RECOMMENDATION FOR SEASONAL INFLUENZA VACCINE COMPOSITION FOR NEW ZEALAND 2010

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CONTENTS

RECOMMENDATIONS

The Australian Influenza Vaccine Committee (AIVC), with a New Zealand representative (Appendix 1), met in Canberra on 2 October 2009 to consult on the influenza vaccine composition for 2009 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.

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1. EPIDEMIOLOGY

It is known that influenza viruses frequently go through antigenic changes, and protection by vaccines is dependent on achieving a good match between vaccine strains and the circulating viruses. Thus, the World Health Organisation (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 has been published in 9 October issue of the *Weekly Epidemiological Record, 2009 84(41):421-436* (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 an 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 for the use in the subsequent year.

Table 1. Influenza Vaccine Recommendations for New Zealand, 1991-2010

Formulation Recommendations		Vaccine used for	A H3N2	A H1N1	B
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

1.1. Overview of World-wide Influenza Activity, March-September 2009

Between February and September 2009, influenza activity was reported in Africa, the Americas, Asia, Europe and Oceania. Activity was higher compared with the same period the previous year and was due to both seasonal influenza and pandemic influenza A(H1N1) 2009 viruses. Following its emergence in March, the pandemic A(H1N1) virus spread rapidly throughout the world, leading to the declaration of an influenza pandemic by WHO on 11 June 2009. The pandemic influenza outbreaks subsequently occurred in all regions of the world and, by July, pandemic A(H1N1) was the predominant influenza virus circulating in many countries in the Americas, Asia, Europe and Oceania.

In the northern hemisphere, outbreaks of pandemic A(H1N1) occurred in many countries in the northern hemisphere during May to August. Following a decline in activity in some countries during July or August, a resurgence was reported in September in some countries in Europe and the Americas. From August, rapid increases in activity were reported in African and Asian countries, for example in Cambodia, China, Japan, Kenya, the Lao People's Democratic Republic, the United Republic of Tanzania and Viet Nam. In addition, seasonal influenza activity was widespread in many countries in February and declined during March and April in some countries. The predominant viruses in Europe and many other countries were A(H3N2), while in Japan and North America higher proportions of A(H1N1) and B viruses were reported. Influenza A(H1N1), A(H3N2) and B viruses co-circulated in varying proportions in many northern hemisphere and tropical countries of Africa and Asia. From June to August, increased activity was reported in some countries in Asia, with regional outbreaks of influenza A(H3N2) in China. Meanwhile,

In the southern hemisphere, pandemic A(H1N1) activity increased rapidly in many countries. Activity peaked in July in some countries, falling to low levels by August or September in Argentina, Australia, Brazil, Chile and New Zealand. In some other countries in the southern hemisphere and in tropical regions of the Americas and Asia, pandemic A(H1N1) influenza virus continued to circulate in September. In addition, seasonal influenza activity began to increase in April, and widespread outbreaks of influenza A(H3N2) were reported in South Africa in June. Influenza A(H3N2) and, to a lesser extent, A(H1N1) circulated in Argentina, Australia and Chile, while New Zealand reported predominantly A(H1N1) activity. Local outbreaks of influenza B occurred in Madagascar and Réunion (France), and B viruses were detected at low levels in many other countries.

From 1 February to 21 September 2009, 37 human cases of influenza A(H5N1), 5 of which were fatal, were confirmed and reported by China, Egypt and Viet Nam, where highly pathogenic avian influenza A(H5N1) is present in poultry. Since December 2003, a total of 440 human cases and 262 deaths have been confirmed in 15 countries. So far, there has been no evidence of sustained human-to-human transmission.
(Excerpted from Weekly Epidemiological Record, 2009 84(41):421-436)

The WHO Collaborating Centre for Reference and Research on Influenza in Melbourne, Australia (Melbourne WHOCC) analysed influenza isolates received from 1 January to 28 September 2009. Pandemic A(H1N1) virus was the predominant strain which accounted for 47.3% (1146/2426) of isolates while 13% (315/2426) were seasonal influenza A(H1N1) and 28.5% (690/2426) were influenza A(H3N2) and 6.8% (166/2426) were influenza B (Figures 2.1 and 2.2 in Appendix 2).

1.2. Influenza Activity in Australia and South Africa, March-September 2009

1.2.1. Australia

Influenza activity in Australia in 2009 was high with some regional variations regarding influenza activities and types/subtypes.

There are seven 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 lab-confirmed cases are required to be reported to State and Territory health departments. In 2009, confirmed pandemic A(H1N1) cases are being received from all jurisdictions through NNDSS except for Victoria and New South Wales (NSW). NSW is also unable to send seasonal influenza notification data. As of 9 October 2009, there were 37,276 confirmed cases of pandemic A(H1N1) influenza in Australia, including 185 associated deaths. Influenza activity in 2009 started earlier than in 2008 and there was a rapid increase in the number of confirmed influenza cases (both seasonal and pandemic (H1N1) 2009) from week 21 (starting 16 May 2009) and peaked in week 30 (staring 20 July 2009). The first wave of the pandemic has lasted approximately 18 weeks, making it a relatively short influenza season in comparison to the previous 5 years (range 21-29 weeks). The high number of confirmed notifications of seasonal influenza seen during May and June are most likely due to the increase in testing for pandemic (H1N1) 2009. Overall, numbers of laboratory confirmed notifications of influenza have been decreasing in the past few weeks.

- **Laboratory Surveillance conducted by the Melbourne WHOCC.** A total of 931 influenza isolates from Australia were received for analysis at the Melbourne WHOCC (Appendix 2) from 1 January to 28 September 2009. 587 pandemic A(H1N1) viruses (69%, 587/931) were isolated, antigenically closely related to A/California/7/2009 (H1N1)v-like strain. 228 (24%, 228/931) of isolates were A(H3N2) viruses with some antigenically related to and some drifted away from A/Brisbane/10/2007-like strain. 94 (10%, 94/931) A(H1N1) viruses were isolated and H1 was antigenically similar to A/Brisbane/59/2007-like strain. Regarding oseltamivir-resistant viruses, one of 250 pandemic A(H1N1) viral isolates tested in NA enzyme inhibition assay showed that it was resistant to oseltamivir and two of 124 pandemic clinical specimens had the H275Y mutation known to confer resistance to oseltamivir. 36 out of 37 seasonal A(H1N1) viruses tested were oseltamivir-resistant.

- **Australian Sentinel Practice Research Network (ASPREN).** This system has GPs who report 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 2009 may be different from that of previous years. ILI presentations to General Practitioners were lower than 2007 and similar to the 2008 rates nationally

- **The emergency department surveillance**. About 49 emergency departments across New South Wales, 8 from Perth and 4 from South Australia participated in the survey. Western Australia emergency department surveillance indicated that influenza activity in 2009 was similar to that of 2007 but higher than that of 2008. New South Wales emergency department surveillance indicated that the 2009 influenza activity has been the highest since 2005

- **Absenteeism Survey**. Australia post conducts an absenteeism survey that consists of national employer of more than 30,000 people in all jurisdictions except NT. The absenteeism data is 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. Absenteeism rates in 2009 have been following the similar trends to those seen in 2007.

- **Death Certificate Survey**. The registered death certificates from the births, deaths and marriages office in New South Wales indicated that influenza and pneumonia deaths in 2009 was lower than 2007.

- **Australian Paediatric Surveillance**. Report on hospital admissions of children aged 15 years and under to Intensive Care Units (ICUs) around Australia following complications due to influenza infection was initiated at the start of June 2009 through the Australian Paediatric Surveillance Unit (APSU). Details of admissions are reported on a weekly basis. In 2009, 124 children have been reported as hospitalised with complications from influenza by APSU. Of the 89 cases, for which data are available, the average age of children admitted to hospital is four years and five months, with an age range from one month to 16 years. Complications were mostly for pneumonia and encephalitis. Thirty-three of the 82 (40%) cases for which data is available had underlying conditions.

(Abridged from a report by Dr Andrea Forde, Department of Health and Ageing, Australia and a report by Dr. Ian Barr, WHO Collaborating Centre for Influenza, Melbourne.)

1.2.2. South Africa

Influenza surveillance in South Africa has been expanded significantly during 2009 and now includes 3 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 9 provinces. This programme focuses on mild infections seen mainly by general practitioners 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 hospitalized patients. This programme includes 11 hospitals covering all 9 provinces and focuses on hospitalised patients with Severe Acute Respiratory-tract Infection (SARI) across the country.

- **SARI surveillance programme** - in 2009 the SARI surveillance programme was established which monitors cases of more severe disease in hospitalised patients. Detailed epidemiologic data are collected on all patients. This programme currently includes 3 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 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 2009, a total of 7108 suspected influenza specimens were processed for which influenza A was detected in 2022 specimens and influenza B in 112 with an isolation rate of 30%. In South Africa, sporadic cases of influenza B were first detected in week 12 and 13 but disappeared again until week 23 when case numbers again began to increase peaking in week 32 and continuing through week 36. In total there were 112 influenza B cases to date (table 1). The first influenza A H3N2 isolates were detected in week 18 and peaked in week 24 with 205 isolates in this week, trailing through to week 35 with a total of 1052 isolates. Only 8 cases of seasonal H1N1 were detected this year from week 22-29.

The first cases of the pandemic influenza A H1N1 virus were detected in week 25 with a number of imported cases in travelers. In the first cases of community circulation were identified in week 27 and transmission is ongoing. Most cases were detected in week 32, but the decrease in detected cases in the following weeks may be due to a change in the testing strategy from all cases to only severe or high risk cases. In total, 909 cases were detected up to week 36 through the active surveillance programmes and routine diagnostic services at National Institute of Communicable Diseases (NICD). A clear distinction can be seen between the seasonal influenza (H3N2) outbreak and the pandemic influenza A H1N1 outbreak resulting in 2 epidemic peaks this year. A national database of all laboratory confirmed cases of pandemic influenza A H1N1 identified by private and public sector laboratories in South Africa has been maintained at NICD since the start of the outbreak. There have been 11 254 laboratory confirmed cases reported by week 37, including 45 deaths. This is however likely an underestimation of the true number of cases. From mid August mainly moderate to severe cases were included in the database, due to a call to medical practitioners to stop testing mild cases.

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

2. INFLUENZA ACTIVITY IN NEW ZEALAND IN 2009

2.1. Overview

Influenza activity during the 2009 New Zealand winter was the second highest recorded in the past 18 years of surveillance. When the 2009 sentinel ILI consultation data were compared to 1992-2008 data, the 2009 cumulative incidence rate of 2241 per 100 000 was the second highest, following 3957 per 100 000 recorded in 1996. The 2009 average weekly consultation rate of 118.7 per 100 000 was the second highest, following 197 per 100 000 in 1996. The 2009 peak consultation rate of 287 per 100 000 was the second highest, following 624 per 100 000 in 1996. In addition, the 2009 influenza hospitalizations (988) were the highest recorded over the period of 1990-2009. The 2009 influenza mortality rate (0.40 per 100 000) was the third highest when compared to that of the 1997-2003 period.

Pandemic influenza A(H1N1)v was the predominant strain detected in New Zealand. This strain represented 56.7% (2746/4845) of all influenza viruses. The pandemic A(H1N1)v strain was antigenically and genetically homogeneous, closely related to the pandemic

A(H1N1)v vaccine candidate strain A/California/7/2009 (H1N1)v. All pandemic influenza A(H1N1)v strains (98) tested were sensitive to oseltamivir.

Among the seasonal influenza viruses, seasonal influenza A(H1N1) was the predominant strain. This strain represented 14.5% (703/4845) of all influenza viruses. All seasonal influenza A(H1N1) strains (53) tested were resistant to oseltamivir. Seasonal influenza A(H3N2) strain represented 1.6% (79/4845) of all influenza viruses. Only a small number of influenza B viruses (6) were detected, representing 0.1% (6/4845) of all influenza viruses.

Based on New Zealand's epidemiological, virological and serological data, as well as cost of vaccine and administration, inclusion of the pandemic (H1N1) 2009 strain in the 2010 seasonal influenza vaccines for the southern hemisphere, would offer an opportunity to achieve increased levels of immunity to pandemic as well as other seasonal influenza strains because:

- pandemic (H1N1) 2009 strain is more likely than the seasonal influenza A(H1N1) strain to predominate in 2010.
- recently published evidence indicates that a single dose of pandemic (H1N1) 2009 vaccine produces an adequate host immune response. This would suggest that it may now be feasible to include the pandemic (H1N1) 2009 strain in the seasonal influenza vaccines.
- other risk-benefit considerations (financial impact, public perceptions, and realities of many southern hemisphere countries with no vaccine manufacturers) support inclusion of the pandemic (H1N1) 2009 strain in the seasonal influenza vaccines.
- a decision to include the pandemic (H1N1) 2009 strain in the seasonal influenza vaccines would assist influenza awareness education and an increased uptake of seasonal influenza vaccine in New Zealand, as well as contribute to the overall global supply of the pandemic vaccines.

2.2. Epidemiology of the New Zealand 2009 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.

New Zealand has made pandemic (H1N1) 2009 a notifiable and quarantineable disease. Seasonal influenza is not a notifiable disease in New Zealand.

2.2.1. Notifiable disease surveillance

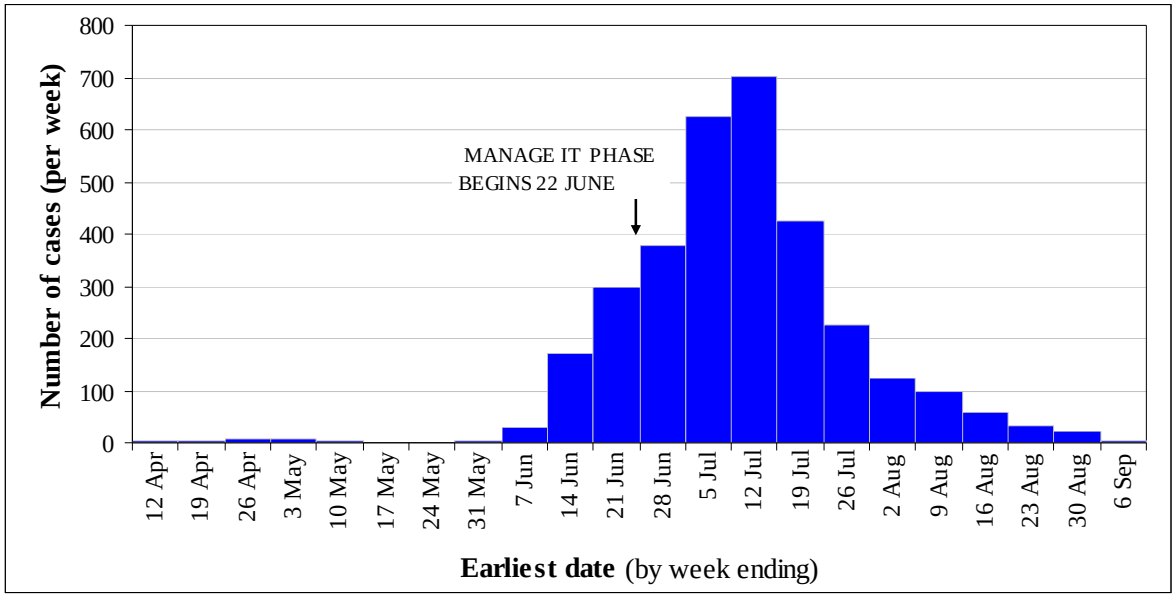
Pandemic (H1N1) 2009 was made a notifiable disease on 30 April 2009. Data are entered into a national web-based database (EpiSurv) operated by the Institute of Environmental Science and Research (ESR) and available for immediate analysis. This system also records hospitalized and fatal cases.

On April 25 2009, New Zealand was the first country in the southern hemisphere to report importation of pandemic influenza A(H1N1) 2009 infection, following the return of an airline flight containing a group of high school students who had travelled in Mexico. A concerted containment effort (e.g. screening arriving airline passengers for ILI, case isolation, quarantine of contacts, and treatment with oseltamivir) by the government, public health officials, border officials, hospitals, primary-care workers and laboratories appeared to delay

establishment of community transmission for several weeks. New Zealand entered its management phase on June 22 after sentinel and nonsentinel surveillance data indicated that 2009 pandemic influenza A(H1N1) had established sustained community transmission.

As of 6 September 2009, a total of 3219 confirmed and probable cases of pandemic (H1N1) 2009 were reported in EpiSurv. The epidemic curve is shown in Figure 1. This epidemic curve was constructed using the earliest date recorded in EpiSurv (onset, hospitalised or report date) and is displayed as cases per week since 6 April 2009. For the purposes of this epidemic curve confirmed and probable cases were combined.

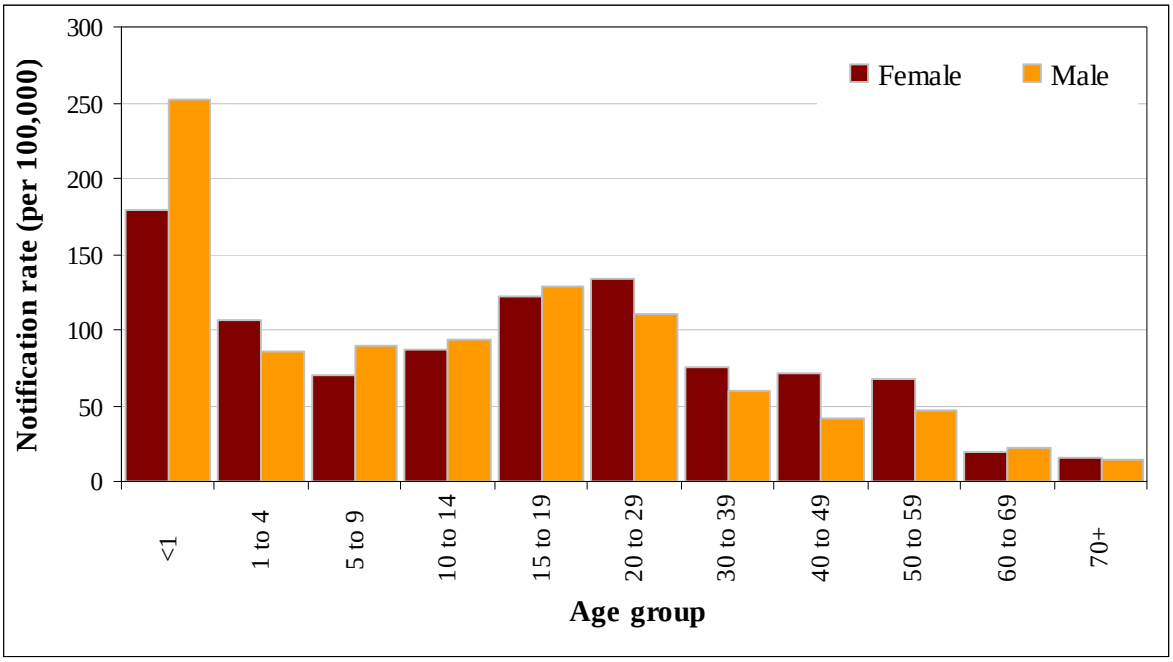
Figure 1. Total cases of pandemic (H1N1) 2009



Confirmed cases n=3150, probable cases n=69

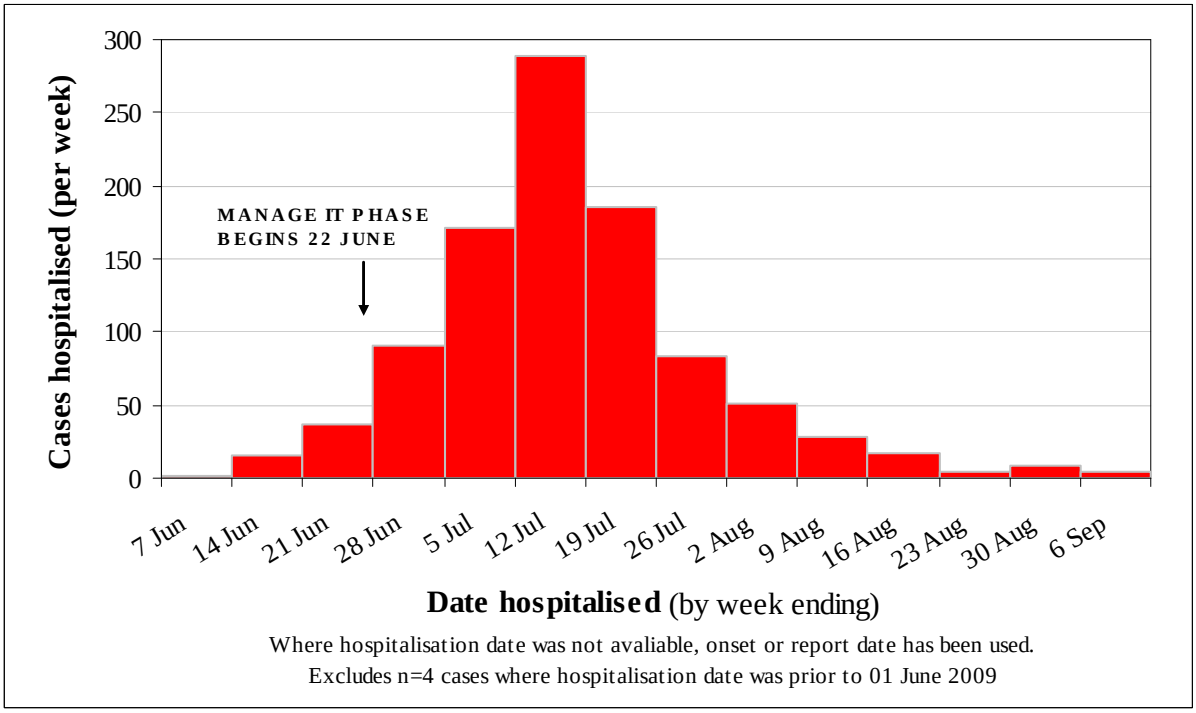
The age standardized rate for cases reported in New Zealand was 75.4 per 100,000. The actual rate is likely to be much higher as only a small proportion of people with symptoms are being tested. The age distribution of cases by gender is shown in Figure 2. The highest reported notification rate for last week was in the under one year old age group followed by persons aged 15-29 years old.

Figure 2 Cumulative rate of pandemic (H1N1) 2009 cases by age and sex



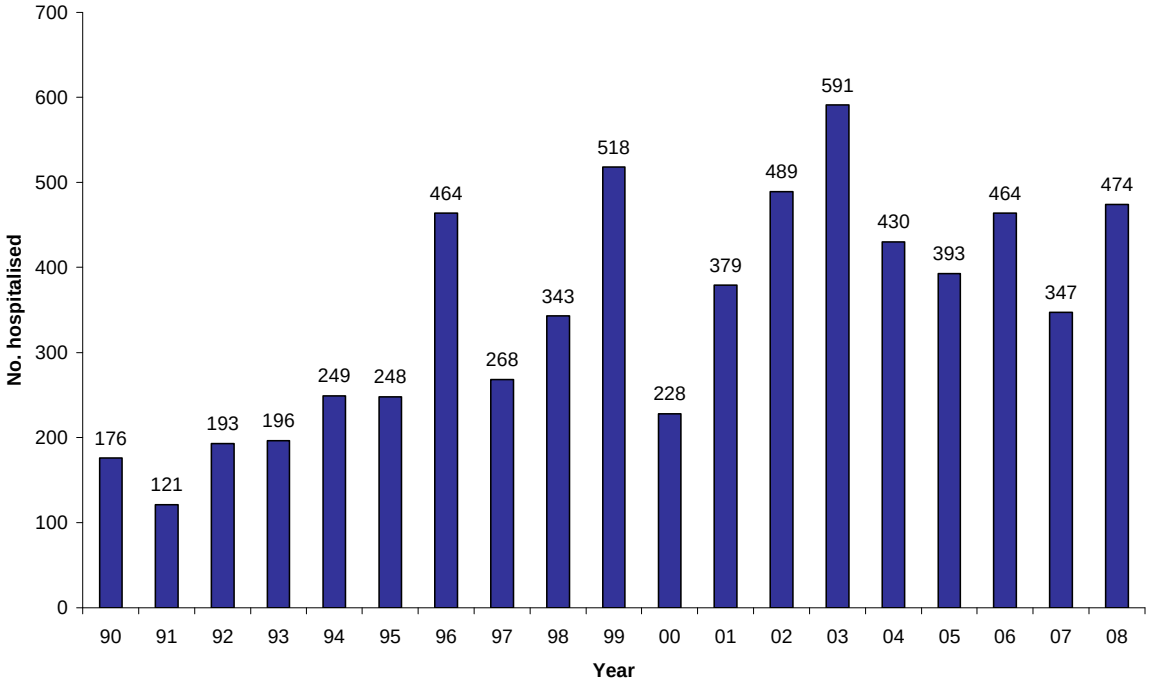
The number of hospitalized cases (as recorded in EpiSurv) since 1 June 2009 is shown in Figure 3. A total of 988 hospitalized cases were reported with the peak of hospitalization occurring in week 28 (July 6-12). Pneumonia was recorded for 300 cases and acute respiratory distress syndrome (ARDS) for 46 cases.

Figure 3 Hospitalised cases of confirmed pandemic A(H1N1) 2009



The 2009 influenza hospitalizations (988) recorded in EpiSurv database were higher than influenza hospitalizations recorded during 1990-2008 (Figure 4).

Figure 4 Influenza hospitalizations, 1990-2008



(Note: Hospital admission data during 1990-2008 for influenza (International Classification of Diseases, ninth revision (subsequently changed to 10th revision), Clinical Modification, ICD-9CM 487 or ICD-10AM J10-J11) was obtained from the New Zealand Health Information Service's National Minimum Dataset (NMDS). Influenza-related hospitalisations were conservatively taken to include only those where influenza was the principal diagnosis.)

Hospitalised cases (N = 193) from the report period 20 July-06 September 2009 were used to identify the risk factors. Chronic respiratory conditions were present in 49.5% of cases for which the information was supplied. Pregnancy information was only reported for females who had answered the question (N = 109). The high proportion of cases with unknown risk factor information should be taken into account in any interpretation of these results.

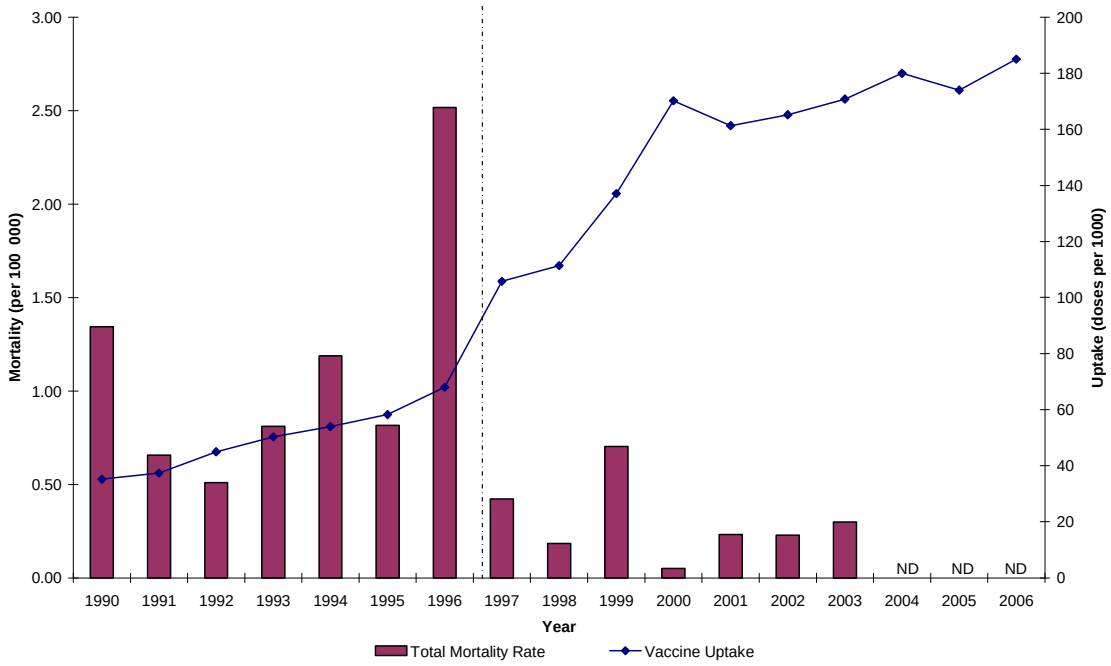
Table 1 : Underlying pre-existing medical conditions or other risk factors for hospitalised cases of pandemic influenza (H1N1) 09[1]

	Yes	Yes (%[2])	No	Unknown	Unknown (%[3])
Cardiac disease	7	8.6	74	112	58.0
Chronic respiratory conditions	47	49.5	48	98	50.8
Diabetes mellitus	11	12.6	76	106	54.9
Haemoglobinopathies	1	1.3	75	117	60.6
Immunosupression	15	18.5	66	112	58.0
Metabolic diseases	4	5.3	72	117	60.6
Morbid obesity	10	12.3	71	112	58.0
Neurological	5	6.5	72	116	60.1
Pregnancy	7	13.7	44	58	53.2
Renal failure	2	2.5	77	114	59.1
Aged care facility resident	3	2.5	116	74	38.3
Contact with infants / children	30	44.8	37	126	65.3

[1] Table includes 193 cases reported between 20/07/09 and 06/09/09 inclusive. Questions relating to pre-existing medical risk factors were only added to the EpiSurv case report form released on 10 July 2009.
[2] Percentage of cases that answered "yes" out of the total number of cases for which the information was supplied.
[3] Percentage of all cases for which the response was 'unknown' or the information was not supplied.

Thirty four deaths have been reported in EpiSurv among pandemic (H1N1) 2009 cases in New Zealand. Of these cases, seventeen were confirmed to have pandemic (H1N1) 2009 virus as the primary cause of death. This gave rise to the mortality rate of 0.40 per 100 000 for 2009. When people have pandemic (H1N1) 2009 virus at the time of death, and it is unclear if it led to the death, normal pathology and testing procedures are carried out. Investigations are continuing on the remaining reported deaths listed in EpiSurv, and it is likely that over time at least some will be added to the number of confirmed deaths due to pandemic (H1N1) 2009 virus, and hence the mortality rate will rise further. The 2009 influenza mortality rate was compared to that of 1990-2003 (Figure 5). It is noted that the 2009 mortality rate was lower than that of the 1990-1996 pre-vaccination period. The 2009 mortality rate was the third highest when compared to that of the 1997-2003 vaccination period. The first (0.7 per 100 000) and second (0.42 per 100 000) highest mortality rates during the vaccination period were recorded in 1999 and 1997 respectively.

Figure 5 Influenza mortality rates, 1990-2003



(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.)

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 24 health districts. Surveillance is conducted during May–September (the southern hemisphere winter) by volunteer sentinel GPs 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. National ILI consultation rates are calculated weekly using the sum of the GP patient populations as the

denominator. Because 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.

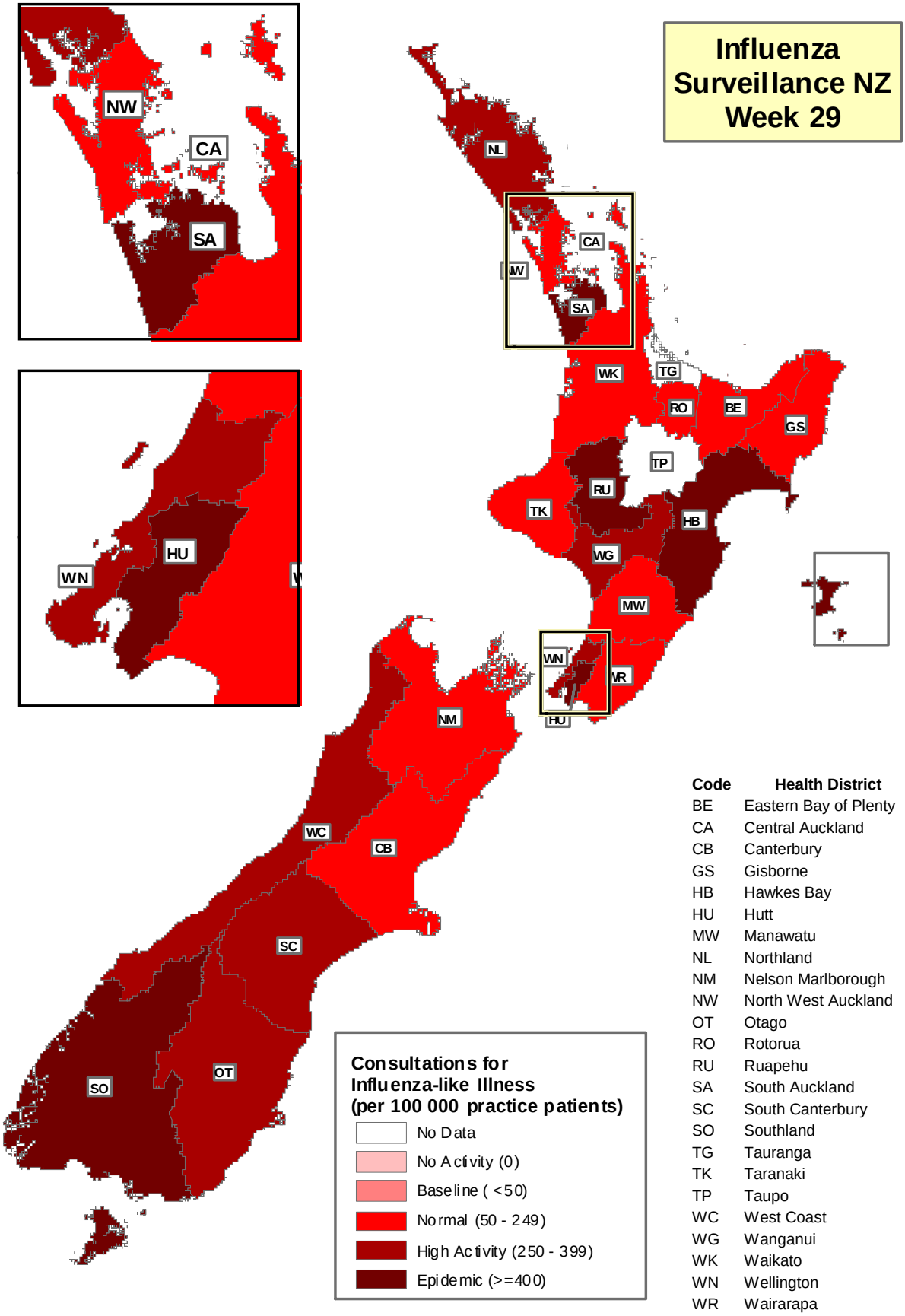
Each participating GP also collects three respiratory samples (i.e., nasopharyngeal or throat swab) each week from each of the first ILI patients examined on Monday, Tuesday, and Wednesday. The GPs forward these samples to the WHO National Influenza Centre at ESR or to hospital virology laboratories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

Sentinel GP surveillance started in May 2009. A total of 101 sentinel GPs were recruited, representing all of the country's 24 health districts and with a combined patient population of 487,131, approximately 12.1% of the New Zealand population. From week 18 (the week ending May 3) through week 36 (the week ending September 6), a total of 8,747 consultations for ILI were reported from the 24 health districts. It is estimated that ILI resulting in a visit to a general practitioner affected over 90,274 New Zealanders. The cumulative incidence of ILI consultation during this period was 2,241.2 per 100,000 population. The average weekly ILI consultation rate during this period was 118.7 per 100 000 population.

As in previous years, 2009 consultation rates for ILI varied greatly among health districts during the study period. Figure 6 shows ILI consultations among health districts during the peak week 29 (July 13-19). Ruapehu had the highest consultation rate (1114.6 per 100 000, 25 cases), followed by Southland (811.1 per 100 000, 72 cases) and Hawke's Bay (595.8 per 100 000, 117 cases).

Weekly national ILI consultation rates for the study period were compared with the same period in 2008 and 2007. From week 18 (the week ending May 3, 2009) through week 23 (June 1-7, 2009), the weekly ILI consultation rate remained below the baseline level of 50 consultations per 100,000 patient population (Figure 7). The ILI rate first crossed the baseline level in week 24 (June 8–14) and increased sharply from week 25 (June 15-21) to week 28 (July 6-12). The ILI consultation rate peaked at 287 consultations per 100,000 patient population in week 29 (July 13-19), approximately three times the peak rate of 95 consultations recorded in 2008. In fact, consultation rates for ILI in New Zealand in 2009 have been the highest observed since 1997 (Figure 8) and the second highest observed since 1992 (Figure 8). Since the week 30 (July 20-26), the influenza activity has been declining.

Figure 6. ILI consultation rates by health district for the peak week 29 (July 13-19)



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

Figure 7. Weekly Consultation Rates for Influenza-like Illness in New Zealand, 2007, 2008, 2009

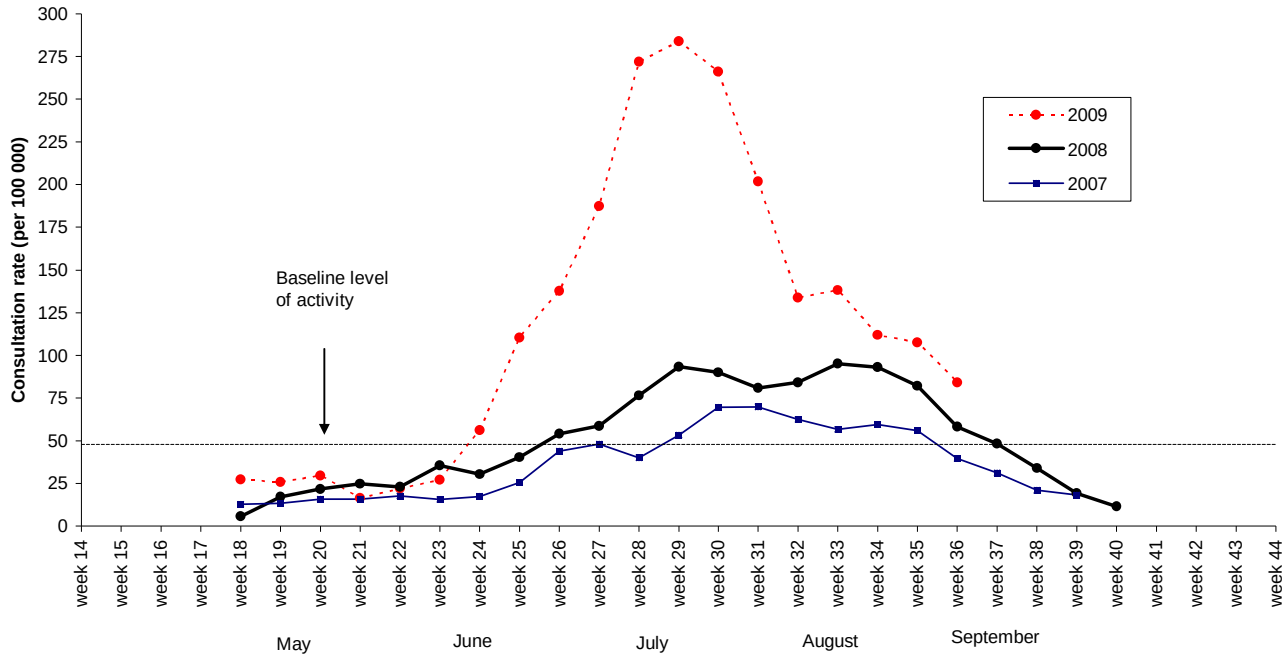
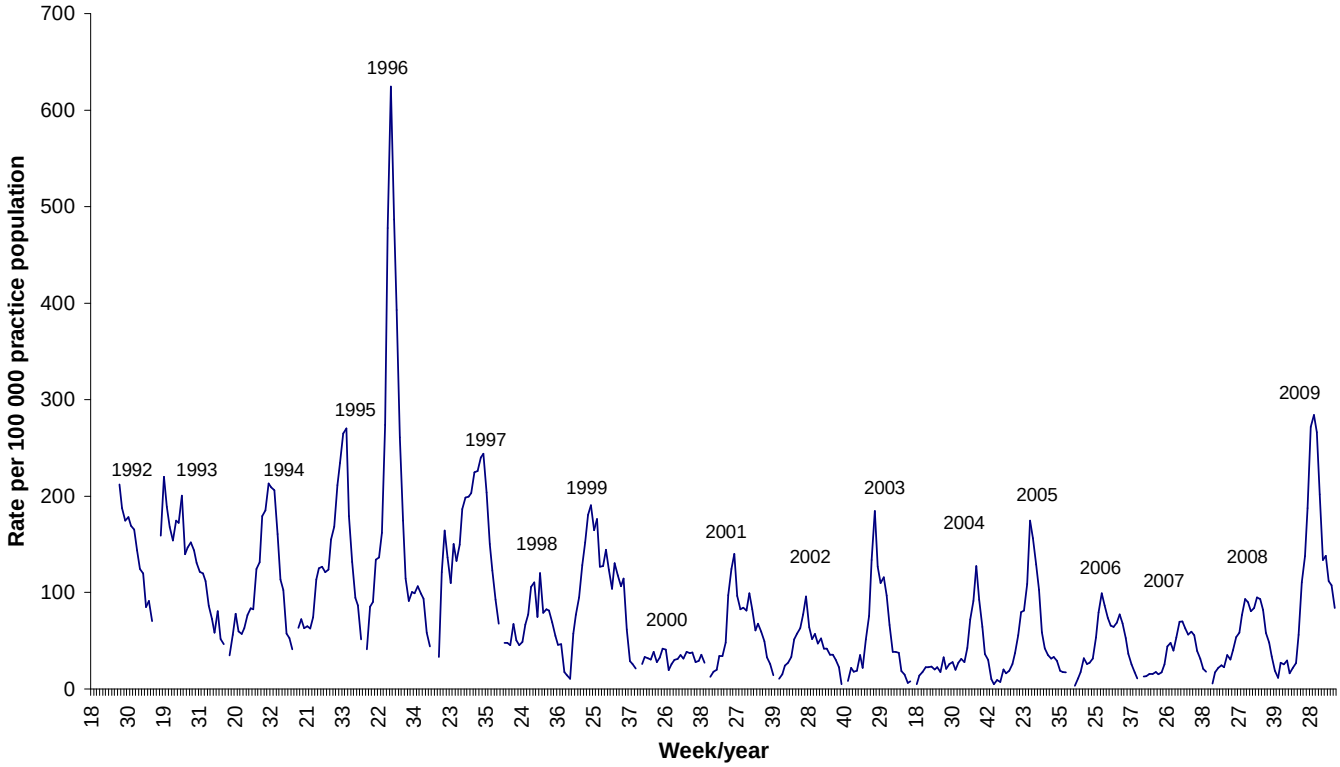


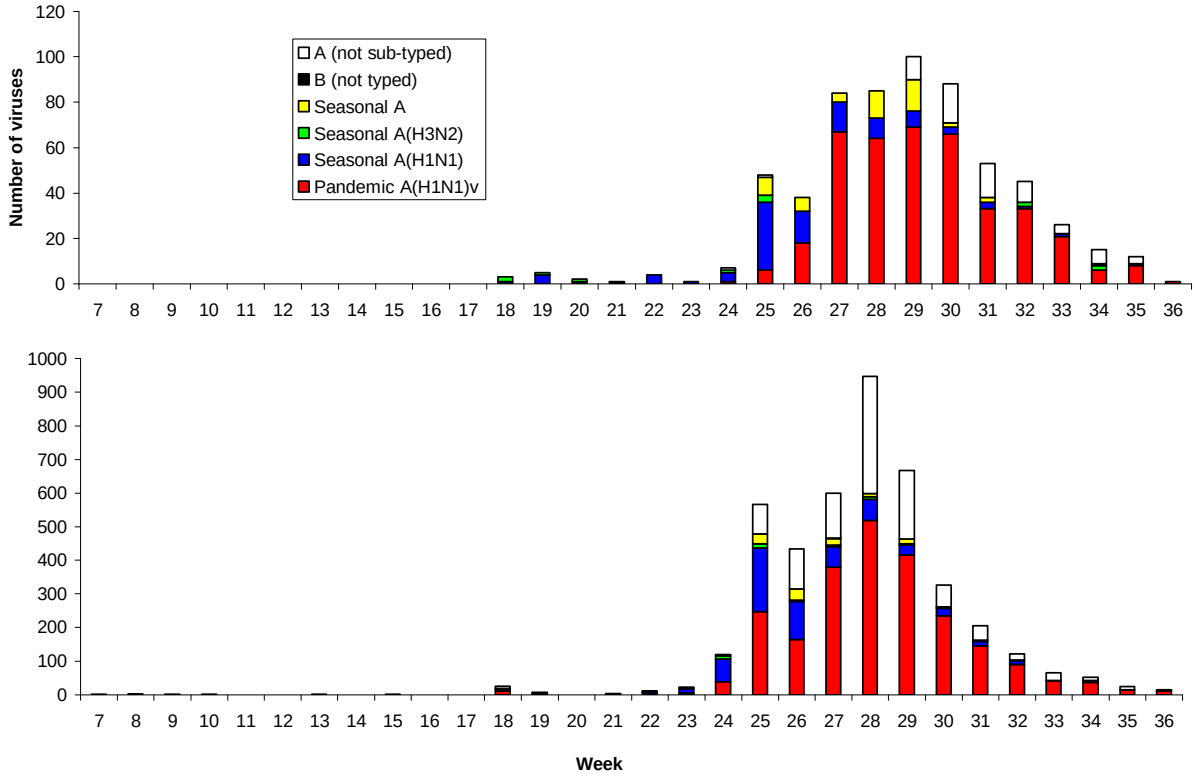
Figure 8. Weekly Consultation Rates for Influenza-like Illness in New Zealand, 1992-2009



During the study period, the highest ILI consultation rates were recorded among children and youths aged ≤19 years. Children aged 1–4 years had the highest ILI consultation rate (245.4 per 100,000 age group population), followed by infants aged <1 year (217.0), and persons aged 5–19 years (133.1), 20–34 years (128.3), 35–49 years (92.2), 50–64 years (77.0) and ≥65 years (31.6).

A total of 2,425 swabs were sent to virology laboratories from sentinel GPs during the study period. From these swabs, 618 influenza viruses were identified. The predominant strain was pandemic (H1N1) 2009 (393) including 125 of pandemic influenza A/California/7/2009 (H1N1)v-like strains, followed by seasonal influenza A (H1N1) (96) including 23 of A/Brisbane/59/2007 (H1N1) – like strains, influenza A not subtyped (66), seasonal influenza A (48), seasonal influenza A (H3N2) (12), and influenza B not typed (3) (Figure 9). The percentage of viruses identified as pandemic (H1N1) 2009 increased from 14% during week 24 (June 8–14) to 80% during week 27 (June 29–July 5).

Figure 9 Number of influenza viruses reported by type and week from sentinel and non-sentinel surveillance



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 from mainly hospital in-patient and outpatients during routine viral diagnosis. In addition, this laboratory network conducted pandemic (H1N1) 2009–related public health surveillance among arriving travellers and the contacts of patients with confirmed pandemic (H1N1) 2009 influenza. During the containment phase (April 25–June 21), when New Zealand public health officials tried to contain transmission from arriving travellers to their close contacts and prevent spread into

the wider community, respiratory samples were collected from most persons with suspected pandemic (H1N1) 2009 influenza. However, during the management phase (June 22 to August 2), when public health officials tried to mitigate the impact of sustained community transmission of the pandemic (H1N1) 2009 virus, the sampling priority was limited to persons with moderate or severe illness or who were vulnerable to severe illness.

A total of 4,227 influenza viruses were reported from the non-sentinel laboratory surveillance network from week 1 (the week ending 4 January 2009) to week 36 (September 1-6). The predominant strain was pandemic (H1N1) 2009 (2353) including 181 of pandemic influenza A/California/7/2009 (H1N1)v-like strains, followed by influenza A not yet subtyped (1086), seasonal influenza A (H1N1) (607) including 100 of A/Brisbane/59/2007 (H1N1) – like strains, seasonal influenza A (111), seasonal influenza A (H3N2) (67) including two A/Brisbane/10/2007 (H3N2) – like strains, and influenza B not typed (3) (Figure 9). The percentage of viruses identified as pandemic (H1N1) 2009 increased from 22% during week 23 (June 1-7) to 63% during week 27 (June 29–July 5).

2.3. Recent strain characterisations

2.3.1. Circulating strains in 2009 in New Zealand

A total of 4845 influenza viruses were detected from sentinel and non-sentinel surveillance in 2009 from weeks 1 to 36 (Figure 10). Table 2 shows influenza virus detections by type and subtype for weeks 1 to 36.

Figure 10. Total Influenza viruses by Type and Week Specimen Taken, 2009

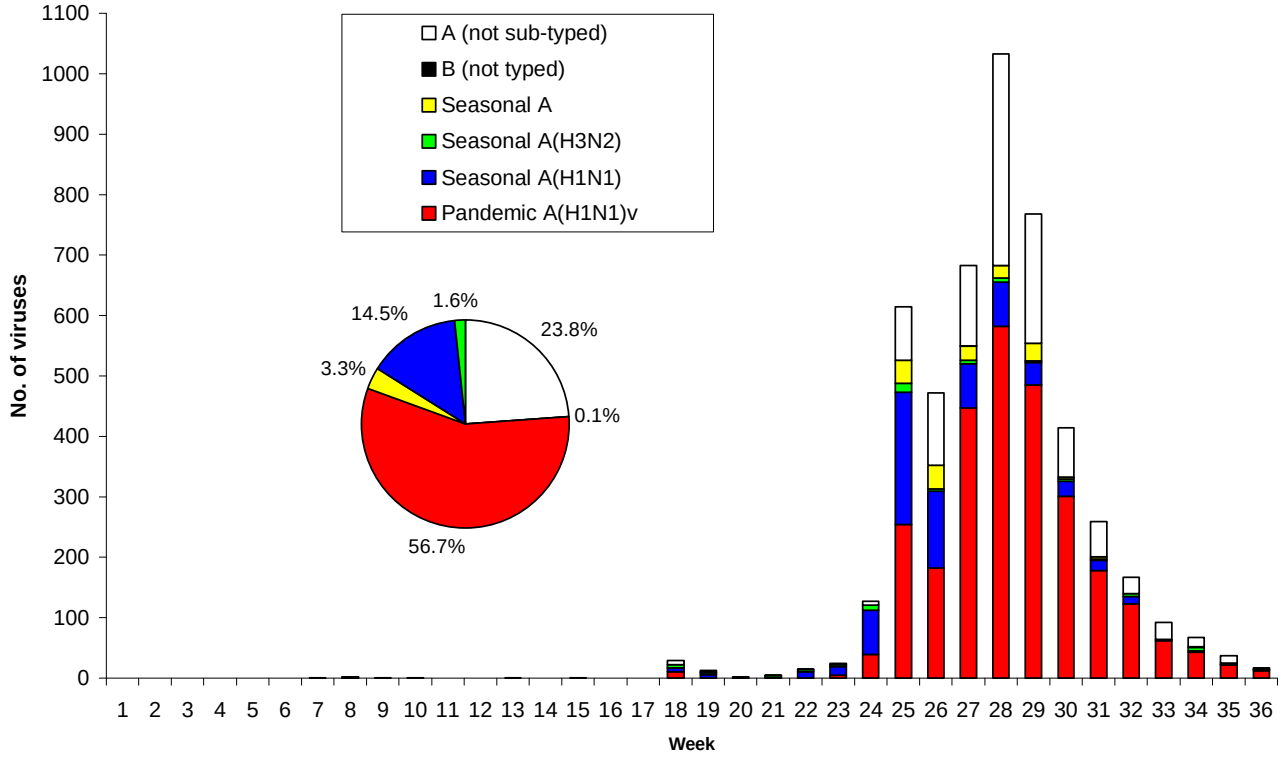


Table 2. Influenza viruses by type and subtype, 2009

Virus	All viruses n=4845 (%)	Typed/Subtyped n= 3534 (%)
Influenza A		
Influenza A (not sub-typed) by PCR	1152 (23.8)	
Seasonal influenza A by PCR	159 (3.3)	
Pandemic A(H1N1)v		
Pandemic A(H1N1)v by PCR	2440 (50.4)	2440 (69.0)
A/California/7/2009 (H1N1)v-like	306 (6.3)	306 (8.7)
Subtotal pandemic A(H1N1)v	**2746 (56.7)**	**2746 (77.7)**
Seasonal Influenza A(H1N1)		
Seasonal Influenza A(H1N1) by PCR	580 (12.0)	580 (16.4)
A/Brisbane/59/2007 (H1N1) - like	123 (2.5)	123 (3.5)
Subtotal seasonal A(H1N1)	**703 (14.5)**	**703 (19.9)**
Influenza A(H3N2)		
Influenza A subtype H3N2 by PCR	77 (1.6)	77 (2.2)
A/Brisbane/10/2007 (H3N2) - like	2 (0.04)	2 (0.06)
Subtotal seasonal A(H3N2)	**79 (1.6)**	**79 (2.2)**
Influenza B		
Influenza B by PCR	6 (0.1)	6 (0.2)
Subtotal B	**6 (0.1)**	**6 (0.2)**
Total	**4845 (100)**	**3534 (100)**

Overall, pandemic A(H1N1)v was the predominant strain among all influenza viruses. The pandemic A(H1N1)v strain represented 56.7% (2746/4845) of all viruses and 77.7% (2746/3534) of all typed and subtyped viruses.

Seasonal influenza A(H1N1) was the predominant strain among all seasonal influenza viruses. It represented 74.2% (703/947) of all seasonal influenza viruses, 14.5% (703/4845) of all viruses and 19.9% (703/3534) of all typed and subtyped viruses.

Seasonal influenza A(H3N2) strain represented 8.3% (79/947) of all seasonal influenza viruses, 1.6% (79/4845) of all viruses and 2.2% (79/3534) of all typed and subtyped viruses.

A very small number of influenza B viruses (6) were detected. Influenza B strain represented 0.6% (6/947) of all seasonal influenza viruses, 0.1% (6/4845) of all viruses and 0.2% (6/3534) of all typed and subtyped viruses.

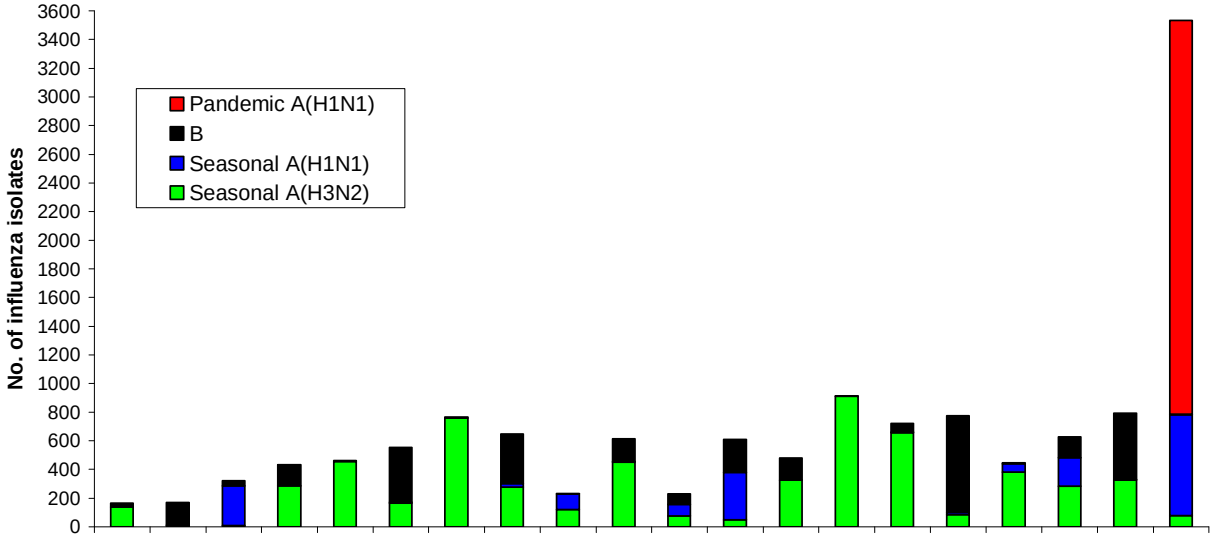
2.3.2. Predominant strains during 1990-2009 in New Zealand

Figure 11 shows the number and percentage of typed and subtyped (not total) influenza viruses from 1990 to 2009. The noticeable changes in terms of predominant patterns are described below:

- Pandemic A(H1N1)v strain has become the predominant strain in 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 hospitalizations during 1990-2008. A A/Wuhan/359/95 (H3N2)-like strain predominated in 1996 with associated 94 deaths (93 out 94 deaths occurred for people aged 65+).
- 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 3 children.

Figure 11. Influenza viruses by type, 1990-2009



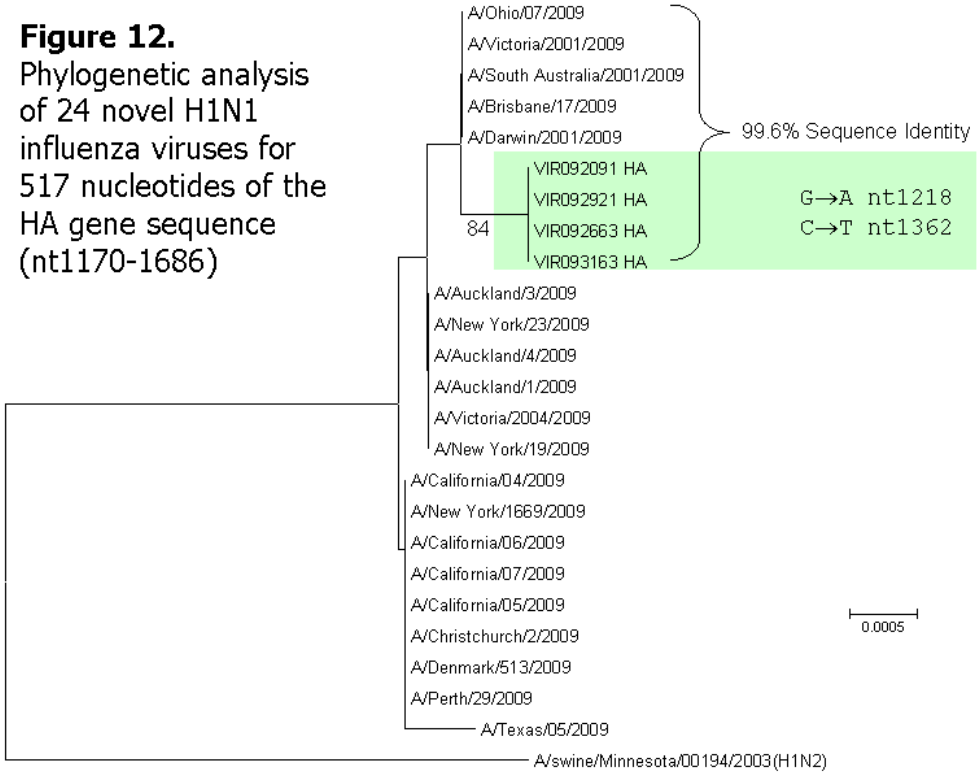
	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
Seasonal A(H1N1)	1%	8%	86%	0%	0%	1%	0%	4%	47%	0%	36%	54%	0%	0%	0%	2%	13%	32%	1%	20%
Seasonal A(H3N2)	83%	0%	3%	66%	99%	30%	99%	43%	52%	74%	33%	8%	68%	100%	91%	11%	86%	45%	41%	2%
B	16%	92%	11%	34%	1%	69%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

2.3.3. Pandemic influenza A(H1N1)v

Representative pandemic influenza A(H1N1)v isolates (306) were antigenically subtyped at the WHO National Influenza Centre at ESR using ferret antisera supplied by the WHO Collaborating Centre (WHOCC) in Melbourne. Some of these isolates were also sent to WHOCC-Melbourne and WHOCC-CDC-Atlanta. Results from these centres all indicated that New Zealand isolates were homogeneous and no drift was observed. New Zealand isolates were antigenically closely related to the pandemic A(H1N1)v vaccine candidate strain A/California/7/2009 (H1N1)v.

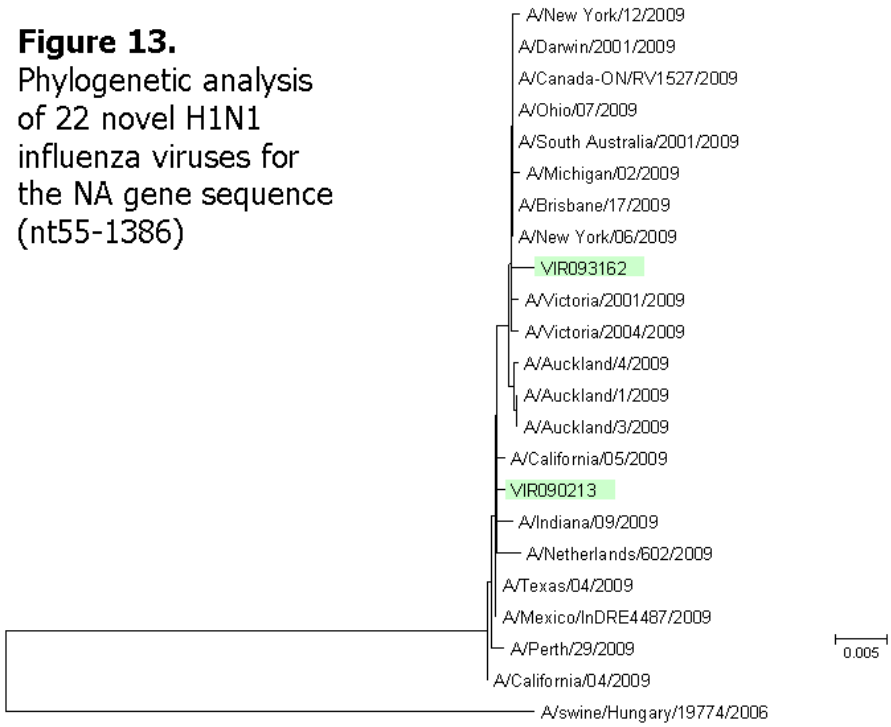
Genetic analysis of the hemagglutinatin (HA) gene of representative pandemic A(H1N1)v showed that the New Zealand isolates were homogeneous and stable (Figure 12). Genetic analysis of the neuraminidase (NA) gene of representative pandemic A(H1N1)v showed that the New Zealand isolates were also homogeneous and stable (Figure 13). No H275Y mutations were detected, suggesting they were sensitive to oseltamivir.

Figure 12.
Phylogenetic analysis of 24 novel H1N1 influenza viruses for 517 nucleotides of the HA gene sequence (nt1170-1686)



Neighbour Joining Tree ; Bootstrap consensus (1000 replicates) ; Maximum Composite Likelihood Model; compiled in MEGA4. Only bootstrap values greater than 50% are shown.

Figure 13.
Phylogenetic analysis of 22 novel H1N1 influenza viruses for the NA gene sequence (nt55-1386)



Neighbour Joining Tree ; Bootstrap consensus (1000 replicates) ; Maximum Composite Likelihood Model; compiled in MEGA4. Only bootstrap values greater than 50% are shown.

2.3.4. Seasonal influenza A(H1N1)

Representative seasonal influenza A(H1N1) isolates (123) 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 and WHOCC-CDC-Atlanta. Results from these centres all indicated that New Zealand isolates were antigenically closely related to the reference strain A/Brisbane/59/2007 (H1N1).

Genetic analysis of the neuraminidase (NA) gene of representative seasonal influenza A(H1N1) strains showed that all New Zealand isolates tested had H275Y mutations, suggesting they were resistant to oseltamivir.

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 closely related to the reference strain A/Brisbane/10/2007 (H3N2).

2.3.6. Influenza B

Of four influenza B PCR positive samples, viral culture was attempted for two samples without recovery at the WHO National Influenza Centre at ESR. The viral culture for the remaining two influenza B samples is still ongoing and will be forwarded to WHOCC-Melbourne.

2.3.7. Oseltamivir resistance

The WHO National Influenza Centre at ESR has established a phenotypic method (fluorometric neuraminidase inhibition assay) for the surveillance of anti-viral drug resistance in influenza viruses. In addition, NIC 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.

Since January 2008, a global emergence and rapid spread of oseltamivir-resistant seasonal influenza AH1N1 viruses has been observed. During the 2009 winter season in New Zealand, a total of 28 seasonal AH1N1 viruses have been tested for the H275Y mutation (histidine-to-tyrosine mutation at the codon of 275 in N1 numbering) which is known to confer resistance to oseltamivir. All 28 viruses had the H275Y mutation. In addition, a total of 25 seasonal AH1N1 viruses were tested using a phenotypic assay called fluorometric neuraminidase inhibition assay. The results of the fluorometric neuraminidase inhibition assay indicated that these viruses had highly reduced sensitivity to oseltamivir with IC50 values in the range of 305-7912 nM, typical of the recently global emerging oseltamivir-resistant A(H1N1) viruses. (Table 3).

Six pandemic influenza A(H1N1)v viruses were sequenced to see whether they possess the H275Y mutation. Among these viruses, three were from samples collected in June 2009 and another three viruses were from samples collected in late April 2009. All six viruses did not possess the H275Y mutation. This indicates that these novel influenza AH1N1 viruses are

sensitive to oseltamivir. In addition, a total of 92 novel influenza AH1N1 09 viruses were tested using the phenotypic assay and all 92 viruses were sensitive to oseltamivir with IC50 values in the range of 0.2 to 0.7 nM (Table 3).

Table 3: Antiviral susceptibility to oseltamivir for influenza AH1N1 viruses in New Zealand from 2006 to 2009.

Influenza type/subtype	***Seasonal AH1N1***				***Novel AH1N1***
Year	2006	2007	2008	2009	2009
Number of viruses	17	138	4	25	92
Mean IC50*	1.84	0.83	728	1399	0.372
Std. dev.	0.71	0.63	136	1990	0.145
Min IC50	0.25	0.01	547	305	0.183
Max IC50	3.099	4.219	870	7912	0.745

**IC50: Concentration of oseltamivir (nM) at which there is 50% inhibition of neuraminidase activity.*

In addition, influenza viruses detected from sentinel and non-sentinel surveillance from a period of 2006 to Jan 2009 have been tested for oseltamivir resistance. Viral isolates from the New Zealand population, collected in 2006 (n=212) and 2007 (n=312) and 2008 (n=245) from the national surveillance program were assayed for susceptibility to oseltamivir (see Table 4).

Table 4: Antiviral susceptibility to oseltamivir during 2006 to Jan 2009 in New Zealand

Influenza type/subtype (neuraminidase)	***Seasonal AH1N1***			***Seasonal AH3N2***			***Influenza B***		
Year	2006	2007	2008-2009 Jan	2006	2007	2008	2006	2007	2008
Number of viruses	17	138	**5**	193	45	107	2	129	134
Mean IC50	1.839	0.8298	*****	0.68	0.43	0.3	34.2	33.97	32.9
Std. dev.	0.7136	0.6295	*****	0.23	0.31	0.3	11.41	16.42	20.2
Min IC50	0.2538	0.0054	**547**	0.22	0.07	0.0	26.13	0.898	0.2
Max IC50	3.099	4.219	**946**	1.36	1.59	2.3	42.27	71.04	104.6
Max Fold Increase	1.7	5.1	**1140**	2.0	3.7	7.1	1.2	2.1	3.2

(*Note: insufficient data for seasonal AH1N1 in 2008-9 to derive a mean and standard deviation value and the 2007 mean was used to give an indication.)

During 2006-2007, all influenza 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 neuraminidase inhibition assay indicated that the four viruses had highly reduced sensitivity to oseltamivir with IC50 values in the range of 500-1700 nM, typical of the recently global emerging oseltamivir-resistant A(H1N1) viruses. Genetic analysis of the neuraminidase gene confirmed that the four viruses had the H275Y mutation (histidine-to-tyrosine at codon 275 in N1 nomenclature), conferring resistance to oseltamivir. These four viruses were isolated from patients aged 2-month-old male infant (1), 15-year-old female (1) and 49-year-old female (2). None of the patients or their close contacts had received Tamiflu prior to sample collection. In January 2009, one seasonal A(H1N1) virus resistant to oseltamivir was identified from a 48 year old male on 22 Jan 2009. The WHO National Influenza Centre at ESR has reported the findings to the WHO.

2.4. Inclusion of the pandemic (H1N1) 2009 strain in the 2010 seasonal influenza vaccines New Zealand perspectives

The biggest challenge for this year's seasonal vaccine recommendation is the question: should the pandemic (H1N1) 2009 strain be included in the seasonal vaccine composition?

2.4.1. Scientific evidence

The epidemiological data from the New Zealand 2009 influenza season indicate that the pandemic (H1N1) 2009 virus became the predominant circulating strain. The antigenic data from New Zealand isolates indicate that the current circulating pandemic (H1N1) 2009 viruses are homogeneous, closely matching the vaccine candidate strain A/California/7/2009 (H1N1)v. The limited serological study for New Zealanders conducted in WHOCC Melbourne and in NIC at ESR indicated that the pandemic (H1N1) 2009 virus does not cross-react with seasonal H1 viruses. This epidemiological, virological and serological data clearly suggests a need to have the pandemic (H1N1) 2009 strain to be included in the seasonal influenza vaccines.

In addition, the probability of the pandemic (H1N1) 2009 strain predominance for 2010 in New Zealand is much higher than seasonal H1 strain. This is based on:

- Historically, all four of the last global influenza pandemics have demonstrated wave patterns with intervals between waves of months to over a year. Three out of the four had second waves with significantly higher mortality than the first wave. Whilst there is no certainty about timing or severity, it is likely that there will be resurgence of pandemic H1N1 next winter, and the emergence of a mutated strain cannot be excluded.

- Should the pandemic influenza H1N1 virus mutate, the virus may become more transmissible, increase in severity, and/or become resistant to antivirals. These factors are subject to considerable uncertainty. A vaccine developed for the current pandemic influenza may provide some cross-protection against a mutated form of pandemic influenza depending on the degree of mutation.

- Whilst the level of infection and hence the level of acquired immunity across the New Zealand population is currently unknown, the transmissibility characteristics of the

pandemic strain, and indication of a relatively low level of infection in New Zealand (Nishiura, Baker and Wilson et al 2009: http://www.nzma.org.nz/journal/122-1299/3722/), support the models that indicate 10-20% of infection across the community. It is reasonable to assume that pandemic (H1N1) 2009 will return and result in sustained transmission at a moderate level and/or become the dominant strain again during the next flu season. The Ministry of Health of New Zealand is planning a sero-prevalence survey in order to gain more robust information on the level of infection and immunity within the community and within specific immunisation target groups.

- New Zealand's epidemiology for seasonal H1 strains indicated that there are only 3 predominant seasons (1992, 2000, and 2001) during the past 20 years from 1990 to 2009. Seasonal H1 strain is the predominant strain for all seasonal influenza viruses in 2009 in New Zealand. Based on this evidence, it would be less likely for seasonal H1 to be the predominant strain again for 2010.

2.4.2. Data on pandemic vaccine trials

In a fast evolving area of pandemic (H1N1) vaccine development, recent publications on pandemic (H1N1) vaccine trials at CSL (Greenberg et al, NEJM 2009;361:10.1056/ NEJMoa0907413), Novartis (Clark et al, NEJM-2009;361:10.1056/NEJMoa0907650) and Sinnvac (http://www.medicalnewstoday.com/articles/162395.php) reported that a single dose of pandemic (H1N1) 09 vaccine was immunogenic in human population. FDA also approved pandemic (H1N1) vaccines as a strain change to each manufacturer's seasonal influenza vaccine (http://www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm181971.htm). The one-dose schedule of the pandemic strain and regulatory approval would make it more feasible for the pandemic (H1N1) 2009 strain to be included in seasonal influenza vaccines.

2.4.3. Other risk-benefit considerations for southern hemisphere countries

- **Vaccine supply:**

New Zealand has supply arrangements in place for pandemic influenza vaccine. However, including the pandemic strain in the seasonal vaccine may enable increased production by allowing manufacturers to focus on producing the seasonal vaccine, to supply southern hemisphere countries.

- **Financial impact:**

If pandemic influenza is not included in the seasonal vaccine, a stand alone pandemic immunisation programme is being developed for New Zealand, but has not yet been agreed. Work to date suggests that a stand alone programme for pandemic influenza will require considerably more resources, than if it were included in an enhanced seasonal influenza programme. New Zealand has yet to complete an economic evaluation but that will be a consideration for government in reaching a decision on whether to approve a stand-alone programme additional to the seasonal immunisation programme.

Inclusion of the pandemic strain in the seasonal vaccine formulation appears likely to be less costly to deliver as well as to manufacture. Such cost-efficiency would be beneficial not only for New Zealand and other southern hemisphere countries, including Pacific countries.

- **Public perceptions:**

Inclusion of the pandemic strain in the seasonal vaccine formulation would be expected to increase the uptake of the seasonal influenza vaccine in New Zealand, increasing population immunity to both pandemic and seasonal influenza viruses. It will also likely provide greater uptake than a stand alone immunisation programme. Further, if monovalent pandemic vaccine and trivalent seasonal vaccines are both offered, there is the risk that there would be public resistance to receiving 2 different influenza vaccines, with resulting risks of a potential decrease of the uptake of the seasonal influenza vaccine. There may also be a public-perceived increased risk of adverse events associated with two injections instead of one injection.

- **Vaccine Manufacture in the Southern Hemisphere:**

Being a relatively small and isolated country, New Zealand, as well as a number of other southern hemisphere countries, face considerable challenges in securing sufficient vaccine in a timely manner. Geographically, Australia is the closest country with vaccine manufacturing capability.
Inclusion of the pandemic strain in the 2010 seasonal vaccine formulation would be a considerable advantage for countries that have no, or limited, access to pharmaceutical/biotechnology producers and/or limited purchasing power compared with larger countries.

2.5. Conclusion

Based on New Zealand's epidemiological, virological and serological data, as well as cost of vaccine and administration, inclusion of the pandemic (H1N1) 2009 strain in the 2010 seasonal influenza vaccines for the southern hemisphere, would offer an opportunity to achieve increased levels of immunity to the pandemic strain as well as other seasonal influenza strains because:

- pandemic (H1N1) 2009 strain is more likely than the seasonal influenza A(H1N1) strain to predominate in 2010.
- recently published evidence indicates that a single dose of pandemic (H1N1) 2009 vaccine produces an adequate host immune response. This would suggest that it may now be feasible to include the pandemic (H1N1) 2009 strain in the seasonal influenza vaccines.
- other risk-benefit considerations (financial impact, public perceptions, and realities of many southern hemisphere countries with no vaccine manufacturers) all favour inclusion of the pandemic (H1N1) 2009 strain in the seasonal influenza vaccines.
- a decision to include the pandemic (H1N1) 2009 strain in the seasonal influenza vaccines would likely assist influenza awareness education and an increased uptake of seasonal influenza vaccine in countries such as New Zealand, as well as contribute to the overall global supply of the pandemic vaccines.

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 shown to be responsible for outbreaks in Mexico in March and April. Outbreaks subsequently occurred in all regions of the world and, by July, pandemic A(H1N1) was the predominant influenza virus circulating in many countries in the Americas,
Asia, Europe and Oceania.

During the 2009 influenza season, 1146 pandemic influenza A(H1N1) isolates were received at the Melbourne WHOCC from 24 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 2746 pandemic influenza A(H1N1) viruses were detected in New Zealand in 2009. Of which 306 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 only 8% low reactors (≥fold reduction compared to homologous titre. CDC-Atlanta reported that 99% of their viruses were A/California/7/2009-like with only 2/801 (<1%) being classified as low reactors (Tables 3.1, 3.2 & 3.3 in Appendix 3). In addition, a total of 91 pandemic A(H1N1) viruses were sequenced in the HA-1 region of the haemagglutinin. The sequence analysis indicated that viruses were very similar with only minor variations with 1-2 amino acids difference compared to the A/California/7/2009 virus (Figure 3.2 in Appendix 3). The neuraminidase (N1) genes of the pandemic viruses were also sequenced, resulting in similar sequence to each other with only 1 or 2 amino acids difference (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. Geometric mean HI titres were lower to a recent seasonal A(H1N1) virus than to the vaccine virus (average reductions: 83%) (WER 83(41), and Table 3.10 in Appendix 3).

In summary, pandemic influenza A(H1N1) viruses became the predominant circulating strain in southern hemisphere countries. In HI tests, the majority of 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 epidemiological, antigenic, genetic and serological data, the WHO consultation recommended vaccines containing a A/California/7/2009 (H1N1)–like strain. The AIVC accepts this recommendation.

3.2. Seasonal influenza A(H1N1)

Influenza A(H1N1) subtype viruses, which re-emerged in 1977, closely resemble strains that circulated until 1956. Because of this, they initially had little impact in the older population. With further antigenic drift in the subtype, there has been evidence of increasing impact in the elderly.

Two antigenically distinct lines of influenza A(H1N1) have circulated in recent years and the current reference strains for these are A/New Caledonia/20/99 and A/Bayern/7/95. An A/New Caledonia/20/99-like strain has been selected as the A(H1) component for vaccine formulations since September 1999, initially because of the increasing incidence of this lineage and the fact that, in humans, vaccines containing viruses of this lineage were found to induce similar antibody responses against both the homologous virus and A/Bayern-like strains whereas the converse was not true. In the past few years, however, viruses with an A/New Caledonia/20/99 like haemagglutinin antigen have completely replaced A/Bayern/7/95-like strains.

During the 2009 influenza season, 315 seasonal influenza A(H1N1) isolates were received at the Melbourne WHOCC from 13 countries with most coming from New Zealand, Australia, Thailand. The virology laboratories in New Zealand use the kit supplied by the Melbourne WHOCC to analyse seasonal influenza A(H1N1) strains. The antiserum used for detecting seasonal influenza A(H1N1) was A/Brisbane/59/2007. 703 seasonal influenza A(H1N1) viruses were detected in New Zealand in 2009 and 123 of them were antigenically subtyped as A/Brisbane/59/2007-like strains.

Among all seasonal influenza A(H1N1) viruses analysed at the Melbourne WHOCC, most of viruses reacted well with ferret sera to A/Brisbane/59/2007 with only some low reactors. In addition, sequence analysis of the seasonal influenza A(H1N1) HA-1 region of the haemagglutinin indicated that viruses all fell into clade 2B with no clade 2C identified. Genetic groupings for the NA were similar to the HA genes with the same viruses falling into Clade 2B. Virtually all viruses sequenced had the oseltamivir resistance substitution of H275Y mutation.

In summary, seasonal influenza A(H1N1) viruses were associated with outbreaks only in a few southern hemisphere countries such as New Zealand. Pandemic A(H1N1) was the predominant circulating A(H1N1) strain in all southern hemisphere countries including New Zealand. The probability of the pandemic A(H1N1) strain predominance for 2010 in southern hemisphere is much higher than seasonal influenza A(H1N1) strain. Serologically, population immunity against pandemic A(H1N1) virus was relatively low. The WHO consultation recommended vaccines containing a pandemic influenza A/California/7/2009 (H1N1)–like strain as the H1 component of the seasonal influenza vaccines. The AIVC accepts this recommendation.

3.3. 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 the Australian Influenza Vaccine Committee (Table 1).

The Melbourne WHOCC has analysed 690 A(H3N2) isolates from 16 countries since January 2009. These viruses made up 28.5% of all viruses analysed at the Centre. Most (74%) of A(H3N2) viruses analysed over this period had reduced activity (8 fold or greater) to ferret sera against A/Brisbane/10/2007 (egg derived virus) and showed better HI titres against ferret sera raised to A/Perth/16/2009-like viruses. HI assays in Tables 5.1, 5.3, 5.4 and 5.5 (Appendix 4) were performed at the Melbourne WHOCC Centre. In addition, HA gene phylogenetic analysis of 2009 A(H3N2) viruses sequenced showed that most viruses were broadly A/Perth/16/2009-like. Viruses in this group had 4 signature amino acid changes at

K158N, N189K, E62K, N144K with some subclades with further changes (Y94H, R261Q or V213A). Sequence analysis of the N2 NA gene from 76 viruses analysed in 2009 showed that the most recent viruses grouped in a similar manner to their HA patterns with the majority having I215V change in the N2 as well as the K173Q change in their HA gene (Figures 5.2 and 5.3 in Appendix 4). Furthermore, vaccines containing influenza A/Brisbane/10/2007 (H3N2)-like antigens stimulated anti-HA antibodies of geometric mean HI titres that were lower to recent isolates than to the vaccine virus (average reductions: younger adults 67%; the elderly 70%). Similar results were obtained in microneutralization tests for a subset of sera (average reductions: younger adults 76%; the elderly 76%). (WER 84(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. The majority of isolates have drifted away antigenically from A/Brisbane/10/2007-like strain and were antigenically similar to A/Perth/16/2009-like strain. Current vaccines containing the A/Brisbane/10/2007 antigen stimulated anti-HA antibodies of geometric mean HI titres that were lower to recent isolates than to the vaccine virus. Based on all epidemiological, antigenic, genetic and serological data, the WHO Consultative Group recommended an A/Perth/16/2009 (H3N2)-like strain. AIVC accepts 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-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 2009. Varying proportions of the two lineages were seen in many countries with B/Yamagata lineage strains circulating in southern hemisphere countries. There were only 6 influenza B viruses detected in New Zealand in 2009.

166 influenza B isolates were received in 2009 at the Melbourne WHOCC from 10 countries (6.8% of total isolates). The majority of isolates (80.9%) were typed as B/Victoria lineage with the majority reacting well with ferret sera raised against egg grown B viruses of this lineage. 19.1% of B viruses were of B/Yamagata lineage and were generally poorly reactive with ferret sera to egg derived B/Florida/4/2006 virus and somewhat react better with ferret antisera against B/Bangladesh/3333/2007 virus. HI assays in Tables 6.1, 6.3, 6.4 were performed at the Melbourne Centre. In addition, sequence analysis of the HA1 gene of recent isolates showed that recent isolates fell into one of the 2 major lineages of B viruses (B/Victoria/2/87 or B/Yamagata/16/88). The B/Victoria lineage viruses mostly grouped either in the B/Brisbane/60/2008 group with signature amino acid changes at S172P, N75K, N165K, V146I, or with the older B/Malaysia/2506/2004-like viruses. Only one virus, B/Sydney/3/2009, fell into the B/Hubei Songzi/51/2008 – B/Fujian Gulou/1272/2006 clade of viruses previously circulating China. 2009 viruses sequenced from the B/Yamagata line fell into one of 3 groups; either B/Florida/4/2006-like (Group 1) with a change at G230S or B/Brisbane/3/2007-like (Group 2) with a change at P108A or B/Bangladesh/3333/2007-like

(Group 3) with a S150I change. The majority of these B/Yamagata-lineage viruses fell into Group 3 (Figures 6.3, 6.4 & 6.5 in Appendix 5). Furthermore, Vaccines containing influenza B/Brisbane/60/2008-like antigen stimulated anti-HA antibodies of similar geometric mean HI titres to the vaccine virus and recent B/Victoria/2/87 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: younger adults 52%; elderly subjects 69%). (WER 84(41), Tables 5.7 to 5.8 in Appendix 5).

In summary, influenza B outbreaks were reported in southern hemisphere countries. The majority of recent isolates was 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 epidemiological, antigenic, genetic and serological data, the WHO consultation recommended a B/Brisbane/60/2008–like strain. The AIVC accepts this recommendation.

4. SUMMARY

It is recommended that the influenza vaccine formulation for New Zealand for 2010 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 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 has been substituted which has the qualities lacking in the prototype strain.

The Australian Influenza Vaccine Committee (AIVC) considered information on international surveillance by WHO, recent data from Australia, New Zealand, South Africa and Argentina on epidemiology and strain characterisation, and the recommendations of the WHO annual consultation on the composition of influenza vaccine for the Southern Hemisphere, held in Melbourne on 19-23 September.

The Committee agreed to adopt the September WHO recommendations. The influenza vaccine components for year 2009 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 viruses are recommended as suitable vaccine strains:

- A/California/7/2009 (H1N1) (NYMC X-179A, NYMC X-181, NYMC X-181A,NIBRG-121, NIBRG-121xp)
- A/Perth/16/2009 (H3N2)- like virus
- B/Brisbane/60/2008

The SRID reference antigens for A/California/7/2009 (H1N1) (X-179A) and (X181¬) strains are available from TGA; reagents for NIBRG-121 and NIBRG-121xp reassortants and antisera suitable for use with all reassortants are available from NIBSC (UK).

The SRID reference antigen for A/Perth/16/2009 (H3N2)- like virus will be available from TGA (Australia) and NIBSC.

The SRID reference antigen and antisera for B/Brisbane/60/2008 are available from TGA and NIBSC.

5. ACKNOWLEDGEMENTS

Ministry of Health, New Zealand

MedSafe at Ministry of Health, New Zealand

The WHO National Influenza Centre and Epidemiology group, ESR

Virus Laboratories in Auckland, Waikato, Wellington and Christchurch Hospitals

Local influenza coordinators within each Public Health Unit

Participants in the National Influenza Surveillance Programme

WHO Collaborating Centre for Influenza, VIDRL-Melbourne, and CDC-Atlanta

National Institute of Communicable Diseases (NICD), Johannesburg, RSA

Australian Influenza Vaccine Committee

APPENDIX 1

The Australia Influenza Vaccine Committee (AIVC) meeting was convened at 1:30 pm on 2 October 2009 in Conference Room 1, TGA, Symonston, Canberra, when overseas participants in the teleconference were connected by Telstra. The New Zealand representative attended the meeting in Canberra.

COMPOSITION OF THE AIVC COMMITTEE (2009)

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

Committee Members:

Ass Prof Gary Grohmann, OLSS, TGA (Chairperson)
Prof Anne Kelso, WHOCC
Dr Ian Barr, WHOCC
*Emeritus Prof Greg Tannock, Macfarlane Burnet Institute
Prof. Ian Gust.
Dr Mike Catton, VIDRL
Dr Heath Kelly, VIDRL
Dr Dominic Dwyer, ICPMR
*Dr David Smith, UWA
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:

Mr David Ryan, CSL Ltd
Mr Peter Schoofs, CSL Ltd
Mr William Cracknell, CSL Ltd
Ms Diana Newport, CSL Ltd
Ms Nicole Schaefer, CSL Ltd
Mr Rodney Daly, 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
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 Lionel Cornu, Baxter Healthcare Pty Ltd
Mr Tony Shelton, Baxter Healthcare Pty Ltd
Dr Maria Fallon, Baxter Healthcare Pty Ltd
Ms Rhonda Owen, OHP, DoHA
Dr Bronwen Harvey, OHP, DoHA
Ms Elizabeth de Somer, Medicines Australia
Mr Michael Sparks, ACT Health
Ms Pearl Bamford, OLSS, TGA
Dr Peter Christian, OLSS,TGA
Ms Sally Goodspeed, OHP, DoHA

*Participating by teleconference

APPENDIX 2

ISOLATES RECEIVED FOR ANALYSIS AT THE AUSTRALIAN WHO COLLABORATING CENTRE

FIGURE 2.1
Influenza isolates received and analysed at the WHO CC for Influenza

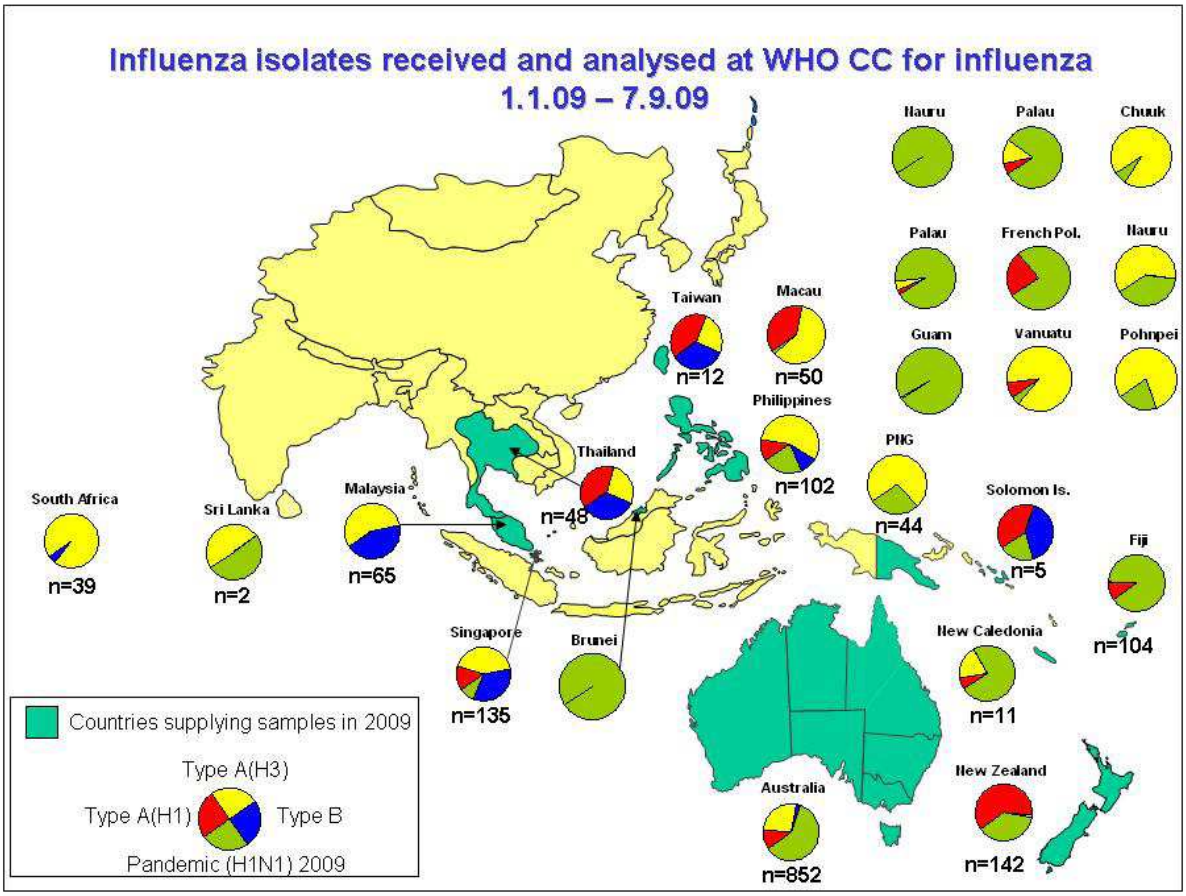
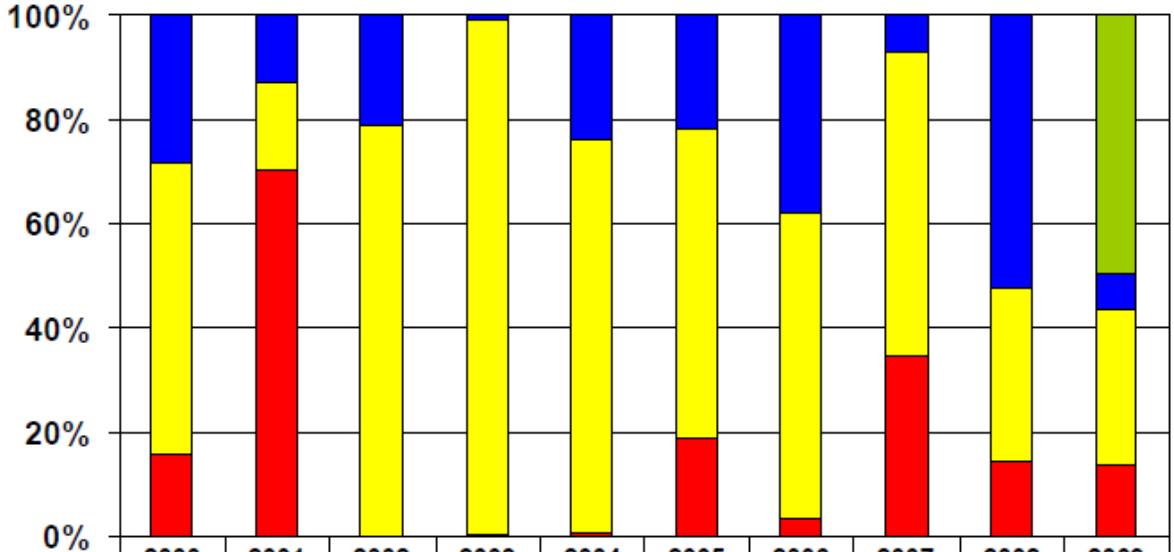


FIGURE 2.1
Influenza isolates received and analysed at the WHO CC for Influenza



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

APPENDIX 3

INFLUENZA A (H1N1)

Table 3.1
Summary – Characterization of Influenza A(H1N1)dpm

	Australia, New Zealand	*Pacific*	SE Asia	Africa	China	Other	Total (%)
March - September 2007							
B/California/7/2009-like	276	13	24	0	1	32	346 (92%)
B/ California/7/2009 (low)*	27	0	3	0	0	0	30 (8%)
Total	303	13	27	0	1	32	376

Table 3.2
Summary – Characterization of Influenza A(H1) 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*	492	24	7	26	175	48	772 (96%)
A/California/07/2009-like **	17				9	1	27 (3%)
A/California/07/2009 (low)***	2						2(<1%)
						Total	
Total	511	24	7	26	184	49	801

* ≤ 2-fold low to vaccine strain
** = 4-fold low to vaccine strain
*** ≥ 8-fold low to vaccine strain

Preliminary Data 09/14/09

Table 3.3

	Compilation: September 3 & 10, 2009	Haemagglutination Inhibition Assay - WHO Influenza Centre, Melbourne					
		Reference Antisera					
		A	B	B	C		
		F999	F19	F14	FS5	Passage	Sample
	Reference Antigens	BRIS/59	CAL/7	CAL/7	AUCK/1	History	Date
A	A/BRISBANE/59/2007	**640**	<20	<20	<20	E3	
	A/CALIFORNIA/4/2009	<20	640	160	320	C2,mdck1	
B	A/CALIFORNIA/7/2009	<20	**640**	**320**	320	E3	
C	A/AUCKLAND/1/2009	<20	320	320	**320**	E2	
	A/AUCKLAND/3/2009	<20	1280	640	320	E2	
	A/AUCKLAND/1/2009	<20	640	320	160	mdck2	
	A/AUCKLAND/3/2009	<20	640	320	320	mdck2	
	Test Ag						
1	A/Victoria/2001/2009	<20	1280	640	320	E3	19/05/2009
2	A/FIJI/2035/2009	<20	1280	640	640	E2	2/07/2009
3	A/PORT MORESBY/2009/2009	<20	1280	640	640	E3	
4	A/DARWIN/2125/2009	<20	1280	640	1280	E2	23/07/2009
5	A/DARWIN/2124/2009	<20	>2560	640	640	E2	9/07/2009
6	A/BRUNEI/2008/2009	<20	1280	640	320	mdck1	16/07/2009
7	A/CANBERRA/2035/2009	<20	1280	320	320	mdck1	4/08/2009
8	A/VICTORIA/528/2009	<20	640	320	320	E3	29/06/2009
9	A/FIJI/2029/2009	<20	1280	320	320	E2	6/07/2009
10	A/TASMANIA/2004/2009	<20	640	320	320	E2	5/07/2009
11	A/PORT MORESBY/2008/2009	<20	640	320	320	E3	
12	A/VICTORIA/2083/2009	<20	640	320	320	E2	23/07/2009
13	A/PERTH/3014/2009	<20	640	320	160	mdck1	15/07/2009
14	A/VICTORIA/541/2009	<20	640	320	160	mdck1	29/07/2009
15	A/SOUTH AUSTRALIA/2019/2009	<20	1280	320	320	MDCKX,MDCK1	21/07/2009
16	A/CANBERRA/2034/2009	<20	640	160	160	mdck1	4/08/2009
17	A/CANBERRA/2036/2009	<20	320	160	160	mdck1	4/08/2009
18	A/TRAT/277/2009	<20	320	160	160	mdck2	27/06/2009
19	A/BANGKOK/288/2009	<20	640	160	160	mdck2	23/06/2009
20	A/BANGKOK/297/2009	<20	320	160	160	mdck2	23/06/2009
21	A/NONG KHAI/347/2009	<20	640	160	320	mdck2	22/07/2009
22	A/SURAT THANI/348/2009	<20	320	160	160	mdck2	27/07/2009
23	A/TASMANIA/2005/2009	<20	640	160	320	E2	3/07/2009
24	A/DARWIN/2126/2009	<20	640	160	160	E2	23/07/2009
25	A/NEW CALEDONIA/2000/2009	<20	320	160	160	mdck1	24/07/2009
26	A/NEW CALEDONIA/2005/2009	<20	320	160	160	mdck1	26/06/2009
27	A/VICTORIA/2112/2009	<20	640	160	160	mdck1	10/08/2009
28	A/SOUTH AUSTRALIA/2020/2009	<20	320	160	80	MDCKX,MDCK1	21/07/2009
29	A/SOUTH AUSTRALIA/2022/2009	<20	320	160	160	MDCKX,MDCK1	23/07/2009
30	A/SOUTH AUSTRALIA/2030/2009	<20	640	160	160	MDCKX,MDCK1	6/08/2009
31	A/WELLINGTON/188/2009	<20	320	160	160	X,MDCK1	10/07/2009
32	A/SAMOA/2/2009	<20	320	160	160	X,MDCK1	10/07/2009
33	A/WELLINGTON/197/2009	<20	320	160	160	X,MDCK1	28/07/2009
34	A/NEW CALEDONIA/2004/2009	<20	320	80	80	mdck1	3/07/2009
35	A/SOUTH AUSTRALIA/2027/2009	<20	160	80	80	MDCKX,MDCK1	30/07/2009
36	A/SOUTH AUSTRALIA/2031/2009	<20	160	80	80	MDCKX,MDCK1	11/08/2009
37	A/WELLINGTON/9/2009	<20	320	80	80	X,MDCK1	9/06/2009
38	A/WELLINGTON/187/2009	<20	320	80	160	X,MDCK1	15/07/2009
39	A/AUCKLAND/268/2009	<20	320	80	80	X,MDCK1	20/07/2009
40	A/AUCKLAND/269/2009	<20	160	80	80	X,MDCK1	20/07/2009
41	A/WELLINGTON/190/2009	<20	320	80	160	X,MDCK1	22/07/2009
42	A/SAMOA/3/2009	<20	320	80	160	X,MDCK1	11/07/2009
43	A/SAMOA/7/2009	<20	320	80	160	X,MDCK1	21/07/2009

44	A/SAMOA/8/2009	<20	320	80	80	X,MDCK1	21/07/2009
45	A/WELLINGTON/191/2009	<20	160	80	80	X,MDCK1	24/07/2009
46	A/WAIKATO/107/2009	<20	160	80	80	X,MDCK1	14/07/2009
47	A/WELLINGTON/198/2009	<20	320	80	80	X,MDCK1	28/07/2009
48	A/PHILIPPINES/3192/2009	<20	160	80	80	MDCK2	24/06/2009
49	A/PHILIPPINES/3367/2009	<20	320	80	80	MDCK3	1/07/2009
50	A/PHILIPPINES/3827/2009	<20	160	80	80	MDCK3	15/07/2009
51	A/PHILIPPINES/2350/2009	<20	320	80	80	MDCK3	15/07/2009
52	A/MACAU/2472/2009	<20	320	80	160	x,mdck1	20/08/2009
53	A/SOUTH AUSTRALIA/2024/2009	<20	80	40	80	MDCKX,MDCK1	28/07/2009
54	A/WAIKATO/108/2009	<20	160	40	80	X,MDCK1	10/07/2009
55	A/PHILIPPINES/3718/2009	<20	80	40	40	MDCK3	14/07/2009
56	A/PHILIPPINES/1577/2009	<20	80	40	80	MDCK2	17/06/2009
57	A/PHILIPPINES/1972/2009	<20	80	40	40	MDCK3	1/07/2009
58	A/VICTORIA/2113/2009	<20	80	40	80	mdck1	21/08/2009
59	A/SOUTH AUSTRALIA/2016/2009	<20	40	20	20	MDCKX,MDCK1	16/07/2009
60	A/SOUTH AUSTRALIA/2023/2009	<20	80	20	40	MDCKX,MDCK1	23/07/2009

FIGURE 3.2
Phylogenetic relationships among influenza A(H1N1)pdm HA1 genes

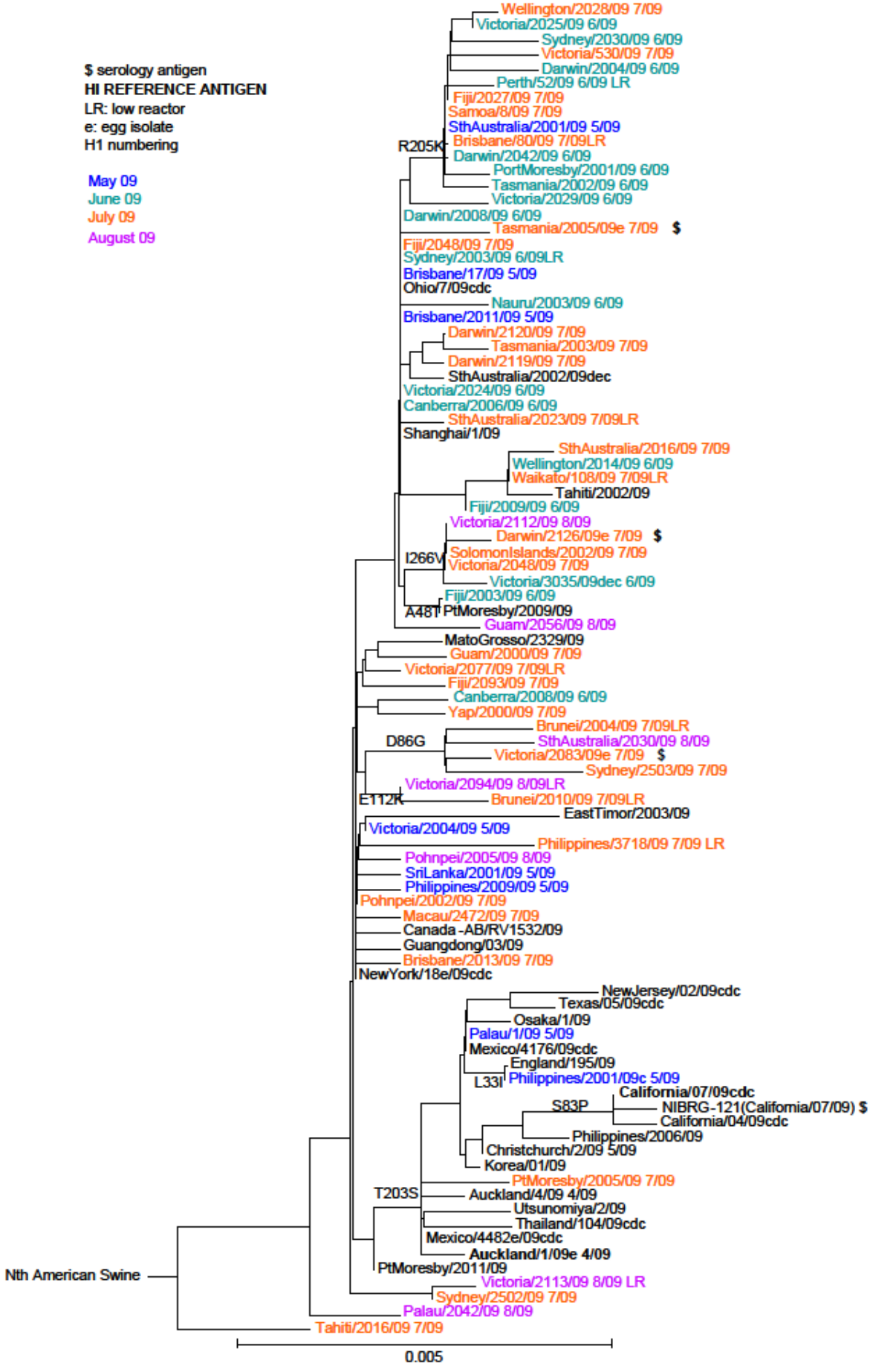


FIGURE 3.3
Phylogenetic relationships among influenza A(H1N1)pdm neuraminidase genes

Pandemic H1N1 2009 Vaccine

For the Australian (2009 serum panel)
A/California/7/2009 (H1N1pdm) (NYMC 179A)
15 & 30µg single doses – code not known

Table 3.10
Haemagglutination inhibition antibody responses
Influenza type A(H1N1)pdm vaccine component
Adults (18 – 64 years)

Population	N	Antigen	Passage History	% Rise	GMT		%>/=40		%>/=160	
					Pre	Post	Pre	Post	Pre	Post
Australian Adults	30	A/Darwin/2126/2009	E2	60	5.0	28.9	0	50	0	33
		A/California/7/2009*	Ex	77	7.8	121.2	10	87	10	60
		A/Tasmania/2005/2009	E2	73	6.8	72.9	7	80	0	50
		A/Brisbane/59/2009#	E3	17	20.0	29.6	43	47	20	27

*Vaccine strain
Seasonal H1N1 virus

APPENDIX 4

INFLUENZA A (H3N2)

Table 5.1
Summary – Characterization of Influenza A(H3N2) from Melbourne Centre

	Australia New Zealand	Pacific	SE Asia	Africa	China	Other	Total (%)
February – September 2005							
A/Wellington/1/04-like	452	0	106	8	32	7	605 (43.8%)
A/Wellington/1/ 04 (low)*	35	0	37	3	14	3	92 (6.7%)
A/California/7/04-like	367	0	94	9	23	0	493 (35.7%)
A/California/7/04 (low)*	119	0	49	2	21	0	191 (13.8%)
Total	973	0	286	22	90	10	1381
October 2005 – February 2006							
A/Wellington/1/04-like	50	0	45	0	0	29	124 (32.2%)
A/Wellington/1/ 04 (low)*	11	0	34	0	18	5	68 (17.7%)
A/California/7/04-like	58	0	60	0	1	29	148 (38.5%)
A/California/7/04 (low)*	3	0	19	0	17	5	44 (11.4%)
Total	122	0	159	0	36	68	384
March - September 2006							
A/Wisconsin/67/2005-like	341	7	40	16	1	0	405 (77.4%)
A/Wisconsin/67/2005 (low)*	106	0	8	4	0	0	118 (22.6%)
Total	447	7	48	20	1	0	523
October 2006 – February 2007							
A/Wisconsin/67/2005-like	67	1	3	0	0	2	73 (50%)
A/Wisconsin/67/2005 (low)*	57	3	11	0	0	2	73 (50%)
Total	124	4	14	0	0	4	146
March – September 2007							
A/Wisconsin/67/2005-like	54	0	20	0	9	0	83 (19%)
A/Wisconsin/67/2005 (low)*	178	0	126	13	31	4	352 (81%)
Total	232	0	146	13	40	4	435
October 2007 – February 2008							
A/Brisbane/10/2007-like	60	0	21	0	26	32	139 (55.8%)
A/Brisbane/10/2007 (low)*	47	0	26	0	23	14	110 (44.1%)
Total	107	0	47	0	49	46	249
March - September 2008							
A/Brisbane/10/2007-like	158	0	106	2	5	41	316 (80.6%)
A/Brisbane/10/2007 (low)*	34	0	36	0	4	2	76 (19.4%)
Total	192	0	142	2	9	43	392
October 2008 – February 2009							
A/Brisbane/10/2007-like	123	0	22	0	0	0	145 (92.9%)
A/Brisbane/10/2007 (low)*	6	0	5	0	0	0	11 (7.1%)
Total	129	0	27	0	0	0	156
March - September 2009							
A/Brisbane/10/2007-like	26	0	49	2	0	18	95 (25.8%)
A/Brisbane/10/2007 (low)*	119	2	77	29	26	20	273 (74.2%)
Total	145	2	126	31	26	38	368

* $\geq$ 8 fold lower in HI assays

TABLE 5.3

	Date: September 2, 2009	Haemagglutination Inhibition Assay - WHO Influenza Centre, Melbourne												
	Sequenced	Reference Antisera												
		1	2	3	4	5	6	7	8	9		10		
		F838	F1154	F897	F968	F1082	F1228	F1391	F1393	F1413	F1412	F1468	Passage	Sample
	Reference Antigens	NY/55	WISC/67	BRIS/9	BRIS/10	URUG/716	BRIS/24	PHIL/16	ST/72	PERTH/16	Perth/15	VIC/208	History	Date
A	A/NEW YORK/55/2004	**1280**	320	320	640	640	640	<40	320	<40	<40	<40	SPFCK3,E4	
B	A/WISCONSIN/67/2005	160	**640**	1280	640	640	640	<40	320	<40	<40	<40	SPFCK3,E5	
C	A/BRISBANE/9/2006	320	1280	**2560**	1280	640	1280	40	320	<40	<40	<40	E5	
D	A/BRISBANE/10/2007	160	320	1280	**1280**	1280	1280	<40	640	<40	<40	<40	E4	
E	NYMCX-175C(A/Uruguay/716/07)	160	320	640	1280	**1280**	1280	<40	640	<40	<40	<40	X,E2	
F	A/BRISBANE/24/2008	160	320	1280	2560	640	**2560**	<40	640	<40	<40	<40	E5	
G	A/PHILIPPINES/16/2009	<40	<40	40	<40	<40	<40	**40**	<40	<40	40	<40	MDCK4	
H	A/SURAT THANI/72/2009	<40	<40	40	<40	40	40	<40	**40**	<40	<40	<40	MDCK4	
I	A/PERTH/16/2009	<40	<40	40	<40	<40	40	640	<40	**640**	640	160	E3	
J	A/VICTORIA/208/2009	40	80	160	80	<40	160	1280	<40	640	640	**1280**	E3	
	Test Ag													
1	A/SYDNEY/602/2009	80	160	640	640	1280	640	<40	320	<40	<40	<40	E4	
2	A/JOHANNESBURG/1196/2009	40	40	160	160	40	80	40	320	<40	40	40	mdck2	13/07/2009
3	A/PHILIPPINES/3188/2009	<40	40	160	80	40	40	320	160	320	320	320	mdck3	24/06/2009
4	A/MACAU/3400/2009	<40	<40	80	80	<40	40	160	80	80	160	40	X,MDCK2	27/07/2009
5	A/MACAU/3418/2009	<40	<40	160	80	40	40	160	80	80	160	80	X,MDCK2	27/07/2009
6	A/JOHANNESBURG/143/2009	<40	40	160	80	40	40	40	80	40	40	40	mdck2	26/05/2009
7	A/JOHANNESBURG/1238/2009	<40	40	160	80	40	80	<40	80	40	40	40	mdck2	14/07/2009
8	A/PORT MORESBY/2/2009	<40	80	80	40	<40	80	640	<40	640	640	320	E3	15/06/2009
9	A/PHILIPPINES/2725/2009	<40	<40	80	40	40	40	640	160	320	320	320	mdck3	3/06/2009
10	A/PHILIPPINES/2722/2009	<40	<40	80	40	<40	40	320	80	160	160	160	mdck2	3/06/2009
11	A/PHILIPPINES/3213/2009	<40	<40	80	40	<40	40	160	80	160	160	160	mdck3	24/06/2009
12	A/MACAU/3425/2009	<40	<40	80	40	<40	40	160	80	80	160	80	X,MDCK2	28/07/2009
13	A/JOHANNESBURG/1237/2009	<40	<40	80	40	<40	40	160	80	80	80	80	mdck2	14/07/2009
14	A/PHILIPPINES/3135/2009	<40	<40	80	40	40	40	160	80	80	160	160	mdck3	24/06/2009
15	A/CANBERRA/21/2009	<40	<40	80	40	<40	<40	80	80	80	160	80	MDCK2	26/07/2009
16	A/CANBERRA/2029/2009	<40	<40	80	<40	<40	40	160	40	40	80	80	mdck3	20/07/2009
17	A/JOHANNESBURG/1166/2009	<40	<40	40	<40	<40	<40	80	<40	40	40	40	mdck2	7/07/2009
18	A/JOHANNESBURG/1250/2009	<40	<40	40	<40	<40	<40	<40	<40	40	40	40	mdck2	15/07/2009
19	A/PHILIPPINES/2990/2009	<40	<40	40	<40	40	40	160	40	80	160	160	mdck3	17/06/2009
20	A/PHILIPPINES/1921/2009	<40	<40	40	<40	40	40	160	40	40	80	40	mdck3	22/04/2009

TABLE 5.4

	Date: September 2, 2009	Haemagglutination Inhibition Assay - WHO Influenza Centre, Melbourne													
		Reference Antisera													
		1	2	3	4	5	6	7	8	9	10	11	12		
		F838	F1154	F897	F968	F1082	F1228	F1391	F1393	F1413	F1412	F1468	2009	Passage	Sample
	Reference Antigens	NY/55	WIS/67	BRI/9	BRI/10	UR/716	BRI/24	PHI/16	ST/72	PER/16	PER/15	VIC/208			
1	A/NEW YORK/55/2004	**1280**	320	320	320	320	320	<40	160	<40	<40	<20	320	SPFCK3,E4	
2	A/WISCONSIN/67/2005	320	**640**	1280	1280	640	1280	80	640	<40	<40	<20	1280	SPFCK3,E5	
3	A/BRISBANE/9/2006	320	1280	**2560**	640	640	640	80	160	<40	<40	<20	1280	E5	
4	A/BRISBANE/10/2007	160	640	640	**1280**	1280	1280	80	640	<40	<40	<20	640	E4	
5	NYMCX-175C(A/Uruguay/716/07)	320	640	1280	1280	**2560**	2560	80	1280	<40	<40	<20	640	X,E2	
6	A/BRISBANE/24/2008	80	320	1280	1280	640	**2560**	80	640	<40	<40	<20	1280	E5	
7	A/PHILIPPINES/16/2009	<40	<40	40	40	<40	<40	**80**	<40	80	80	<20	160	MDCK4	
8	A/SURAT THANI/72/2009	<40	<40	40	40	<40	40	40	**160**	<40	<40	<20	160	MDCK4	
9	A/PERTH/16/2009	<40	<40	40	<40	<40	<40	640	<40	**640**	640	160	320	E3	
10	A/VICTORIA/208/2009	<40	40	80	40	<40	80	1280	<40	640	640	**320**	320	E3	
	Test Ag														
1	A/PERTH/107/2009	<40	<40	80	80	40	40	40	80	<40	<40	<20	160	MDCKX,MDCK2	21/06/2009
2	A/PERTH/403/2009	<40	40	80	80	40	80	640	80	640	640	160	320	mdck1	6/07/2009
3	A/PERTH/405/2009	<40	<40	80	80	<40	40	320	80	160	160	80	160	mdck1	4/07/2009
4	A/MACAU/2314/2009	<40	40	160	80	40	40	320	80	320	160	80	320	x,mdck1	3/07/2009
5	A/PERTH/413/2009	<40	<40	80	80	<40	40	320	80	320	160	80	160	mdck2	15/07/2009
6	A/PERTH/93/2009	<40	<40	80	40	<40	40	160	80	160	80	40	160	MDCKX,MDCK2	16/06/2009
7	A/PERTH/117/2009	<40	<40	40	40	<40	<40	160	<40	160	80	<20	160	MDCKX,MDCK2	29/06/2009
8	A/CAMBODIA/5/2009	<40	<40	40	40	<40	40	160	80	80	80	40	160	p3,mdck1	1/06/2009
9	A/CAMBODIA/7/2009	<40	<40	40	40	<40	<40	160	<40	160	160	40	160	p3,mdck1	24/06/2009
10	A/CAMBODIA/8/2009	<40	<40	40	40	<40	<40	160	40	80	80	40	160	p3,mdck1	16/06/2009
11	A/PERTH/402/2009	<40	<40	40	40	<40	<40	80	80	80	40	40	80	mdck1	6/07/2009
12	A/CAMBODIA/3/2009	<40	<40	80	40	<40	<40	160	40	160	160	80	160	p2,mdck1	16/06/2009
13	A/MACAU/2503/2009	<40	<40	80	40	<40	<40	160	40	160	80	40	80	x,mdck1	7/07/2009
14	A/MACAU/2578/2009	<40	<40	40	40	<40	<40	80	<40	80	80	40	80	x,mdck1	9/07/2009
15	A/MACAU/2650/2009	<40	40	80	40	<40	40	320	80	320	160	80	160	x,mdck1	10/07/2009
16	A/NEW CALEDONIA/3/2009	<40	<40	80	40	<40	40	160	80	80	80	40	80	mdck1	26/07/2009

TABLE 5.5

	Date: August 24, 2009	Haemagglutination Inhibition Assay - WHO Influenza Centre, Melbourne														
		Reference Antisera														
		1	2	3	4	5	6	7	8	9	10	11				
		F838	F1154	F897	F1466	F1082	F1228	F1391	F1393	F1413	F1467	F1468	F1412	2009	Passage	Sample
	Reference Antigens	NY/55	WIS/67	BRI/9	Bri/10	UR/716	BRI/24	PHI/16	ST/72	PER/16	VIC/208	VIC/208	PER/15	sera		
1	A/NEW YORK/55/2004	**640**	320	320	160	320	320	<40	320	<40	<20	<20	<40	1280	SPFCK3,E4	
2	A/WISCONSIN/67/2005	320	**640**	2560	640	640	1280	<40	640	<40	<20	<20	<40	2560	SPFCK3,E5	
3	A/BRISBANE/9/2006	320	640	**2560**	640	640	640	<40	160	<40	<20	<20	<40	2560	E5	
4	A/BRISBANE/10/2007	160	640	1280	**640**	1280	2560	<40	640	<40	80	40	<40	1280	E4	
5	NYMCX-175C(A/Uruguay/716/07)	160	320	1280	640	**2560**	2560	<40	1280	<40	<20	40	<40	2560	X,E2	
6	A/BRISBANE/24/2008	<40	320	1280	640	640	**2560**	<40	640	<40	<20	80	40	2560	E5	
7	A/PHILIPPINES/16/2009	<40	<40	40	<20	<40	<40	**160**	<40	<40	<20	20	<40	320	MDCK4	
8	A/SURAT THANI/72/2009	<40	<40	40	<20	<40	<40	<40	**160**	<40	<20	20	<40	320	MDCK4	
9	A/PERTH/16/2009	<40	<40	40	<20	<40	<40	640	<40	**1280**	320	160	320	1280	E3	
10	A/VICTORIA/208/2009	<40	160	320	40	40	160	640	320	640	**160**	160	80	1280	MDCK2	
11	A/VICTORIA/208/2009	<40	320	320	320	<40	320	2560	<40	1280	1280	**640**	320	2560	E3	
	Test Ag															
1	A/BRISBANE/89/2009	<40	40	320	160	<40	80	640	320	640	160	320	160	1280	mdck4	22/06/2009
2	A/DARWIN/11/2009	<40	<40	160	80	<40	40	320	160	320	320	320	160	640	mdck2	29/06/2009
3	A/VICTORIA/226/2009	<40	40	160	160	<40	80	640	160	640	320	320	320	1280	MDCK2	23/07/2009
4	A/VICTORIA/229/2009	<40	<40	160	80	<40	40	320	160	640	160	320	160	1280	MDCK2	24/07/2009
5	A/PERTH/77/2009	<40	40	160	80	<40	80	640	160	320	160	160	160	640	MDCKX,MDCK1	8/06/2009
6	A/MACAU/2321/2009	<40	40	160	80	<40	80	320	160	320	320	320	160	640	x,mdck1	3/07/2009
7	A/PERTH/78/2009	<40	40	160	40	<40	40	160	160	320	160	160	320	640	MDCKX,MDCK1	10/06/2009
8	A/PERTH/80/2009	<40	40	160	160	40	80	640	80	640	320	320	320	1280	MDCKX,MDCK1	6/06/2009
9	A/PERTH/82/2009	<40	<40	80	80	<40	40	320	160	320	160	160	160	320	MDCKX,MDCK2	8/06/2009
10	A/VICTORIA/224/2009	<40	<40	80	80	<40	40	160	160	320	160	160	160	320	mdck2	20/07/2009
11	A/BRISBANE/63/2009	<40	<40	80	40	<40	40	160	160	160	160	160	80	320	mdck3	17/06/2009
12	A/VICTORIA/223/2009	<40	<40	80	40	<40	<40	160	<40	160	160	160	80	320	mdck2	20/07/2009
13	A/BRISBANE/65/2009	<40	<40	80	40	<40	40	80	80	80	160	160	80	320	mdck4	22/06/2009
14	A/VICTORIA/227/2009	<40	<40	80	40	<40	<40	160	80	160	160	160	80	640	MDCK2	23/07/2009
15	A/BRISBANE/64/2009	<40	<40	80	40	<40	40	160	<40	160	80	80	80	320	mdck3	17/06/2009
16	A/VICTORIA/222/2009	<40	<40	80	40	<40	<40	160	<40	320	80	160	80	320	mdck2	20/07/2009
17	A/DARWIN/12/2009	<40	<40	80	40	<40	40	160	<40	80	80	80	80	320	mdck2	30/06/2009
18	A/VICTORIA/228/2009	<40	<40	80	40	<40	40	160	80	160	160	160	80	320	MDCK2	24/07/2009
19	A/PERTH/83/2009	<40	<40	80	40	<40	<40	160	80	160	80	80	80	320	MDCKX,MDCK2	9/06/2009
20	A/MACAU/2337/2009	<40	<40	80	40	<40	40	320	80	320	160	160	160	640	x,mdck1	3/07/2009
21	A/CAMBODIA/15/2009	<40	<40	40	40	<40	<40	160	<40	160	80	160	160	320	p3,mdck1	16/06/2009

FIGURE 5.2
Phylogenetic relationships among influenza A(H3) HA1 genes

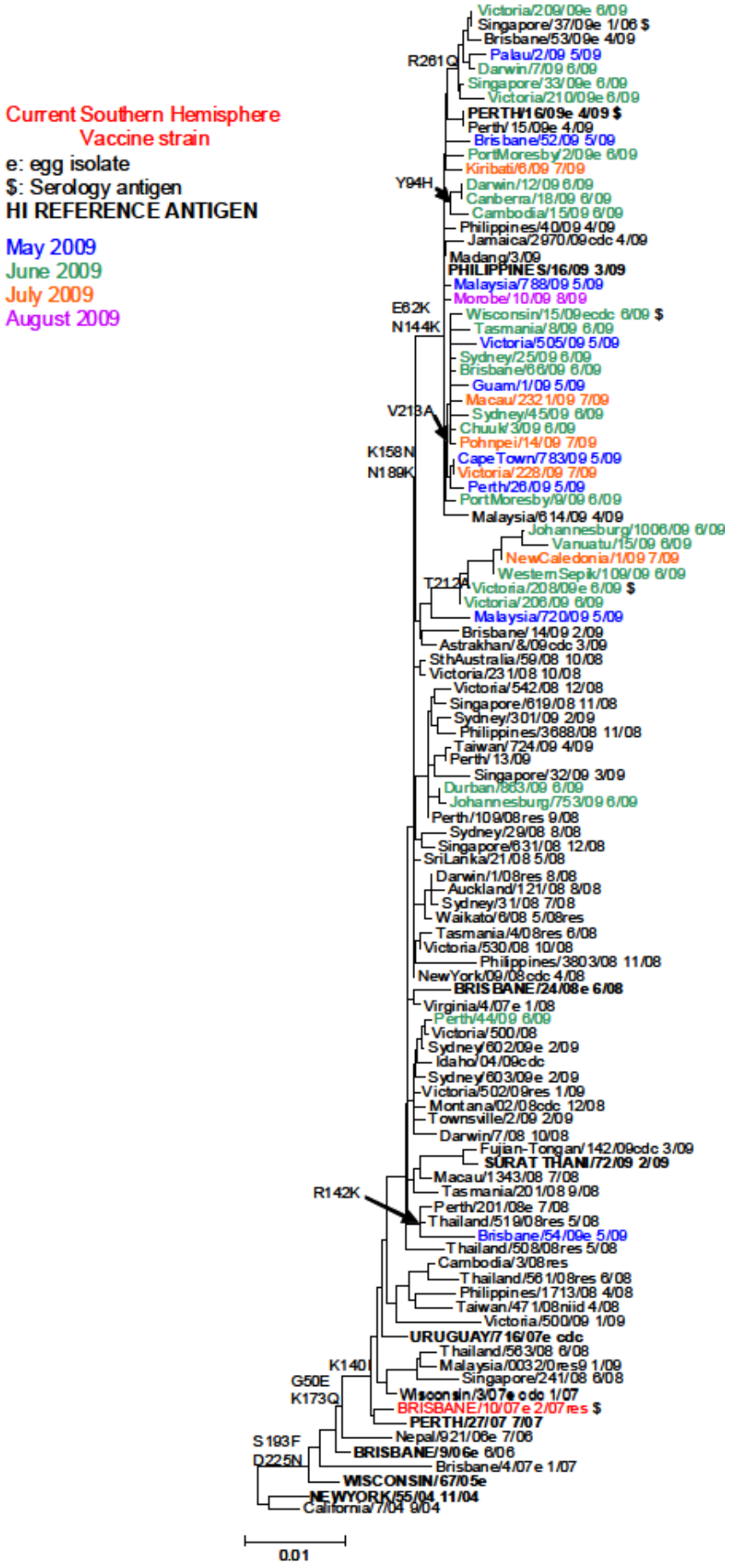


FIGURE 5.3
Phylogenetic relationships among influenza N2 neuraminidase genes 2009

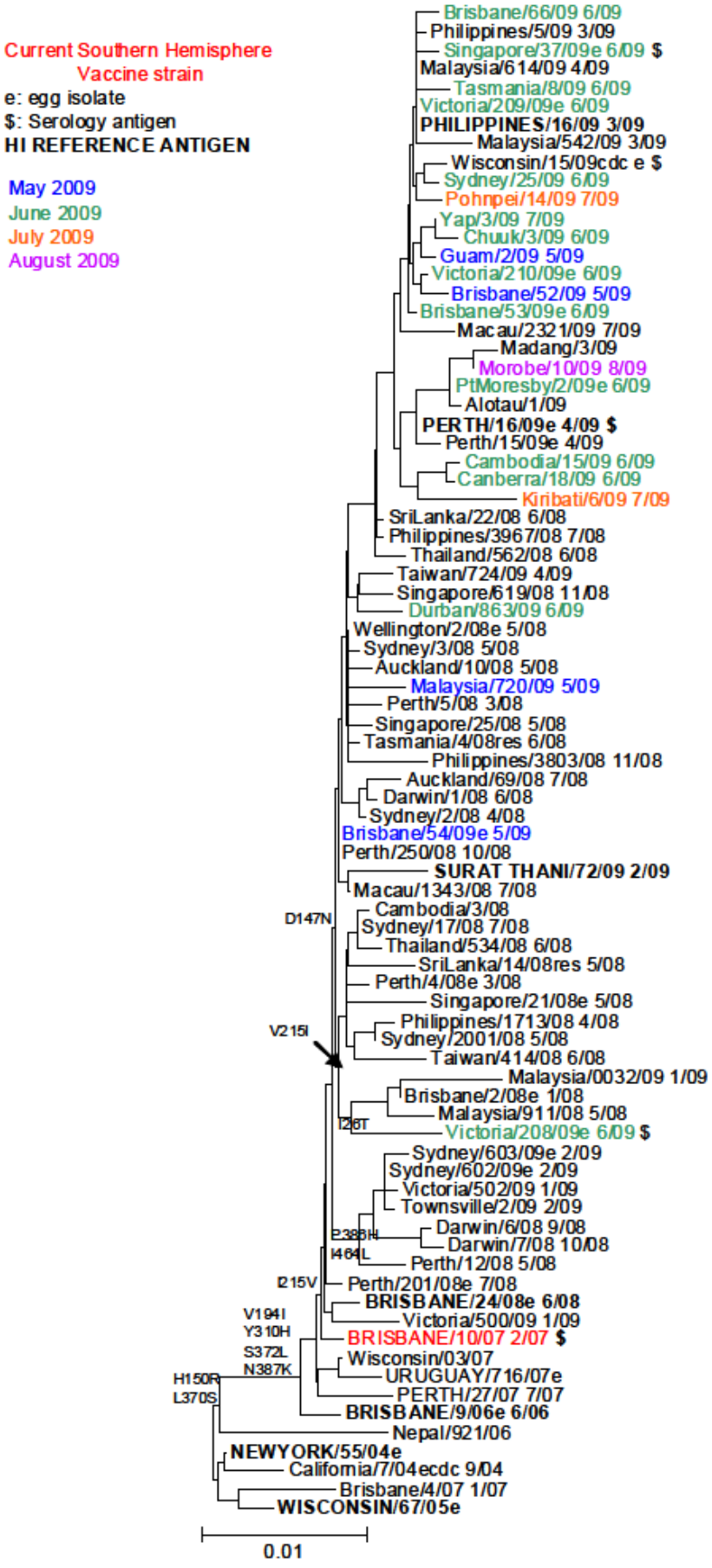


Table 5.12
Haemagglutination-inhibition antibody responses
Influenza type A(H1) vaccine component
Young Adults

Population	N	Antigen	Passage History	% Rise	GMT		%≥40		%≥160	
					Pre	Post	Pre	Post	Pre	Post
Australian Younger Adult	20	A/Brisbane/10/2007*	E3	75	10.0	105.5	15	90	5	55
		A/Perth/16/2009	E3	60	5.9	31.4	5	55	0	10
		A/Victoria/208/2009	E3	60	5.9	29.3	5	60	0	10
		A/Singapore/37/2009	E2	50	5.7	25.5	5	50	0	10
		A/Wisconsin/15/2009	E3	50	5.5	20.0	5	40	0	5
European Younger Adult	24	A/Brisbane/10/2007*	E3	58	8.9	42.4	13	71	0	25
		A/Perth/16/2009	E3	50	5.8	9.4	0	17	0	0
		A/Victoria/208/2009	E3	42	6.9	20.0	4	42	0	0
		A/Singapore/37/2009	E2	42	5.9	15.0	0	33	0	0
		A/Wisconsin/15/2009	E3	50	5.2	11.5	0	40	0	0
Japanese Younger Adult	24	A/Brisbane/10/2007*	E3	37	7.9	27.5	3	33	0	10
		A/Perth/16/2009	E3	8	5.8	9.4	4	21	0	0
		A/Victoria/208/2009	E3	2	7.3	13.7	4	29	0	0
		A/Singapore/37/2009	E2	21	5.5	8.9	0	17	0	0
		A/Wisconsin/15/2009	E3	13	5.3	7.3	0	0	0	13

Table 5.13
Haemagglutination-inhibition antibody responses
Influenza type A(H1) vaccine component
Older Adults

Population	N	Antigen	Passage History	% Rise	GMT		%≥40		%≥160	
					Pre	Post	Pre	Post	Pre	Post
Australian Older Adult	20	A/Brisbane/10/2007*	E3	70	28.3	125.5	60	95	5	65
		A/Perth/16/2009	E3	55	9.7	32.5	5	60	0	10
		A/Victoria/208/2009	E3	50	12.7	37.3	10	70	0	5
		A/Singapore/37/2009	E2	50	9.7	32.5	10	60	0	15
		A/Wisconsin/15/2009	E3	50	6.6	21.4	0	40	0	5
European Older Adult	24	A/Brisbane/10/2007*	E3	50	6.7	24.5	4	54	0	8
		A/Perth/16/2009	E3	25	5.6	9.4	0	17	0	0
		A/Victoria/208/2009	E3	29	5.8	9.7	4	8	0	0
		A/Singapore/37/2009	E2	29	5.3	8.7	0	13	0	0
		A/Wisconsin/15/2009	E3	17	5.0	7.1	0	16	0	0
Japanese Older Adult	24	A/Brisbane/10/2007*	E3	63	9.4	35.6	17	67	0	29
		A/Perth/16/2009	E3	27	5.6	10.6	3	13	0	3
		A/Victoria/208/2009	E3	33	7.3	15.0	4	29	0	0
		A/Singapore/37/2009	E2	29	5.5	9.7	4	8	0	4
		A/Wisconsin/15/2009	E3	25	5.8	9.2	0	0	0	8

* Vaccine Strain

APPENDIX 5

INFLUENZA B

Table 6.1
Summary – Characterization of Influenza A(H1N1)dpm

	Australia, New Zealand	Pacific	SE Asia	Africa	China	Other	Total (%)
March - September 2006							
B/Malaysia/2506/2004-like	100	7	62	5	14	2	190 (49.8%)
B/Malaysia/2506/2004 (low)*	69	4	43	4	7	2	129 (33.8%)
B/Shanghai/361/2002-like	12	0	33	1	1	1	48 (12.7%)
B/Shanghai/361/2002 (low)*	2	0	12	0	0	0	14 (3.7%)
Total	183	11	150	10	22	5	381
October 2006 – February 2007							
B/Malaysia/2506/2004-like	8	0	5	0	0	0	13 (32.5%)
B/ Malaysia/2506/ (low)*	19	0	6	0	0	0	25 (62.5%)
B/Shanghai/361/2002-like	0	0	0	0	0	0	0 (0%)
B/Shanghai/361/2002 (low)*	0	0	1	0	0	1	2 (5%)
Total	27	0	12	0	0	1	40
March – October 2007							
B/Malaysia/2506/2004-like	0	0	11	1	0	0	12 (9.8%)
B/ Malaysia/2506/ (low)*	12	0	21	4	0	0	37 (29.8%)
B/Florida/7/2004-like	31	0	41	2	1	0	75 (60.4%)
B/Florida/7/2004 (low)*	0	0	0	0	0	0	0 (0%)
Total	43	0	73	7	1	0	124
October 2007 – February 2008							
B/Malaysia/2506/2004-like	2	0	0	0	0	3	5 (5.4%)
B/ Malaysia/2506/ (low)*	1	0	8	0	0	1	10 (10.7%)
B/Florida/7/2004-like	29	0	28	0	0	8	65 (69.9%)
B/Florida/7/2004 (low)*	5	0	3	0	1	4	13 (14.%)
Total	37	0	39	0	1	16	93
March – September 2008							
B/Malaysia/2506/2004-like	5	0	6	0	1	0	12 (2.3%)
B/ Malaysia/2506/ (low)*	134	2	27	2	1	3	169 (31.9%)
B/Florida/7/2004-like	120	0	42	6	6	0	174 (32.9%)
B/Florida/7/2004 (low)*	97	0	23	0	9	45	174 (32.9%)
Total	356	2	98	8	17	48	529
October 2008 – February 2009							
B/Malaysia/2505/2004-like	14	0	5	0	0	0	19 (3.7%)
B/ Malaysia/2505/ (low)*	299	0	13	0	0	9	321 (63.4%)
B/Florida/7/2004-like	53	0	9	0	0	1	63 (12.4%)
B/Florida/7/2004 (low)*	62	0	14	0	0	28	104 (20.5%)
Total	428	0	41	0	0	38	507
March - September 2009							
B/Brisbane/60/2008-like	4	0	24	0	0	10	38 (55.9%)
B/Brisbane/60/2008 (low)*	2	1	9	0	0	5	17 (25%)
B/Florida/7/2004-like	0	0	0	0	0	0	0
B/Florida/7/2004 (low)*	3	0	8	0	0	2	13 (19.1%)
Total	9	1	41	0	0	17	68

* $\geq$ 8 fold lower in HI assays

TABLE 6.3
Victoria Lineage

	Date: September 16, 2009	Haemagglutination Inhibition Assay - WHO Influenza Centre, Melbourne												
		Reference Antisera												
		1	2	3	4	5	6	7	8	9	10			
		F1096	F1173	F1233	F1236	F1235	F1362	F1364	F1363	F1469	F997	MAB	Passage	Sample
	Reference Antigens	MAL/2506	VIC/304	BRIS/60	BRIS/60	BRIS/33	TOWN/2	HK/90	TEXAS/26	SING/14	FLOR/4	172	History	Date
1	B/MALAYSIA/2506/2004	**1280**	640	20	320	640	40	640	160	80	<20	<20	E4	
2	B/VICTORIA/304/2006	1280	**320**	<20	320	640	40	320	160	80	<20	20	E4	
3	B/BRISBANE/60/2008-c	20	40	**80**	80	640	40	160	20	<20	<20	320	MDCK6	
4	B/BRISBANE/60/2008-e	1280	160	40	**640**	>2560	80	640	320	20	<20	320	E6	
5	B/BRISBANE/33/2008	1280	320	80	1280	**>2560**	80	1280	640	40	<20	640	E3	
6	B/TOWNSVILLE/2/2008	20	40	80	160	1280	**40**	320	40	<20	<20	320	MDCK4	
7	B/HONG KONG/90/2008	1280	160	40	640	1280	80	**1280**	320	20	<20	640	E3	
8	B/TEXAS/26/2008	640	160	40	160	1280	80	320	**640**	20	<20	640	E5	
9	B/SINGAPORE/14/2009	40	80	<20	<20	80	<20	80	20	**80**	<20	<20	MDCKX,MDCK3	
10	B/FLORIDA/4/2006	160	40	<20	40	20	<20	<20	20	<20	**640**	<20	E4	
	Test Ag													
1	B/HUBEI-XILING/37/2009	1280	320	<20	160	640	20	160	320	80	<20	<20	E3+2, E1	
2	B/HUBEI-XILING/35/2009	1280	640	20	160	640	20	320	160	160	<20	20	E1/E2, E2	
3	B/CAMBODIA/3/2009	40	160	160	160	1280	80	640	80	20	<20	640	p2,mdck1	2/04/2009
4	B/CAMBODIA/6/2009	40	80	160	160	1280	40	320	80	<20	<20	1280	p2,mdck1	1/06/2009
5	B/CHANTHABURI/284/2009	40	160	160	160	1280	40	640	80	20	<20	1280	MDCK1, MDCK2	23/06/2009
6	B/SURAT THANI/97/2009	20	80	160	160	1280	80	640	80	<20	<20	1280	MDCK2, MDCK3	20/04/2009
7	B/TRAT/257/2009	20	160	160	160	1280	40	640	40	<20	<20	640	MDCK1, MDCK2	2/06/2009
8	B/CHANTHABURI/329/2009	20	80	80	160	1280	40	320	80	20	<20	1280	MDCK1, MDCK2	2/07/2009
9	B/NONG KHAI/332/2009	640	160	<20	80	160	<20	80	40	40	<20	<20	MDCK1, MDCK2	3/07/2009
10	B/CAMBODIA/1/2009	20	40	160	80	640	40	320	40	<20	<20	640	p3,mdck1	19/02/2009
11	B/CAMBODIA/2/2009	20	40	80	80	640	40	320	40	<20	<20	1280	p2,mdck1	11/03/2009
12	B/CAMBODIA/5/2009	20	40	80	80	1280	40	320	40	<20	<20	640	p3,mdck1	22/04/2009
13	B/CHANTHABURI/124/2009	20	80	80	80	1280	40	320	40	<20	<20	1280	MDCK2, MDCK3	6/05/2009
14	B/CHANTHABURI/199/2009	20	80	80	80	1280	80	640	80	<20	<20	1280	MDCK2, MDCK3	26/05/2009
15	B/TRAT/338/2009	20	80	80	80	1280	40	320	40	<20	<20	640	MDCK1, MDCK2	1/07/2009
16	B/NONG KHAI/269/2009	320	160	<20	40	160	20	160	40	40	<20	<20	MDCK2, MDCK3	5/06/2009
17	B/CAMBODIA/4/2009	20	40	40	40	640	40	160	20	<20	<20	1280	p2,mdck1	18/04/2009
18	B/WASHINGTON/1/2009	80	20	<20	20	40	20	160	80	<20	<20	320	E4	
19	B/SONGKHLA/80/2009	20	<20	<20	<20	<20	<20	<20	<20	<20	80	<20	MDCK2, MDCK3	11/03/2009

TABLE 6.4
Victoria Lineage

	Date: August 5, 2009	Haemagglutination Inhibition Assay - WHO Influenza Centre, Melbourne										
		Reference Antisera										
		1	2	3	4	5	6	7	8	9		
		F1096	F1173	F1233	F1236	F1235	F1362	F1364	F1363	F997	Passage	Sample
		MAL/2506	VIC/304	BRIS/60	BRIS/60	BRIS/33	TOWN/2	HK/90	TEXAS/26	FLOR/4	History	Date
1	B/MALAYSIA/2506/2004	**1280**	320	<20	160	640	20	160	160	<20	E4	
2	B/VICTORIA/304/2006	1280	**320**	<20	160	640	20	160	160	<20	E4	
3	B/BRISBANE/60/2008	20	80	**160**	160	1280	40	320	40	<20	MDCK6	
4	B/BRISBANE/60/2008	1280	320	80	**640**	1280	80	1280	320	<20	E6	
5	B/BRISBANE/33/2008	1280	320	80	640	**1280**	80	1280	640	<20	E3	
6	B/TOWNSVILLE/2/2008	20	80	160	160	1280	**80**	320	80	<20	MDCK4	
7	B/HONG KONG/90/2008	1280	320	80	640	1280	80	**1280**	320	<20	E3	
8	B/TEXAS/26/2008	640	160	40	320	1280	40	640	**640**	<20	E5	
9	B/FLORIDA/4/2006	160	20	<20	40	<20	<20	<20	<20	**640**	E4	
	Test Ag											
1	B/SURAT THANI/18/2009	40	160	320	160	>2560	80	640	80	<20	MDCK3	9/01/2009
2	B/SURAT THANI/71/2009	40	160	160	160	1280	80	320	40	<20	MDCK2,SIAT1	20/02/2009
3	B/SYDNEY/4/2009	40	80	160	160	1280	80	320	40	<20	MDCKX,MDCK1	4/05/2009
4	B/SYDNEY/1/2009	20	80	160	160	1280	80	320	80	<20	MDCKX,MDCK1	1/04/2009
5	B/SYDNEY/99/2008	1280	320	<20	160	640	20	160	160	<20	mdckx.mdck1	25/08/2008
6	B/SYDNEY/2/2009	20	80	160	80	1280	40	320	40	<20	MDCKX,MDCK1	31/03/2009
7	B/SINGAPORE/8/2009	20	80	160	80	1280	40	320	40	<20	MDCK1, MDCK2	20/02/2009
8	B/SINGAPORE/22/2009	160	320	<20	<20	160	<20	80	20	<20	MDCK1, MDCK2	2/06/2009
9	B/PHILIPPINES/10/2009	80	320	<20	<20	80	<20	40	20	<20	mdck3	10/03/2009
10	B/SINGAPORE/12/2009	80	320	<20	<20	80	<20	40	<20	<20	MDCK1, MDCK2	11/04/2009
11	B/SYDNEY/3/2009	40	160	<20	<20	40	<20	40	<20	<20	MDCKX,MDCK1	5/05/2009
12	B/SINGAPORE/17/2009	40	160	<20	<20	40	<20	40	<20	<20	MDCK1, MDCK2	22/04/2009

FIGURE 6.3
Phylogenetic relationships among influenza B HA1 genes 2009
B/Victoria Lineage

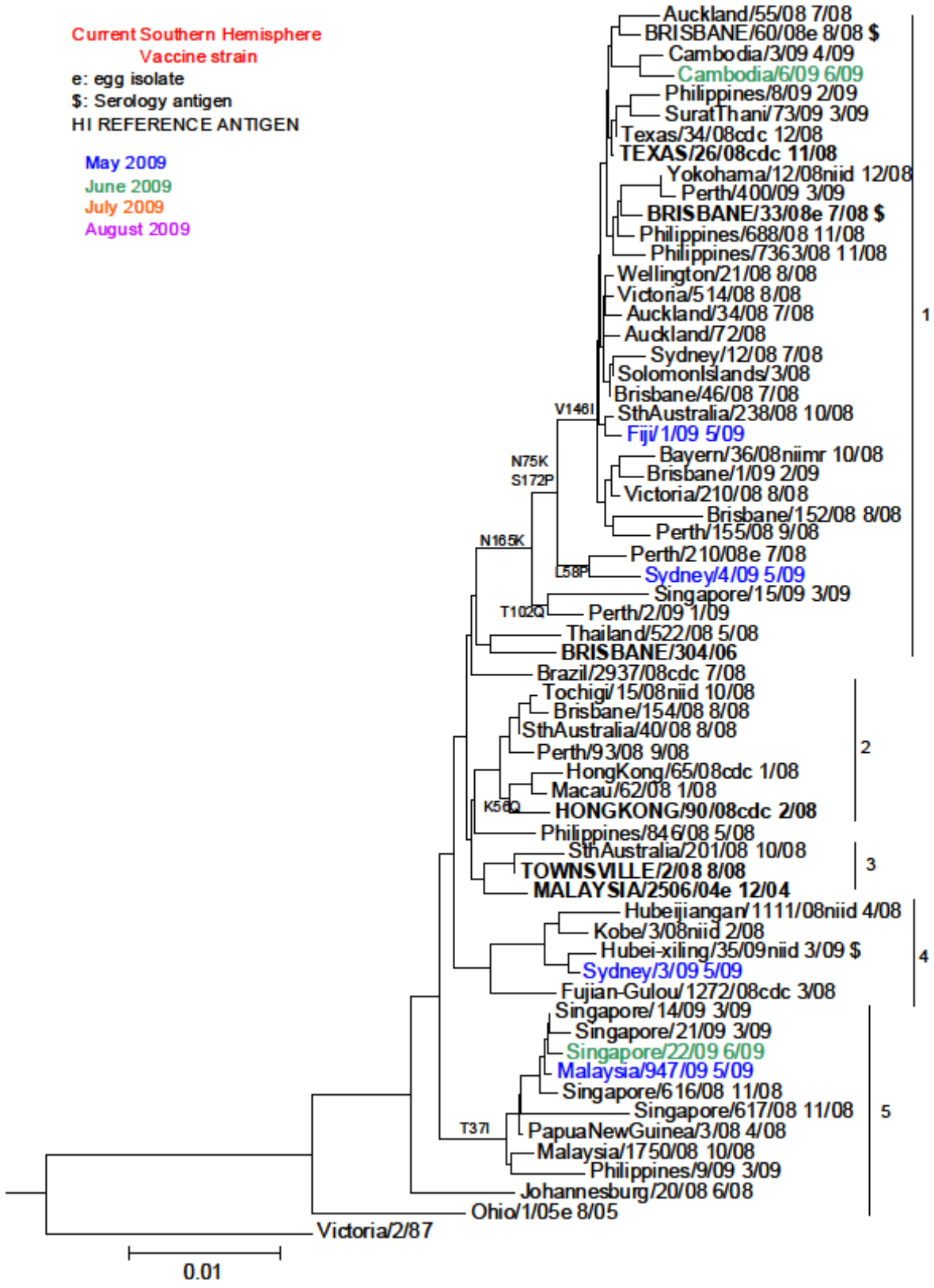


FIGURE 6.4
Phylogenetic relationships among influenza B HA1 genes 2009
B/Yamagata Lineage

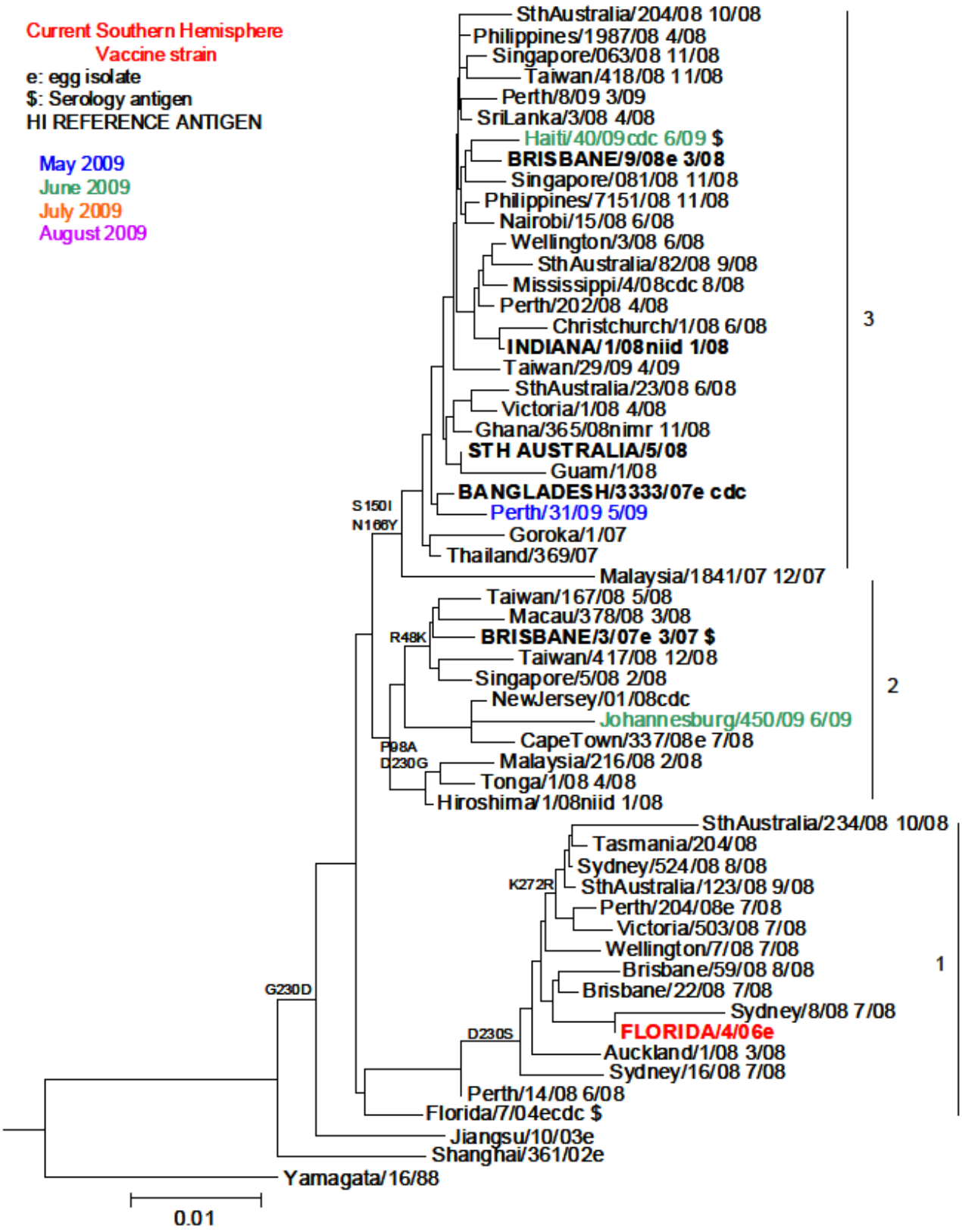


FIGURE 6.5
Phylogenetic relationships among influenza B neuraminidase genes 2009

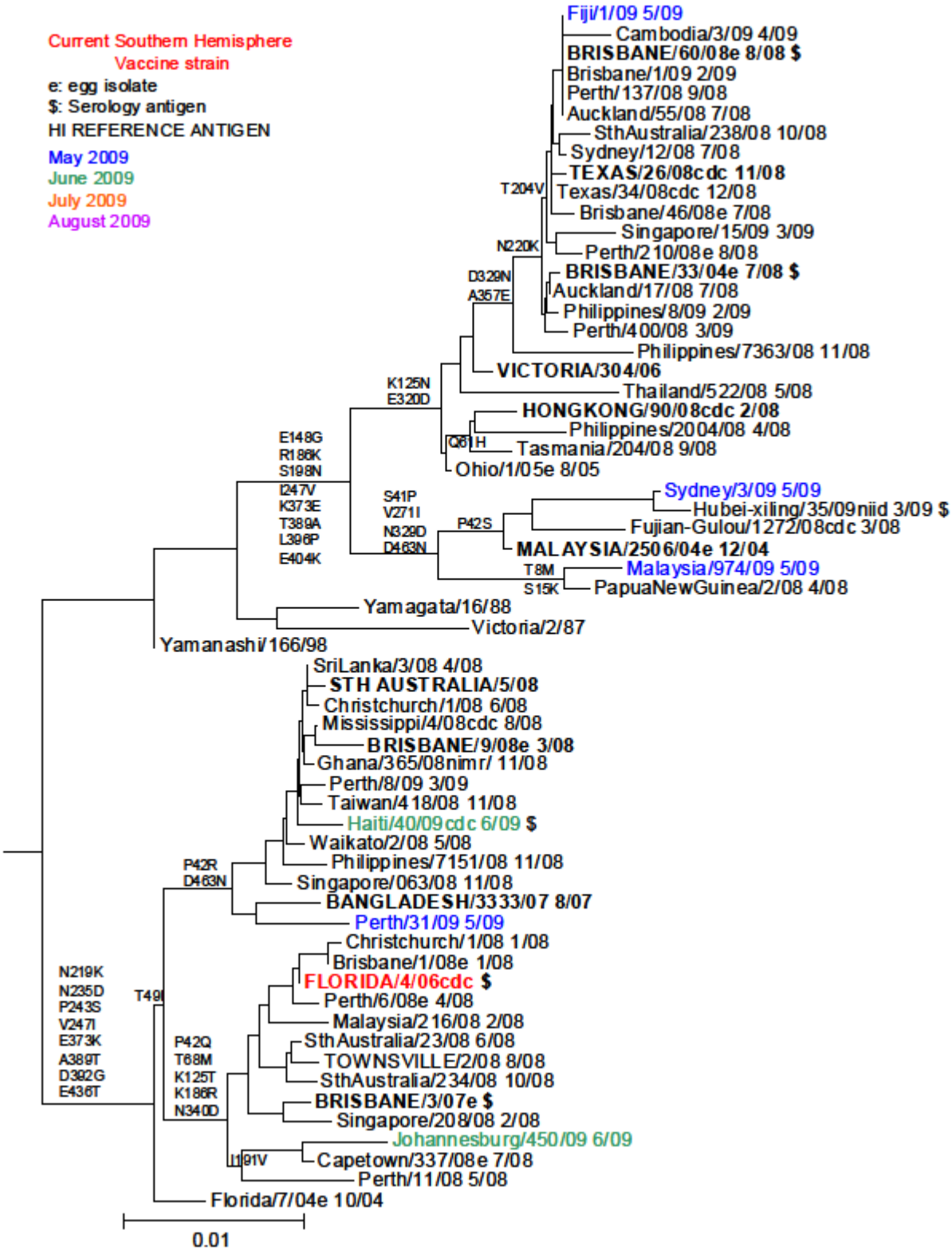


Table 5.7
Haemagglutination inhibition antibody responses
Influenza type B vaccine component
Young Adults

Population	N	Antigen	Passage History	% Rise	GMT		%>/=40		%>/=160	
					Pre	Post	Pre	Post	Pre	Post
Australian Younger Adult	20	B/Brisbane/60/2008^	E4	20	14.1	26.4	20	45	10	20
		B/Brisbane/3/2007*+	E3	65	117.1	519.6	95	100	45	95
		B/Hebei-Yiling/37/2009^	E6	5	13.7	20.0	21	30	13	25
European Younger Adult	24	B/Brisbane/60/2008*^	E4	33	17.3	53.4	42	71	8	29
		B/Brisbane/3/2007+	E3	33	38.9	77.7	58	79	21	33
		B/Hebei-Yiling/37/2009^	E6	21	13.3	33.6	29	58	4	21
Japanese Younger Adult	24	B/Brisbane/60/2008^	E4	13	27.5	30.8	58	58	21	21
		B/Brisbane/3/2007*+	E3	25	116.4	213.5	92	100	58	75
		B/Hebei-Yiling/37/2009^	E6	4	25.2	26.7	46	50	42	46

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	20	B/Brisbane/60/2008^	E4	20	20.0	34.8	35	65	5	10
		B/Brisbane/3/2007*+	E3	30	95.1	242.4	95	100	45	90
		B/Hebei-Yiling/37/2009^	E6	20	16.2	27.3	35	55	5	10
European Older Adult	12	B/Brisbane/60/2008*^	E4	54	9.2	42.4	21	67	4	25
		B/Brisbane/3/2007+	E3	38	109.0	23.1	21	42	0	13
		B/Hebei-Yiling/37/2009^	E6	67	7.7	28.3	11	72	0	28
European Older Adult	13	B/Brisbane/60/2008^	E4	13	20.0	30.8	46	54	17	21
		B/Brisbane/3/2007*+	E3	50	20.0	80.0	33	88	4	38
		B/Hebei-Yiling/37/2009^	E6	17	15.4	25.9	38	50	8	17

*Vaccine strain
^B/Vic – like viruses

APPENDIX 6

WHO RECOMMENDATION FOR INFLUENZA VACCINES

2009, 84, 421–436 No. 41

World Health Organization
Organisation mondiale de la Santé

Weekly epidemiological record
Relevé épidémiologique hebdomadaire

9 OCTOBER 2009, 84th YEAR / 9 OCTOBRE 2009, 84e ANNÉE
No. 41, 2009, 84, 421–436
http://www.who.int/wer

Contents

Sommaire

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Geneva

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Recommended composition of influenza virus vaccines for use in the 2010 influenza season (southern hemisphere winter)

September 2009

WHO convenes technical meetings[1] in February and September every year to recommend the composition of influenza vaccines[2] for the northern and southern hemispheres, respectively. This recommendation relates to the composition of vaccines for the forthcoming influenza season in the southern hemisphere (May to October 2010). A recommendation will be made in February 2010 relating to vaccines that will be used for the influenza season in the northern hemisphere (November 2010 to April 2011). For countries in equatorial regions, epidemiological considerations will influence which recommendation (February or September) individual national authorities consider more appropriate.

Influenza activity, February – September 2009

Between February and September 2009, influenza activity was reported in Africa, the Americas, Asia, Europe and Oceania (*Table 1*). Activity was higher compared with the same period the previous year[3] and was due to both seasonal influenza and pandemic influenza A(H1N1) 2009 viruses. Following its emergence in March, the pandemic A(H1N1) virus spread rapidly throughout the world, leading to the declaration of an influenza pandemic by WHO on 11 June 2009.[4]

1 See http://www.who.int/csr/disease/influenza/vaccinerecommendations/en/index.html

2 A description of the process of influenza vaccine virus selection and development is available at: http://www.who.int/gb/pip/pdf_files/Fluvaccvirusselection.pdf

3 See http://www.who.int/wer/2008/wer8341/en/index.html

4 See http://www.who.int/mediacentre/news/statements/2009/h1n1_pandemic_phase6_20090611/en/index.html

Recommandation relative à la composition des vaccins antigrippaux pour la saison 2010 (prochain hiver dans l'hémisphère Sud)

Septembre 2009

L'OMS organise chaque année des réunions techniques[1] en février et en septembre pour recommander la composition des vaccins contre la grippe saisonnière[2] pour les hémisphères Nord et Sud, respectivement. La présente recommandation s'applique à la composition des vaccins contre la grippe saisonnière pour l'hiver prochain dans l'hémisphère Sud (mai à octobre 2010). Une recommandation relative aux vaccins à utiliser pendant la saison grippale de l'hémisphère Nord (novembre 2010 à avril 2011) sera formulée en février 2010. Pour les pays des régions équatoriales, les autorités nationales s'appuieront sur des considérations épidémiologiques pour déterminer laquelle des deux recommandations est la plus adaptée (février ou septembre).

Activité grippale, février-septembre 2009

Entre février et septembre 2009, on a signalé une activité grippale en Afrique, dans les Amériques, en Asie, en Europe et en Océanie (*Tableau 1*). L'activité a été plus importante qu'au cours de la même période de l'année précédente[3] et a été due aussi bien au virus de la grippe saisonnière qu'au virus de la grippe pandémique A (H1N1) 2009. Suite à l'émergence de ce dernier en mars, ce virus s'est répandu très rapidement partout dans le monde, conduisant à la déclaration par l'OMS de la pandémie grippale le 11 juin 2009.[4]

1 Voir http://www.who.int/csr/disease/influenza/vaccinerecommandations/en/index.html.

2 On trouvera une description du procédé de sélection et de mise au point des virus vaccins grippaux à l'adresse suivante: http://www.who.int/gb/pip/pdf_files/Fluvaccvirusselection.pdf.

3 Voir http://www.who.int/wer/2008/wer8341/en/index.html.

4 Voir http://www.who.int/mediacentre/news/statements/2009/h1n1_pandemic_phase6_20090611/en/index.html.

Table 1 **Extent and type of influenza activity worldwide, February–August 2009**
Tableau 1 **Etendue et type d'activité grippale dans le monde, février-août 2009**

Country, area or territory – Pays, région ou territoire	February – Février	March – Mars	April – Avril	May – Mai	June – Juin	July – Juillet	August – Août
Africa – Afrique							
Algeria – Algérie					H1(pdm)	H1(pdm)	H1(pdm)
Angola							H1(pdm)
Botswana						H1(pdm)	H1(pdm)
Cameroon – Cameroun	•H1, •B		•H1		••••H3	•H1, ••••H3	••H3, H1(pdm)
Cape Verde – Cap Vert						H1(pdm)	•H1, •H3
Côte d'Ivoire	•H1, •H3, •B	•H3, •B	•H1, •H3, •B, H1(pdm)	••H1, ••H3, •B, H1(pdm)	•H3, •B, H1(pdm)	•H1, •H3, H1(pdm)	
Democratic Republic of the Congo – République démocratique du Congo							H1(pdm)
Djibouti						••H3, ••B	H1(pdm)
Egypt – Egypte	•B	•B	•H1, • B	•H1, •B	H1(pdm)	H1(pdm)	
Ethiopia – Ethiopie					H1(pdm)		
France, Mayotte							•A, H1(pdm)
France, Réunion					•B	••B, H1(pdm), •H3	••B, H1(pdm), •A
Gabon						H1(pdm)	
Ghana	•B		•H3, •B	•H1	•H1, •H3, •B	•H3	H1(pdm)
Kenya	•H1,•H3, •B	•H1,•H3	•H1,•H3	•H1, H1(pdm)	•H3, H1(pdm)	••H1, •B, H1(pdm)	•H1, •H3, •B, H1(pdm)
Libyan Arab Jamahiriya – Jamahiriya arabe lybienne						H1(pdm)	
Madagascar	•H1, •H3	•H3	•H1, •H3	•H1, •H3, •B	•H1, •H3, ••B	•H3, ••B	••B
Mauritius – Maurice					•H3, H1(pdm)	•H3, •B	
Morocco – Maroc	•H1	•B	•B		•A, H1(pdm)	•H1, H1(pdm)	H1(pdm)
Mozambique							H1(pdm)
Namibia – Namibie						H1(pdm)	H1(pdm)
Nigeria – Nigéria		•A	•H3	•H3	•H3	•A	
Senegal – Sénégal					••H3	•H3	
Seychelles						H1(pdm)	
Somalia – Somalie							H1(pdm)
South Africa – Afrique du Sud			••H3	•H1, •••H3, •B	••••H3, •B, H1(pdm)	•H1, •••H3, •B, H1(pdm)	••H3, H1(pdm)
Sudan – Soudan						H1(pdm)	H1(pdm)
Swaziland							H1(pdm)
Tunisia – Tunisie	•H1, ••••H3, •B	•H1, ••••H3, •B	••H3, •B		•H1, •B, H1(pdm)	•H3	•B, H1(pdm)
Uganda – Ouganda				H1(pdm)	H1(pdm)		
United Republic of Tanzania – République-Unie de Tanzanie				H1(pdm)	H1(pdm)		
Zambia – Zambie						H1(pdm)	H1(pdm)
Zimbabwe						H1(pdm)	H1(pdm)
America – Amériques							
Antigua and Barbuda – Antigua-et-Barbuda						H1(pdm)	H1(pdm)
Argentina – Argentine			H1(pdm)	••H3, ••H1, H1(pdm)	••H3, H1(pdm)	H1(pdm)	H1(pdm)
Bahamas				H1(pdm)	H1(pdm)		
Barbados – La Barbade				•H3	H1(pdm)		H1(pdm)
Belize						H1(pdm)	
Bolivia (Plurinational State of) – Bolivie (Etat plurinational de)				H1(pdm)	H1(pdm)	H1(pdm)	H1(pdm)
Brazil – Brésil	•B,	•H1, •B	•H1, H1(pdm)	•H1, •H3, •B, H1(pdm)	•••A, •H1, •H3, •B, H1(pdm)	•••A, •H3, •B, H1(pdm)	H1(pdm)
Canada	••H1, •H3, •••B	••H1, •H3, •••B	••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)
Chile – Chili	•H1		•H1	•H1,•H3, H1(pdm)	•H3, H1(pdm)	•••H3,•B, H1(pdm)	H1(pdm)
Colombia – Colombie	•H3, •B	•H1	•H1, •H3, H1(pdm)	•H1, •H3, H1(pdm)	••••H3, 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
Costa Rica			••••B, H1(pdm)	••••H1, •B, H1(pdm)	••••H3, ••••B, •H1, H1(pdm)	H1(pdm)	H1(pdm)
Cuba				H1(pdm)	H1(pdm)		
Dominica – Dominique					H1(pdm)		
Dominican Republic – République dominicaine				•H1, •B, H1(pdm)	•H3, H1(pdm)	H1(pdm)	H1(pdm)
Ecuador – Equateur	•H1, •H3	•H3		•H1, •H3, •B, H1(pdm)	•H1, •••H3, •B, H1(pdm)	•H3, H1(pdm)	H1(pdm)
El Salvador			H1(pdm)	•H1, •B, H1(pdm)	••H1, •B, H1(pdm)	••H1	
France, French Guiana – Guyane française	•H3, •B	•H3	•H3, •B,	•H3, •B,	•H3	•H1, •H3, H1(pdm)	•H1, •H3, •B, H1(pdm)
France, Guadeloupe		•H3			•H3, H1(pdm)	H1(pdm)	H1(pdm), •H3
France, Martinique	•H3				H1(pdm)	•H1, H1(pdm)	•H1, H1(pdm)
France, Saint Barthélemy							H1(pdm)
France, Saint Martin						H1(pdm)	
Grenada – Grenade							H1(pdm)
Guatemala		•B, •H1	•H1, H1(pdm)	••H1, •H3, H1(pdm)	•H3, ••••B,	•H3, •B	
Guyana – Guyane						H1(pdm)	H1(pdm)
Haiti					•B, H1(pdm)	•H3, •B, H1(pdm)	
Honduras			•H3	•H1, •H3, •B, H1(pdm)	•••H3, •••B, H1(pdm)	••H3, H1(pdm)	
Jamaica – Jamaïque		•H1, •B	•H1, •H3		•H3, H1(pdm)		
Mexico – Mexique	•H1, •H3, •B, H1(pdm)	•H1, ••H3, ••B, H1(pdm)	•••H1, •••H3, H1(pdm)	H1(pdm)	H1(pdm)	H1(pdm)	H1(pdm)
Nicaragua					••••H1, H1(pdm)	H1(pdm)	H1(pdm)
Panama	•A, •B	•A, •B		•H1, H1(pdm)	H1(pdm)	H1(pdm)	
Paraguay			H1(pdm)	•H3, H1(pdm)	•H1, •H3, H1(pdm)	H1(pdm)	H1(pdm)
Peru – Pérou	•A, •B	•A, •B	•A	••H1, H1(pdm)			
Puerto Rico – Porto Rico				H1(pdm)	H1(pdm)	H1(pdm)	H1(pdm)
Saint Kitts and Nevis – Saint Kitts et Nevis						H1(pdm)	
Saint Lucia – Sainte-Lucie						H1(pdm)	
Saint Vincent and the Grenadines – Saint Vincent et les Grenadines							H1(pdm)
Suriname					•H3, H1(pdm)	H1(pdm)	H1(pdm)
Trinidad and Tobago – Trinité et Tobago		•H3	H1(pdm)	H1(pdm)	H1(pdm)		
United Kingdom, Anguilla – Royaume-Uni, Anguilla					•H3		H1(pdm)
United Kingdom, Bermuda – Royaume-Uni, Bermudes				H1(pdm)	H1(pdm)		
United Kingdom, British Virgin Islands – Royaume-Uni, Iles Vierges britanniques					H1(pdm)		
United Kingdom, Cayman Islands – Royaume-Uni, Iles Caïman				•H1	•H1, •H3, H1(pdm)		
United States of America – Etats-Unis d'Amérique	••••H1, ••H3, ••••B	•••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)
United States of America, Virgin Islands – Etats-Unis d'Amériques, Iles Vierges							H1(pdm)
Uruguay	•A	•A		•A, H1(pdm)	•H1, •B, H1(pdm)	H1(pdm)	H1(pdm)
Venezuela (Bolivarian Republic of) – Venezuela (République bolivarienne du)					H1(pdm)		
Asia							
Afghanistan					H1(pdm)	H1(pdm)	
Azerbaijan – Azerbaïdjan				•B	•B		H1(pdm)
Bahrain – Bahrein					H1(pdm)	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
Bangladesh		•H3	•H3	•H3	•H3, •B, H1(pdm)	H1(pdm)	
Bhutan – Bhoutan					H1(pdm)	H1(pdm)	H1(pdm)
Brunei Darussalam – Brunéi Darussalam					H1(pdm)	H1(pdm)	H1(pdm)
Cambodia – Cambodge					H1(pdm)	H1(pdm)	••H3, H1(pdm)
China – Chine	•H1, •H3, •B	•H1, •H3, ••B	•H1, •H3,••B	•H1, •H3, •B, H1(pdm)	••H1, ••H3, •B	••H1, •••H3, •B, H1(pdm)	••H1, •••H3, •B
Taiwan, China – Taïwan, Chine	••H1, •H3	•H1, •H3	•B	•H3, H1(pdm)	H1(pdm)	H1(pdm)	H1(pdm)
China (Hong Kong SAR) – Chine (RAS Hong Kong)	••H1, •H3, •B	•H1, •H3, •B	•H1, •H3, •B	•H1, •H3, •B, H1(pdm)	•H1, •H3, •B, H1(pdm)	•H1, ••H3, •B, H1(pdm)	•H1, ••H3, •B, H1(pdm)
Democratic People's Republic of Korea				H1(pdm)	H1(pdm)	H1(pdm)	H1(pdm)
Indonesia – Indonésie					H1(pdm)	H1(pdm)	H1(pdm)
India – Inde	•H1	•H1			H1(pdm)	H1(pdm)	H1(pdm)
Iran (Islamic Republic of) – Iran (République islamique d')	•H3, •B	•H1		•B	•H3, H1(pdm)	•H1, •H3, •B, H1(pdm)	H1(pdm)
Iraq					H1(pdm)	H1(pdm)	
Israel – Israël	•••H3,•B	•••H1, •H3, •B	•H1, • H3, • B	•H1, •H3, •B	H1(pdm)	H1(pdm)	H1(pdm)
Japan – Japon	••••H1, ••H3, ••••B	••H1, •H3, ••••B	•H1, ••H3, ••B	•H1, •••H3, •B, H1(pdm)	•H1, ••H3, •B, H1(pdm)	•H1, •H3, •B, H1(pdm)	•H1, •H3, H1(pdm)
Jordan – Jordanie					H1(pdm)	H1(pdm)	H1(pdm)
Kazakhstan	•A	•A,•B	•A, •B	•A, •B		H1(pdm)	H1(pdm)
Kuwait – Koweït				H1(pdm)	H1(pdm)	H1(pdm)	
Kyrgyzstan	•H3	• H1, •H3				•H1	•H3, H1(pdm)
Lao People's Democratic Republic – République démocratique populaire lao					H1(pdm)	H1(pdm)	H1(pdm)
Lebanon – Liban				H1(pdm)	H1(pdm)	H1(pdm)	H1(pdm)
Malaysia – Malaysie	•H3	•B	•H3, •B	•H3, •B	H1(pdm)	H1(pdm)	H1(pdm)
Mongolia – Mongolie	•••H1	•H1					
Nepal – Népal					H1(pdm)	H1(pdm)	H1(pdm)
Myanmar					H1(pdm)	H1(pdm)	H1(pdm)
Oman			•H3, •B	•H3, •B	H1(pdm)	H1(pdm)	H1(pdm)
Pakistan	•H3, •B				H1(pdm)	•A	•A
Philippines	•H1, •H3	•H1, •H3	•H1, •H3	H1(pdm)	H1(pdm)	H1(pdm)	H1(pdm)
Qatar					H1(pdm)		
Republic of Korea – République de Corée			H1(pdm)	•H3, H1(pdm)	H1(pdm)	•H1, •H3, H1(pdm)	•H3, •B, H1(pdm)
Saudi Arabia – Arabie saoudite					H1(pdm)	H1(pdm)	H1(pdm)
Singapore – Singapour	•B	•H1	•H3, •B	•H1, •H3, H1(pdm)	•H3, •B, H1(pdm)	H1(pdm)	H1(pdm)
Sri Lanka			•H1	•H1	•H1, H1(pdm)	•H1, •B, H1(pdm)	•H3, •B, H1(pdm)
Syrian Arab Republic – République arabe syrienne						H1(pdm)	H1(pdm)
Thailand – Thaïlande				H1(pdm)	H1(pdm)	H1(pdm)	H1(pdm)
United Arab Emirates – Emirats arabes unis				H1(pdm)	H1(pdm)	H1(pdm)	H1(pdm)
Uzbekistan						H1(pdm)	H1(pdm)
Viet Nam			•H3, •B	•H3	H1(pdm)	H1(pdm)	H1(pdm)
Yemen – Yémen					H1(pdm)	H1(pdm)	H1(pdm)
Europe							
Albania – Albanie	•H3			•B		H1(pdm)	H1(pdm)
Andorra – Andorre						H1(pdm)	
Austria – Autriche	••••H3	•H3, •B	•B	H1(pdm)	H1(pdm)	H1(pdm)	H1(pdm)
Belarus – Bélarus	••••H3	•••A, •B	•A, •B			•A	
Belgium – Belgique	•H1, ••••H3, •B	••••H3, •B	•B	H1(pdm)	H1(pdm)	H1(pdm)	H1(pdm)
Bosnia and Herzegovina – Bosnie-Herzégovine	••••H3					H1(pdm)	H1(pdm)
Bulgaria – Bulgarie	••H3		•H3, •B		H1(pdm)	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
Croatia – Croatie	••••H3, •B	••H3, •••• B	•H3, ••B			•H1	
Cyprus – Chypre					H1(pdm)	H1(pdm)	H1(pdm)
Czech Republic – République tchèque	•H1, ••••H3, •B	••H3, ••B	•A, •B	H1(pdm)	H1(pdm)		
Denmark – Danemark	••••H3	•H1, •H3, •B	•H1, •B	•H1, •H3, •B, H1(pdm)	•H1, •H3, •B, H1(pdm)	H1(pdm)	H1(pdm)
Estonia – Estonie	••••H3, •B	••••H3, ••B	•H1, ••H3, ••B	•H3, •B	•A , •B, H1(pdm)	H1(pdm)	H1(pdm)
Finland – Finlande	•H1, ••••H3, •B	•H1, ••••H3	•H1, ••H3, •B	•B, H1(pdm)			
France	•H1, ••••H3, •B	•H3, ••B	•H3,•B, H1(pdm)	•H1, •H3, H1(pdm)	•H1, •H3, •B H1(pdm)	•H1, •H3, H1(pdm)	•H1, •H3, •B, H1(pdm)
Georgia – Georgie	•H3,•B	•H1, •H3, •B	•B	•B		H1(pdm)	H1(pdm)
Germany – Allemagne	•H1, ••••H3, •B	•H1, •••H3, ••B	•B	H1(pdm)	H1(pdm)	H1(pdm)	H1(pdm)
Greece – Grèce	•H3	••H3, ••B	•H3, •B	•H3, H1(pdm)	H1(pdm)	•H3, H1(pdm)	H1(pdm)
Hungary – Hongrie	••••H3, •B	••••H3, •B	•A, •B		H1(pdm)	H1(pdm)	H1(pdm)
Iceland – Islande					H1(pdm)		
Ireland – Irlande				H1(pdm)	H1(pdm)	H1(pdm)	H1(pdm)
Italy – Italie	•H1, •••H3, •B	•H3, •B	•H3, •B	•H1	•H1, •H3, H1(pdm)	•H1, •H3, H1(pdm)	H1(pdm)
Latvia – Lettonie	•H1, •••H3, •B	•••H3, •B	•H1, • H3, • B	•H1, • H3, • B		H1(pdm)	H1(pdm)
Liechtenstein							H1(pdm)
Lithuania – Lithuanie	••H3, •B				H1(pdm)	H1(pdm)	H1(pdm)
Luxembourg	••••H3	••H3	•B	•H3	H1(pdm)	H1(pdm)	H1(pdm)
Malta – Malte					H1(pdm)	H1(pdm)	H1(pdm)
Monaco					H1(pdm)		
Montenegro					H1(pdm)		H1(pdm)
Netherlands – Pays-Bas	•H1, ••••H3, •B	••••H3, •B	•A, •B, H1(pdm)	H1(pdm)	H1(pdm)	H1(pdm)	H1(pdm)
Norway – Norvège	•H1, ••••H3	••••H3	•H1,•H3, •B	•H3, •B, H1(pdm)	•H3, •B, H1(pdm)	•H3, •B, H1(pdm)	•H3, •B, H1(pdm)
Poland – Pologne	•H1, •••H3,•B	••H3, •B	•H3, •B	•H1, •H3, H1(pdm)	•H1, •H3, H1(pdm)	H1(pdm)	H1(pdm)
Portugal	••H3	•H3		•B, H1(pdm)	•H3,•B, H1(pdm)	H1(pdm)	H1(pdm)
Republic of Moldova – République de Moldavie		•H3,• B			H1(pdm)		
Romania – Roumanie	•••H3	•••H3	••H3	•A, •B, H1(pdm)	•H1, •B, H1(pdm)	•H3, H1(pdm)	H1(pdm)
Russian Federation – Fédération de Russie	••H1, ••H3, ••B	•H1, ••H3, ••B	• H1, ••H3, ••B	•H1, •H3, •B, H1(pdm)	•H1, •H3, •B	•H1, •H3,• B, H1(pdm)	H1(pdm)
Serbia – Serbie	•H3,••B	••H3, ••B			H1(pdm)	H1(pdm)	H1(pdm)
Slovakia – Slovaquie	•••H3,•B	••H3, •B	•B	H1(pdm)	H1(pdm)	H1(pdm)	H1(pdm)
Slovenia – Slovénie	••••H3	•••H3	••H1, •H3, •B	•H3, •B	H1(pdm)	H1(pdm)	H1(pdm)
Spain – Espagne	••H3,•B	•H3, ••B	•B, H1(pdm)	•B, H1(pdm)	H1(pdm)	H1(pdm)	H1(pdm)
Sweden – Suède	•H1, ••••H3	••H3, •B	•H3, •B	•A, •B, H1(pdm)	•A, •B, H1(pdm)	H1(pdm)	H1(pdm)
Switzerland – Suisse	••••H3, ••B	••••H3, •B	•B	•B, H1(pdm)		H1(pdm)	H1(pdm)
The former Yugoslav Republic of Macedonia – Ex-République yougoslave de Macédoine					H1(pdm)	H1(pdm)	H1(pdm)
Turkey – Turquie		•H3, ••B	•B	•B, H1(pdm)			H1(pdm)
Ukraine	••H3, •B	••••H3, •B	••H3, •B	•B, H1(pdm)	•B		
United Kingdom of Great Britain and Northern Ireland – Royaume-Uni et Irlande du Nord	••H1, ••H3, ••B	•H1,•H3, •B	••H3, ••B, H1(pdm)	•H1,•H3, •B, H1(pdm)	H1(pdm)	•H3, H1(pdm)	H1(pdm)
Oceania – Océanie							
Australia – Australie	•H1	•H1,•H3, •B	•H1,•H3, •B	•H1,•H3, H1(pdm)	•H1,••H3, H1(pdm)	•H1,••H3, H1(pdm)	•H1,•H3, H1(pdm)
Fiji – Fidji			•H1	•H1	H1(pdm)	H1(pdm)	
France, New Caledonia – Nouvelle Calédonie				•H1, •H3	••H1, •H3, H1(pdm)	•H1,••H3, H1(pdm)	•••H3, H1(pdm)
France, Tahiti			•H1,	•H1, H1(pdm)	H1(pdm),	•A, H1(pdm)	•A, H1(pdm)
France, Wallis and Futuna – Wallis et Futuna							H1(pdm)
Kiribati					H1(pdm)	••H3, H1(pdm)	
Maldives						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
Marshall Islands – Iles Marshall							H1(pdm)
Micronesia (Federated States of), Chuuk – Micronésie (Etats fédérés de), Chuuk					••H3, H1(pdm)	••H3, H1(pdm)	H1(pdm)
Micronesia (Federated States of), Pohnpei – Micronésie (Etats fédérés de), Pohnpei					••H3, H1(pdm)	••H3, H1(pdm)	H1(pdm)
Micronesia (Federated States of), Yap – Micronésie (Etats fédérés de), Yap					•H3	•••H3, H1(pdm)	H1(pdm)
Nauru					H1(pdm)	H1(pdm)	
New Zealand – Nouvelle Zélande		•H1, •H3	•H1, •H3, •B, H1(pdm)	•••H1, ••H3, •B	•••H1, •H3, •B, H1(pdm)	•H1, •H3, H1(pdm)	•H1, •H3, H1(pdm)
Palau – Palaos				•H3, •H1, H1(pdm)	•H3, H1(pdm)	H1(pdm)	•H3, H1(pdm)
Papua New Guinea – Papouasie Nouvelle-Guinée				•H3	••H3, H1(pdm)	•H3, H1(pdm)	•H3
Timor-Leste							H1(pdm)
Tonga						H1(pdm)	H1(pdm)
United States of America, American Samoa – Etats-Unis d'Amérique, Samoa Américaine					•H1	H1(pdm)	
United States of America, Guam – Etats-Unis d'Amérique, Guam				•H3	H1(pdm)	H1(pdm)	H1(pdm)
Vanuatu					•H1, ••H3, H1(pdm)	•H1, ••H3	

Data in *Table 1* were provided by the Global Influenza Surveillance Network. – Les données du *Tableau 1* ont été fournies par le réseau mondial de surveillance de la grippe.

• = Sporadic activity – Activité sporadique
•• = Local activity – Activité locale
••• = 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

Seasonal influenza

In the northern hemisphere, influenza activity was widespread in many countries in February and declined during March and April in some countries. The predominant viruses in Europe and many other countries were A(H3N2), while in Japan and North America higher proportions of A(H1N1) and B viruses were reported. Influenza A(H1N1), A(H3N2) and B viruses co-circulated in varying proportions in many northern hemisphere and tropical countries of Africa and Asia. From June to August, increased activity was reported in some countries in Asia, with regional outbreaks of influenza A(H3N2) in China.

In the southern hemisphere, influenza activity began to increase in April, and widespread outbreaks of influenza A(H3N2) were reported in South Africa in June. Influenza A(H3N2) and, to a lesser extent, A(H1N1) circulated in Argentina, Australia and Chile, while New Zealand reported predominantly A(H1N1) activity. Local outbreaks of influenza B occurred in Madagascar and Réunion (France), and B viruses were detected at low levels in many other countries.

Grippe saisonnière

Dans l'hémisphère Nord, l'activité grippale a été largement répandue dans de nombreux pays en février et a ensuite décliné en mars et en avril dans certains d'entre eux. Les virus A (H3N2) ont prédominé en Europe et dans de nombreux autres pays, tandis que des proportions plus élevées de virus A (H1N1) et B ont été rapportées au Japon et en Amérique du Nord. Les virus grippaux A (H1N1), A (H3N2) et B ont circulé en même temps dans des proportions diverses dans de nombreux pays de l'hémisphère Nord, ainsi que dans des pays tropicaux d'Afrique et d'Asie. Entre juin et août, une activité accrue a été rapportée dans certains pays d'Asie, avec des flambées régionales de grippe A (H3N2) en Chine.

Dans l'hémisphère Sud, l'activité grippale a commencé à s'accroître en avril et des flambées étendues de grippe A (H3N2) ont été signalées en Afrique du Sud en juin. La grippe A (H3N2) et, dans une moindre mesure, la grippe A (H1N1) ont circulé en Argentine, en Australie et au Chili, tandis que la Nouvelle Zélande a surtout signalé une activité de la grippe A (H1N1). Des flambées locales de grippe B se sont produites à Madagascar et à la Réunion (France) et des virus B ont été détectés à des niveaux faibles dans de nombreux autres pays.

Pandemic A(H1N1) influenza

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

Outbreaks of pandemic A(H1N1) occurred in many countries in the northern hemisphere during May to August. Following a decline in activity in some countries during July or August, a resurgence was reported in September in some countries in Europe and the Americas. From August, rapid increases in activity were reported in African and Asian countries, for example in Cambodia, China, Japan, Kenya, the Lao People's Democratic Republic, the United Republic of Tanzania and Viet Nam.

In the southern hemisphere, pandemic A(H1N1) activity increased rapidly in many countries. Activity peaked in July in some countries, falling to low levels by August or September in Argentina, Australia, Brazil, Chile and New Zealand. In some other countries in the southern hemisphere and in tropical regions of the Americas and Asia, pandemic A(H1N1) influenza virus continued to circulate in September.

The extent and type/subtype of reported influenza activity worldwide are summarized in *Table 1.*

Influenza A(H5N1)

From 1 February to 21 September 2009, 37 human cases of influenza A(H5N1), 5 of which were fatal, were confirmed and reported by China, Egypt and Viet Nam, where highly pathogenic avian influenza A(H5N1) is present in poultry. Since December 2003, a total of 440 human cases and 262 deaths have been confirmed in 15 countries.[5] So far, there has been no evidence of sustained human-to-human transmission.

Antigenic and genetic characteristics of recent isolates

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 viruses are of prime importance in determining vaccine composition. These relationships are evaluated mainly in haemagglutination inhibition (HI) tests with postinfection ferret antisera against egg embryoes and cell grown reference and vaccine viruses, using red blood cells principally from turkeys and guinea-pigs, 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 (HA) and neuraminidase (NA) genes help to define the

[5] See http://www.who.int/csr/disease/avian_influenza/country/cases_table_2009_08_31/en/index.html

Grippe pandémique A (H1N1)

Le virus pandémique A (H1N1) a été détecté pour la première fois en avril aux États-Unis et il a été établi qu'il était responsable de flambées survenues au Mexique en mars et en avril. Par la suite, des flambées se sont produites dans toutes les régions du monde et au mois de juillet le virus de la grippe pandémique A (H1N1) était le principal virus grippal circulant dans de nombreux pays des Amériques, d'Asie, d'Europe et d'Océanie.

Des flambées de grippe pandémique A (H1N1) se sont produites dans de nombreux pays de l'hémisphère Nord entre mai et août. Suite à un déclin d'activité observé dans certains pays au cours des mois de juillet ou août, une résurgence a été signalée en septembre dans quelques pays d'Europe et des Amériques. À partir d'août, des augmentations rapides d'activité ont été signalées dans les pays d'Afrique et d'Asie, par exemple au Cambodge, en Chine, au Japon, au Kenya, en République démocratique populaire lao, en République Unie de Tanzanie et au Viet Nam.

Dans l'hémisphère Sud, l'activité de la grippe pandémique A (H1N1) a rapidement augmenté dans de nombreux pays. Elle a atteint un pic en juillet dans certains pays, déclinant ensuite jusqu'à des niveaux faibles en août ou en septembre, en Argentine, en Australie, au Brésil, au Chili et en Nouvelle-Zélande. Dans certains autres pays de l'hémisphère Sud et dans les régions tropicales des Amériques et d'Asie, le virus de la grippe pandémique A (H1N1) a continué de circuler en septembre.

L'étendue et le type/sous-type d'activité grippale rapportée dans le monde sont résumés dans le *Tableau 1.*

Grippe A (H5N1)

Du 1er février au 21 septembre 2009, 37 cas humains de grippe A (H5N1), dont 5 mortels, ont été confirmés et notifiés par la Chine, l'Egypte et le Viet Nam, où la grippe aviaire A (H5N1) hautement pathogène est présente chez les volailles. Depuis décembre 2003, 440 cas humains et 262 décès ont été confirmés au total dans 15 pays.[5] Jusqu'ici, rien ne permet de penser qu'il y ait eu une transmission interhumaine soutenue.

Caractéristiques antigéniques et génétiques des isolements récents

On combine des analyses antigéniques et génétiques pour identifier les variants antigéniques émergents susceptibles d'avoir une importance épidémique à l'avenir et dont l'inclusion dans les vaccins peut être envisagée. Les rapports antigéniques entre virus contemporains et virus vaccins revêtent une importance capitale pour déterminer la composition des vaccins. Ces rapports sont principalement évalués par des épreuves d'inhibition de l'hémagglutination (IH) réalisées au moyen d'immunsérums de furet post infection en présence de virus de référence cultivés sur oeufs embryonnés ou en culture cellulaire et de virus vaccins, en prenant des hématies de dindes et de cobayes, essentiellement, mais aussi d'autres espèces le cas échéant. Les épreuves de neutralisation virale fournissent des données complémentaires. La cartographie antigénique sert d'outil analytique supplémentaire permettant de visualiser et d'intégrer les données antigéniques. Des analyses phylogénétiques des

[5] Voir http://www.int/csr/disease/avian_influenza/country/cases_table_2009_08_31/en/index.html.

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.

Influenza A(H1N1) viruses

The majority of influenza A(H1N1) viruses detected worldwide during this period were pandemic A(H1N1); a decreasing proportion was seasonal A(H1N1). HI tests using postinfection ferret antisera indicated that pandemic A(H1N1) viruses were antigenically homogeneous and closely related to the vaccine virus A/California/7/2009 (*Table 2*). Sequence analysis of the pandemic A(H1N1) viruses indicated that they were genetically homogeneous. Seasonal A(H1N1) viruses are distinct from the pandemic A(H1N1) viruses; most were antigenically and genetically closely related to A/Brisbane/59/2007.

Influenza A(H3N2) viruses

In HI tests with postinfection ferret antisera, many viruses were antigenically closely related to the current vaccine viruses A/Brisbane/10/2007 and A/Uruguay/716/2007. Since March, increasing proportions of viruses have been antigenically and genetically distinguishable from the vaccine viruses and closely related to A/Perth/16/2009 and A/Hong Kong/1985/2009 reference viruses (*Table 3*).

gènes de l'hémagglutinine (HA) et de la neuraminidase (NA) aident à définir la parenté génétique existant entre les variants antigéniques et leurs prédécesseurs et à comprendre la base moléculaire de la dérive antigénique. La propagation des variants antigéniques associés aux flambées de grippe dans les différents pays constituent également un critère important de sélection de vaccins candidats appropriés sur le plan épidémiologique.

Virus grippaux A (H1N1)

La majorité des virus grippaux A (H1N1) détectés dans le monde au cours de cette période étaient des virus de la grippe pandémique; une proportion décroissante d'entre eux était constituée de virus A (H1N1) de la grippe saisonnière. Les épreuves d'IH réalisées au moyen d'immunsérums de furet post-infection ont indiqué que les virus de la grippe pandémique A (H1N1) étaient homogènes sur le plan antigénique et étroitement apparentés au virus vaccin A/California/7/2009 (*Tableau 2*). L'analyse des séquences des virus de la grippe pandémique A (H1N1) a indiqué qu'ils étaient génétiquement homogènes. Les virus de la grippe saisonnière A (H1N1) sont distincts des virus de la grippe pandémique A (H1N1); la plupart d'entre eux étaient étroitement apparentés sur le plan antigénique et génétique au virus A/Brisbane/59/2007.

Virus grippaux A (H3N2)

Dans les épreuves d'IH réalisées au moyen d'immunsérums de furets post-infection, de nombreux virus étaient étroitement apparentés sur le plan antigénique aux virus vaccins actuels A/Brisbane/10/2007 et A/Uruguay/716/2007. Depuis le mois de mars, des proportions croissantes de virus ont été distinctes des virus vaccins sur le plan antigénique et génétique et étroitement apparentées aux virus de référence A/Perth/2009 et A/Hong Kong/1985/2009 (*Tableau 3*).

Table 2 **Results of haemagglutination inhibition tests of pandemic A(H1N1) influenza viruses with postinfection ferret antisera**
Tableau 2 **Résultats des épreuves d'inhibition de l'hémagglutination pratiquées à l'aide d'immunsérums de furet post-infection pour les virus de la grippe pandémique A (H1N1)**

	A/California/7/2009	A/Narita/1/2009	A/Brisbane/59/2007
Antigens – Antigènes			
A/California/7/2009	2560	2560	10
A/Narita/1/2009	2560	5120	40
A/Brisbane/59/2007[a]	5	5	1280
Recent isolates – Isolements récents			
A/Argentina/08/2009	2560	2560	10
A/Chile/7109/2009	2560	2560	10
A/Denmark/528/2009[b]	1280	5120	10
A/England/195/2009	1280	2560	20
A/Florida/12/2009	5120	5120	20
A/Haiti/89/2009	2560	2560	20
A/Kenya/31/2009	1280	1280	10
A/Kobe/91992/2009	2560	5120	10
A/Laos/1294/2009	2560	5120	10
A/Mexico/4108/2009	2560	ND	40
A/Myanmar/60/2009	2560	5120	10
A/New Zealand/876/2009	2560	2560	20
A/Panama/4264/2009	2560	2560	10
A/Paraguay/912/2009	5120	5120	40
A/Sichuan/sw11/2009	2560	ND	10
A/Uruguay/706/2009	5120	2560	20

ND = not determined – Non défini
[a] Seasonal A(H1N1) vaccine virus – Virus de la grippe saisonnière A(H1N1)
[b] Oseltamivir-resistant – Résistant à l'oseltamivir

Table 3 **Results of haemagglutination inhibition tests of influenza A(H3N2) viruses with postinfection ferret antisera**
Tableau 3 **Résultats des épreuves d'inhibition de l'hémagglutination pratiquées à l'aide d'immunsérums de furets post-infection pour les virus grippaux A (H3N2)**

	A/Brisbane/10/2007	A/HK/1985/2009	A/Perth/16/2009
Antigens – Antigènes			
A/Brisbane/10/2007	1280	<40	40
A/Uruguay/716/2007	2560	80	<40
A/Hong Kong/1985/2009	80	2560	1280
A/Perth/16/2009	<40	320	1280
Recent isolates – Isolements récents			
A/Cameroon/350/2009	320	80	80
A/Ghana/FS1110/2009	320	80	40
A/Iceland/6043/2009	640	40	<40
A/Lithuania/142K/2009	1280	40	80
A/Victoria/212/2009	640	ND	<40
A/Columbia/227/2009	80	1280	640
A/Costa Rica/5179/2009	80	ND	640
A/Ghana/FS1267/2009	80	2560	2560
A/Iran/755/2009	80	2560	2560
A/Johannesburg/385/2009	160	2560	640
A/Luxembourg/791/2009	80	5120	2560
A/Myanmar/77/2009	160	1280	1280
A/Philippines/2725/2009	40	ND	640
A/Singapore/33/2009	<40	5120	640
A/Wisconsin/15/2009	<40	2560	1280

ND = not determined – Non défini

Influenza B viruses

Influenza B viruses of both the B/Victoria/2/87 and the B/Yamagata/16/88 lineages circulated and B/Victoria/2/87 lineage viruses continued to predominate.

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. The majority of B/Yamagata/16/88 lineage viruses were closely related to the previous vaccine viruses B/Florida/4/2006 and B/Brisbane/3/2007.

Resistance to influenza antiviral drugs

Neuraminidase inhibitors

The majority of pandemic A(H1N1) viruses were sensitive to the neuraminidase inhibitors oseltamivir and zanamivir. The few cases of resistance to oseltamivir among pandemic A(H1N1) viruses were linked to use of this drug for prophylaxis or treatment and were due to the histidine to tyrosine amino acid substitution at residue 275 (H275Y) in the neuraminidase. There were no reports of oseltamivir-resistant A(H3N2) or B viruses, but the majority of seasonal A(H1N1) viruses circulating were oseltamivir-resistant.[6] No zanamivir resistant viruses were reported.

M2 inhibitors

All pandemic A(H1N1) viruses and most A(H3N2) viruses were resistant to the M2 inhibitors, amantadine and rimantadine, while the majority of seasonal A(H1N1) viruses were sensitive. Resistance to these antiviral drugs remained predominantly associated with

[6] http://www.who.int/csr/disease/influenza/h1n1_table/en/index.html

Virus grippaux B

Des virus grippaux B des lignées B/Victoria/2/87 et B/Yamagata/16/88 ont circulé et ceux de la lignée B/Victoria/2/87 ont continué d'être prédominants.

Dans les épreuves d'IH réalisées au moyen d'immunsérums de furets post-infection, la majorité des virus de la lignée B/Victoria/2/87 étaient étroitement apparentés sur le plan antigénique au virus B/Brisbane/60/2008. La majorité des virus de la lignée B/Yamagata/16/88 étaient étroitement apparentés aux virus vaccins précédents B/Florida/4/2006 et B/Brisbane/3/2007.

Résistance aux antiviraux utilisés contre la grippe

Inhibiteurs de la neuraminidase

La majorité des virus de la grippe pandémique A (H1N1) ont été sensibles à l'oseltamivir et au zanamivir, des inhibiteurs de la neuraminidase. Les quelques cas de résistance à l'oseltamivir recensés parmi ces virus ont été liés à l'utilisation de ce médicament pour la prophylaxie ou le traitement et étaient dû à la substitution de l'histidine par la tyrosine (acides aminés) au niveau du résidu 275 (H275Y) de la neuraminidase. Aucun rapport n'a fait état d'une résistance des virus grippaux A (H3N2) ou B à l'oseltamivir, mais la majorité des virus de la grippe saisonnière A (H1N1) circulants étaient résistants à l'oseltamivir.[6] Aucun virus résistant au zanamivir n'a été signalé.

Inhibiteurs de la protéine M2

Tous les virus de la grippe pandémique A (H1N1) et la plupart des virus de la grippe A (H3N2) étaient résistants à l'amantadine et à la rimantadine, des inhibiteurs de la protéine M2, tandis que la majorité des virus de la grippe saisonnière A (H1N1) y étaient sensibles. La résistance à ces antiviraux est

[6] Voir http://www.who.int/csr/disease/influenza/h1n1_table/en/index.html.

a serine to asparagine substitution at residue 31 (S31N) of the M2 ion channel protein. A small number of seasonal A(H1N1) viruses were resistant to both oseltamivir and M2 inhibitors.

Studies with inactivated influenza virus vaccines

The presence of antibodies to the HA of recent virus isolates was determined by HI tests in 8 panels of sera from younger adult and elderly subjects who had received seasonal trivalent inactivated vaccines. The trivalent vaccines contained the antigens of A/Brisbane/59/2007 (H1N1) and A/Uruguay/716/2007 (H3N2); for the B component, vaccines contained B/Brisbane/60/2008 or B/Florida/4/2006. Only panels from recipients who had received vaccine containing B/Brisbane/60/2008 were used for the analysis of recent influenza B virus isolates. For all panels of sera, the antibody responses to the seasonal A(H1N1) vaccine component were not considered due to the predominance of pandemic A(H1N1) viruses in the world. In addition, 2 panels of sera from subjects participating in clinical trials of pandemic A(H1N1) vaccines were analysed.

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. Geometric mean HI titres were lower to a recent seasonal A(H1N1) virus than to the vaccine virus (average reductions: 83%).

Vaccines containing influenza A/Brisbane/10/2007 (H3N2)-like antigens stimulated anti-HA antibodies of geometric mean HI titres that were lower to recent isolates than to the vaccine virus (average reductions: younger adults 67%; the elderly 70%). Similar results were obtained in microneutralization tests for a subset of sera (average reductions: younger adults 76%; the elderly 76%).

Vaccines containing influenza B/Brisbane/60/2008-like antigen stimulated anti-HA antibodies of similar geometric mean HI titres to the vaccine virus and recent B/Victoria/2/87 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: younger adults 52%; elderly subjects 69%).

Recommended composition of influenza virus vaccines for use in the 2010 influenza season

Pandemic influenza A(H1N1) viruses emerged in March and spread globally to become predominant, while seasonal influenza A(H1N1), A(H3N2) and B viruses co-circulated to a lesser extent in many countries during the period February to September 2009.

Pandemic A(H1N1) viruses were antigenically and genetically similar to A/California/7/2009-like viruses. Vaccines containing A/California/7/2009 antigens stimu-

restée principalement associée à une substitution de la sérine par l'asparagine au niveau du résidu 31 (S31N) de la protéine M2 servant de canal ionique. Un petit nombre de virus de la grippe saisonnière A (H1N1) étaient résistants aussi bien à l'oseltamivir qu'aux inhibiteurs de la protéine M2.

Etudes sur les vaccins antigrippaux à virus inactivés

La présence d'anticorps dirigés contre l'hémagglutinine des isolements viraux récents a été déterminée par des épreuves d'IH appliquées à 8 batteries de sérums d'adultes jeunes et de personnes âgées ayant reçu des vaccins trivalents inactivés contre la grippe saisonnière. Ces vaccins renfermaient des antigènes des virus A/Brisbane/59/2007 (H1N1) et A/Uruguay/716/2007 (H3N2); pour la composante B, ils renfermaient les antigènes des virus B/Brisbane/60/2008 ou B/Florida/4/2006. Seules les batteries de sérums des sujets ayant reçu un vaccin contenant l'antigène du virus B/Brisbane/60/2008 ont été utilisées pour l'analyse des isolement récents de virus grippal B. Pour toutes les batteries de sérums, les réponses en anticorps dirigées contre la composante de la grippe saisonnière A (H1N1) n'ont pas été étudiées en raison de la prédominance des virus de la grippe pandémique A (H1N1) dans le monde. De plus, 2 batteries de sérums de sujets participant à des essais cliniques des vaccins contre la grippe pandémique A (H1N1) ont été analysées.

Les vaccins renfermant des antigènes de virus de type A/California/7/2009 ont suscité la formation d'anticorps HA dont les titres moyens géométriques IH contre les virus vaccins et les isolements récents de virus de la grippe pandémique A (H1N1) étaient comparables. Les titres moyens géométriques étaient moins élevés contre un virus récent de la grippe saisonnière A (H1N1) que contre le virus vaccin (réduction moyenne: 83%).

Les vaccins contenant des antigènes de virus de type B/Brisbane/10/2007 (H3N2) ont suscité la formation d'anticorps HA dont les titres moyens géométriques étaient moins élevés contre les isolements récents que contre le virus vaccin (réductions moyennes: jeunes adultes 67%; personnes âgées 70%). Des résultats analogues ont été obtenus pour une sous-série de sérums dans des épreuves de microneutralisation (réductions moyennes: jeunes adultes 76%; personnes âgées 76%).

Les vaccins contenant des antigènes de virus de type B/Brisbane/60/2008 ont suscité la formation d'anticorps HA dont les titres moyens géométriques contre le virus vaccin et les isolements récents de la lignée B/Victoria/2/87 étaient analogues. Toutefois, les titres moyens géométriques ont été quelque peu moins élevés contre les virus récents de la ligne B/Yamagata/16/88 que contre le virus vaccin (réductions moyennes: jeunes adultes 52%, personnes âgées 69%).

Recommandation relative à la composition des vaccins antigrippaux pour la saison 2010

Les virus de la grippe pandémique A (H1N1) sont apparus en mars et se sont propagés dans le monde pour y devenir prédominants, tandis que les virus de la grippe saisonnière A (H1N1), A (H3N2) et B ont circulé de façon concomitante dans une moindre mesure dans de nombreux pays au cours de la période s'étendant de février à septembre 2009.

Les virus de la grippe pandémique A (H1N1) étaient analogues sur le plan antigénique et génétique aux virus de type A/California/7/2009. Les vaccins contenant les antigènes du virus

lated anti-HA antibodies of similar titres against the vaccine virus and recent pandemic A(H1N1) viruses.

Seasonal influenza A(H1N1) viruses were associated with very few outbreaks and the numbers of isolates diminished significantly by August. The majority of recent viruses were antigenically and genetically similar to the vaccine virus A/Brisbane/59/2007.

Influenza A(H3N2) viruses were associated with outbreaks in several countries. The majority of recent viruses were antigenically and genetically distinguishable from the vaccine viruses A/Brisbane/10/2007 and A/Uruguay/716/2007 and were closely related to A/Perth/16/2009-like reference viruses. Current vaccines containing A/Uruguay/716/2007 antigens stimulated anti-HA antibodies with titres that were consistently lower to recent influenza A(H3N2) viruses.

Influenza B outbreaks were reported in several countries. 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 recent B/Yamagata/16/88 lineage viruses were antigenically closely related to B/Florida/4/2006. 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 consistently lower against recent viruses of the B/Yamagata/16/88 lineage.

It is recommended that vaccines for use in the 2010 influenza season (southern hemisphere winter) contain the following:

– an A/California/7/2009 (H1N1)-like virus;

– an A/Perth/16/2009 (H3N2)-like virus;

– a B/Brisbane/60/2008-like virus.

Il est recommandé que les vaccins utilisés au cours de la saison grippale 2010 (hiver de l'hémisphère Sud) renferment les souches suivantes:

– un virus de type A/California/7/2009 (H1N1);

– un virus de type A/Perth/16/2009 (H3N2);

– un virus de type B/Brisbane/60/2008.

As in previous years, national 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.[7]

Vaccine viruses (including reassortants) and reagents for use in the laboratory standardization of inactivated vaccine may be obtained from: Immunobiology Section, Office of Laboratory and Scientific Services, Therapeutic Goods Administration, P.O. Box 100, Woden, ACT 2606 Australia (fax: +61 2 6232 8564, e-mail: 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, England (fax: +44 1707 641050, e-mail: enquiries@nibsc.hpa.org.uk, web site: http://www.nibsc.ac.uk/flu_

A/California/7/2009 ont suscité la formation d'anticorps HA ayant des titres analogues contre le virus vaccin et contre les virus récents de la grippe pandémique A (H1N1).

Les virus de la grippe saisonnière A (H1N1) ont été associés à très peu de flambées et le nombre de leurs isolements avait nettement diminué au mois d'août. La majorité des virus récents étaient comparables sur le plan antigénique et génétique au virus vaccin A/Brisbane/59/2007.

Les virus grippaux A (H3N2) ont été associés à des flambées dans plusieurs pays. La majorité des virus récents étaient distincts sur le plan antigénique et génétique des virus vaccins A/Brisbane/10/2007 et A/Uruguay/716/2007 et étaient étroitement apparentés aux virus de référence de type A/Perth/16/2009. Les vaccins actuels contenant les antigènes du virus A/Uruguay/716/2007 ont suscité la formation d'anticorps HA dont les titres ont été régulièrement moins élevés contre les virus grippaux A (H3N2) récents.

Des flambées de grippe B ont été signalées dans plusieurs pays. Si les virus des lignées B/Victoria/2/87 et B/Yamagata/16/88 ont circulé en même temps, ce sont ceux de la lignée B/Victoria/2/87 qui ont prédominé. La majorité des virus récents de cette lignée étaient étroitement apparentés sur le plan antigénique et génétique au virus B/Brisbane/60/2008. La plupart des virus récents de la lignée B/Yamagata/16/88 étaient étroitement apparentés sur le plan antigénique au virus B/Florida/4/2006. Les vaccins actuels contenant les antigènes du virus B/Brisbane/60/2008 ont suscité la formation d'anticorps HA dont les titres contre les virus vaccins et les virus récents de la lignée B/Victoria/2/87 étaient comparables; toutefois, les titres d'anticorps ont été régulièrement moins élevés contre les virus récents de la lignée B/Yamagata/16/88.

Comme lors des années précédentes, les autorités nationales de contrôle devront approuver la composition et la formulation des vaccins utilisés dans chaque pays. Les autorités nationales de santé publique sont responsables de la formulation des recommandations relatives à l'utilisation du vaccin. L'OMS a publié des recommandations relatives à la prévention de la grippe.[7]

Les virus vaccins (y compris réassortis) et les réactifs nécessaires à la standardisation en laboratoire du vaccin inactivé peuvent être obtenus auprès des organismes suivants: Immunobiology Section, Office of Laboratory and Scienfitic Services, Therapeutic Goods Aministration, P.O. Box 100, Woden, ACT 2606 Australia (télécopie: +61 2 6232 8564, courriel: influenza.standards@tga.gov.au; site Web: 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, Angleterre (télécopie: +44 1707 641050, courriel: enquiries@nibsc.hpa.org.uk, site Web: http://www.nibsc.ac.uk/flu_site/index.html); ou Division of

[7] See http://www.who.int/docstore/wer/pdf/2002/wer7728.pdf

[7] Voir http://www..who.int/docstore/wer/pdf/200/wer7728.pdf

site/index.html); or 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).

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, VIC 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/flu/); or the WHO Collaborating Centre for Reference and Research on Influenza, MRC National Institute for Medical Research, The Ridgeway, Mill Hill, London NW7 1AA, England (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. ▩

Product Quality, Center for Biologics Evaluation and Research, Food and Drug Administration, 1401 Rockville Pike, Rochkville, MD 20892, United States (télécopie: +1 301 480 9748).

Les demandes de virus de référence nécessaires à l'analyse antigénique doivent être adressées au Centre collaborateur OMS de référence et de recherche pour la grippe, VIDRL, 10 Wreckyn Street, North Melbourne, VIC 3051, Australia (télécopie: +61 3 9342 3939, site Web: http://www.influenzacentre.org); au Centre collaborateur OMS de référence et de recherche pour la grippe, National Institute of Infectious Diseases, Gakuen 4-7-1, Musashi-Murayama, Tokyo 208-0011, Japan (télécopie: +81 42 561 6149 or +81 42 565 2498, site Web: http://www.nih.go.jp/niid/index.html); au 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, Unites States (télécopie: +1 404 639 0080, site Web: http://www.cdc.gov/flu/); ou the WHO Collaborating Center for Reference and Research on Influenza, MRC National Institute for Medical Research, The Ridgeway, Mill Hill, London NW7 1AA, Angleterre (télécopie: +44 208 906 4477, site Web: http://www.nimr.mrc.ac.uk/wic/). Des données épidémiologiques actualisées peuvent être consultées sur le site Web de l'OMS à l'adresse suivante: http://www.who.int/influenza. ▩

Antigenic and genetic characteristics of influenza A(H5N1) viruses and candidate vaccine viruses developed for potential use in human vaccines

September 2009

Since their reemergence in 2003, influenza A(H5N1) influenza viruses have become endemic in some countries and continue to cause outbreaks in poultry and sporadic human infections. Despite the emergence of the pandemic A(H1N1) 2009 virus, the zoonotic and pandemic threats posed by H5N1 viruses remain. The H5N1 viruses have continued to diversify both genetically and antigenically, leading to the need for multiple candidate vaccine viruses. The development of representative H5N1 candidate vaccine viruses, coordinated by WHO, remains an essential component of the overall global strategy for pandemic preparedness. This summary provides an update on the characterization of H5N1 viruses isolated from birds and humans and the current status of the development of candidate H5N1 vaccine viruses.

Comparisons of the candidate H5N1 vaccine viruses with respect to immunogenicity and their relationship to newly emerging H5N1 viruses are ongoing and will be updated periodically by WHO. An update of current and completed H5N1 vaccine clinical trials is available at http://www.who.int/vaccine_research/diseases/influenza/flu_trials_tables/en/index.html.

Influenza A(H5N1) activity from February to September 2009

A(H5N1) viruses have continued to be detected in birds in Africa and Asia. Human infections have been reported

Caractéristiques antigéniques et génétiques des virus grippaux A (H5N1) et des virus vaccins candidats mis au point en vue d'une utilisation potentielle dans des vaccins destinés à l'homme

Septembre 2009

Depuis leur réémergence en 2003, les virus grippaux A (H5N1) sont devenus endémiques dans certains pays et continuent de provoquer des flambées chez les volailles et des infections sporadiques chez l'homme. En dépit de l'émergence du virus de la grippe pandémique A (H1N1) 2009, les menaces que font peser sur le plan zoonosique et pandémique les virus H5N1 demeurent. Ces virus ont continué à se diversifier tant sur le plan génétique qu'antigénique conduisant à la nécessité de disposer de multiples virus vaccins candidats. La mise au point de virus vaccins H5N1 candidats représentatifs, coordonnée par l'OMS, reste une composante essentielle de la stratégie mondiale de préparation à une pandémie. Le présent résumé fait le point de la caractérisation des virus H5N1 isolés chez les oiseaux et chez l'homme et indique l'état actuel d'avancement des virus vaccins H5N1 candidats.

Des comparaisons entre ces virus vaccins H5N1 candidats portant sur l'immunogénicité et leur rapport avec les virus H5N1 apparus depuis peu sont en cours, et seront périodiquement actualisées par l'OMS. Une mise à jour relative aux essais cliniques en cours et achevés portant sur les vaccins contre les virus H5N1 est disponible à l'adresse suivante: http://www.who.int/vaccine_research/diseases/influenza/flu_trials_tables/en/index.html.

Activité de la grippe A (H5N1) de février à septembre 2009

Les virus A (H5N1) ont continué d'être détectés chez des oiseaux en Afrique et en Asie. Des infections humaines ont été rappor-

Table 1 **Influenza A(H5N1) activity reported from February to September 2009**
Tableau 1 **Activité de la grippe A (H5N1) rapportée de février à septembre 2009**

Country, area or territory – Pays, région ou territoire	Host – Hôte	Genetic clade – Clade génétique
Bangladesh	Domestic poultry – Volaille domestique	2.2
China – Chine	Human – Homme	2.3.4
	Domestic poultry – Volaille domestique	unknown – inconnu
	Wild birds – Oiseaux sauvages	unknown – inconnu
China, Hong Kong SAR – Chine, Hong Kong RAS	Domestic poultry – Volaille domestique	2.3.2 and 2.3.4 – 2.3.2 et 2.3.4
	Wild Birds – Oiseaux sauvages	2.3.2 and 2.3.4 – 2.3.2 et 2.3.4
Egypt – Égypte	Humans – Homme	2.2.1
	Domestic poultry – Volaille domestique	2.2.1
India – Inde	Domestic poultry – Volaille domestique	unknown – inconnu
Indonesia – Indonésie	Domestic poultry – Volaille domestique	2.1 clades
Lao People's Democratic Republic – République démocratique populaire lao	Domestic poultry – Volaille domestique	2.3.4
Mongolia – Mongolie	Wild birds – Oiseaux sauvages	2.3.2
Nepal – Népal	Domestic poultry – Volaille domestique	unknown – inconnu
Russian Federation – Fédération de Russie	Wild birds – Oiseaux sauvages	2.3.2
Viet Nam	Humans – Homme	unknown – inconnu
	Domestic poultry – Volaille domestique	2.3.4

to WHO from China, Egypt and Viet Nam, countries that have also declared outbreaks in birds (*Table 1*).

Antigenic and genetic characteristics

A nomenclature for phylogenetic relationships among the haemagglutinin (HA) genes of H5N1 viruses was devised in consultation with representatives of the Food and Agriculture Organization of the United Nations (FAO), the World Organisation for Animal Health (OIE) and WHO. This nomenclature is updated when novel genetic clades emerge and can be found at http://www.who.int/csr/disease/avian_influenza/guidelines/nomenclature/en/index.html.

Viruses characterized during this period fall within the following clades:

Clade 2.2 viruses were detected in chickens in Bangladesh and their genetic characteristics were similar to those of viruses circulating in Bangladesh during 2008 (*Figure 1*). Data are not available on the antigenic properties of these viruses.

Clade 2.2.1 viruses continue to circulate in poultry in Egypt, with sporadic transmission to humans. Viruses isolated during this period were genetically similar to those isolated during 2007 and 2008 (*Figure 1*). Data are not available on the antigenic properties of the 2009 viruses.

Clade 2.3.2 viruses have continued to be detected in poultry and wild birds in China Hong Kong Special Administrative Region (Hong Kong SAR) and were detected for the first time in wild birds in Southwestern Siberia (Russian Federation) and Mongolia. These viruses were genetically similar to clade 2.3.2 viruses isolated in previous years (*Figure 1*). The viruses isolated in Hong Kong SAR were antigenically closely related to previous clade 2.3.2 viruses.

Clade 2.3.4 viruses were detected in poultry and wild birds in Hong Kong SAR, and in poultry in Viet Nam

tées à l'OMS par la Chine, l'Égypte et le Viet Nam, pays qui ont également fait état de flambées chez les oiseaux (*Tableau 1*).

Caractéristiques antigéniques et génétiques

Une nomenclature des rapports phylogénétiques entre les gènes de l'hémagglutinine (HA) des différents virus H5N1 a été élaborée en consultation avec des représentants de l'Organisation des Nations Unies pour l'Alimentation et l'Agriculture (FAO), de l'Organisation mondiale de la Santé animale (OIE) et de l'OMS. Cette nomenclature est actualisée lorsque de nouveaux clades génétiques apparaissent et peut être consultée à l'adresse suivante: http://www.who.int/csr/disease/avian_influenza/guidelines/nomenclature/en/index.html.

Les virus caractérisés au cours de cette période se répartissent dans les clades suivants:

Des virus appartenant au *clade 2.2* ont été détectés chez des poulets au Bangladesh et leurs caractéristiques génétiques étaient semblables à celles des virus ayant circulé au Bangladesh en 2008 (*Figure 1*). On ne dispose pas de données relatives aux propriétés antigéniques de ces virus.

Des virus appartenant au *clade 2.2.1* continuent de circuler chez les volailles en Égypte avec une transmission sporadique à l'homme. Les virus isolés au cours de cette période étaient comparables sur le plan génétique à ceux isolés en 2007 et 2008 (*Figure 1*). On ne dispose pas de données sur les propriétés antigéniques des virus 2009.

Des virus appartenant au *clade 2.3.2* ont continué d'être détectés chez des volailles et des oiseaux sauvages en Chine, région administrative spéciale de Hong Kong (Hong Kong RAS) et ont été retrouvés pour la première fois chez des oiseaux sauvages dans le sud-ouest de la Sibérie (Fédération de Russie) et en Mongolie. Ces virus étaient comparables sur le plan génétique aux virus du clade 2.3.2 isolés les années précédentes (*Figure 1*). Les virus isolés à Hong Kong étaient étroitement apparentés sur le plan antigénique aux virus du clade 2.3.2 isolés précédemment.

Des virus appartenant au *clade 2.3.4* ont été retrouvés chez des volailles et des oiseaux sauvages à Hong Kong RAS et chez des

Fig. 1 **Phylogenetic relationships of H5N1 virus haemagglutinin genes showing availability of vaccine strains**

Fig. 1. **Rapports phylogénétiques entre les gènes de l'hémagglutinine des virus H5N1 montrant la disponibilité des souches vaccinales.**

* Viruses for which vaccine strains are available – Virus pour lesquels on dispose de souches vaccinales – Virus pour lesquels on dispose de souches vaccinales

** Viruses for which vaccine strains are pending – Virus pour lesquels des souches vaccinales sont en attente – Virus pour lesquels les souches vaccinales sont en attente

*** Viruses for which vaccine strains are proposed – Virus pour lesquels des souches vaccinales sont proposées – Virus pour lesquels des souches vaccinales sont proposées

We gratefully acknowledge the contributions of the originating laboratories and countries that have provided samples and/or submitted sequence data to DDBJ, EMBL-Bank, GenBank, GISAID and other public databases. Sequence has also been provided by the National Influenza Center at the Central Public Health Laboratory, Ministry of Health and the National Laboratory for Veterinary Quality Control on Poultry Production (NLQP), Egypt. Recent viruses (where date of isolation known) are shown in italics.– Nous remercions tout particulièrement pour leurs contributions les laboratoires et pays d'origine qui ont fourni des échantillons et/ou soumis des données relatives aux séquences au DDBJ, à l'EMBL-Bank, à la GenBank, au GISAID et autres banques de données publiques. Des données de ce type ont également été fournies par le Centre national d'Étude de la Grippe du Laboratoire central de Santé publique, Ministère de la Santé, et par le Laboratoire national de contrôle de la qualité vétérinaire de la production de volaille, Égypte. Les virus récents (dont on connaît la date d'isolement) sont indiqués en italiques.

and the Lao People's Democratic Republic. A human case in China was reported in February. The viruses isolated in Hong Kong SAR were genetically similar to viruses isolated in Hong Kong SAR in 2008 (*Figure 1*) and were antigenically related to the candidate vaccine virus A/chicken/Hong Kong/AP156/2008. Viruses isolated in Viet Nam and the Lao People's Democratic Republic. A human case in China was reported in February. The viruses isolated in Hong Kong SAR were genetically similar to viruses isolated in Hong Kong SAR in 2008 (*Figure 1*) and were antigenically related to the candidate vaccine virus A/chicken/Hong Kong/AP156/2008. Viruses isolated in Viet Nam et en République démocratique populaire lao. Un cas a été notifié chez l'homme en Chine en février. Les virus isolés à Hong Kong (RAS de Chine) étaient comparables sur le plan génétique à ceux qui y avaient été isolés en 2008 (*Figure 1*) et apparentés sur le plan antigénique au virus vaccin candidat A/chicken/Hong Kong/AP156/2008. Les virus isolés au volailles au Viet Nam et en République démocratique populaire lao. Un cas a été notifié chez l'homme en Chine en février. Les virus isolés à Hong Kong (RAS de Chine) étaient comparables sur le plan génétique à ceux qui y avaient été isolés en 2008 (*Figure 1*) et apparentés sur le plan antigénique au virus vaccin candidat A/chicken/Hong Kong/AP156/2008. Les virus isolés au

Table 2 **Results of haemagglutination inhibition tests of A(H5N1) viruses with postinfection ferret antisera**
Tableau 2 **Résultats des épreuves d'inhibition de l'hémagglutination pratiquées à l'aide d'immunsérums de furet postinfection pour les virus A (H5N1)**

	Clade	1 VN/1203	2.1 IND/5	2.2 bhg/QI	2.2.1 EG/321	2.3.2 ck/KO	2.3.4 ANH/1	2.3.4 jwe/HK	2.3.4 dk/LO	2.3.4 ck/VN/35
Reference antigens – Antigènes de référence										
A/Viet Nam/1203/2004	1	**640**	5	160	5	5	5	5	10	320
A/Indonesia/5/2005	2.1	5	**640**	160	160	5	80	5	5	40
A/bh goose/Qinghai/1A/05 X PR8	2.2	20	320	**640**	320	5	5	80	20	40
A/Egypt/321-NAMRU3/2007	2.2.1	5	320	320	**1280**	5	5	80	10	40
A/chicken/Korea/GIMJE/08	2.3.2	5	5	80	5	**160**	5	5	5	80
A/Anhui/1/05	2.3.4	10	80	80	40	5	**2560**	320	320	640
A/Jap white eye/Hong Kong/1038/06	2.3.4	5	40	640	160	5	2560	**1280**	640	320
A/duck/Laos/3295/06	2.3.4	5	5	80	5	5	320	80	**80**	80
A/chicken/Viet Nam/NCVD-35/08	2.3.4	5	20	160	5	5	160	20	160	**640**
Representative test antigens – Antigènes testés représentatifs										
A/chicken/Viet Nam/NCVD-279/09	2.3.4	5	5	80	5	5	320	80	80	160
A/chicken/Viet Nam/NCVD-282/09	2.3.4	5	5	80	40	5	80	20	40	320
A/chicken/Viet Nam/NCVD-283/09	2.3.4	5	5	40	5	5	80	5	80	640

Table 3 **Status of H5N1 vaccine virus development (September 2009)**
Tableau 3 **État d'avancement des virus vaccins H5N1 (septembre 2009)**

Reassortants with regulatory approval – Virus réassortis approuvés par l'autorité de réglementation

Virus	Clade	Institution*	Availability – Disponibilité
A/Cambodia/R0405050/2007	1	NIBSC	Yes – Oui
A/Viet Nam/1203/2004	1	CDC and SJ/HKU/NIAID	Yes – Oui
A/Viet Nam/1194/2004	1	NIBSC	Yes – Oui
A/duck/Hunan/795/2002	2.1	SJ/HKU/NIAID	Yes – Oui
A/Indonesia/5/2005	2.1	CDC	Requires Indonesian Government permission – Nécessite l'autorisation du Gouvernement indonésien
A/bar-headed goose/Qinghai/1A/200 5	2.2	SJ/HKU/NIAID	Yes – Oui
A/whooper swan/Mongolia/244/2005	2.2	SJ/NIAID	Yes – Oui
A/Egypt/2321/2007	2.2.1	CDC	Yes – Oui
A/turkey/Turkey/1/2005	2.2.1	NIBSC	Yes – Oui
A/Anhui/1/2005	2.3.4	CDC	Yes – Oui
A/duck/Laos/3295/2006	2.3.4	FDA	Yes – Oui
A/Japanese white-eye/Hong Kong/1038/2006	2.3.4	SJ/HKU/NIAID	Yes – Oui
A/goose/Guiyang/337/2006	4	SJ/HKU/NIAID	Yes – Oui

Reassortants prepared and awaiting regulatory approval – Virus réassortis préparés et dans l'attente d'une approbation par l'autorité de réglementation

Virus	Clade	Institution*	Availability – Disponibilité
A/chicken/India/NIV33487/2006	2.2	CDC/NIV	Pending – En attente
A/Egypt/3300-NAMRU3/2008	2.2	CDC	Pending – En attente
A/common magpie/Hong Kong/5052/2007	2.3.2	SJ/HKU/NIAID	Pending – En attente
A/chicken/Viet Nam/NCVD-016/2008-like	7	CDC	Pending – En attente

Viruses proposed by WHO for candidate vaccine preparation – Virus proposés par l'OMS pour la préparation de vaccins candidats

Virus	Clade	Institution*
A/chicken/Hong Kong/AP156/2008-like	2.3.4	SJ/HKU/NIAID
A/chicken/Viet Nam/NCDV-03/2008	7	CDC

* CDC = Centers for Disease Control and Prevention, USA – *Centers for Diseases Control and Prevention*, Etats-Unis
FDA = Food and Drug Administration, USA – *Food and Drug Administration*, Etats-Unis
NIAID = National Institute of Allergy and Infectious Diseases, National Institute of Health, USA – L'Institut National d'Allergie et de Maladies Infectieuses, Institut national de la santé, Etats-Unis
NIBSC = National Institute for Biological Standards and Control, England – *National Institute for Biological Standards and Control*, Angleterre
NIV = National Institute of virology, India – Institut national de virologie, Inde
SJ = St Jude Children's Research Hospital, USA – Hôpital pour enfants St Jude, Etats-Unis
HKU = University of Hong Kong, China Hong Kong SAR – Université de Hong Kong, Hong Kong (région administrative spéciale de Chine)

lated in Viet Nam were genetically diverse. These viruses were antigenically closely related to the candidate vaccine virus A/duck/Laos/3295/2006 (*Table 2*).

A(H5N1) candidate vaccine viruses

Based on the available data, no new candidate A(H5N1) vaccine viruses are proposed at this time. The available candidate H5N1 vaccine viruses are listed in *Table 3*. On the basis of the geographical spread, epidemiology, and antigenic and genetic properties of the H5N1 viruses, national authorities may recommend the use of one or more of these for pilot lot vaccine production, clinical trial and subsequent stockpiling of vaccines, should such national policies exist.

Additional H5N1 candidate vaccine viruses may be developed as the viruses continue to evolve and will be announced as they become available. Institutions, companies and others interested in pandemic vaccine development who wish to receive candidate vaccine viruses, should contact the WHO Global Influenza Program at GISN@who.int or the institutions listed in announcements published on the WHO web site http://www.who.int/csr/disease/avian_influenza/guidelinestopics/en/index5.html ■

Viet Nam présentaient une diversité génétique. Ils étaient étroitement apparentés sur le plan antigénique au virus vaccin candidat A/duck/Laos/3295/2006 (*Tableau 2*).

Virus vaccins A (H5N1) candidats

Compte tenu des données disponibles, aucun nouveau virus vaccin A (H5N1) candidat n'est proposé pour le moment. On trouvera dans le *Tableau 3* la liste des virus vaccins A (H5N1) candidats disponibles. Sur la base de la propagation géographique, de l'épidémiologie et des propriétés antigéniques et génétiques des virus H5N1, les autorités nationales peuvent recommander l'utilisation d'un ou plusieurs d'entre eux pour la production de lots de vaccins pilotes, la réalisation d'essais cliniques et le stockage ultérieur des vaccins, si des politiques nationales de ce type existent.

Au fur et à mesure de l'évolution de ces virus, des virus vaccins H5N1 candidats supplémentaires seront peut être mis au point; ils seront annoncés dès qu'ils seront disponibles. Les institutions, firmes et autres parties intéressées par la mise au point d'un vaccin contre la grippe pandémique A (H5N1) qui souhaitent recevoir des virus vaccins candidats doivent prendre contact avec le Programme mondial de lutte contre la grippe de l'OMS à l'adresse suivante: GISN@who.int ou les institutions qui figurent dans les annonces postées sur le site Web de l'OMS: http://www.who.int/csr/disease/avian_inflenza/guidelinestopics/en/index5.html. ■

WHO web sites on infectious diseases
Sites internet de l'OMS sur les maladies infectieuses

Avian influenza	**http://www.who.int/csr/disease/avian_influenza/en/**	Grippe aviaire
Buruli ulcer	**http://www.who.int/gtb-buruli**	Ulcère de Buruli
Child and adolescent health and development	**http://www.who.int/child_adolescent_health/en/**	Santé et développement des enfants et des adolescents
Cholera	**http://www.who.int/cholera/**	Choléra
Deliberate use of biological and chemical agents	**http://www.who.int/csr/delibepidemics/**	Usage délibéré d'agents chimiques et biologiques
Dengue (DengueNet)	**http://who.int/denguenet**	Dengue (DengueNet)
Epidemic and pandemic surveillance and response	**http://www.who.int/csr/en/**	Alerte et action en cas d'épidémie et de pandémie
Eradication/elimination programmes	**http://www.who.int/infectious-disease-news/**	Programmes d'éradication/élimination
Geographical information systems (GIS)	**http://www.who.int/csr/mapping/**	Systèmes d'information géographique
Global atlas of infectious diseases	**http://globalatlas.who.int**	Atlas mondial des maladies infectieuses
Global Outbreak Alert and Response Network (GOARN)	**http://www.who.int/csr/outbreaknetwork/en/**	Réseau mondial d'alerte et d'action en cas d'épidémie (GOARN)
Health topics	**http://www.who.int/topics**	La santé de A à Z
Influenza	**http://www.who.int/csr/disease/influenza/en/**	Grippe
Influenza network (FluNet)	**http://who.int/flunet**	Réseau grippe (FluNet)
International Health Regulations	**http://www.who.int/csr/ihr/en/**	Règlement sanitaire international
International travel and health	**http://www.who.int/ith/**	Voyages internationaux et santé
Intestinal parasites	**http://www.who.int/wormcontrol/**	Parasites intestinaux
Leishmaniasis	**http://www.who.int/leishmaniasis**	Leishmaniose
Leprosy	**http://www.who.int/lep/**	Lèpre
Lymphatic filariasis	**http://www.who.int/lymphatic_filariasis/en/**	Filariose lymphatique
Malaria	**http://www.who.int/malaria**	Paludisme
Neglected tropical diseases	**http://www.who.int/neglected_diseases/en/**	Maladies tropicales négligées
Outbreak news	**http://www.who.int/csr/don**	Flambées d'épidémies
Poliomyelitis	**http://www.polioeradication.org/casecount.asp**	Poliomyélite
Rabies network (RABNET)	**http://www.who.int/rabies**	Réseau rage (RABNET)
Report on infectious diseases	**http://www.who.int/infectious-disease-report/**	Rapport sur les maladies infectieuses
Salmonella surveillance network	**http://www.who.int/salmsurv**	Réseau de surveillance de la salmonellose
Smallpox	**http://www.who.int/csr/disease/smallpox/**	Variole
Schistosomiasis	**http://www.who.int/schistosomiasis/en**	Schistosomiase
Tropical disease research	**http://www.who.int/tdr/**	Recherche sur les maladies tropicales
Tuberculosis	**http://www.who.int/tb/** and/et **http://www.stoptb.org**	Tuberculose
Vaccines	**http://www.who.int/immunization/en/**	Vaccins
Weekly Epidemiological Record	**http://www.who.int/wer/**	Relevé épidémiologique hebdomadaire
WHO Lyon Office for National Epidemic Preparedness and Response	**http://www.who.int/csr/ihr/lyon/en/index.html**	Bureau OMS de Lyon pour la préparation et la réponse des pays aux épidémies
WHO Pesticide Evaluation Scheme (WHOPES)	**http://www.who.int/whopes**	Schéma OMS d'évaluation des pesticides (WHOPES)
WHO Mediterranean Centre for Vulnerability Reduction, Tunis	**http://wmc.who.int/**	Centre Méditerranéen de l'OMS pour la Réduction de la Vulnérabilité à Tunis (WMC)
Yellow fever	**http://www.who.int/csr/disease/yellowfev/en/**	Fièvre jaune