RECOMMENDATION FOR INFLUENZA VACCINE COMPOSITION 2008

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RECOMMENDATION FOR INFLUENZA VACCINE COMPOSITION 2008

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- A(H3N2) an A/Brisbane/10/2007 (H3N2) - like strain
- B a B/Florida/4/2006 - like strain

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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 5 October issue of the *Weekly Epidemiological Record, 2007 82(40):345-356* (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.

1.1. Overview of World-wide Influenza Activity, March-September 2007

Between February and September 2007, influenza activity was reported in Africa, the Americas, Asia, Europe and Oceania. In some countries, influenza activity was higher than in
recent years, for example in Argentina and Australia.

In the northern hemisphere, influenza continued to cause outbreaks in Asia, Europe and North America. In the United States, A(H1N1) viruses predominated, while in Canada and Europe A(H3N2) viruses predominated. Influenza A(H1N1) and B viruses co-circulated with A(H3N2) viruses in several countries in Asia, Eastern Europe and the Middle-East. Influenza activity declined in April, except in the Russian Federation, where activity continued throughout June, and in Hong Kong Special Administrative Region of China (Hong Kong SAR), where outbreaks caused by A(H3N2) viruses occurred in July.

In the southern hemisphere, influenza activity began in April in South America, increased in May, remained high throughout July and declined in August. In Oceania and South Africa, activity started in June, peaked in July to August and declined in September. Influenza A(H3N2) and B viruses co-circulated and provoked outbreaks in South America, while in Oceania A(H3N2) and A(H1N1) viruses co-circulated and caused outbreaks in Australia. Outbreaks due to A(H1N1) viruses were reported in New Zealand in July, and in South Africa in August.

Between February and 19 September 2007, 58 confirmed human cases with 36 deaths from influenza A(H5N1) were reported to WHO from Cambodia, China, Egypt, Indonesia, the Lao People's Democratic Republic, Nigeria and Viet Nam. Since November 2003, a total of 328 human cases with 200 deaths have been confirmed from 12 countries. The WHO influenza pandemic preparedness level remains unchanged at Phase 3. To date, there has been no evidence of sustained human-to-human transmission. The current status of the development of candidate A(H5N1) vaccine viruses as well as guidance for national authorities and vaccine companies on the selection of candidate viruses for use in vaccine development are available at: http://www.who.int/csr/disease/avian_influenza/guidelines/h5n1virus/en/index.html. *(Excerpted from Weekly Epidemiological Record, 2007 82(40):345-356)*

The WHO Collaborating Centre for Reference and Research on Influenza in Melbourne, Australia (Melbourne WHOCC) analysed influenza isolates received from 1 January to 26 September 2007. Influenza A(H3N2) was the predominant strain which accounted for 58% (505/878) of isolates while 27% (241/878) were influenza A(H1N1) and 15% (132/878) were influenza B (Figures 2.1 and Table 2.1 in Appendix 2).

1.2. Southern Hemisphere Influenza Activity, March-September 2007

1.2.1. New Zealand

Influenza is not a notifiable disease in New Zealand. A national influenza surveillance system was set up in 1991 as part of the WHO global programme for influenza surveillance. The purpose of influenza surveillance is:

- to describe the incidence and distribution of influenza in the community;
- to detect influenza epidemics within the community in order to assist public health intervention;
- to identify the predominant strains to help plan for effective influenza vaccines for the subsequent year.

There are two forms of influenza surveillance in New Zealand:

1) Sentinel surveillance. This is operated nationally by ESR and locally by surveillance co-ordinators within the public health service in each of 24 health districts. The system operates during the winter "influenza season", usually from May through September each year. Based on the population and geographic distribution, about 90 voluntary sentinel general practitioners throughout the country are recruited into the system, covering roughly 10% of the New Zealand population. This system provides two types of surveillance information, one being disease information and the other being strain information. Every week, each sentinel practice provides consultation data (the number of cases of influenza-like illness) to the WHO National Influenza Centre at ESR. This allows the measurement of the incidence and distribution of influenza. In addition, each

sentinel practice provides throat/nasopharyngeal swabs from the first patient seen with an influenza-like illness on Monday, Tuesday and Wednesday of each week. These samples are forwarded to four virology laboratories around the country for viral isolation and identification. Some hospital virology laboratories refer influenza isolates to the WHO National Influenza Centre at ESR for further typing. This provides the national data on predominant strains. The combined information on disease incidence and predominant strain is reported to MoH and WHO weekly, monthly and annually. The weekly report, *Influenza Weekly Update*, is distributed in a printed format or accessible on ESR's website (http://www.surv.esr.cri.nz/virology/influenza_weekly_update.php).

2) Laboratory-based surveillance. This system is operated all year around by the four regional virology laboratories at Auckland, Waikato, Christchurch and Wellington and by one public health virology lab, the WHO National Influenza Centre at ESR. This system is conducted by sampling hospital in-patients and outpatients during routine viral diagnosis. The viral isolation data are reported nationally in *Virology Weekly Report*, and distributed in a printed format or on ESR's website (http://www.esr.cri.nz/virology/virology_weekly_report.php)

The data on consultation rates from 1991 to 2000 were reviewed and the thresholds used to describe influenza-like activity were defined (Table 2) *(New Zealand Public Health Report 2000 8(2): 9-13).*

Sentinel influenza surveillance started in May 2007. The peak of the influenza activity in 2007 is lower than 2006 and 2005 (Figure 1). It peaked in weeks 30 and 31, 3 weeks later than the peak in 2006. The consultation rate remained at the baseline level from week 18 to week 28 (in the middle of June). Then it increased rapidly and reached the peak in weeks 30 and 31 (at the beginning of July) with the consultation rate for flu-like illness at 70/100,000. The influenza activity continued for 4 weeks and then fell below the baseline level in week 36 (at the beginning of September). Since then, it has remained below the baseline level. When weekly consultation rates for ILI from 1992-2007 were compared (Figure 2), influenza activity in 2007 is the second lowest after 2000.

Influenza isolates were reported weekly by sentinel and laboratory-based surveillance (Figure 3). There are three interesting features of influenza activity in 2007: 1) The viral isolation for sentinel surveillance peaked in week 30 with 30 viral isolations, the same week as the peak of the ILI consultation. 2) The viral isolation for laboratory-based surveillance peaked in week 34 with 79 viral isolations, 4 weeks later than the peak of the viral isolation for sentinel surveillance. 3) A greater proportion of influenza viruses were isolated from sentinel surveillance in 2007 (48%) than in 2006 (40%). A total of 684 influenza viruses were reported by sentinel and laboratory-based surveillance from weeks 1 to 39 in 2007. Sentinel surveillance yielded 326 (48%, 326/684) influenza viruses and laboratory-based surveillance reported 358(52%, 358/684) influenza viruses. In 2006, 305 influenza viruses (40%, 305/758) were detected from sentinel surveillance and 453 (60%, 453/758) from laboratory-based surveillance. The increase in the proportion of influenza isolates resulting from sentinel surveillance could reflect widespread community outbreaks of influenza and/or fewer hospitalisations in 2007.

A total of 684 influenza viruses were isolated in 2007 from weeks 1 to 39 (Figure 4). Overall, influenza A was the predominant type with 557 isolates (81%, 557/684). There were 127 influenza B isolations in 2007, consisting of 19% (127/684) of total isolates.

Among 557 influenza A viruses, 293 influenza A viruses are yet to be subtyped. 161 influenza A(H1N1) viruses were identified with 143 viruses being subtyped as influenza A/New Calendonia/20/1999 strains, 2 as A/Solomon/3/3006 strains and 16 as A(H1N1) not antigenically subtyped (detected by PCR). In addition, 103 influenza A(H3N2) viruses were identified with 38 viruses being subtyped as A/Wisconsin/67/2005 strains, 2 as A/California/7/2004 strains and 63 as A(H3N2) not antigenically subtyped (detected by PCR). Overall, influenza A/New Calendonia/20/1999 (H1N1)-like strain was the predominant strain.

Among 127 influenza B viruses, 57 were typed as B/Shanghai/361/2002-like strains three as B/Malaysia/2506/2004-like strains and 67 as influenza B viruses yet to be antigenically typed.

Figure 5 shows the temporal distribution of influenza A and B viruses in 2007. Three main antigenic strains (A/New Calendonia/20/1999, A/Wisconsin/67/2005 and B/Shanghai/361/2002) co-circulated throughout the winter season

Figure 6 shows the percentage of influenza isolates by type from 1990 to 2007. A total of 324 influenza isolates have been typed and sub-typed. Influenza A(H1N1), A(H3N2) and B viruses consist of 49.7%, 31.8% and 18.5% of all typed/sub-typed isolates respectively.

Figure 7 shows age group comparison between sentinel and laboratory-based surveillance. It is interesting to note again that the age group between 0-1 years and 1-4 years and patients over 65 years were represented more in laboratory-based surveillance than in sentinel surveillance. This is consistent with the findings from the past 3-4 years. This may reflect the fact that influenza presented more severely in the very young and the elderly populations, resulting in hospitalisations.

Due to vaccine breakthrough and/or failure observed in 2004 (Influenza Annual Report, 2004), the need for surveying influenza vaccine breakthrough/failure was discussed and agreed by health professionals around the country. When GPs take swabs from 3 ILI patients each week, specimen request forms with necessary demographic information are required to be provided. One extra question is included to record whether the patient has been vaccinated against influenza in the same year as the onset of ILI.

A total of 13 vaccine breakthrough cases were recorded from the national influenza database (Table 3) from weeks 1 to 39, comprising 1.9% of total isolates (13/684). The clinical effectiveness of influenza vaccines depends on the immunocompetence of the recipient, previous exposure to influenza and influenza vaccines, and the closeness of the match between the vaccine and circulating influenza strains. Of 13 vaccine breakthrough cases, 9 cases (69%, 9/13) occurred in age groups >50 years. Immunological senescence may explain a higher proportion of vaccine breakthrough cases in the elderly population. In addition, six vaccine breakthrough cases had influenza A(H3N2) viruses and 5 with influenza B viruses. None of A(H1N1) viruses were isolated from the vaccine breakthrough cases even though A(H1N1) was the predominant subtype in 2007.

In addition, 269 ILI cases had information on vaccination history from the ESRLab database for sentinel surveillance specimens. Among them, 42 had influenza vaccination in the same year as the onset of ILI and 227 had none. There were 8 (19%, 8/42) vaccinated patients whose specimens yielded influenza viruses.

1.2.2. Australia

Influenza activity in Australia in 2007 was moderate to severe nation-wide with some regional variation regarding influenza types/subtypes. Some paediatric sudden death cases were reported with influenza virus isolations.

There are six 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. The NNDSS data indicated that the influenza activity was much higher in 2007 than in 2006. The activity peaked in week 33, one week earlier than in 2006. Young children aged 0-4 years had the highest influenza notifications compared with other age groups. The Queensland notification was the highest compared with other jurisdictions. Forty-four influenza notification cases had influenza vaccinations.

- Laboratory Surveillance conducted by the Melbourne WHOCC. A total of 484 influenza isolates from Australia were received for analysis at the Melbourne WHOCC (Appendix 2) from 1 January to 26 September 2007. 58.3% (282/484) of isolates were A(H3N2) viruses, antigenically related to A/Wisconsin/67/2005-like strain. 165 (34.1%, 165/484) A(H1N1) viruses were isolated and H1 was antigenically similar to A/New Caledonia/20/99-like strain. 37 influenza B viruses (7.6%, 37/484) were isolated with co-circulation of B/Yamagata and B/Victoria lineage viruses. Influenza A/Wisconsin/67/2005 viruses were isolated from three sudden death children aged 2, 2 and 3 years from Western Australia. One sudden death child aged 2 from Queensland had influenza AH1N1 virus detected. Influenza A (not yet subtyped) was also detected from a sudden death child aged 2 from New South Wales.

- Australian Sentinel Practice Research Network (ASPREN). In 2007, ASPREN consists of 39-80 general practices from Western Australia, Victoria, New South Wales and South Australia. New cases of influenza-like-illness (ILI) are reported per 1000 consultation per week all-year-around. This information is forwarded to Commonwealth fortnightly. Since January 2004, all sentinel GP surveillance schemes use the same case definition of ILI. ASPREN showed that the consultation rates for influenza-like illness in 2007 were higher than 2006 and peaked in July.

- The emergency department surveillance in New South Wales. This surveillance indicated higher influenza activity in 2007 than in 2006. About 30 emergency departments participated in the survey. The peak was recorded in August with the ILI rate at 9/1000 consultations.

- 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. The absenteeism data in 2007 indicated a higher absenteeism during the winter of 2007 compared with 2006.

- 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 2007 reached over 200 per 1000 deaths.

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

1.2.3. South Africa

Influenza activity during the South African 2007 winter season was monitored by the Viral Watch sentinel surveillance programme. This program has been expanded in 2007 to include 7 of the 9 provinces. Seventy five of the 140 sites are situated in Johannesburg and surrounding areas.

The 2007 influenza season started later than the previous two years. After sporadic isolates during April to June, the numbers of isolates made per week increased markedly from week 26 (the last week of June) onward. The average onset of the influenza season in South Africa over the past 23 years is week 23 (the first week of June), with a range of week 15 (mid-April) to week 28 (mid-July). Week 31 (the first week of August) appears to have been the peak of the 2007 influenza season with the highest number of specimens (134) and isolates (72), an isolation rate of 52%, as well as accounting for 15% of all influenza isolates made this season to date. Although the number of specimens and isolates started to decline from week 35 (the last week of August), influenza is still circulating.

A total of 516 influenza isolations were made, of which, 386 influenza A viruses and 130 influenza B viruses. Of the 386 influenza A isolates, 139 were further identified as influenza A(H1N1), and 160 as A(H3N2). Of 130 influenza B viruses, 62 were further identified as B/Malaysia/2506/2004-like while 52 as B/Shanghai/361/02-like viruses. Significant antigenic drift has been observed among A(H1N1), A(H3N2) and B/Yamagata-lineage viruses.

Sequence analysis was conducted for influenza A(H1N1), A(H3N2) and B:

- Influenza A(H1N1): The HA1 subunit revealed the H1 viruses isolated during the season showed that the majority of the isolates clustered into two groups. While all the isolates in these groups shared two common amino acid substitutions relative to the A/Solomon Islands/3/06 virus (R73K and T128V), the group 'B' viruses had one further change at R188M. The group 'A' viruses exhibited more extensive drift from the /Solomon Islands/3/06 strain with a further five changes at residues 35, 145, 188, 193 and 273.
- Influenza A(H3N2): Molecular characterization of the HA1 subunit of the H3s revealed that the majority of the viruses sequenced from different provinces in the country were very uniform and showed substantial drift from the A/Wisconsin/67/05 vaccine strain. All shared the common amino acid substitution K140I and the majority also had the G50E change seen in many H3s isolated elsewhere. Some of the South African strains exhibited an unusual D7Y substitution while several of the earlier H3s viruses had a distinctive change at 83 (K-R) instead. The isolates were more closely related to the A/Brisbane/10/7 strain with sporadic substitutions at a number of residues.
- Influenza B: The phylogenetic tree was constructed from analysis of the HA1 subunit of representative South African 2007 influenza B viruses from both the B/Victoria/2/87 and B/Yamagata/16/88 genetic lineages. The B/Victoria/02/07-lineage influenza B isolates showed little drift from the B/Malaysia/2506/04 vaccine strain with two common amino acid differences compared to the latter. The South African B/Yamagata-lineage viruses were related to other recent B viruses such as B/Hong Kong/141/07.

Influenza virus was isolated from the respiratory specimens of 25 patients who had received influenza vaccine prior to the onset of the season. Patients were aged between 5 and 79 years (median 53). Twenty-one of the 25 isolates were influenza A, of which 5 have been further

identified as A H1N1 and 14 as A H3N2. The influenza B isolates were identified as B Malaysia/2506/04-like (2) and B Shanghai/361/02-like (2).

In summary, the influenza season in South Africa began later than the previous two years with the peak of activity occurring in week 31. Influenza A H3N2 and H1N1 accounted for the majority of virus isolates, while influenza B strains were isolated later in the season. All the viruses which were characterized in more detail at both the antigenic and genetic levels exhibited significant drift from the respective vaccine strains as has been reported for many other countries

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

2. RECENT STRAIN CHARACTERISATION AND LIKELY VACCINE CANDIDATES

2.1. 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 2007 influenza season, an increasing number of A(H1N1) viruses were isolated in New Zealand, Australia and some Southeast Asian countries. At least 3 paediatric and adult deaths were associated with influenza A(H1N1) infection in Australia in 2007.

The virology laboratories in New Zealand use the kit supplied by Melbourne WHOCC to analyse influenza A(H1N1) strains. The antiserum used for detecting A(H1) was A/New Caledonia/20/99. There were 143 influenza A/New Caledonia (H1N1)-like virus isolations in New Zealand in 2007.

Since January 2007, the Melbourne WHOCC has analysed 241 A(H1) isolates from 9 countries. 21% of these viruses were of A/New Caledonia/20/99-lineage and 79% of A/Solomon Islands/3/2006 lineage (Tables 3.1, 3.2 & 3.3 in Appendix 3). Some viruses reacted well with A/New Caledonia/20/99 ferret antisera and post-vaccination human serum pools however the majority of viruses had titres 8-fold lower (greater) to the homologous A/New Caledonia/20/99 titre. Some of these low reactors were well inhibited by ferret sera derived from A/Solomon Island/3/2006-like egg-grown viruses (A/Solomon Islands/3/2006, A/Hong Kong/2652/2006, A/Fukishima/141/2006) but most viruses were better covered with ferret sera raised to cell-grown viruses

(eg, A/Hong Kong/2652/2006 and A/Brisbane/59/2007). In addition, sequence analysis of the A(H1) HA-1 region of the haemagglutinin indicated that viruses could be grouped into 2 major clades. Group 1 contained mainly older viruses and early 2006 viruses with a Y256K (eg, A/Wellington/15/2005) although there were still some viruses from 2007 that fell in this group (eg, A/Brisbane/47/2007 and A/Cape Town/106/2007). The Group 2 viruses have a number of amino acid changes including T90K, Y101H, R149K, R212K, T269N and two further subgroups with changes at R192K and K81R respectively (Figure 3.2, Table 3.7 in Appendix 3). The majority of Australian isolates (including fatal cases) fell into the subgroup with K144E, D45N changes. Twenty-five neuraminidase (N1) genes were sequenced. Some genetic drift has been seen in the neuraminidase from the A/New Caledonia/20/99 with most strains clustering in a similar manner as they did with the HA1 (Figure 3.3 in Appendix 3). Furthermore, vaccines containing influenza A/Solomon Islands/3/2006 (H1N1) antigen stimulated postimmunization production of antibodies to HA at titres >= 40 to the influenza A(H1N1) vaccine virus in the sera of 100% of adults and 88% of elderly people. Although the average postimmunization geometric mean HI titres were 76% lower to recent isolates compared with the vaccine virus, the proportions of sera with titres >=40 were similar to those against the vaccine virus (WER 82(40), and Tables 3.8 and 3.9 in Appendix 3).

In summary, influenza A(H1N1) viruses were associated with outbreaks in southern hemisphere countries including New Zealand. In HI tests, the majority of isolates were antigenically similar to A/Solomon Islands/3/2006-like strain. Current vaccines containing A/Solomon Islands/3/2006 antigen stimulated HA antibodies against recent A(H1N1) influenza isolates, which were of similar titre and frequency to those against the vaccine virus. Based on all epidemiological, antigenic, genetic and serological data, the WHO consultation recommended vaccines containing a A/Solomon Islands/3/2006 (H1N1)–like strain. The AIVC accepts this recommendation.

2.2. 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 505 A(H3N2) isolates from 11 countries since January 2007. These viruses made up the majority (57.5%) of all viruses analysed at the Centre. Only 19% of the viruses reacted well with ferret antisera raised to egg-grown A/Wisconsin/67/2005 or A/Hiroshima/52/2005 viruses. A significant proportion of viruses (81%) had reduced reactivity (8 fold or greater) with these reference antisera (Tables 4.1 and 4.2 in Appendix 4). Tables 4.3 & 4.4 (Appendix 4) show the HI titres (fold increased/decreased) obtained with the isolates using ferret sera against A/Wisconsin/67/2005 compared with the homologous titres. In addition, genetic analysis indicated that four main groups were apparent from the A(H3) HA1 sequencing. Group 1 contained viruses isolated mainly from early in 2007 (eg A/Christchurch/3/2007). Group 2 viruses had the characteristic changes at R142G, L157S and K173E and contained the reference virus A/Nepal/921/2006 and some early 2007 Australian viruses. Group 3 with changes at G50E and K140I contained the bulk of the 2007 viruses from Australia and South Africa including the 3 fatal paediatric cases in Western Australia. A fourth group had a further change at K173N
(eg, Sydney/215/2007). Sequence analysis of the N2 NA gene from 56 viruses analysed in 2007 showed that the most recent viruses had several changes and formed their own distinct

subgroup similar to A/Brisbane/10/2007 which a subpopulation had a NA that grouped with A/Wisconsin/67/2005 (Figures 4.2 and 4.3, Table 4.8 in Appendix 4). Furthermore, vaccines containing influenza A/Wisconsin/67/2005(H3N2)-like antigens stimulated postimmunization production of antibodies to HA at titres >= 40 to the vaccine virus in the sera of 100% of children, 92% of adults and 88% of elderly people. When sera were tested against recent isolates, the corresponding proportions were somewhat lower: 85% of children, 59% of adult and 40% of elderly people. The average postimmunization geometric mean HI titres were lower to recent isolates than to the vaccine virus (reductions: children 33%; adults 47%; the elderly 60%). (WER 82(40), and Tables 4.7 and 4.8 in Appendix 4).

In summary, influenza A(H3N2) viruses were associated with widespread outbreaks in many southern hemisphere countries including New Zealand. Most recent isolates had antigenically drifted away from the vaccine virus A/Wisconsin/67/2005. Current vaccines containing the A/Wisconsin/67/2005(H3N2) antigen stimulated HA antibodies against recent influenza A(H3N2) isolates that were somewhat lower in titre and frequency than to the vaccine virus. Based on all epidemiological, antigenic, genetic and serological data, the WHO Consultative Group recommended an A/Brisbane/10/2007 (H3N2)-like strain. AIVC accepts this recommendation.

2.3. 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/Shanghai/361/2002) 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/Malaysia/2504/2004). For reasons not wholly understood, these remained geographically restricted to Asia until 2001. In 2002 the B/Malaysia/2504/2004-like strains were the predominant viruses worldwide.

Both recent B/Victoria-like strains (B/Malaysia/2504/2004 is the current reference strain) and B/Yamagata-like strains (B/Shanghai/361/2002 is the current reference strain) continued to be isolated worldwide in 2007. Varying proportions of the two lineages were seen in many countries with B/Yamagata lineage strains predominating in New Zealand and Australia but with small numbers.

132 influenza B isolates were received in 2007 at the Melbourne WHOCC from 10 countries (15% of total isolates). The majority of isolates (60%) were typed as B/Yamagata-like and reacted well to ferret sera raised against egg grown B viruses of this lineage (e.g. B/Florida/4/2006). The remaining 40% of B viruses were typed as B/Victoria-like and reacted poorly with ferret sera raised against egg-derived viruses of this lineage (e.g. B/Malaysia/2506/2004) but much better with ferret sera to cell-grown viruses (e.g. B/Malaysia/174/2006) (Tables 5.1, 5.2, 5.3 in Appendix 5). Table 5.4 (appendix 5) shows the HI titres (fold increased/decreased) obtained with the isolates using ferret sera against B/Malaysia/2506/2004 or B/Florida/4/2006 compared with the homologous titres. In addition, sequence analysis of the HA1 gene of recent isolates showed that they fell into one of the 2 major lineages of B viruses (B/Victoria/2/87 or B/Yamagata/16/88), consistent with their antigenic typing. Viruses sequenced from the B/Yamagata line showed a small number of changes from the previous vaccine strain B/Jiangsu/10/2003 including changes at V252M and P108A. The B/Victoria lineage viruses showed little drift from the current reference vaccine virus B/Malaysia/2506/2004. All 14 B viruses analysed in 2007 had an NA sequence

of the B/Yamagata lineage but were divided into 2 subgroups that were similar to B/Florida/7/2004 or B/Malaysia/2506/2004. Both subgroups showed continued genetic drift (Figures 5.2, 5.3, 5.4 & 5.5, & Table 5.8 in Appendix 5). Furthermore, vaccines containing influenza B/Malaysia/2506/2004 antigen stimulated postimmunization production of antibodies to HA at titres >= 40 to the vaccine virus in the sera of 59% of children, 75% of adults and 70% of elderly people. In adults and the elderly, the corresponding proportions were similar for recent B/Malaysia/2506/2004-like viruses and recent B/Yamagata/16/88 lineage virus. In children, the proportions were similar for the vaccine viruses and recent B/Malaysia/2506/2004-like isolates, but were somewhat lower (22%) for recent B/Yamagata/16/88 lineage isolates. In children, adults and the elderly, the average postimmunization geometric mean HI titres and proportions of titres >= 40 to recent B/Malaysia/2506/2004-like isolates were similar to those to the vaccine virus, but titres to recent B/Yamagata/16/88 lineage viruses were somewhat reduced (reductions: children 52%; adults 47%; and the elderly 34% (WER 82(40), Tables 5.7 to 5.8 in Appendix 5).

In summary, influenza B outbreaks were reported in southern hemisphere countries including New Zealand. The majority of recent isolates was antigenically similar to B/Florida/4/2006 (B/Yamagata/16/88 lineage). Current vaccines containing B/Malaysia/2506/2004 antigen stimulated HA antibodies that were similar in titre to recently isolated B/Malaysia/2506/2004 – like viruses. However, the average postimmunisation geometric mean HI titres to recent B/Yamagata/16/88 lineage viruses were reduced. Based on all epidemiological, antigenic, genetic and serological data, the WHO consultation recommended vaccines containing a B/Florida/4/2006–like strain. The AIVC accepts this recommendation.

3. SUMMARY

It is recommended that the influenza vaccine formulation for New Zealand in 2008 is:

- A(H1N1) an A/Solomon Islands/3/2006 (H1N1) - like strain
- A(H3N2) an A/Brisbane/10/2007 (H3N2) - like strain
- B a B/Florida/4/2006 - like strain

3.1. 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 Geneva on 17-19 September.

The Committee agreed to adopt the September WHO recommendations. The influenza vaccine components for year 2008 season should contain the following:

A (H1N1):	an A/Solomon Islands/3/2006 (H1N1) - like strain,	15 µg HA per dose
A (H3N2):	an A/Brisbane/10/2007 (H3N2) - like strain,	15 µg HA per dose
B:	a B/Florida/4/2006 - like strain,	15 µg HA per dose

The following viruses are suitable vaccine strains:

- A/Solomon Islands/3/2006 (H1N1) (IVR-145)
- A/Brisbane/10/2007 (H3N2) (IVR-147)
- B/Florida/4/2006 or B/Brisbane/3/2007

- The SRID reference standard reagents for A/Solomon Islands/3/2006 (H1N1) (IVR-145) strain are available from NIBSC (UK).
- The SRID reference standard reagents for A/Brisbane/10/2007 (H3N2) (IVR-147) and B/Brisbane/3/2007 will be available from TGA following calibration in December 2007.

4. ACKNOWLEDGEMENTS

The WHO National Influenza Centre, ESR

Virus Laboratories in Auckland, Waikato and Christchurch Hospitals

Participants in the National Influenza Surveillance Programme

WHO Collaborating Centre for Influenza, CSL, Melbourne

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

Australian Influenza Vaccine Committee

Regional Public Health in Wellington

Table 1. Influenza Vaccine Recommendations for New Zealand, 1991-2008

Formulation Recommendations		Vaccine used for	A H3N2	A H1N1	B
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

Table 2. Thresholds Used to Describe Influenza Activity*

Term used		Consultation rate (per 100,000 population)
Baseline		<= 49
Normal seasonal activity	low	50-99
	moderate	100-149
	high	150-249
higher than expected		250-399
severe epidemic		>= 400

*Note: This was published in *New Zealand Public Health Report 2001, 8(1):9-12* "Influenza surveillance and immunisation in New Zealand, 1990-1999"

Figure 1. Weekly Consultation Rates for Influenza-like Illness in New Zealand, 2005, 2006, 2007

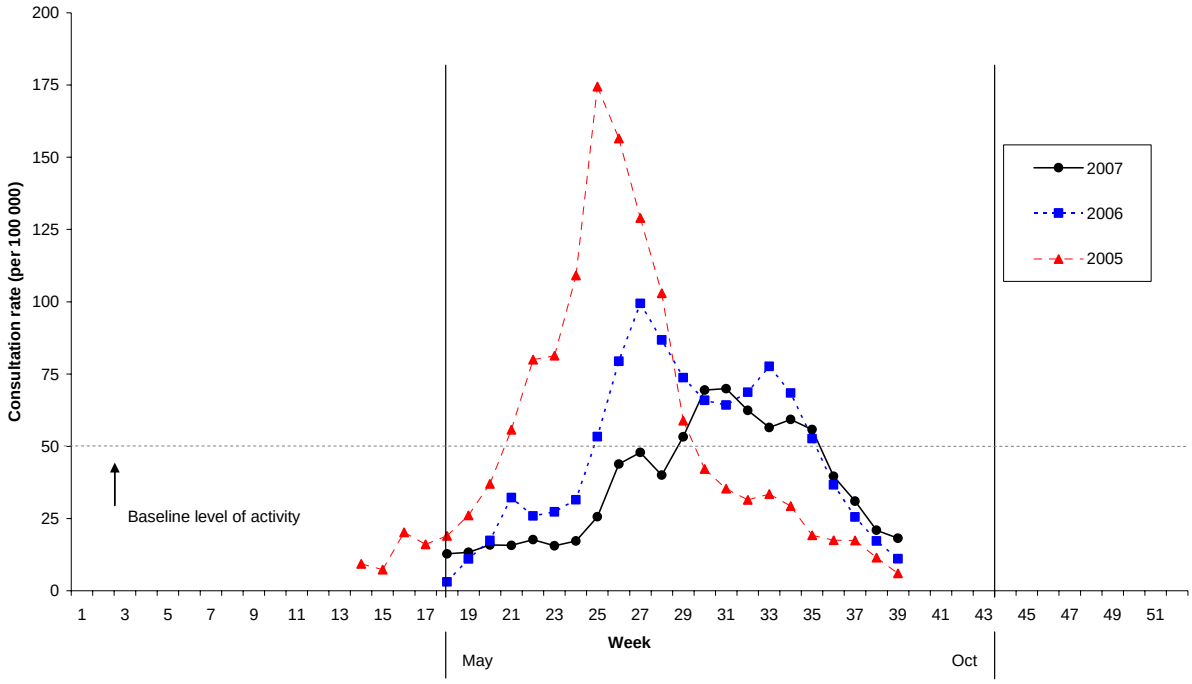


Figure 2. Weekly Consultation Rates for Influenzea-like Illness in New Zealand 1992-2007

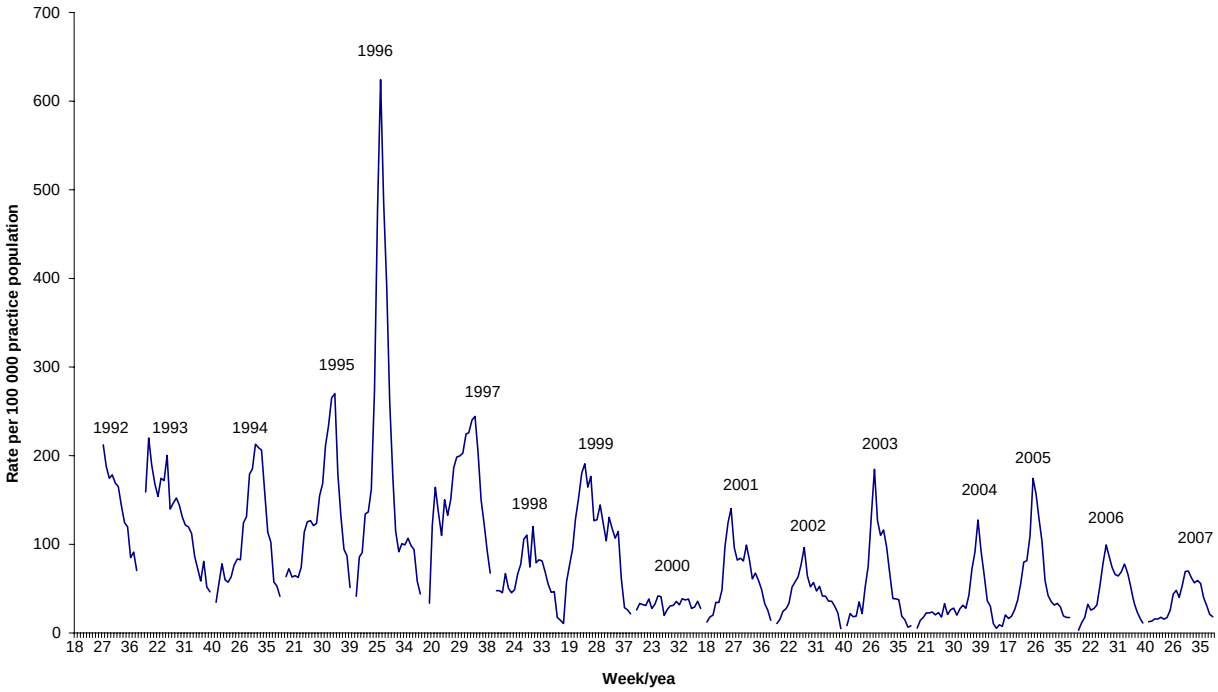


Figure 3. Total Influenza Isolates by Surveillance Type and Week Specimen Taken, 2007

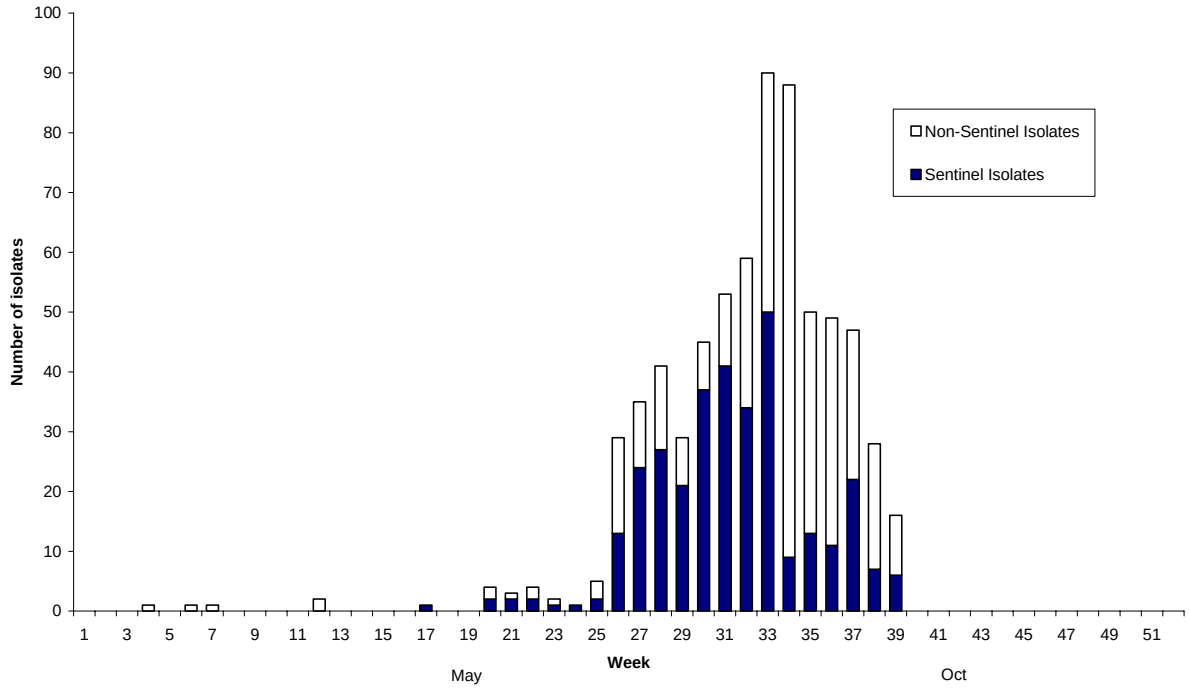


Figure 4. Total Influenza Isolates by Type and Week Specimen Taken, 2007

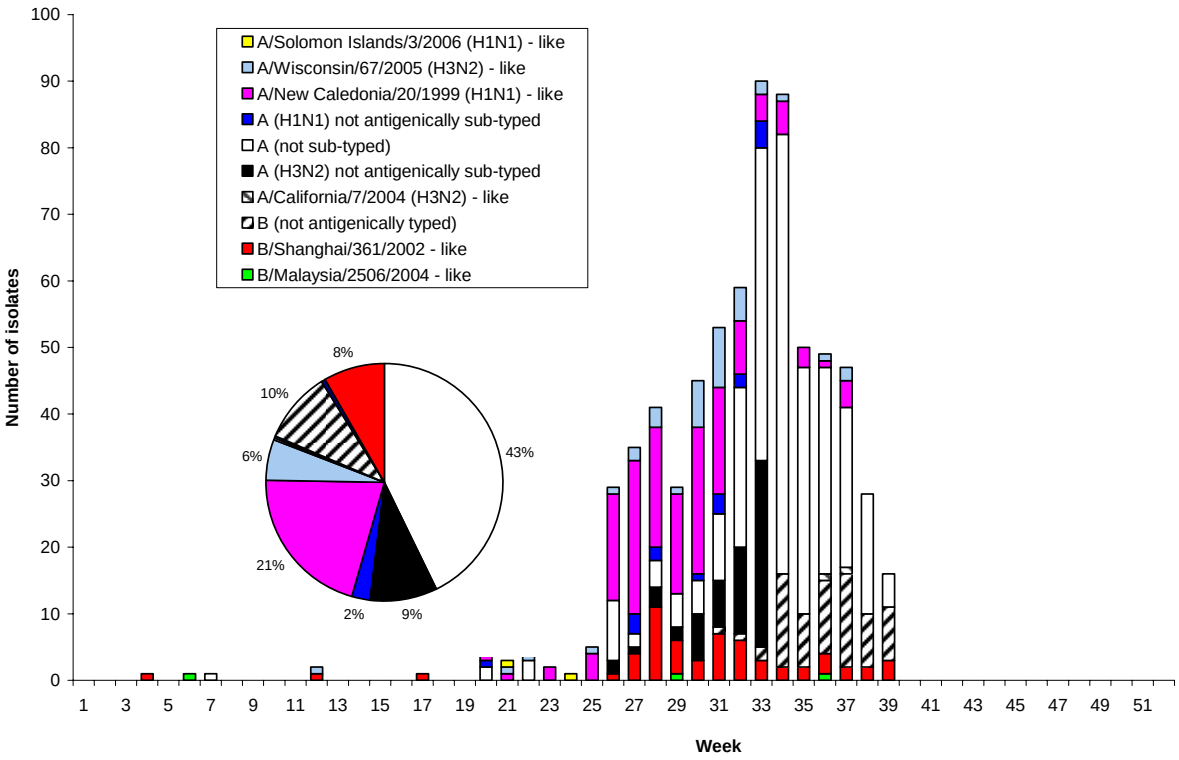


Figure 5. Total Influenza Virus Isolates by Type and Week Specimen Taken, 2007

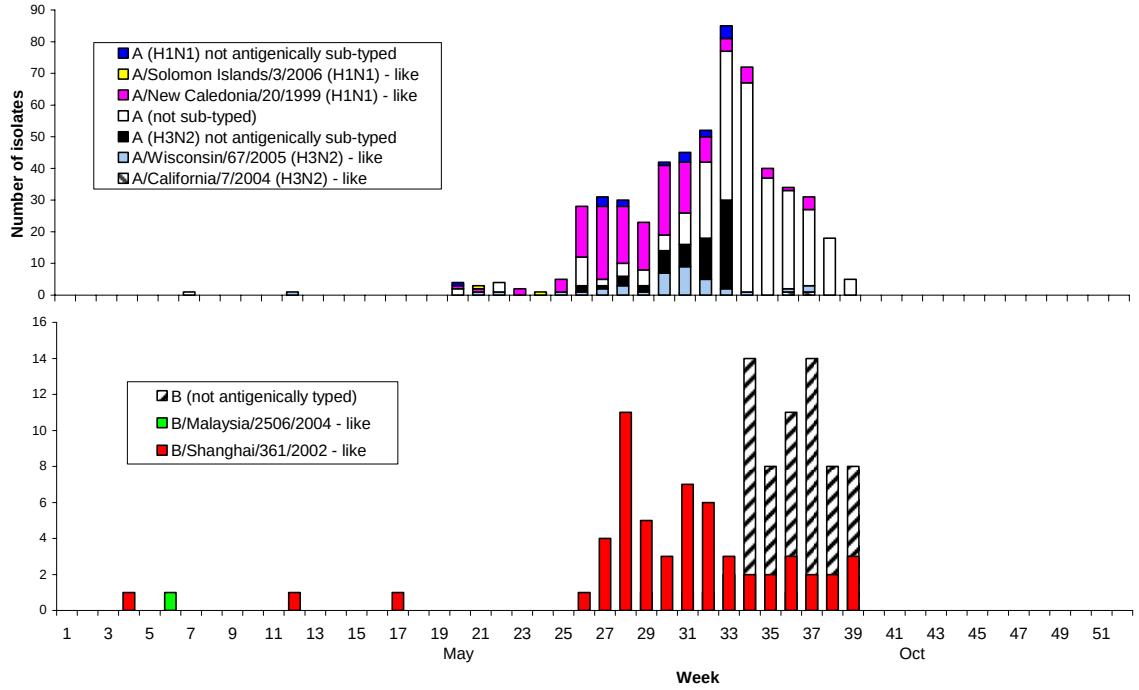
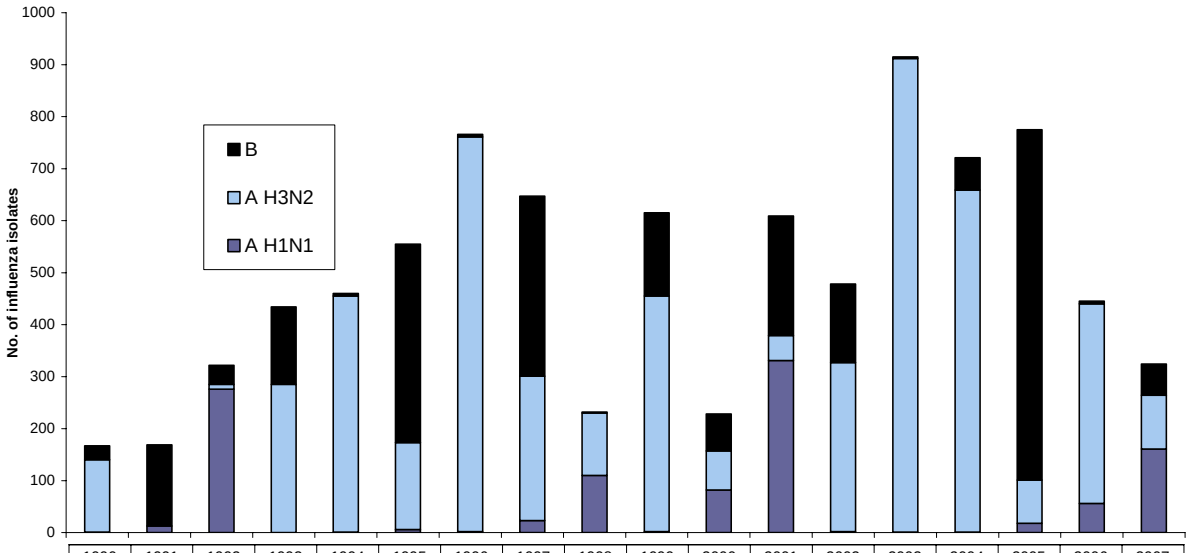


Figure 6. Influenza Isolates by Type, 1990-2007



	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007
B	16%	92%	11%	34%	1%	69%	1%	53%	1%	26%	31%	38%	32%	0%	9%	87%	1%	19%
A H3N2	83%	0%	3%	66%	99%	30%	99%	43%	52%	74%	33%	8%	68%	100%	91%	11%	86%	32%
A H1N1	1%	8%	86%	0%	0%	1%	0%	4%	47%	0%	36%	54%	0%	0%	0%	2%	13%	50%

Figure 7. Comparison of Sentinel and Laboratory-based Surveillance by Age Group, 2007

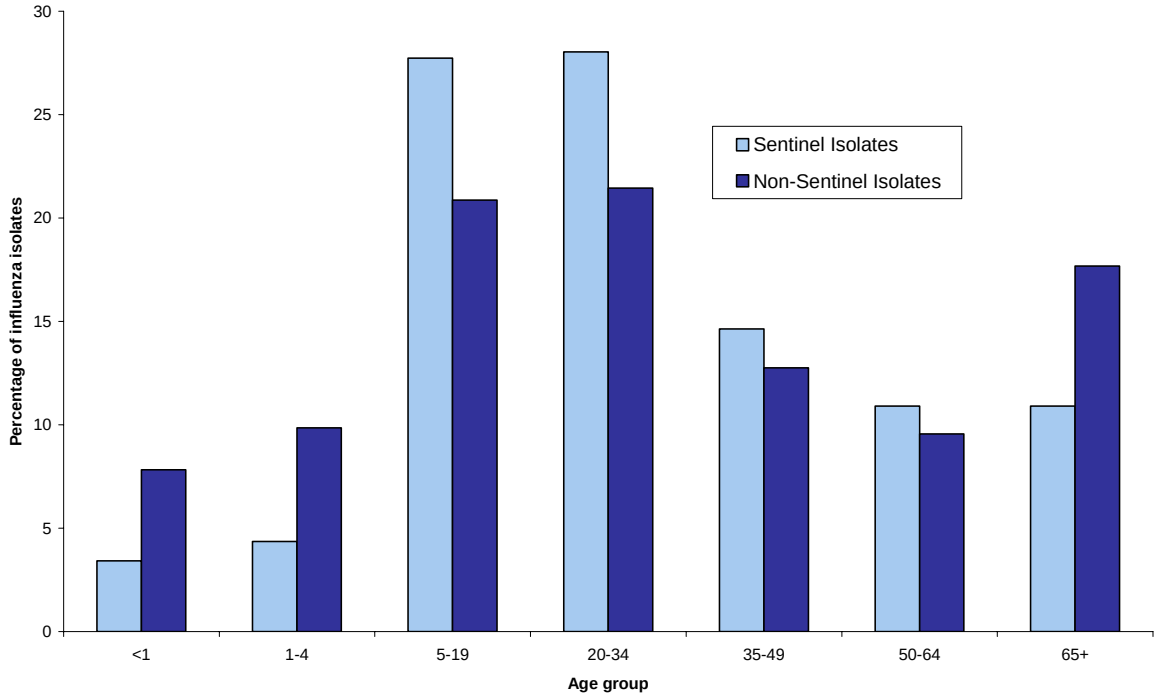


Table 3. Vaccine Breakthrough Cases by Age Groups, 2007

Age Group	Influenza A not subtyped	A/Wisconsin /67/2005 (H3N2)	AH3N2 (PCR)	Influenza B (PCR)	B/Shanghai/ 361/2002	Subtotal
20-34 yrs		2			1	3
35-49 yrs			1			1
50-64 yrs	1	2		1	1	5
65 + yrs	1	1		2		4
Subtotal	**2**	**5**	**1**	**3**	**2**	**13**

APPENDIX 1

The Australia Influenza Vaccine Committee (AIVC) meeting was convened at 1:30 pm on 3 October 2007 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 (2007)

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

Members: Dr Gary Grohmann, TGAL, TGA (**Chairperson**)
Prof Ann Kelso, WHO Collaborating Centre for Reference and Research on Influenza
Dr Ian Barr, WHO Collaborating Centre for Reference and Research on Influenza
Prof Ian Gust, Melbourne University
Prof Gordon Ada, JCSMR
Prof Greg Tannock, RMIT
Dr Mike Catton, VIDRL
Dr Heath Kelly, VIDRL
Dr David Smith, UWA
Dr Grahame Dickson, DSEB, TGA
Dr Leslee Roberts, OHP, DoHA
Dr Alan Hampson, Interflu Pty Ltd
Dr Sue Huang, CDI, ESR, NZ
*Prof Barry Schoub, National Institute for Communicable Diseases, SA
*Dr Terry Besselaar, National Institute for Communicable Diseases, SA
Thérèse Marengo, TGAL, TGA (**Secretary**)
Dr Rohan Hammett, PMA, TGA (apologies)
Dr Dominic Dwyer, ICPMR (apologies)

Observers: Mr David Ryan, CSL Ltd
Mr Peter Schoofs, CSL Ltd
Mr William Cracknell, CSL Ltd
Ms Christine Wadey, CSL Ltd
Dr Victor Carey, Sanofi Pasteur
Ms Crissa Kyriasis, GlaxoSmithKline Australia Pty Ltd
Mr Shane Patella, GlaxoSmithKline Australia Pty Ltd
Mr Tony Wilson-Williams, Solvay Biosciences Pty Ltd
Mr George Weber, Novartis Vaccines
Dr Stephen Pasaribu, Baxter
Dr Larry Kelly, Director TGAL, TGA
Dr Nick Medveczky, TGAL, TGA
Dr Tania Dalla Pozza, TGAL, TGA
Mr Chris Boswell, TGAL, TGA
Ms Derna Waters, TGAL, TGA
Mr Chris Boswell, TGAL, TGA
Ms Derna Waters, TGAL, TGA

* Participating by telephone

APPENDIX 2

ISOLATES RECEIVED FOR ANALYSIS AT THE AUSTRALIAN WHO COLLABORATING CENTRE

APPENDIX 3

INFLUENZA A (H1N1)

APPENDIX 4

INFLUENZA A (H3N2)

APPENDIX 5

INFLUENZA B

APPENDIX 6

WHO RECOMMENDATION FOR INFLUENZA VACCINES