9	BRIS/10	URUG/716	PHIL/16	ST/72	PER/16	SING/37	VIC/208	RHO. IS	PER/519	VIC/8		
A	A/WISCONSIN/67/2005	**320**	320	320	320	20	320	<20	<20	20	20	20	40	SPFCK3,E5	
B	A/BRISBANE/9/2006	160	**160**	320	320	20	320	<20	<20	<20	20	20	20	E5	
C	A/BRISBANE/10/2007	320	320	**640**	1280	20	640	20	20	40	40	80	80	E3	
D	NYMCX-175C(A/Uruguay/716/07)	320	160	320	**1280**	<20	640	<20	<20	20	<20	20	20	X,E2	
E	A/PHILIPPINES/16/2009	<20	20	80	20	**320**	160	160	320	160	160	640	640	MDCK4	
F	A/SURAT THANI/72/2009	<20	20	<20	<20	40	**320**	20	20	20	40	80	80	MDCK4	
G	A/PERTH/16/2009	<20	<20	<20	<20	320	<20	**320**	320	320	320	320	160	E4	
H	A/SINGAPORE/37/2009	<20	<20	<20	<20	320	20	320	**320**	320	320	320	320	E3	
I	A/VICTORIA/208/2009	160	40	320	20	>2560	80	>2560	>2560	**1280**	1280	>2560	>2560	E3	
J	A/RHODE ISLAND	20	<20	<20	<20	80	<20	320	80	320	**640**	640	1280	E5	
K	A/PERTH/519/2010	20	40	80	20	160	80	160	80	160	160	**160**	320	MDCK1	
L	A/VICTORIA/8/2010	20	40	40	20	320	160	160	160	320	160	320	**640**	MDCK2	
M	A/VICTORIA/8/2010	<20	20	20	40	320	40	320	160	320	320	640	1280	E3	
	Test Ag.														
1	A/VICTORIA/532/2010	80	80	320	80	1280	320	1280	1280	1280	1280	>2560	1280	MDCK1	16/08/2010
2	A/PERTH/27/2010	40	20	80	40	640	160	640	320	640	320	1280	1280	MDCKX,MDCK1	08/07/2010
3	A/PERTH/23/2010	40	20	80	40	320	80	640	320	640	320	640	1280	MDCKX,MDCK1	29/06/2010
4	A/PERTH/501/2010	20	40	80	20	320	160	320	320	320	160	640	1280	MDCK2	20/05/2010
5	A/NEWCASTLE/4/2010	20	20	80	20	320	80	320	160	320	320	640	1280	MDCK1	25/06/2010
6	A/VICTORIA/552/2010	20	40	80	40	320	160	320	320	320	160	640	1280	mdck1	27/08/2010
7	A/PERTH/30/2010	20	40	80	20	320	160	320	320	320	320	640	1280	MDCKX,MDCK2	13/07/2010
8	A/PERTH/501/2010	<20	20	20	40	160	20	160	80	320	320	320	640	E3	
9	A/TASMANIA/3/2010	<20	40	80	20	320	160	160	160	160	320	320	640	mdck2	05/08/2010
10	A/BRISBANE/55/2010	20	20	40	20	160	80	160	160	160	160	160	320	mdck3	30/07/2010
11	A/PHILIPPINES/2050/2010	20	20	40	<20	160	80	160	160	160	160	320	640	MDCK3	17/08/2010
12	A/HYOGO/3004/2010	20	20	40	20	160	80	160	160	160	160	320	640	mdck5	17/05/2010
13	A/SRI LANKA/19/2010	<20	20	40	<20	160	40	80	80	80	80	160	320	MDCKX,MDCK2	18/05/2010
14	A/BRISBANE/46/2010	<20	20	40	<20	80	80	80	80	80	80	80	160	mdck4	11/07/2010
15	A/HIROSHIMA-C/27/2010	<20	20	20	<20	80	40	80	80	80	40	80	160	mdck5	05/2010
16	A/PANAMA/307149/2010	<20	20	40	20	80	80	80	80	80	80	80	160	C1/C2,MDCK1	06/2010
17	A/ALABAMA/5/2010	<20	20	20	<20	80	80	40	40	80	40	80	160	M1/C2,MDCK1	07/2010

FIGURE 5.2 Phylogenetic relationships among influenza A(H3) HA genes

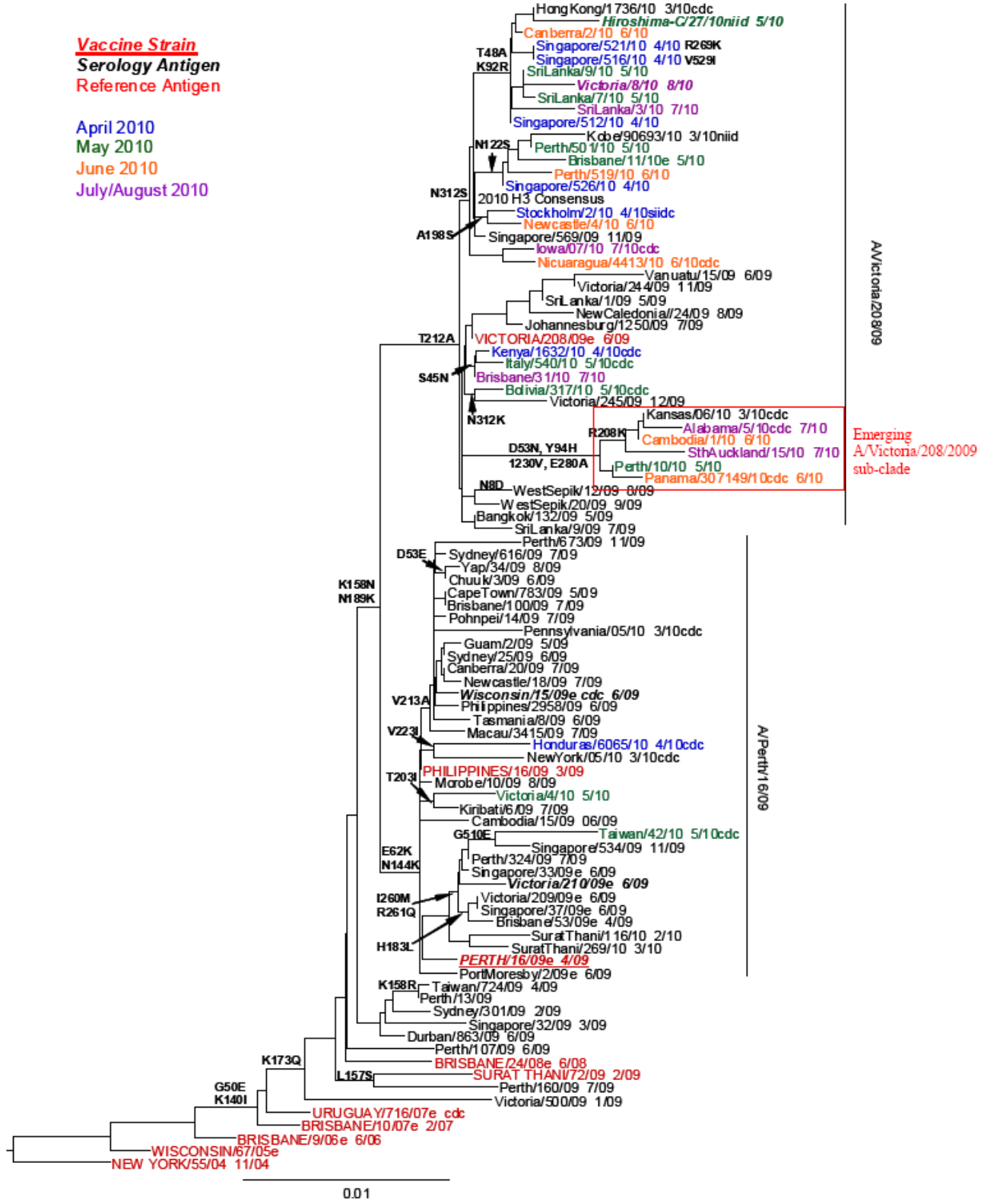
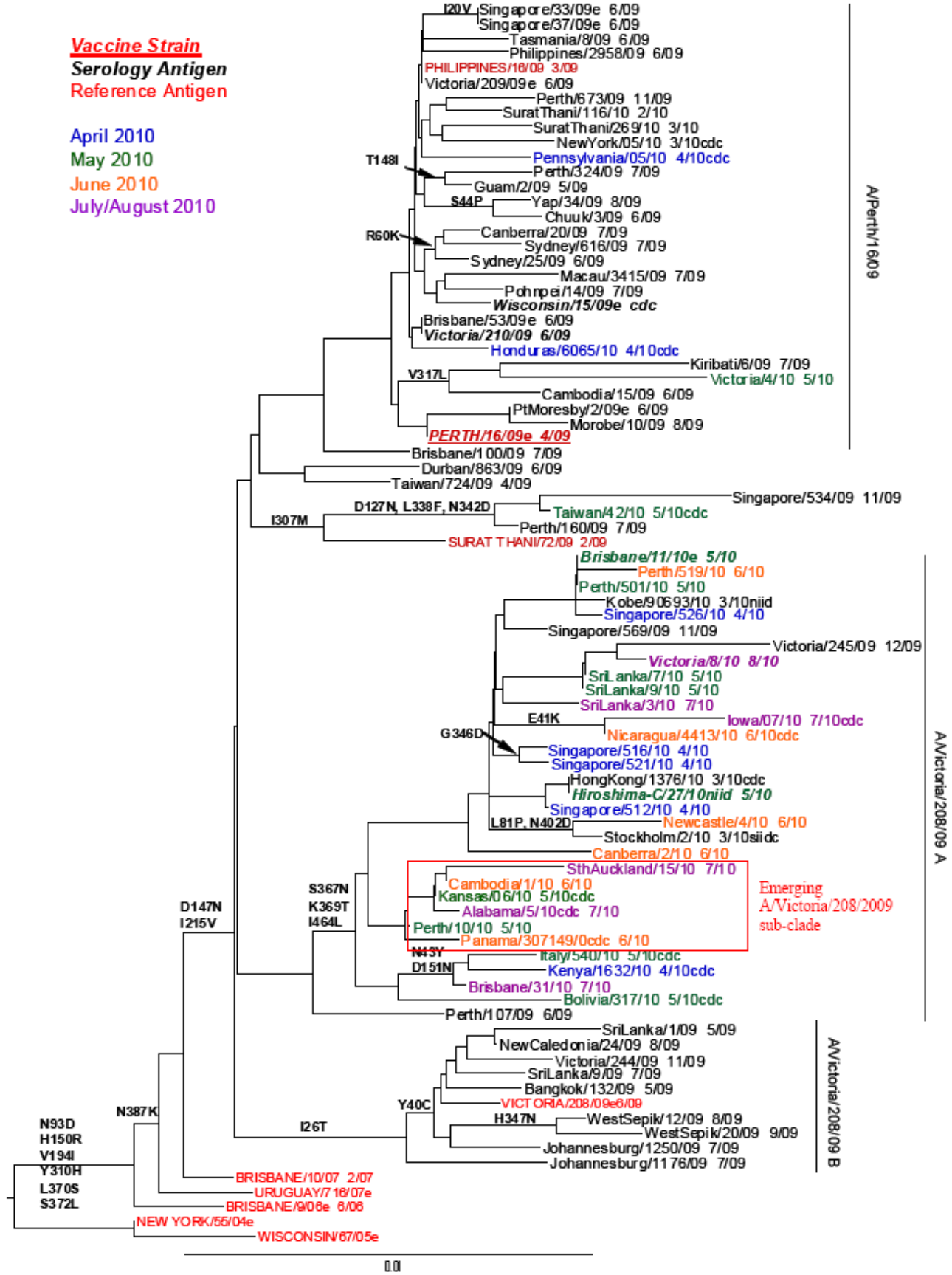


FIGURE 5.3 Phylogenetic relationships among influenza N2 neuraminidase genes



Human Serological Studies

Seasonal Influenza Vaccine

Collaborative assays were performed in 5 laboratories using panels of pre- and postimmunisation sera from young adults and older adults. Panels were derived from recipients of the 2010 Australian vaccine and the 2010-2001 European vaccine.

Australian H3 2010 vaccine	A/Wisconsin/15/2009 (H3N2) (NYMC X-183)
European H3 2010-2001 vaccine	A/Victoria/210/2009 (H3N2) (NYMC X-187)

TABLE 5.12 Haemagglutination-inhibition antibody responses
Influenza type A(H3N2) vaccine component
Young Adults

Population	N	Antigen	Passage History	% Rise	GMT		%>/=40		%>/=160	
					Pre	Post	Pre	Post	Pre	Post
Australian Younger Adult	24	A/Perth/16/2009	E4	75	8.9	67.3	17	75	0	46
		A/Rhode Island/1/2010	E5	71	7.9	53.4	8	67	4	42
		A/Brisbane/11/2010	E4	71	7.1	43.6	8	67	0	25
		A/Victoria/8/2010	E3	79	7.9	61.7	8	75	8	29
		A/Hiroshima-C/27/2010	MDCK5	17	5.8	10.6	0	8	0	0
European Younger Adult	24	A/Perth/16/2009	E4	79	6.5	61.7	4	71	4	42
		A/Rhode Island/1/2010	E5	75	5.6	49.0	4	67	0	29
		A/Brisbane/11/2010	E4	71	5.5	30.0	4	58	0	13
		A/Victoria/8/2010	E3	79	5.9	56.6	4	75	0	42
		A/Hiroshima-C/27/2010	MDCK5	29	5.0	8.7	0	8	0	0

TABLE 5.13 Haemagglutination-inhibition antibody responses
Influenza type A(H3N2) vaccine component
Older Adults

Population	N	Antigen	Passage History	% Rise	GMT		%>/=40		%>/=160	
					Pre	Post	Pre	Post	Pre	Post
Australian Older Adult	24	A/Perth/16/2009	E4	67	10.6	84.7	17	79	8	50
		A/Rhode Island/1/2010	E5	63	8.9	69.2	4	79	4	46
		A/Brisbane/11/2010	E4	71	8.7	56.6	17	71	4	46
		A/Victoria/8/2010	E3	71	12.6	77.7	21	79	4	54
		A/Hiroshima-C/27/2010	MDCK5	29	5.6	9.7	0	8	0	0
European Older Adult	24	A/Perth/16/2009	E4	71	5.3	50.4	0	63	0	29
		A/Rhode Island/1/2010	E5	75	5.1	46.2	0	58	0	29
		A/Brisbane/11/2010	E4	54	5.3	28.3	0	46	0	25
		A/Victoria/8/2010	E3	67	5.5	43.6	0	50	0	38
		A/Hiroshima-C/27/2010	MDCK5	21	5.0	8.4	0	17	0	0

* Vaccine Strain

APPENDIX 5 - Influenza B

TABLE 6.1 Summary – Antigenic Characterisation of Influenza B from the Melbourne WHO CC

	Australia, New Zealand	Pacific	SE Asia	Africa	East Asia	South Asia	Total (%)
October 2007 – February 2008							
B/Malaysia/2506/2004-like	3	0	3	0	0	0	6 (2.3%)
B/ Malaysia/2506/2004 (low)*	3	0	25	0	0	0	28 (10.9%)
B/Florida/4/2006-like	112	1	51	0	5	0	169 (65.5%)
B/Florida/4/2006 (low)*	31	0	9	0	15	0	55 (21.3%)
Total	149	1	88	0	20	0	258
March – September 2008							
B/Malaysia/2506/2004-like	9	0	11	0	1	0	21 (3.3%)
B/ Malaysia/2506/2004 (low)*	192	2	27	2	2	0	225 (34.9%)
B/Florida/4/2006-like	169	0	39	6	10	2	224 (34.8%)
B/Florida/4/2006 (low)*	110	0	28	25	9	2	174 (27.0%)
Total	480	2	105	33	22	2	644
October 2008 – February 2009							
B/Malaysia/2506/2004-like	15	0	4	0	0	0	19 (3.7%)
B/ Malaysia/2506/2004 (low)*	306	0	10	0	0	0	316 (61.4%)
B/Florida/4/2006-like	67	0	9	0	1	0	77 (14.9%)
B/Florida/4/2006 (low)*	91	0	7	2	3	0	103 (20.0%)
Total	479	0	30	2	4	0	515
March - September 2009							
B/Brisbane/60/2008-like	4	0	40	0	0	0	44 (37.0%)
B/Brisbane/60/2008 (low)*	2	1	21	0	0	0	24 (20.2%)
B/Malaysia/2506/2004-like	1	0	2	0	0	0	3 (2.5%)
B/Malaysia/2506/2004 (low)*	1	0	32	0	0	0	33 (27.7%)
B/Florida/4/2006-like	0	0	2	0	0	0	2 (1.7%)
B/Florida/4/2006 (low)*	3	0	10	0	0	0	13 (10.9%)
Total	11	1	107	0	0	0	119
October 2009 – February 2010							
B/Brisbane/60/2008-like	0	0	3	1	1	0	5 (10.4%)
B/Brisbane/60/2008 (low)*	1	0	2	0	0	1	4 (8.3%)
B/Malaysia/2506/2004-like	0	0	10	0	0	0	10 (20.8%)
B/Malaysia/2506/2004 (low)*	0	0	25	0	0	0	25 (52.1%)
B/Florida/4/2006-like	0	0	3	0	0	0	3 (6.3%)
B/Florida/4/2006 (low)*	0	0	1	0	0	0	1 (2.1%)
Total	1	0	44	1	1	1	48
March - September 2010							
B/Brisbane/60/2008-like	5	0	83	13	11	0	112 (59.9%)
B/Brisbane/60/2008 (low)*	0	0	2	0	17	0	19 (10.2%)
B/Malaysia/2506/2004-like	0	0	4	0	0	0	4 (2.1%)
B/Malaysia/2506/2004 (low)*	0	0	42	0	1	0	43 (23.0%)
B/Florida/4/2006-like	0	0	0	1	0	0	1 (0.5%)
B/Florida/4/2006 (low)*	1	0	1	1	5	0	8 (4.3%)
Total	6	0	132	15	34	0	187

* $\geq$ 8 fold lower in HI assays

TABLE 6.3 B/Victoria Lineage

	21 September 2010	Haemagglutination Inhibition Assay - WHO Influenza Centre, Melbourne												
		Reference Antisera												
		A	B	C	D	E	F	G	H	I	J			
	Sequenced	F1175	F1173	F1233	F1236	F1235	F1364	F1640	F1658	F1659	F1688	Mab	Passage	Sample
	Turkey RBC	MAL/2506	VIC/304	BRIS/60	BRIS/60	BRIS/33	HK/90	PHIL/6363	SING/616	SING/616	HK/259	172	History	Date
	Reference Antigens													
A	B/MALAYSIA/2506/2004	**1280**	640	<20	320	640	320	1280	1280	320	640	<80	E5	
B	B/VICTORIA/304/2006	640	**640**	<20	320	640	320	1280	1280	160	640	<80	E4	
C	B/BRISBANE/60/2008	20	40	**160**	160	640	320	80	40	<20	160	1280	MDCK6	
D	B/BRISBANE/60/2008	320	320	160	**1280**	>2560	1280	640	640	160	>2560	1280	E6	
E	B/BRISBANE/33/2008	160	320	80	640	**1280**	640	320	320	80	1280	640	E4	
F	B/HONG KONG/90/2008	320	320	80	640	>2560	**1280**	640	1280	320	1280	1280	E3	
G	B/PHILIPPINES/6363/2009	320	320	<20	160	320	160	**640**	640	160	320	<80	MDCK5	
H	B/SINGAPORE/616/2008	320	320	<20	160	320	160	640	**640**	320	320	<80	MDCK4	
I	B/SINGAPORE/616/2008	320	320	<20	160	320	160	640	1280	**320**	320	<80	E2	
J	B/HONG KONG/259/2010	320	320	80	640	>2560	1280	640	640	80	**1280**	640	E4	
	Test Antigens													
1	B/CHIANG RAI/341/2010	20	160	320	320	1280	640	320	80	<20	320	640	MDCK2	07/07/2010
2	B/NEW CALEDONIA/3/2010	20	80	160	160	1280	320	160	40	<20	160	320	mdck1	27/07/2010
3	B/NEW CALEDONIA/8/2010	20	80	160	160	1280	320	160	40	<20	160	320	MDCK1	13/08/2010
4	B/NEW CALEDONIA/10/2010	20	80	160	160	1280	320	160	80	<20	160	640	MDCK1	17/08/2010
5	B/NEW CALEDONIA/12/2010	20	80	160	160	1280	320	160	80	<20	160	320	MDCK1	23/08/2010
6	B/NEW CALEDONIA/14/2010	20	80	160	160	1280	320	160	40	<20	160	<80	MDCK1	25/08/2010
7	B/CHIANG RAI/404/2010	<20	80	160	160	1280	320	320	40	<20	160	640	MDCK2	02/08/2010
8	B/NAKHONRATCHASIMA/413/2010	20	80	160	160	1280	320	160	40	<20	160	640	MDCK2	16/07/2010
9	B/CHIANG RAI/417/2010	20	80	160	160	1280	320	160	40	<20	160	640	MDCK2	29/07/2010
10	B/TAK/418/2010	<20	80	160	160	1280	320	160	40	<20	160	640	MDCK2	03/08/2010
11	B/BANGKOK/422/2010	20	80	160	160	1280	640	160	40	<20	160	640	MDCK2	03/08/2010
12	B/NOTHABURI/424/2010	20	80	80	160	1280	320	160	40	<20	160	640	MDCK3	02/08/2010
13	B/NOTHABURI/437/2010	20	80	160	160	1280	320	160	40	<20	160	640	MDCK2	09/08/2010
14	B/SURAT THANI/438/2010	20	80	160	160	1280	320	160	40	<20	160	640	MDCK2	08/08/2010
15	B/BANGKOK/448/2010	<20	80	160	160	1280	320	160	40	<20	160	640	MDCK2	10/08/2010
16	B/NOTHABURI/474/2010	20	80	160	160	1280	320	160	40	<20	160	640	MDCK2	16/08/2010
17	B/CHIANG RAI/476/2010	20	80	160	160	1280	320	320	80	<20	160	640	MDCK2	09/08/2010
18	B/NEW CALEDONIA/1/2010	20	80	160	160	1280	320	160	80	<20	160	640	MDCK1	16/07/2010
19	B/NEW CALEDONIA/4/2010	20	40	160	160	1280	320	160	40	<20	160	640	mdck1	28/07/2010
20	B/NEW CALEDONIA/7/2010	20	80	160	160	1280	320	160	40	<20	160	640	MDCK1	12/08/2010
21	B/BANGKOK/399/2010	20	80	160	160	640	320	160	40	<20	160	640	MDCK2	28/07/2010
22	B/NOTHABURI/443/2010	<20	160	80	160	640	320	320	40	<20	160	640	MDCK3	03/08/2010
23	B/BANGKOK/479/2010	<20	80	160	160	640	320	160	40	<20	160	640	MDCK2	19/08/2010
24	B/SURAT THANI/492/2010	<20	40	160	160	640	320	160	40	<20	160	640	MDCK2	15/08/2010
25	B/NEW CALEDONIA/16/2010	20	80	160	160	640	320	160	40	<20	160	640	MDCK1	22/07/2010
26	B/SURAT THANI/408/2010	20	80	80	80	1280	320	160	40	<20	160	640	MDCK2	28/07/2010
27	B/JOHANNESBURG/20/2010	20	40	80	80	640	320	80	40	<20	160	640	mdck3	24/06/2010
28	B/BANGKOK/475/2010	<20	40	80	80	640	160	160	40	<20	160	640	MDCK2	16/08/2010
29	B/BANGKOK/495/2010	<20	80	160	80	640	320	160	40	<20	160	640	MDCKX,MDCK1	23/08/2010
30	B/NEW CALEDONIA/5/2010	20	40	80	80	640	320	80	40	<20	160	640	MDCK1	05/08/2010
31	B/NEW CALEDONIA/11/2010	20	20	<20	40	80	40	80	80	<20	<20	<80	MDCK1	19/08/2010

TABLE 6.4 B/Victoria Lineage

	Compilation: 14 & 17 September 2010	Haemagglutination Inhibition Assay - WHO Influenza Centre, Melbourne												
		Reference Antisera												
		A	B	C	D	E	F	G	H	I	J			
	Sequenced	F1175	F1173	F1233	F1236	F1235	F1364	F1640	F1658	F1659	F1688	Mab	Passage	Sample
	Turkey RBC	MAL/2506	VIC/304	BRIS/60	BRIS/60	BRIS/33	HK/90	PHIL/6363	SING/616	SING/616	HK/259	172	History	Date
	Reference Antigens													
A	B/MALAYSIA/2506/2004	**640**	320	<20	160	320	320	1280	1280	320	640	<80	E5	
B	B/VICTORIA/304/2006	640	**640**	<20	320	1280	320	1280	1280	320	640	<80	E4	
C	B/BRISBANE/60/2008	20	40	**160**	160	1280	320	80	40	<20	160	1280	MDCK6	
D	B/BRISBANE/60/2008	160	320	80	**640**	1280	1280	640	640	160	1280	1280	E6	
E	B/BRISBANE/33/2008	160	160	80	640	**1280**	640	320	320	80	1280	640	E4	
F	B/HONG KONG/90/2008	160	320	80	640	1280	**1280**	640	640	320	1280	640	E3	
G	B/PHILIPPINES/6363/2009	320	320	<20	160	320	320	**640**	640	160	320	<80	MDCK5	
H	B/SINGAPORE/616/2008	320	320	<20	160	320	160	640	**640**	320	320	<80	MDCK4	
I	B/SINGAPORE/616/2008	320	320	<20	160	320	160	640	1280	**320**	320	<80	E2	
J	B/HONG KONG/259/2010	320	160	80	640	>2560	1280	640	640	160	**>2560**	1280	E4	
	Test Antigens													
1	B/MALAYSIA/228/2010	1280	320	160	640	>2560	1280	320	320	<20	640	320	MDCKX,MDCK1	12/05/2010
2	B/JOHANNESBURG/105/2010	40	160	160	320	>2560	640	160	80	20	320	1280	mdck2	04/08/2010
3	B/PANAMA/307237/2010	160	160	80	320	1280	640	320	640	160	640	1280	E3	09/09/2010
4	B/BOLIVIA/104/2010	160	160	80	320	640	320	320	640	80	320	80	E3	09/09/2010
5	B/SYDNEY/201/2010	<20	160	320	320	>2560	640	160	<20	<20	320	640	mdckx,mdck1	23/08/2010
6	B/BRISBANE/1/2010	<20	160	160	320	1280	640	320	160	<20	320	320	MDCK1,MDCK2	11/08/2010
7	B/PHILIPPINES/2112/2010	20	80	160	160	1280	320	160	40	<20	160	640	MDCK3	24/05/2010
8	B/JOHANNESBURG/28/2010	20	80	160	160	1280	320	160	40	<20	160	640	mdck3	28/06/2010
9	B/JOHANNESBURG/49/2010	20	80	160	160	1280	320	160	40	<20	160	1280	mdck3	02/07/2010
10	B/JOHANNESBURG/57/2010	20	80	160	160	1280	640	160	40	20	160	1280	mdck3	06/07/2010
11	B/JOHANNESBURG/100/2010	20	80	160	160	1280	320	160	40	<20	160	1280	mdck2	02/08/2010
12	B/JOHANNESBURG/102/2010	20	80	160	160	1280	320	160	40	<20	160	1280	mdck2	03/08/2010
13	B/NEW CALEDONIA/13/2010	20	160	160	160	1280	320	160	80	<20	160	1280	mdck1	25/08/2010
14	B/NEW CALEDONIA/15/2010	20	80	160	160	1280	320	160	40	<20	160	1280	mdck1	27/08/2010
15	B/JOHANNESBURG/12/2010	20	160	320	160	1280	640	160	80	20	320	2560	mdck2	22/06/2010
16	B/JOHANNESBURG/97/2010	20	80	160	160	1280	320	80	40	<20	160	640	mdck2	30/07/2010
17	B/SYDNEY/202/2010	20	80	160	160	1280	320	160	40	<20	160	640	MDCKX, MDCK1	26/08/2010
18	B/PHILIPPINES/2576/2010	20	80	160	160	1280	640	80	<20	<20	160	640	MDCK2	28/09/2010
19	B/VICTORIA/507/2010	<20	80	160	160	1280	640	80	<20	<20	160	1280	mdck1	02/09/2010
20	B/JEONBUK/1111/2010	40	80	160	160	1280	320	80	<20	<20	160	640	MDCK-P3	30/03/2010
21	B/BRISBANE/2/2010	<20	80	160	160	1280	320	80	<20	<20	160	320	MDCK2,MDCK3	11/08/2010
22	B/JOHANNESBURG/25/2010	20	80	160	80	1280	320	160	40	<20	160	1280	mdck3	29/06/2010
23	B/INCHEON/4302/2010	20	80	80	80	640	320	40	<20	<20	160	1280	MDCK-P3	28/12/2009
24	B/GYEONGGI/1681/2010	20	40	160	80	640	320	80	<20	<20	160	640	MDCK-P3	12/04/2010
25	B/PHILIPPINES/2848/2010	<20	40	80	80	640	320	80	<20	<20	160	640	MDCK2	12/07/2010
26	B/DAEGU/1186/2010	20	80	80	80	640	160	80	20	<20	160	640	MDCK-P3	01/04/2010
27	B/PHILIPPINES/2537/2010	80	160	<20	<20	80	<20	640	160	20	<20	<80	MDCK2	28/06/2010
28	B/PHILIPPINES/1617/2010	80	160	<20	<20	<20	<20	640	160	<20	<20	<80	MDCK2	6/04/2010
29	B/PHILIPPINES/2217/2010	80	160	<20	<20	<20	<20	640	160	<20	<20	<80	MDCK2	1/06/2010
30	B/PHILIPPINES/2788/2010	80	160	<20	<20	<20	<20	640	160	<20	<20	<80	MDCK2	5/07/2010
31	B/PHILIPPINES/666/2010	40	160	<20	<20	<20	<20	640	160	<20	<20	<80	MDCK2	17/05/2010
32	B/PHILIPPINES/2242/2010	80	160	<20	<20	20	20	640	160	<20	<20	<80	MDCK3	7/06/2010

TABLE 6.5 B/Victoria Lineage

	26 August 2010	Haemagglutination Inhibition Assay - WHO Influenza Centre, Melbourne												
		Reference Antisera												
		A	B	C	D	E	F	G	H	I	J			
	Sequenced		F1173	F1233	F1236	F1235	F1364	F1640	F1658	F1659	F1688	Mab	Passage	Sample
	Turkey RBC	MAL/2506	VIC/304	BRI/60	BRI/60	BRI/33	HK/90	PHIL/6363	SING/616	SING/616	HK/259	172	History	Date
	Reference Antigens													
A	B/MALAYSIA/2506/2004	**1280**	320	<20	320	320	160	640	640	160	640	<20	E5	
B	B/VICTORIA/304/2006	1280	**640**	<20	320	640	320	640	640	160	640	<80	E4	
C	B/BRISBANE/60/2008 – cell	20	40	**80**	80	640	160	40	<20	<20	160	640	MDCK6	
D	B/BRISBANE/60/2008 – egg	640	160	80	**320**	1280	640	320	320	80	1280	320	E4	
E	B/BRISBANE/33/2008	1280	640	160	1280	**>2560**	1280	640	640	80	1280	640	E3	
F	B/HONG KONG/90/2008	1280	320	80	640	>2560	**1280**	640	640	320	1280	640	E3	
G	B/PHILIPPINES/6363/2009	1280	320	<20	160	640	320	**640**	640	160	320	<80	MDCK5	
H	B/SINGAPORE/616/2008 –cell	320	160	<20	160	320	160	640	**640**	320	160	<80	MDCK2	
I	B/SINGAPORE/616/2008 –egg	1280	320	<20	160	320	160	640	640	**320**	320	<80	E2	
J	B/HONG KONG/259/2010	640	160	40	320	1280	640	320	320	40	**1280**	640	E4	
	Test Ag													
1	B/TAIWAN/11/2010	640	160	80	320	1280	640	320	320	160	1280	80	E1+2,E1	
2	B/MIE/6/2010	1280	160	40	320	1280	640	320	320	80	1280	160	E1+2,E1	
3	B/CAMBODIA/1/2010	20	40	320	160	1280	320	80	<20	<20	160	320	mdck2	10/01/2010
4	B/DAEGU/1611/2010	20	40	320	160	1280	320	80	<20	<20	160	640	MDCK-P3	10/04/2010
5	B/CHRISTCHURCH/1/2010	20	80	160	160	1280	320	80	<20	<20	160	640	MDCKX,MDCK1	30/06/2010
6	B/CAMBODIA/3/2010	20	40	160	160	1280	320	80	<20	<20	160	640	mdck2	01/02/2010
7	B/CAMBODIA/8/2010	20	40	160	160	640	320	80	<20	<20	160	640	MDCK0,MDCK1	05/03/2010
8	B/CAMBODIA/2/2010	20	40	160	80	1280	320	80	<20	<20	160	640	mdck2	14/01/2010
9	B/VICTORIA/503/2010	20	40	160	80	1280	320	80	20	<20	160	640	MDCK1	11/08/2010
10	B/DAEGU/1614/2010	<20	40	160	80	1280	320	80	<20	<20	160	640	MDCK-P3	09/04/2010
11	B/DAEGU/1314/2010	20	40	160	80	1280	320	80	<20	<20	160	160	MDCK-P3	03/04/2010
12	B/CAMBODIA/5/2010	20	40	160	80	640	320	80	<20	<20	160	320	mdck2	13/07/2010
13	B/CAMBODIA/6/2010	20	40	160	80	640	320	80	<20	<20	160	640	MDCK2	13/07/2010
14	B/VICTORIA/504/2010	20	40	160	80	640	320	80	<20	<20	160	640	MDCK1	13/08/2010
15	B/DAEGU/1513/2010	20	40	160	80	640	320	80	<20	<20	160	640	MDCK-P3	08/04/2010
16	B/CAMBODIA/7/2010	20	40	80	80	640	320	80	<20	<20	160	640	MDCK2	07/07/2010
17	B/CAMBODIA/4/2010	20	<20	80	40	320	80	40	<20	<20	<20	320	mdck2	05/07/2010

FIGURE 6.3 Phylogenetic relationships among influenza B HA genes of the B/Victoria Lineage

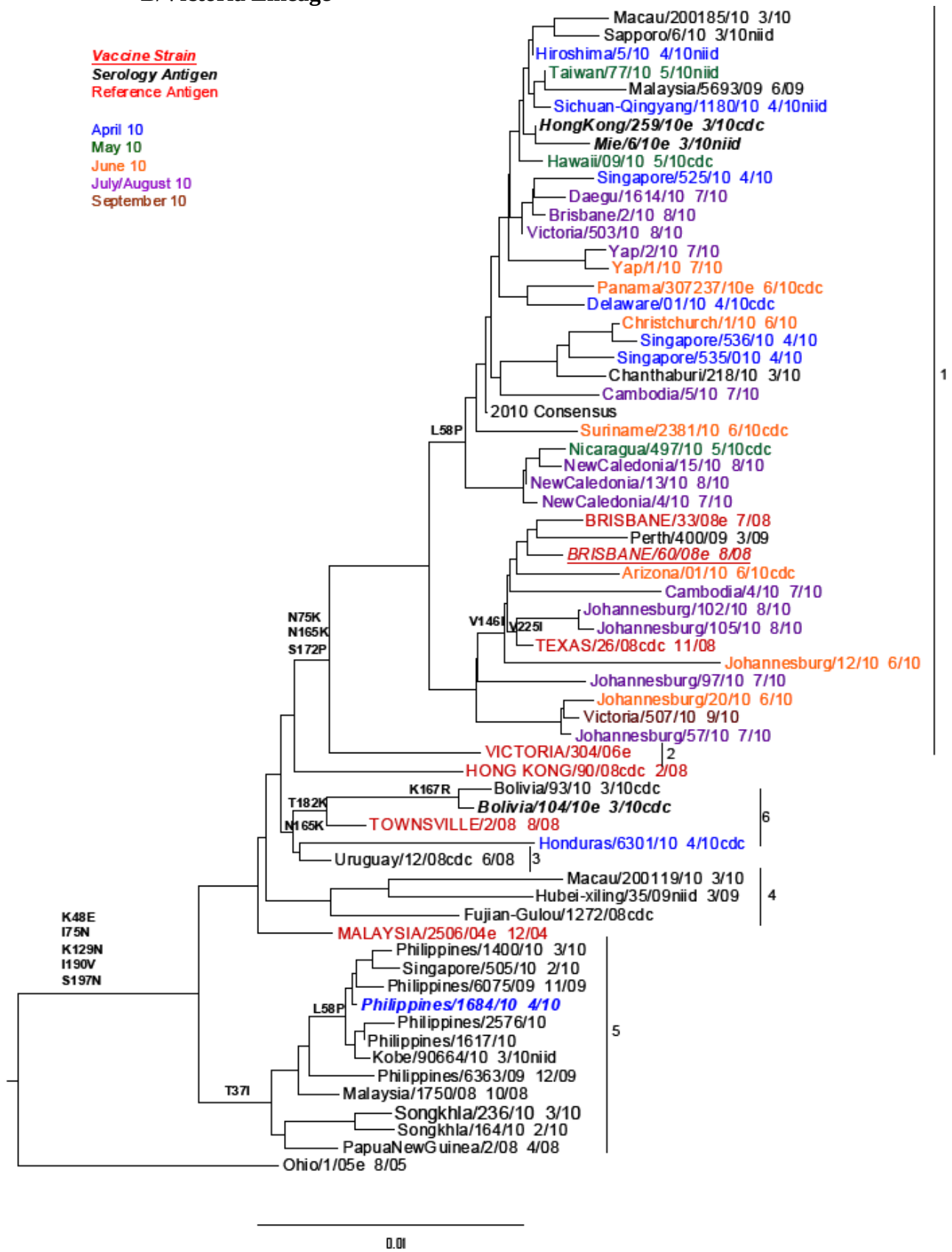


FIGURE 6.4 Phylogenetic relationships among influenza B HA genes of the Yamagata Lineage

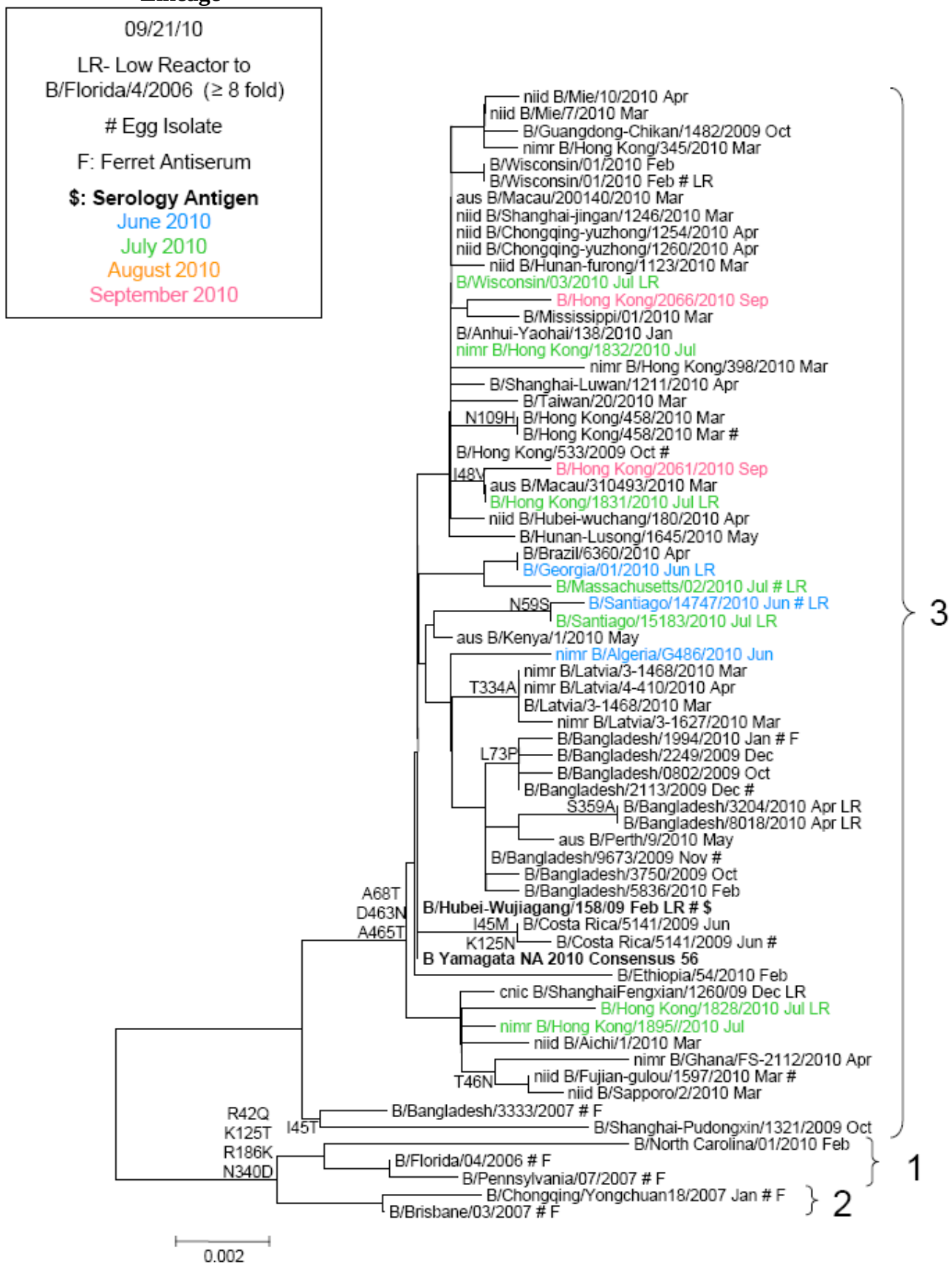


FIGURE 6.5 Phylogenetic relationships among influenza B neuraminidase genes 2010

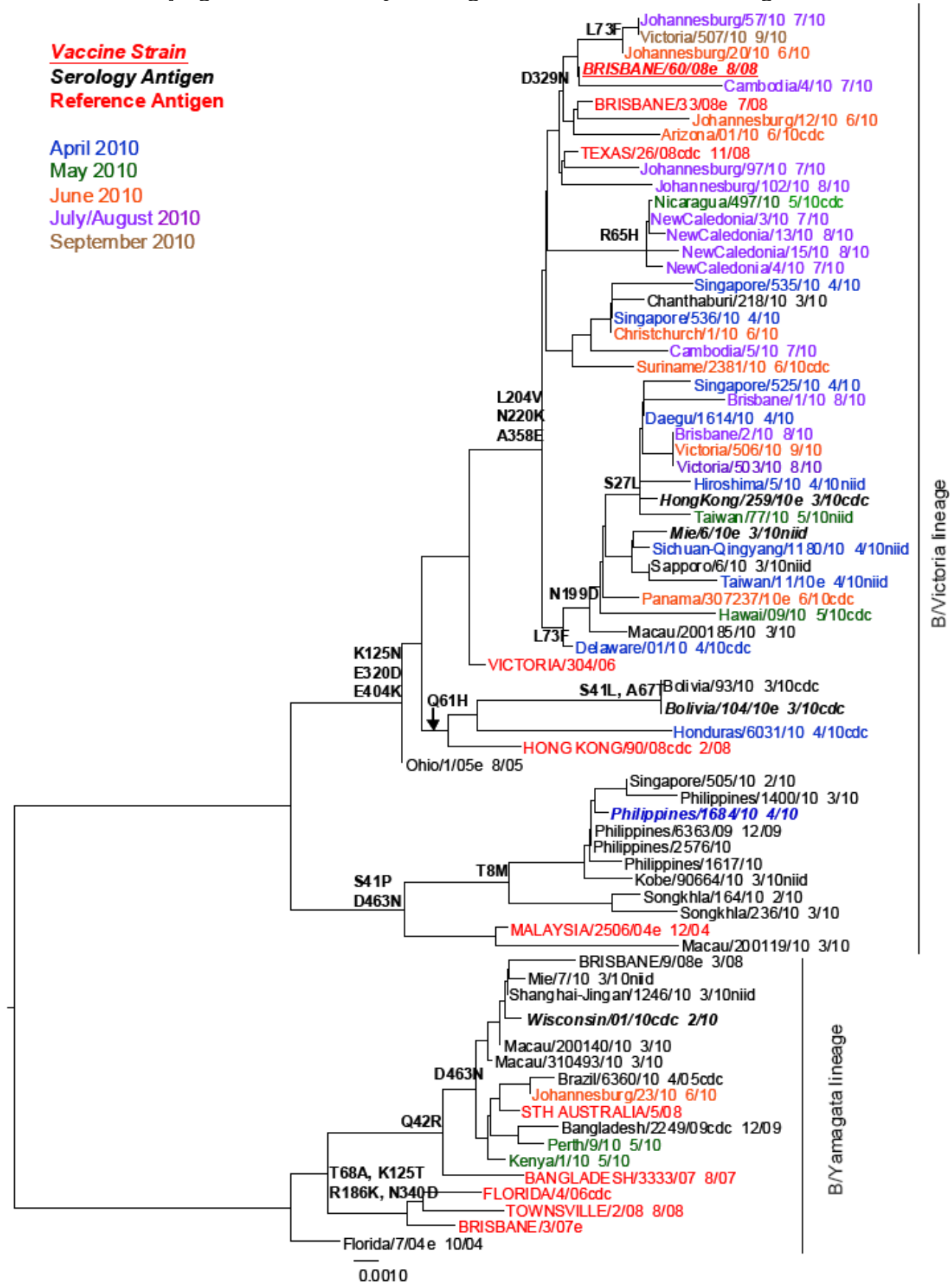


TABLE 5.7 Haemagglutination inhibition antibody responses Influenza type B vaccine component (Young Adults)

Population	N	Antigen	Passage History	% Rise	GMT		%>/=40		%>/=160	
					Pre	Post	Pre	Post	Pre	Post
Australian Younger Adult	24	B/Brisbane/60/2008*^	E4	50	30.0	97.9	50	79	29	50
		B/Hong Kong/259/2010^	E4	46	42.4	106.8	54	79	33	50
		B/Mie/6/2010^	E4	46	35.6	106.8	54	79	29	50
		B/Bolivia/104/2010^	E3	54	47.6	155.4	46	67	38	58
		B/Brisbane/3/2007+	E3	8	95.1	155.4	67	79	38	54
		B/Wisconsin/1/2010+	E4	21	43.6	80.0	46	58	25	41
European Younger Adults	24	B/Brisbane/60/2008*^	E4	88	8.7	155.4	13	92	4	58
		B/Hong Kong/259/2010^	E4	110	8.7	219.8	13	88	4	67
		B/Mie/6/2010^	E4	92	9.4	219.8	13	88	4	58
		B/Bolivia/104/2010^	E3	92	10.6	239.7	8	96	4	63
		B/Brisbane/3/2007+	E3	88	16.8	134.5	29	79	21	54
		B/Wisconsin/1/2010+	E4	58	10.0	50.4	21	63	4	38

TABLE 5.8 Haemagglutination inhibition antibody responses Influenza type B vaccine component (Older Adults)

Population	N	Antigen	Passage History	% Rise	GMT		%>/=40		%>/=160	
					Pre	Post	Pre	Post	Pre	Post
Australian Older Adult	24	B/Brisbane/60/2008*^	E4	71	8.9	46.2	21	67	4	21
		B/Hong Kong/259/2010^	E4	67	11.2	56.6	21	79	4	21
		B/Mie/6/2010^	E4	63	10.3	47.6	13	71	4	25
		B/Bolivia/104/2010^	E3	58	13.7	56.6	29	58	4	21
		B/Brisbane/3/2007+	E3	8	41.2	92.4	58	63	25	33
		B/Wisconsin/1/2010+	E4	29	21.8	46.2	38	46	21	29
European Older Adults	24	B/Brisbane/60/2008*^	E4	58	6.3	28.3	8	58	0	21
		B/Hong Kong/259/2010^	E4	58	6.9	43.6	8	67	4	3
		B/Mie/6/2010^	E4	50	6.9	33.6	8	50	4	25
		B/Bolivia/104/2010^	E3	67	7.5	46.2	17	83	6	33
		B/Brisbane/3/2007+	E3	39	7.7	21.2	17	56	6	17
		B/Wisconsin/1/2010+	E4	33	6.7	15.4	8	38	0	8

*Vaccine strain
^B/Vic – lineage viruses
+B/Yam – lineage viruses

APPENDIX 6 - WHO Recommendation for Influenza Vaccines

Recommended viruses of influenza vaccines for use in the 2011 influenza season

(southern hemisphere)

September 2010

(Reformatted from the Weekly Epidemiological Record, 2010 85(41):401-412)

WHO convenes technical consultations[2] in February and September each year to recommend viruses for inclusion in influenza vaccines[3] for the northern and southern hemispheres, respectively. This recommendation relates to the influenza vaccines for the forthcoming influenza season in the southern hemisphere (2011). A recommendation will be made in February 2011 relating to vaccines that will be used for the influenza season in the northern hemisphere (2011–2012). For countries in equatorial regions, epidemiological considerations will influence which recommendation (February or September) individual national and regional authorities consider more appropriate.

Influenza activity, February – September 2010

Between February and September 2010, influenza was active worldwide and reported in Africa, the Americas, Asia, Europe and Oceania. In many countries activity was low compared with the same period in 2009; it was due to both pandemic influenza A(H1N1) and seasonal A(H3N2) and B viruses. In general, outbreaks due to pandemic A(H1N1) viruses decreased during this period, leading to the declaration of the post-pandemic phase by WHO on 10 August 2010.[4]

In the southern hemisphere, influenza activity was variable in the different regions. Pandemic A(H1N1) viruses predominated in some countries, such as Australia, Colombia and New Zealand. In general, activity increased from July and had declined in most countries by September.

In the northern hemisphere, influenza activity generally declined from February and was very low in Europe and North America compared to the same period in the previous year. In Asia, widespread outbreaks of pandemic A(H1N1) occurred in India; regional pandemic A(H1N1) activity was reported in Bhutan, Cambodia, China and Malaysia, and localized activity was reported in Nepal.

Seasonal influenza A(H3N2) or B viruses predominated in some African and South American countries, and regional activity of A(H3N2) and B viruses was experienced in China. Confirmed cases of seasonal A(H1N1) viruses were rare.

In tropical areas, many countries experienced outbreaks of varying intensity of pandemic A(H1N1), A(H3N2) and B influenza. The extent and type of influenza activity worldwide are summarized in *Table 1*.

Influenza A(H5N1) and A(H9N2)

From 17 February 2010 to 26 September 2010, 27 human cases of A(H5N1), 12 of which were fatal, were confirmed and reported by Cambodia, China, Egypt, Indonesia and Viet Nam, where highly pathogenic avian Influenza A(H5N1) is present in poultry. Since December 2003, a total of 505 cases with 300 deaths have been confirmed in 15 countries.[5] To date there has been no evidence of sustained human-to-human transmission.

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[2] See http://www.who.int/csr/disease/Influenza/vaccinerecommendations/en/index.html; accessed October 2010.

[3] A description of the process of influenza vaccine virus selection and development is available at: http://apps.who.int/gb/pip/pdf_fi %20les/Fluvaccvirusselection.pdf

[4] See http://www.who.int/mediacentre/news/statements/2010/h1n1_vpc_20100810/en/index.html; accessed October 2010.

[5] See http://www.who.int/csr/disease/avian_Influenza/country/cases_table_2010_08_31/en/index.html; accessed October 2010.

No human cases of Influenza A(H9N2) were reported during the period from February to September 2010.

Antigenic and genetic characteristics of recent isolates

Influenza A(H1N1) viruses

The vast majority of A(H1N1) viruses detected worldwide during this period were pandemic A(H1N1); only a small number of seasonal A(H1N1) viruses were confirmed. Haemagglutination inhibition (HI) tests using postinfection ferret antisera indicated that pandemic A(H1N1) viruses remained antigenically homogeneous and closely related to the vaccine virus A/California/7/2009. Sequence analysis of pandemic A(H1N1) viruses indicated increasing genetic heterogeneity. A small number of viruses showed reductions in reactivity in HI assays with some ferret antisera raised against a panel of representative viruses including the vaccine virus, but they did not form distinct genetic subclades.

The small number of seasonal A(H1N1) viruses, from China, were generally antigenically and genetically closely related to A/Brisbane/59/2007.

Influenza A(H3N2) viruses

The majority of A(H3N2) viruses collected between February and September 2010 were antigenically closely related to A/Perth/16/2009, the vaccine virus for the northern hemisphere 2010–2011 season. This relationship assessed using panels of postinfection ferret antisera in HI assays and was supported by virus neutralization assays. Phylogenetically, the haemagglutinin (HA) genes of recent viruses fell into two distinct genetic clades represented by A/Perth/16/2009 and A/Victoria/208/2009, with the majority falling within the A/Victoria/208/2009 clade. Emergence of phylogenetic subgroups within the A/Victoria/208/2009 clade has been observed but viruses within these clades, and emerging subgroups, were antigenically similar to A/Perth/16/2009.

Influenza B viruses

Influenza B viruses of both the B/Victoria/2/87 and the B/Yamagata/16/88 lineages circulated, with B/Victoria/2/87 lineage viruses continuing to predominate. However, in China, B/Yamagata/16/88 lineage viruses have recently predominated although circulating at low levels.

In HI tests with postinfection ferret antisera, the majority of the B/Victoria/2/87 lineage viruses were antigenically closely related to the vaccine virus B/Brisbane/60/2008, while two antigenically distinguishable groups were detected in Asia and South America, represented by B/Philippines/1617/2010 and B/Bolivia/104/2010, respectively. Most recently isolated B/Yamagata/16/88 lineage viruses were antigenically distinguishable from the previous vaccine virus B/Florida/4/2006 and were more closely related to both B/Bangladesh/3333/2007 and B/Wisconsin/1/2010.

Resistance to Influenza antiviral drugs

Neuraminidase inhibitors

The vast majority of pandemic A(H1N1) viruses were sensitive to oseltamivir. The small number of oseltamivir-resistant pandemic A(H1N1) viruses detected were mostly linked to use of this drug for prophylaxis or treatment; in all of these cases, resistance was due to a histidine to tyrosine substitution at amino acid 275 (H275Y) in the neuraminidase. There were no reports of oseltamivir-resistant A(H3N2) or B viruses. No zanamivir-resistant viruses were confi rmed. Updates are available at http://www.who.int/csr/disease/Influenza/h1n1_table/en/index.html

Table 1 **Extent and type of influenza activity worldwide, February 2010 – September 2010**
Tableau 1 **Etendue et type d'activité grippale saisonnière dans le monde, février 2010-septembre 2010**

Country, area or territory – Pays, région ou territoire	February – Février	March – Mars	April – Avril	May – Mai	June – Juin	July – Juillet	August – Août	September – Septembre
Africa – Afrique								
Algeria – Algérie	•H3, •H1(pdm)			•H1(pdm)	•B			
Angola	•B	•B	•H3, •B, •H1(pdm)	•B, •H1(pdm)				
Cameroon – Cameroun	•H1(pdm)	•H3, •B, •H1(pdm)	•B, •H1(pdm)	•B	•B, •H1(pdm)	•H3, •B	•B	•B, •H1(pdm)
Central African Republic – République centrafricaine					•B	•H1(pdm)		
Côte d'Ivoire	•H3, •H1(pdm)	•H3, •••H1(pdm)	••H1(pdm)	H3, •B, •H1(pdm)	•H3, •H1(pdm)			
Democratic Republic of the Congo – République démocratique du Congo	•H3	•H3, •B, •H1(pdm)	•H3, •B, •H1(pdm)	•H3, •B	•H3, •B	•B		
Egypt – Egypte	•H3, •B, •H1(pdm)	•H3, B, •••H1(pdm)	•B, •H1(pdm)	•H1(pdm)				
Ethiopia – Ethiopie	•B, •H1(pdm)	•H1(pdm)	•A					
France, Réunion			•A	•A, •H1(pdm)	•H1(pdm)	•B, •H1(pdm)	•A, •B, •H1(pdm)	•A, •B, •H1(pdm)
Ghana	•H3, ••H1(pdm)	••H3, ••H1(pdm)	•H3, •B, ••••H1(pdm)	•H3, ••H1(pdm)	•H3, ••H1(pdm)	•H3, •H1(pdm)	•H1(pdm)	•H1, •B, •H1(pdm)
Kenya	•B, •H1(pdm)	•H3, •B, •H1(pdm)	•H3, •B, •H1(pdm)	•H3	•H3, •B, •H1(pdm)	•H3, •H1(pdm)	•H3, •B, •H1(pdm)	•H3, •B
Madagascar	•H3, ••H1(pdm)	•H3, •B, •H1(pdm)	•H3, •B, •H1(pdm)	•H3	•H3	•H3, •H1(pdm)	•H3, •B, •H1(pdm)	•H3, •H1(pdm)
Mali						•B		
Mauritania – Mauritanie					•B	•B	•H3	
Mauritius – Maurice						•B, •H1(pdm)	•H3, •B, •H1(pdm)	
Guinea-Bissau – Guinée Bissau						•H3, •B, •H1(pdm)		
Rwanda	•H3, •B, •H1(pdm)	•H3, •B, •H1(pdm)	•H3, •B, •H1(pdm)	•B, •H1(pdm)	•B	•B	•B	•B
Senegal – Sénégal	•H3, •••H1(pdm)	••H1(pdm)		•B	•B	•B	•H3, •B	
South Africa – Afrique du Sud	•B		•B	•B	•H3, •B, •H1(pdm)	••H3, ••B, •H1(pdm)	•H3, ••B, ••H1(pdm)	•H3, ••B, •H1(pdm)
Tunisia – Tunisie	•H3, •B, •H1(pdm)	•H3	•B					
Uganda – Ouganda	•B, •H1(pdm)	•H3, •B, •H1(pdm)	•H3, •H1(pdm)	•H3	•H3, •B	•H3		
United Republic of Tanzania – République-Unie de Tanzanie	•H3, •B, •H1(pdm)	•B, •H1(pdm)	•H3, •H1(pdm)	••H3, •H1(pdm)	••H3, •H1(pdm)	•H3, •B	•B	•H3, •B
Zambia – Zambie	•B	•H3, •B, •H1(pdm)	•H3, •B, •H1(pdm)					
America – Amériques								
Argentina – Argentine	•B	•H3, •B, •H1(pdm)	••H3, ••B, •H1(pdm)	•H3, ••B, •H1(pdm)	••B, •H1(pdm)	•H3, ••B, •H1(pdm)	•A, ••B	
Bahamas	••H1(pdm)	•••H1(pdm)						

Table 1 *(continued)* – Tableau 1 *(suite)*

Country, area or territory – Pays, région ou territoire	February – Février	March – Mars	April – Avril	May – Mai	June – Juin	July – Juillet	August – Août	September – Septembre
Asia – Asie								
Afghanistan	•H1(pdm)	•H1(pdm)			•H1(pdm)			
Bangladesh	•B,•H1(pdm)	•B,•H1(pdm)	•B,•H1(pdm)	•B,•H1(pdm)	•B,•H1(pdm)	•H3,•B, ••H1(pdm)	•H3,•B, •H1(pdm)	•B,•H1(pdm)
Bhutan – Bhoutan				••H1(pdm)	•••H1(pdm)	••H1(pdm)		
Cambodia – Cambodge	•H3,•B, •H1(pdm)	•B,••H1(pdm)	•B		•H3,•B, •H1(pdm)	•H3,•B, •••H1(pdm)	•H3,•B, •••H1(pdm)	•B, •••H1(pdm)
China – Chine	•H1,•H3, •••B, ••H1(pdm)	•H1,•H3, •••B, •••H1(pdm)	•H1, •H3, •••B, •H1(pdm)	•H1,••H3, •••B, •H1(pdm)	•H1,•H3, •••B, •H1(pdm)	•H1,••H3, •••B, •H1(pdm)	•H1,•••H3, ••B,•H1(pdm)	••H3,••B, •H1(pdm)
Hong Kong SAR – Hong Kong, RAS	•H3,•B, ••H1(pdm)	•H3,••B, ••H1(pdm)	•H1,•H3,•B, •H1(pdm)	•H3,•B, •H1(pdm)	•H3,•B, •H1(pdm)	•H3,•B, •H1(pdm)	•H3,•B, •H1(pdm)	•H3,•B, •H1(pdm)
Taiwan – Taïwan	•H1(pdm)	•B, •H1(pdm)	•B	•B, •H3				
Democratic People's Republic of Korea – République populaire démocratique de Corée		•H1(pdm), •B	•H1(pdm), •B					
Indonesia – Indonésie	•H3,•B	•H3,•B, •H1(pdm)	•H3,•B, •H1(pdm)	•H3,•B, •H1(pdm)	•H3,•B, •H1(pdm)	•H3,•B, •H1(pdm)	•B	
India – Inde	•B, ••••H1(pdm)	•B, ••••H1(pdm)	•B, ••••H1(pdm)	•B,•H1(pdm)	•B,•H1(pdm)	•H3,•B, ••••H1(pdm)	•H3,•B, ••••H1(pdm)	•H3,•B, ••••H1(pdm)
Iran (Islamic Republic of) – Iran (République islamique d')	•H3,•B, •H1(pdm)	•B,•H1(pdm)	•B	•B	•H3,•B	•B	•B	•B
Israel – Israël		•H1(pdm)						
Japan – Japon	•H3,•B	•H3,•B, •H1(pdm)	•H3,•B, •H1(pdm)	•H3,•B, •H1(pdm)	•H3,•B, •H1(pdm)	•H3,•B, •H1(pdm)	•H3,•B, •H1(pdm)	•H3, •B, •H1(pdm)
Kazakhstan		•B,•H1(pdm)	•B	•B				
Kyrgyzstan				•B				
Malaysia – Malaisie		••H1(pdm)	•••H1(pdm)	•••H1(pdm)	••H1(pdm)	•H1(pdm)		
Maldives						•H1(pdm)		
Mongolia – Mongolie	••B,•H1(pdm)	••••B, •H1(pdm)	•B					
Nepal – Népal						••H1(pdm)	••H1(pdm)	•B, •H1(pdm)
Oman	•H1(pdm)	•B,•H1(pdm)	•H3,•B, •H1(pdm)	•B				
Pakistan	•B	•H1(pdm)	•H3		•H3,•B			•A
Philippines	•B,•H1(pdm)	•B,•H1(pdm)	•B,•H1(pdm)	•H3,•B, •H1(pdm)	•H3,•B, •H1(pdm)	•H3,•B, •H1(pdm)		
Republic of Korea – République de Corée	•H3,•B, ••H1(pdm)	••B,•H1(pdm)	•H3,•••B, •H1(pdm)	••B,•H1(pdm)	•H3,•B, •H1(pdm)			
Singapore – Singapour		•H3,•B, ••H1(pdm)	•H3,•B, ••H1(pdm)	•H3,•H1(pdm)	••H3, •H1(pdm)	••H3, •H1(pdm)	••H3, ••B, •H1(pdm)	••H3, ••B, •H1(pdm)
Sri Lanka	•H3,•H1(pdm)	•H3,•H1(pdm)	•H3,•H1(pdm)	••H3	•H3	•H3,•B		
Tajikistan – Tadjikistan	•B,•H1(pdm)							
Thailand – Thaïlande	•H3,•B, •H1(pdm)	•H3,•B, •H1(pdm)	•H3,•B, •H1(pdm)	•H3,•B, •H1(pdm)	•H3,•B, •H1(pdm)	•H3,•B, •••H1(pdm)	•H3,•B, •H1(pdm)	•H3,•B
Viet Nam		•B						

Table 1 *(continued)* – Tableau 1 *(suite)*

Country, area or territory – Pays, région ou territoire	February – Février	March – Mars	April – Avril	May – Mai	June – Juin	July – Juillet	August – Août	September – Septembre
Europe								
Austria – Autriche	•H1(pdm)							
Belarus – Bélarus	•H1(pdm)	•H1(pdm)	•B, •H1(pdm)	•B, •H1(pdm)				
Belgium – Belgique	•B, •H1(pdm)	•B, •H1(pdm)	•B	•B				
Bosnia and Herzegovina – Bosnie-Herzégovine	•H1(pdm)	•H1(pdm)						
Bulgaria – Bulgarie	•B, •H1(pdm)							
Croatia – Croatie	•H1(pdm)	•H1(pdm)						
Cyprus – Chypre		•H1(pdm)	•B, •H1(pdm)					
Czech Republic – République tchèque	•H1(pdm)	•H1(pdm)		•B, •H1(pdm)				
Denmark – Danemark	•H1(pdm)	•H1(pdm)	•H1(pdm)	•B		•B		
Estonia – Estonie	•B, •H1(pdm)	•B, •H1(pdm)	•B, •H1(pdm)	•H1(pdm)		•H1(pdm)		
France	•B, •H1(pdm)	•B, •H1(pdm)	•B, •H1(pdm)	•B, •H1(pdm)	•B	•H3	•B	•B
Georgia – Georgie	•••H1(pdm)	•••H1(pdm)	•B, •H1(pdm)	•B				
Germany – Allemagne	•B, •H1(pdm)	•B, •H1(pdm)	•H1(pdm)	•B				
Greece – Grèce	•••H1(pdm)	•H1(pdm)	•H1(pdm)	•H3, •H1(pdm)				
Hungary – Hongrie	•H1(pdm)	•H1(pdm)	•H1(pdm)	•H1(pdm)				
Iceland – Islande	•H1(pdm)							
Ireland – Irlande	•A	•A	•A	•A				
Italy – Italie	•B, •H1(pdm)	•B	•B	•H3, •B	•H1(pdm)			
Latvia – Lettonie	•B, •H1(pdm)	•B, •H1(pdm)	•B	•B				
Lithuania – Lithuanie	•H1(pdm)		•B	•H1(pdm)				
Luxembourg	•H1(pdm)	•H1(pdm)	•B, •H1(pdm)	•H1(pdm)				
Malta – Malte	•H1(pdm)	•H1(pdm)	•H1(pdm)	•B				
Montenegro	•H1(pdm)							
Netherlands – Pays-Bas	•H1(pdm)	•H1(pdm)	•B	•H1(pdm)				•B
Norway – Norvège	•B, •H1(pdm)	•B, •H1(pdm)	•B, •H1(pdm)	•B	•B, •H1(pdm)	•B, •H1(pdm)	•H3	
Poland – Pologne	•B, •H1(pdm)	••H1(pdm)	•B	•B, •H1(pdm)	•H1(pdm)			•H1(pdm)
Portugal	•H1(pdm)	•H1(pdm)	•H1(pdm)					
Republic of Moldova – République de Moldavie	••H1(pdm)	•H1(pdm)						
Romania – Roumanie	•B, •H1(pdm)	•H1(pdm)	•H1(pdm)	•H3				
Russian Federation – Fédération de Russie	•H3, •••B, •••H1(pdm)	•H3, •••B, ••H1(pdm)	•H3, ••B, ••H1(pdm)	•H3, •B, •H1(pdm)	•H3, •B, •H1(pdm)			
Serbia – Serbie	•H1(pdm)	•H1(pdm)	•H1(pdm)					
Slovakia – Slovaquie	•H1(pdm)	•H1(pdm)	•H3, •H1(pdm)					
Slovenia – Slovénie	•H1(pdm)		•B	•B	•B			
Spain – Espagne	•B, •H1(pdm)	•B, •H1(pdm)	•B, •H1(pdm)	•B, •H1(pdm)	•B	•B		
Sweden – Suède	••B, •H1(pdm)	••B, •H1(pdm)	•H3, ••B, •H1(pdm)	•B, •H1(pdm)				

Table 1 *(continued)* – Tableau 1 *(suite)*

Country, area or territory – Pays, région ou territoire	February – Février	March – Mars	April – Avril	May – Mai	June – Juin	July – Juillet	August – Août	September – Septembre
Europe								
Austria – Autriche	•H1(pdm)							
Belarus – Bélarus	•H1(pdm)	•H1(pdm)	•B, •H1(pdm)	•B, •H1(pdm)				
Belgium – Belgique	•B, •H1(pdm)	•B, •H1(pdm)	•B	•B				
Bosnia and Herzegovina – Bosnie-Herzégovine	•H1(pdm)	•H1(pdm)						
Bulgaria – Bulgarie	•B, •H1(pdm)							
Croatia – Croatie	•H1(pdm)	•H1(pdm)						
Cyprus – Chypre		•H1(pdm)	•B, •H1(pdm)					
Czech Republic – République tchèque	•H1(pdm)	•H1(pdm)		•B, •H1(pdm)				
Denmark – Danemark	•H1(pdm)	•H1(pdm)	•H1(pdm)	•B		•B		
Estonia – Estonie	•B, •H1(pdm)	•B, •H1(pdm)	•B, •H1(pdm)	•H1(pdm)		•H1(pdm)		
France	•B, •H1(pdm)	•B, •H1(pdm)	•B, •H1(pdm)	•B, •H1(pdm)	•B	•H3	•B	•B
Georgia – Georgie	•••H1(pdm)	•••H1(pdm)	•B, •H1(pdm)	•B				
Germany – Allemagne	•B, •H1(pdm)	•B, •H1(pdm)	•H1(pdm)	•B				
Greece – Grèce	•••H1(pdm)	•H1(pdm)	•H1(pdm)	•H3, •H1(pdm)				
Hungary – Hongrie	•H1(pdm)	•H1(pdm)	•H1(pdm)	•H1(pdm)				
Iceland – Islande	•H1(pdm)							
Ireland – Irlande	•A	•A	•A	•A				
Italy – Italie	•B, •H1(pdm)	•B	•B	•H3, •B	•H1(pdm)			
Latvia – Lettonie	•B, •H1(pdm)	•B, •H1(pdm)	•B	•B				
Lithuania – Lithuanie	•H1(pdm)		•B	•H1(pdm)				
Luxembourg	•H1(pdm)	•H1(pdm)	•B, •H1(pdm)	•H1(pdm)				
Malta – Malte	•H1(pdm)	•H1(pdm)	•H1(pdm)	•B				
Montenegro	•H1(pdm)							
Netherlands – Pays-Bas	•H1(pdm)	•H1(pdm)	•B	•H1(pdm)				•B
Norway – Norvège	•B, •H1(pdm)	•B, •H1(pdm)	•B, •H1(pdm)	•B	•B, •H1(pdm)	•B, •H1(pdm)	•H3	
Poland – Pologne	•B, •H1(pdm)	••H1(pdm)	•B	•B, •H1(pdm)	•H1(pdm)			•H1(pdm)
Portugal	•H1(pdm)	•H1(pdm)	•H1(pdm)					
Republic of Moldova – République de Moldavie	••H1(pdm)	•H1(pdm)						
Romania – Roumanie	•B, •H1(pdm)	•H1(pdm)	•H1(pdm)	•H3				
Russian Federation – Fédération de Russie	•H3, •••B, •••H1(pdm)	•H3, •••B, ••H1(pdm)	•H3, ••B, ••H1(pdm)	•H3, •B, •H1(pdm)	•H3, •B, •H1(pdm)			
Serbia – Serbie	•H1(pdm)	•H1(pdm)	•H1(pdm)					
Slovakia – Slovaquie	•H1(pdm)	•H1(pdm)	•H3, •H1(pdm)					
Slovenia – Slovénie	•H1(pdm)		•B	•B	•B			
Spain – Espagne	•B, •H1(pdm)	•B, •H1(pdm)	•B, •H1(pdm)	•B, •H1(pdm)	•B	•B		
Sweden – Suède	••B, •H1(pdm)	••B, •H1(pdm)	•H3, ••B, •H1(pdm)	•B, •H1(pdm)				

Table 1 *(continued)* – Tableau 1 *(suite)*

Country, area or territory – Pays, région ou territoire	February – Février	March – Mars	April – Avril	May – Mai	June – Juin	July – Juillet	August – Août	September – Septembre
Switzerland – Suisse	•B, •H1(pdm)	•H1(pdm)	•B, •H1(pdm)	•B			•H1(pdm)	
The former Yugoslav Republic of Macedonia – Ex-République yougoslave de Macédoine	•H1(pdm)							
Turkey – Turquie	•B, •H1(pdm)	•B						
Ukraine	•B, ••H1(pdm)	••B, •H1(pdm)	••B, •H1(pdm)	••B				
United Kingdom of Great Britain and Northern Ireland – Royaume-Uni et Irlande du Nord	•B, •H1(pdm)	•B, •H1(pdm)	•B, •H1(pdm)	•B, •H1(pdm)	•B		•H1(pdm)	•H3
Oceania – Océanie								
Australia – Australie	•H3, •B, •H1(pdm)	•H3, •H1(pdm)	•H3, •B, •H1(pdm)	•H3, •B, •H1(pdm)	•H3, •B, •H1(pdm)	•H3, •B, ••H1(pdm)	•H3, •B, ••••H1(pdm)	••••H1(pdm)
France, New Caledonia – Nouvelle Calédonie						••B, •H1pdm	••B	••B
New Zealand – Nouvelle Zélande				•H1(pdm)	•H3, •B, •H1(pdm)	•B, •••H1(pdm)	•H3, •B, •••H1(pdm)	••H1pdm

Data in *Table 1* were provided by the Global Influenza Surveillance Network and other partners. – Les données du *Tableau 1* ont été fournies par le réseau mondial de surveillance de la grippe et d'autres partenaires.

• = Sporadic activity – Activité sporadique
•• = Local activity – Activité locale
••• = Regional outbreaks – Flambées régionales
•••• = Widespread outbreaks – Flambées étendues

A = Influenza A (not subtyped) – Grippe A (sous-type non déterminé)
B = Influenza B – Grippe B
H1 = Influenza A(H1N1) – Grippe A(H1N1)
H3 = Influenza A(H3N2) – H3 = Grippe A(H3N2)
H1(pdm) = Pandemic A (H1N1) 2009 – H1 (pdm) = grippe pandémique A (H1N1) 2009

M2 inhibitors

The vast majority of pandemic A(H1N1) viruses and all tested A(H3N2) viruses were resistant to the M2 inhibitors, amantadine and rimantadine. Resistance to these antiviral drugs remained predominantly associated with a serine to asparagine substitution at amino acid 31 (S31N) of the M2 protein.

Studies with inactivated Influenza virus vaccines

The presence of antibodies to the HA of recent virus isolates, in 9 panels of sera from children, adults and elderly adults who had received seasonal trivalent inactivated vaccines, was determined by HI assay. The trivalent vaccines contained the antigens of either A/California/7/2009 (pandemic H1N1)-like or A/Brisbane/59/2007 (seasonal H1N1)-like, either A/Uruguay/716/2007 or A/Perth/16/2009-like viruses (H3N2), and B/Brisbane/60/2008. Only panels from recipients who had received vaccines containing A/California/7/2009-like and A/Perth/16/2009-like were considered for the analysis of recent pandemic A(H1N1) and A(H3N2) virus isolates. For all panels of sera, the antibody responses to the seasonal A(H1N1) vaccine component were not considered due to the extremely low circulation of seasonal A(H1N1) viruses in the world.

Vaccines containing A/California/7/2009 (H1N1)-like antigens stimulated anti-HA antibodies of similar geometric mean HI titres to the vaccine virus and recent pandemic A(H1N1) isolates. For a small number of pandemic A(H1N1) viruses, the geometric mean HI titres of human post-vaccination sera were lower than titres to the vaccine virus (average reductions: adults, 68%; elderly adults, 55%). 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 microneutralization tests using a subset of sera.

Vaccines containing Influenza B/Brisbane/60/2008-like antigens stimulated anti-HA antibodies of similar geometric mean HI titres to the vaccine virus and recent B/Victoria/2/87 lineage isolates. Geometric mean HI titres were somewhat lower to recent B/Yamagata/16/88 lineage viruses than to the most recent B/Victoria/2/87 lineage vaccine virus for adults and elderly adults (average reductions: adults, 37%; elderly adults, 27%).

Recommended composition of Influenza virus vaccines for use in the 2011 Influenza season

Pandemic Influenza A(H1N1) viruses emerged in March 2009 and continued to circulate, while seasonal A(H3N2) and B viruses circulated at increasing levels in some countries during the period from February to September 2010. Seasonal Influenza A(H1N1) viruses were rarely detected.

Pandemic A(H1N1) viruses were antigenically and genetically similar to A/California/7/2009. Vaccines containing A/California/7/2009 antigens stimulated anti-HA antibodies of similar titres against the vaccine virus and recent pandemic A(H1N1) viruses.

Very few seasonal Influenza A(H1N1) viruses were reported. Of these, the majority were antigenically and genetically similar to the previous vaccine virus A/Brisbane/59/2007.

Sporadic to widespread Influenza A(H3N2) activity was reported in several countries. The majority of recent viruses were antigenically and genetically similar to the vaccine virus A/Perth/16/2009. Vaccines containing A/Perth/16/2009-like antigens stimulated anti-HA antibodies of similar titres against the vaccine virus and recently circulating A(H3N2) viruses.

Influenza B activity was reported in several countries with regional activity being reported in Argentina, Bolivia, Chile, China, Mongolia, Nicaragua, Republic of Korea, Russian Federation and South Africa. While viruses of both B/Victoria/2/87 and B/Yamagata/16/88 lineages co-circulated, B/Victoria/2/87 lineage viruses predominated. 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 distinguishable from the previous vaccine virus B/Florida/4/2006 and were more closely related to both B/Bangladesh/3333/2007 and B/Wisconsin/1/2010. Current vaccines containing B/Brisbane/60/2008 antigens stimulated anti-HA antibodies that had similar titres against the vaccine viruses and recent viruses of the B/Victoria/2/87 lineage; however, titres were lower to recent viruses of the B/Yamagata/16/88 lineage.

It is expected that pandemic A(H1N1), A(H3N2) and B viruses will co-circulate in the 2011 southern hemisphere Influenza season.

As in previous years, national or regional control authorities approve the composition and formulation of vaccines used in each country. National public health authorities are responsible for making recommendations regarding the use of the vaccine. WHO has published recommendations on the prevention of Influenza.[6]

The status of development and availability of candidate vaccine viruses and potency testing reagents can be accessed on the relevant WHO website.[7]

Vaccine viruses (including reassortants) and reagents for use in the laboratory standardization of inactivated vaccine may be obtained from: Immunobiology Section, Offi ce of Laboratory and Scientific Services, Monitoring and Compliance Group, Therapeutic Goods Administration, P.O.

[6] See http://www.who.int/docstore/wer/pdf/2002/wer7728.pdf; accessed October 2010.
[7] See http://www.who.int/csr/disease/infl uenza/vaccinerecommendations2/en/index.html; accessed October 2010.

Box 100, Woden ACT, 2606 Australia (fax: +61 2 6232 8564, email: Influenza.standards@tga.gov.au; web site: http://www.tga.gov.au); Division of Virology, National Institute for Biological Standards and Control, Health Protection Agency, Blanche Lane, South Mimms, Potters Bar, Hertfordshire, EN6 3QG UK (fax: +44 1707 641050, e-mail: enquiries@nibsc.hpa.org.uk, web site: http://www.nibsc.ac.uk/flu_site/index.html); Division of Product Quality, Center for Biologics Evaluation and Research, Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20892, United States (fax: +1 301 480 9748); or Center for Influenza Virus Research, National Institute of Infectious Diseases, Gakuen 4-7-1, Musashi-Muayama, Tokyo 208-0011, Japan (fax. +81 42 561 6156).

It is recommended that the following viruses be used for influenza vaccines in the 2011 influenza season (southern hemisphere):

- an A/California/7/2009 (H1N1)-like virus;
- an A/Perth/16/2009 (H3N2)-like virus;*
- a B/Brisbane/60/2008-like virus.

* A/Wisconsin/15/2009 and A/Victoria/210/2009 are A/Perth/16/2009-like viruses.

Requests for reference viruses for antigenic analysis should be addressed to the WHO Collaborating Centre for Reference and Research on Influenza, VIDRL, 10 Wreckyn Street, North Melbourne, Victoria 3051, Australia (fax: +61 3 9342 3939, web site: http://www.influenzacentre.org); the WHO Collaborating Centre for Reference and Research on Influenza, National Institute of Infectious Diseases, Gakuen 4-7-1, Musashi-Murayama, Tokyo 208-0011, Japan (fax: +81 42 561 6149 or +81 42 565 2498, web site: http://www.nih.go.jp/niid/index.html); the WHO Collaborating Center for Surveillance, Epidemiology and Control of Influenza, Centers for Disease Control and Prevention, 1600 Clifton Road, Mail Stop G16, Atlanta, GA 30333, United States (fax: +1 404 639 0080, web site: http://www.cdc.gov/fl u/); or the WHO Collaborating Centre for Reference and Research on Influenza, MRC National Institute for Medical Research, The Ridgeway, Mill Hill, London NW7 1AA, UK (fax: +44 208 906 4477, web site: http://www.nimr.mrc.ac.uk/wic/). Updated epidemiological information is available on the WHO web site at http://www.who.int/influenza.

WHO web sites on infectious diseases

Avian influenza	**http://www.who.int/csr/disease/avian_influenza/en/**
Buruli ulcer	**http://www.who.int/buruli/en/**
Child and adolescent health and development	**http://www.who.int/child_adolescent_health/en/**
Cholera	**http://www.who.int/cholera/en/**
Deliberate use of biological and chemical agents	**http://www.who.int/csr/delibepidemics/informationresources/en/**
Dengue (DengueNet)	**http://apps.who.int/globalatlas**
Epidemic and pandemic surveillance and response	**http://www.who.int/csr/en/**
Eradication/elimination programmes	**http://www.who.int/infectious-disease-news/**
Filariasis	**http://www.filariasis.org**
Geographical information systems (GIS)	**http://www.who.int/health_mapping/en/**
Global atlas of infectious diseases	**http://globalatlas.who.int**
Global Outbreak Alert and Response Network (GOARN)	**http://www.who.int/csr/outbreaknetwork/en/**
Health topics	**http://www.who.int/topics/en**
Influenza	**http://www.who.int/csr/disease/influenza/en/**
Influenza network (FluNet)	**http://who.int/flunet**
International Health Regulations	**http://www.who.int/ihr/en/**
International travel and health	**http://www.who.int/ith/en/**
Intestinal parasites	**http://www.who.int/wormcontrol/en**
Leishmaniasis	**http://www.who.int/leishmaniasis/en**
Leprosy	**http://www.who.int/lep/en**
Lymphatic filariasis	**http://www.who.int/lymphatic_filariasis/en/**
Malaria	**http://www.who.int/malaria/en**
Neglected tropical diseases	**http://www.who.int/neglected_diseases/en/**
Outbreak news	**http://www.who.int/csr/don/en**
Poliomyelitis	**http://www.polioeradication.org/casecount.asp**
Rabies network (RABNET)	**http://www.who.int/rabies/en**
Report on infectious diseases	**http://www.who.int/infectious-disease-report/**
Global Foodborne Infections Network (GFN)	**http://www.who.int/gfn/en**
Smallpox	**http://www.who.int/csr/disease/smallpox/en**
Schistosomiasis	**http://www.3.imperial.ac.uk/schisto**
Tropical disease research	**http://www.who.int/tdr/**
Tuberculosis	**http://www.who.int/tb/en** and/et **http://www.stoptb.org**
Immunization, Vaccines and Biologicals	**http://www.who.int/immunization/en/**
Weekly Epidemiological Record	**http://www.who.int/wer/**
WHO Lyon Office for National Epidemic Preparedness and Response	**http://www.who.int/ihr/lyon/en/index.html**
WHO Pesticide Evaluation Scheme (WHOPES)	**http://www.who.int/whopes/en**
WHO Mediterranean Centre for Vulnerability Reduction, Tunis	**http://wmc.who.int/**
Yellow fever	**http://www.who.int/csr/disease/yellowfev/en/**