

**RECOMMENDATION FOR INFLUENZA
VACCINE COMPOSITION 2007**

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VACCINE COMPOSITION 2007**

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by

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RECOMMENDATIONS

The Australian Influenza Vaccine Committee (AIVC), with a New Zealand representative (Appendix 1), met in Canberra on 4 October 2006 to consult on the influenza vaccine composition for 2007. The recommended composition was:

- A(H1N1) an A/New Caledonia/20/99-like strain
- A(H3N2) an A/Wisconsin/67/2005 - like strain
- B a B/Malaysia/2506/2004 - 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 13 October issue of the *Weekly Epidemiological Record, 2006 81(41):385-396* (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 2006

Between February and September 2006, influenza activity was reported in Africa, the Americas, Asia, Europe and Oceania. In general, activity was low compared with the same period in recent years.

In the northern hemisphere, influenza activity continued in North America and Asia, declining in April, except in Hong Kong Special Administrative Region (SAR) of China, where outbreaks occurred from March to July. In Europe, activity increased in February, quickly reached a peak and declined in April. In North America and some Eastern European countries, influenza A(H3N2) viruses predominated and caused outbreaks, while in other European countries, influenza B viruses predominated. In Asia, influenza A(H1N1), A(H3N2) and B viruses cocirculated.

In the southern hemisphere, influenza activity began in April. Overall activity was mild to low. In South America, influenza A(H1N1) viruses predominated but circulated locally and were responsible for an outbreak in Brazil. While outbreaks caused by influenza A(H3N2) occurred in New Zealand and South Africa, activity remained low in other parts of Africa and Oceania.

Between February and 19 September 2006, 87 confirmed human cases with 59 deaths from influenza A(H5N1) were reported to WHO from Azerbaijan, Cambodia, China, Djibouti, Egypt, Indonesia, Iraq and Thailand. Since November 2003, a total of 247 human cases have been confirmed from 10 countries. The WHO influenza pandemic preparedness level remains unchanged at Phase 3. So far, there has been no evidence of sustained human-to-human transmission. The current status of the development of new candidate H5N1 vaccine viruses and 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/h5n1virus2006_08_18/en/index.html

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 2006. Influenza A(H3N2) was the predominant strain which accounted for 55.6% (657/1182) of isolates while 19% (225/1182) were influenza A(H1N1) and 25.4% (300/1182) were influenza B (Figures 2.1 and Table 2.1 in Appendix 2).

1.2 Southern Hemisphere Influenza Activity, March-September 2006

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 80 voluntary sentinel general practitioners throughout the country are recruited into the system. 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 five 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.esr.cri.nz/flu>).

- 2) Laboratory-based surveillance. This system is operated all year around by the four regional virology laboratories at Auckland, Waikato, Christchurch and Dunedin 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 2006. The peak of the influenza activity in 2006 is lower but broader than 2005 and 2004. The consultation rate remained at the baseline level from week 18 to week 24 (in the middle of June). The activity increased rapidly and reached the first peak in week 27 (at the beginning of July) with the consultation rate for flu-like illness at 99/100,000. The peak activity continued for 6 weeks and reached the second peak in week 33 (in the middle of August). Then influenza activity started to decline and reached the baseline level in week 36 (at the beginning of September). Since then, it has remained at the baseline level. When weekly consultation rates for ILI from 1992-2006 were compared, influenza activity in 2006 is at the low-to-moderate level. In particular, comparison of the data for the last 7 years (2000 to 2006) indicates that influenza activity in 2006 is the third lowest to 2000 and 2002.

Influenza isolates were reported weekly by sentinel and laboratory-based surveillance. Influenza isolations in 2006 have two interesting features: 1) The peak of viral isolation was in week 29 (92), 2 weeks later than the first peak of the ILI consultation. 2) A greater proportion of influenza viruses were isolated from sentinel surveillance in 2006 (40%) than in 2005 (33%). Sentinel surveillance yielded 305 (40%, 305/758) influenza viruses and laboratory-based surveillance isolated 453 (60%, 453/758) influenza viruses, whereas 276 (33%, 276/826) influenza viruses were from sentinel surveillance and 550 (67%, 550/826) from laboratory-based surveillance in 2005. The increase in the proportion of influenza isolates resulting from sentinel surveillance could reflect widespread community outbreaks of influenza and/or fewer hospitalisations in 2006.

A total of 758 influenza viruses were isolated in 2006 from weeks 1 to 38 (Figure 4). Overall, influenza A was the predominant type with 753 isolates (99%, 753/758). There were only five influenza B isolations in 2006 with two of B/Malaysia/2506/2004-like strains and two of B/Shanghai/361/2002-like strains and one influenza B yet to be typed. Of 753 influenza A isolates, influenza A/New York/55/2004 (H3N2)-like strain was the predominant strain (50%, 381/758). In addition, 48 of influenza A/New Caledonia/20/99 (H1N1) – like strains were isolated. There were 324 of influenza A isolates yet to be sub-typed. Of these, 262 were from the Canterbury region.

Figure 5 shows the temporal distribution of influenza A and B viruses in 2006. Influenza B viruses scattered throughout the season. Influenza A(H1N1) viruses emerged in the late season, co-circulating with influenza A(H3N2) viruses.

Figure 6 shows the percentage of influenza isolates by type from 1990 to 2006. A total of 434 influenza isolates have been typed and sub-typed. Influenza A(H3N2), A(H1N1) and B viruses consist of 88%, 11% and 1% 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. A total of 52 patients (7%, 52/758) in 0-4 age group and >65 age group yielded influenza viruses in 2006. 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 26 vaccine breakthrough cases were recorded from the national influenza database (Table 3), comprising 3.4% of total isolates (26/758). 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 26 vaccine breakthrough cases, 17 cases (65%, 17/26) occurred in age groups >50 years. Immunological senescence may explain a higher proportion of vaccine breakthrough cases in the elderly population. In addition, three vaccine cases had influenza A/Wisconsin/67/2005 – low reactors. This indicated 12 % of vaccine breakthrough might be due to the continuing drift of the virus, resulting in a lower match between the circulating virus and the vaccine.

In addition, 260 ILI cases had information on vaccination history from the ESRLab database for sentinel surveillance specimens. Among them, 31 had influenza vaccination in the same year as the onset of ILI and 229 had none. There were 12 (38.7%, 12/31) vaccinated patients whose specimens yielded influenza viruses. Of these, one case (8.3%, 1/12) had an A/New York/55/2004 (H3N2) –low reactor.

1.2.2 Australia

There are three forms of laboratory surveillance system in Australia for influenza strain characterisation: The first form is called 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 is lower in 2006 than in 2005. The activity peaked in week 34, two weeks later than in 2005. The second form is laboratory virology serology surveillance system (LabVISE). About 12 to 25 laboratories report the basic strain identification. This system has been operating since 1982. In 2006, about 960 influenza isolations were reported from LabVISE. The third form is the laboratory surveillance conducted by the Melbourne WHOCC. In addition, Australian Sentinel Practice Research Network (ASPREN) conducts influenza disease surveillance (influenza-like-illness). In 2006, ASPREN consists of 39-80 general practices from Western Australia, Victoria and Northern Territory. 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 2006 peaked during July in Western Australia, August in Victoria and Queensland, whilst the tropical influenza activity in Northern Territory peaked in February, July and September. New South Wales replaced ASPREN surveillance with emergency department surveillance in 2006. About 30 emergency departments participated in the survey. The peak was recorded in late August with the ILI rate at 1-5/1000 consultations. Furthermore, 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 was supplied weekly per jurisdiction. The percentage of sick leave for three days or more continuously is reported. The absenteeism data in 2006 indicated a broad peak of absenteeism during the winter. The increased absenteeism in August overlapped well with the peak detected by the NNDSS data.

A total of 440 influenza isolates from Australia were received for analysis at the Melbourne WHOCC (Appendix 2) from 1 January to 26 September 2006. 63.6% (280/440) of isolates were A(H3N2) viruses, antigenically related to A/Wisconsin/67/2005-like strain. 13 (3%, 13/440) A(H1N1) viruses were isolated and H1 was antigenically similar to A/New Caledonia/20/99-like strain. 147 influenza B viruses (33.4%, 147/440) were isolated with co-circulation of B/Malaysia and B/Shanghai lineage viruses.

(Abridged from a report by Dr Moira McKinnon, 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 2006 winter season was monitored mainly in Johannesburg and surrounding areas but also included other areas in the country. This was made possible by expanding the National Viral Watch to include centres from the Eastern Cape, KwaZulu/Natal and Western Cape Provinces.

Both subtypes of influenza A and B viruses circulated during the season but the predominant virus subtype isolated was A H3N2. The first influenza isolate of the season was made from a specimen collected in Johannesburg on 27 March (week 13), after which sporadic isolates were made. From week 18, (week starting 1 May), isolates were made on a regular basis, with the largest number being made in week 23 (week starting 4 June). The last isolate was made from a specimen collected on 19 September.

A total of 547 influenza isolations were made i.e. 498 influenza A virus and 49 influenza B. Of the influenza A isolates, five were identified as A/Caledonia/20/99-like (H1N1), 353 as A/Wisconsin/67/2005-like (H3N2) and 140 were untyped. A proportion of the A/Wisconsin/67/2005-like viruses showed low reactivity in HI tests. The majority of the influenza B isolates (40) was identified as B/Malaysia/2506/2004-like while 4 were B/Shanghai/361/02-like viruses.

Sequence analysis of the HA1 subunit revealed the H1 viruses isolated during the season showed very little genetic drift from the A/New Caledonia/20/99 vaccine strain. The molecular characterisation of representative influenza H3N2 isolates revealed that the viruses circulating in South Africa exhibited extensive genetic drift relative to the A/California/7/2004 vaccine strain. They shared a greater homology with the A/Wisconsin/67/05 strain with the characteristic S193F and D225N mutations seen in the

A/Wisconsin/67/05-like viruses. All the isolates differed from the A/Wisconsin/67/05 strain at residues 122 (D – N), 195 (H – Y) and 223 (I – V). Sporadic mutations were seen at residues 188 (D – N), 196 (A – T) and 269 (R - K). The phylogenetic tree constructed from analysis of the HA1 subunit of representative South African 2006 influenza B viruses from both the B/Victoria/2/87 and B/Yamagata/16/88 viruses. The 2006 B/Victoria/2/87-like isolates were closely homologous to the B/Malaysia/2506/04 vaccine strain and shared only one common amino acid change at position 109 (K – N). In the B/Shanghai-like viruses, substitutions were seen at residues 37 (I – T), 40 (H – Y), 131 (L – P) and 252 (V – M). Sporadic changes were seen at several other residues.

Thirty nine of the 547 (7,0 %) specimens which were positive for influenza were from patients whom had received the influenza vaccine. Influenza A was isolated from 34 of these, with 26 identified as subtype H3N2 and 8 untyped. The remaining 5 vaccine failures were infected with an influenza B/Malaysia/2506/04-like virus. Patients with vaccine failure were observed from all age groups.

In summary, influenza activity in South Africa during the 2006 winter season was predominantly mild with some localized outbreaks of influenza A H3N2. The majority of viruses isolated in 2006 were influenza A H3N2 in contrast to the 2005 season where influenza A H1N1 viruses were the predominant subtype. The majority of the South African H3N2 viruses reacted well with the A/Wisconsin/67/05 northern hemisphere vaccine strain, but there were a small number of low reactors which have also been seen in other countries with H3N2 activity this year.

(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 February 1998, 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 2001-2002 season, it was found that genetic reassortant influenza viruses with H1N2 antigens were circulating and were the predominant H1 viruses in certain areas, particularly the UK. The haemagglutinin of these viruses was derived from the A/New Caledonia lineage whereas the neuraminidase and the other 6 genes of the viruses were

derived from the contemporary A(H3N2) human strains. The A(H1N2) viruses have only rarely been reported in recent times and no A(H1N2) was detected globally in 2006.

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 48 influenza A/New Caledonia (H1N1)-like virus isolations in New Zealand in 2006.

Since January 2006, the Melbourne WHOCC has analysed 225 A(H1) isolates from 11 countries with most coming from the Philippines (90). All were A/New Caledonia/20/99-lineage viruses (Tables 3.1 & 3.2 in Appendix 3). Most viruses reacted well with A/New Caledonia/20/99 ferret antisera and post-vaccination human serum pools however an increasing proportion (29%) of low reactors (8 fold or more) were observed. In addition, sequence analysis of the A(H1) HA-1 region of the haemagglutinin indicated that viruses could be grouped into 2 major clades. One group contained mainly older viruses and early 2006 viruses with a Y256F (eg A/Wellington/15/2005) and the other group having a number of amino acid changes including K90T, H101Y, K149R, K212R, N269T and smaller subgroups with changes at R192K and K81R respectively (Figure 3.2 in Appendix 3). The majority of recent isolates was in these two subgroups. Nineteen 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 tree with subgroups represented by A/Victoria/500/2006 and A/Philippines/1392/2006 (Figure 3.3, Table 3.4 in Appendix 3). Furthermore, vaccines containing influenza A/New Caledonia/20/99 (H1N1) antigen stimulated postimmunization production of antibodies to HA at titres ≥ 40 to the influenza A(H1N1) vaccine virus in the sera of 55% of children, 75% of adults and 62% of elderly people. In children and adults, the proportions of titres ≥ 40 to recent isolates were similar, but only 38% of elderly people had titres ≥ 40 to recent isolates. The average postimmunization geometric mean HI titres to recent isolates were not significantly different from those to the vaccine virus (WER 81(41), and Tables 3.6 and 3.7 in Appendix 3).

In summary, influenza A(H1N1) viruses were associated with outbreaks in southern hemisphere countries. In HI tests, the majority of isolates were antigenically similar to A/New Caledonia/20/99. Influenza A (H1N2) viruses were not reported. Current vaccines containing A/New Caledonia/20/99 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/New Caledonia/20/99 –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). In the 2006 winter in New Zealand, influenza A(H3N2) was the predominant subtype.

The Melbourne WHOCC has analysed 657 A(H3N2) isolates from 11 countries since January 2006. These viruses made up the majority (55.8%) of all viruses analysed at the Centre. Approximately half of the viruses reacted well with ferret antisera raised to

A/Wisconsin/67/2005 or A/Hiroshima/52/2005. A significant proportion of viruses (34%) had reduced reactivity (8 fold or greater) with these reference antisera. The ESR national influenza reference laboratory also recorded a significant percentage (32%, 47/146) of A(H3N2) viruses that were A/Wisconsin/67/2005-low reactors. Tables 4.1 and 4.2 (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 three main groups were apparent from the A(H3) HA1 sequencing. Group 1 contained viruses isolated mainly from early in 2006 (eg A/Thailand/86/2006). Group 2 viruses had the characteristic changes at S193F and D225N and these viruses contained a number of “low reactors” in HI assays (eg A/Brisbane/64/2006). Group 3 viruses were largely made up of viruses with G50E change and also contained a number of “low reactors” in HI assays. Sequence analysis of the N2 NA gene from viruses analysed in 2006 showed that the most recent viruses had several changes compared to 2004-5 viruses and formed their own distinct subgroups (Figures 4.2 and 4.3, Table 4.6 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 89% of adults and 85% of elderly people. For representative recent isolates, the proportions with titres ≥ 40 were somewhat lower; 69% of adult and 71% of elderly people. For adults and the elderly, the average postimmunization geometric mean HI titres to recent isolates were somewhat lower (WER 81(41), and Tables 4.8 and 4.9 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 were antigenically similar to the vaccine viruses A/Wisconsin/67/2005 and A/Hiroshima/52/2005. 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/Wisconsin/67/2005-like virus as A(H3N2) vaccine component for 2007 and the AIVC accepts this recommendation.

2.3 Influenza B

Two distinct lines of influenza B have been observed during recent years, initially from 1990 when the B/Panama/45/90 variant of influenza B was first observed. This strain and its further variants (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 2006. Varying proportions of the two lineages were seen in many countries with B/Malaysia lineage strains predominating worldwide.

300 influenza B isolates were received in 2006 at the Melbourne WHOCC from 11 countries (25.4%) of total isolates). The majority of isolates (78.7%) were typed as B/Malaysia/2504/2004-like but reacted poorly to ferret sera raised against egg-grown B viruses of this lineage. The remaining 21.1% of B viruses were typed as

B/Shanghai/361/2002-like, reacting well with ferret sera raised against viruses of this lineage. A significant proportion of viruses (41% and 44%) had reduced reactivity (8 fold or greater) with the antisera against B/Malaysia/2504/2004 like and B/Shanghai/361/2002 –like strains respectively. Tables 5.1 and 5.2 (appendix 5) show the HI titres (fold increased/decreased) obtained with the isolates using ferret sera against B/Hong Kong/330/2001 or B/Shanghai/361/2002 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 for the B/Yamagata line showed minor changes from the B/Jiangsu/10/2003-like strains and also had the M252I change. The B/Victoria lineage viruses showed little drift from the current reference viruses B/Malaysia/2504/2004. All B viruses analysed in 2006 had an NA sequence of the B/Yamagata lineage and were divided into 2 subgroups that were similar to B/Jiangsu/10/2003 or B/Shenzen/654/99. Both subgroups showed continued drift (Figures 5.2, 5.3, 5.4, & 5.5, Table 5.6 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 81% of adults and 75% of elderly people. In adults and the elderly, the postimmunization average geometric mean HI titres and proportions of titres ≥ 40 to recent B/Malaysia/2506/2004-like isolates (B/Victoria/2/87 lineage) were similar (WER 81(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 similar to B/Malaysia/2506/2004 (B/Victoria/2/87 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. Based on all epidemiological, antigenic, genetic and serological data, the WHO consultation recommended vaccines containing a B/Malaysia/2506/2004–like strain. The AIVC accepts this recommendation.

3 SUMMARY

It is recommended that the influenza vaccine formulation for New Zealand in 2007 is:

- A(H1N1) an A/New Caledonia/20/99-like strain
- A(H3N2) an A/Wisconsin/67/2005 - like strain
- B a B/Malaysia/2506/2004-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 and South Africa 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 18-20 September. The Committee agreed to adopt the September WHO recommendations. The influenza vaccine components for year 2007 season should contain the following:

A (H1N1):	an A/New Caledonia/20/99 (H1N1) - like strain,	15 µg HA per
dose		
A (H3N2):	an A/Wisconsin/67/2005 (H3N2) - like strain,	15 µg HA per
dose		
B:	a B/Malaysia/2506/2004 - like strain,	15 µg HA per
dose		

The following viruses are suitable vaccine strains:

- A/New Caledonia/20/99 (IVR-116)
- A/ Wisconsin/67/2005 (NYMCX-161B) or A/Hiroshima/52/2005 (IVR-142)
- B/Malaysia/2506/2004

The SRID reference standard reagents for all the above vaccine strains are available from NIBSC (UK).

4 ACKNOWLEDGEMENTS

The WHO National Influenza Centre, ESR

Virus Laboratories in Auckland, Waikato, Christchurch and Dunedin Hospitals

Participants in the National Influenza Surveillance Programme

WHO Influenza Collaborating Centre, CSL, Melbourne

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

Australian Influenza Vaccine Committee

Regional Public Health in Wellington

Table 1. Influenza Vaccine Recommended Formulations 1990-2007

Formulation Recommendations		Vaccine used for	A H3N2	A H1N1	B
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/Moscow/10/99	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-like 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, 2004, 2005, 2006

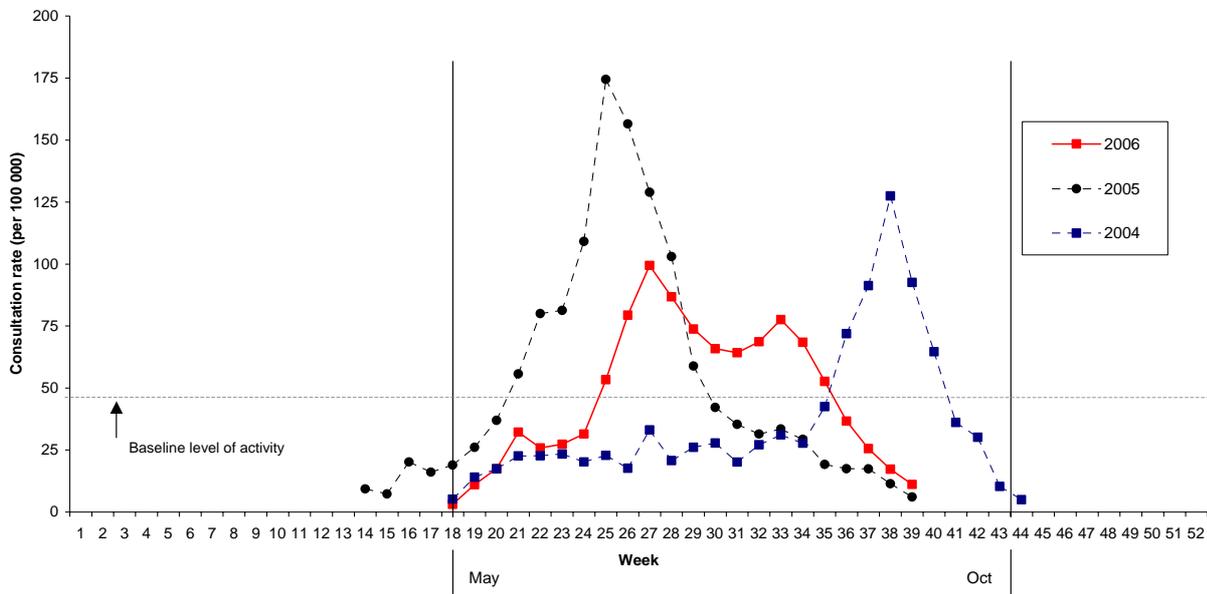


Figure 2. Weekly Consultation Rates for Influenza-like Illness in New Zealand 1992-2006

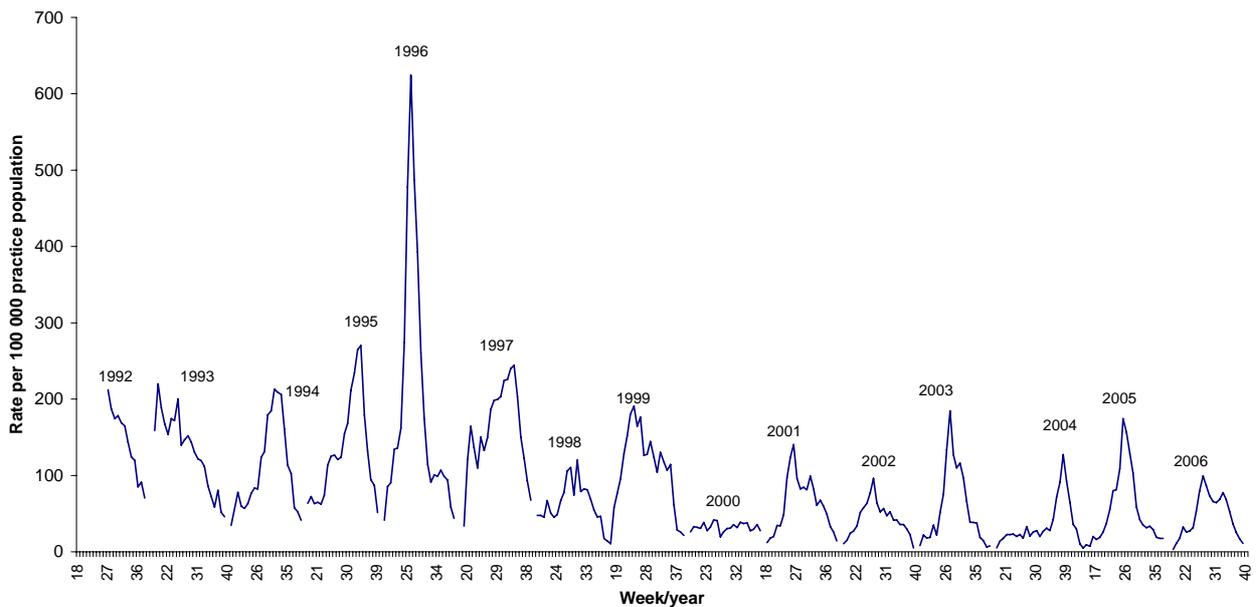


Figure 3. Total Influenza Isolates by Surveillance Type and Week Specimen Taken, 2006

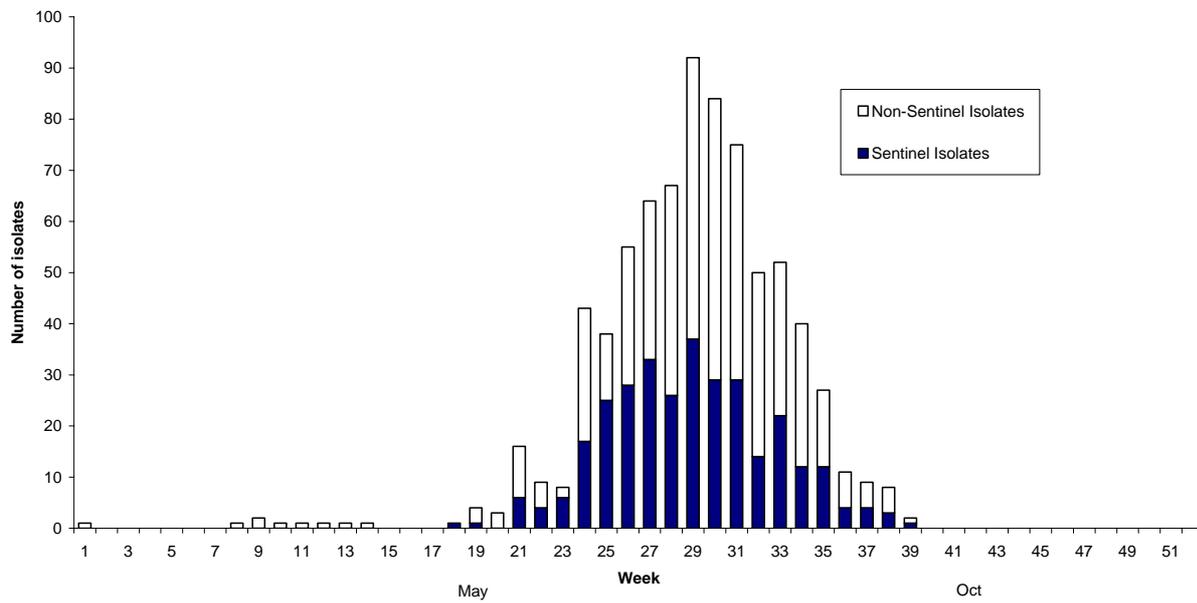


Figure 4. Total Influenza Isolates by Type and Week Specimen Taken, 2006

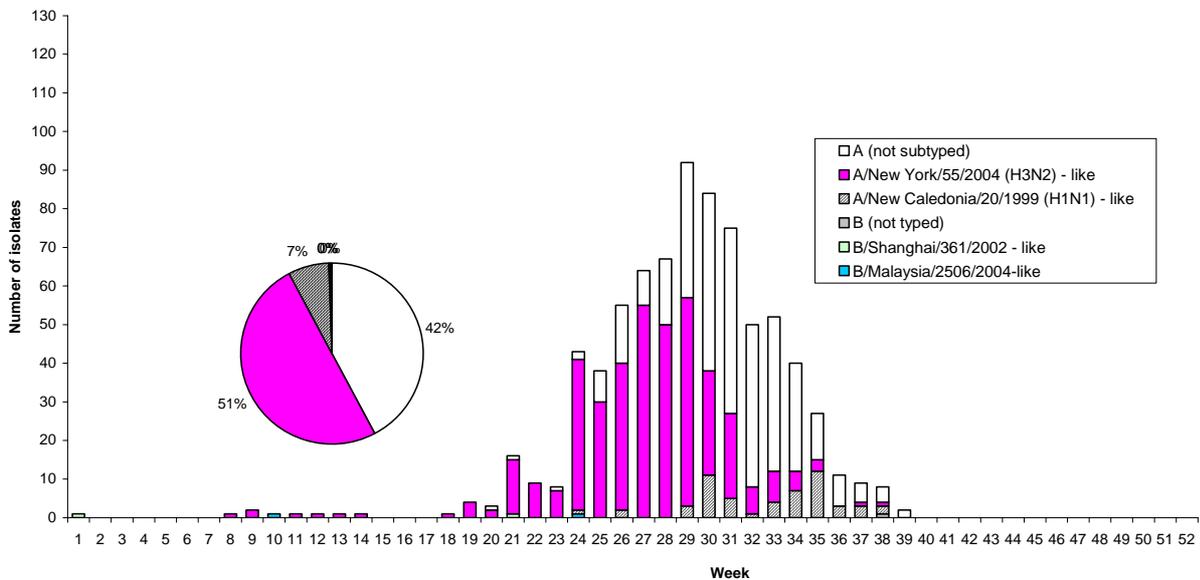


Figure 5. Total Influenza Virus Isolates by Type and Week Specimen Taken, 2006

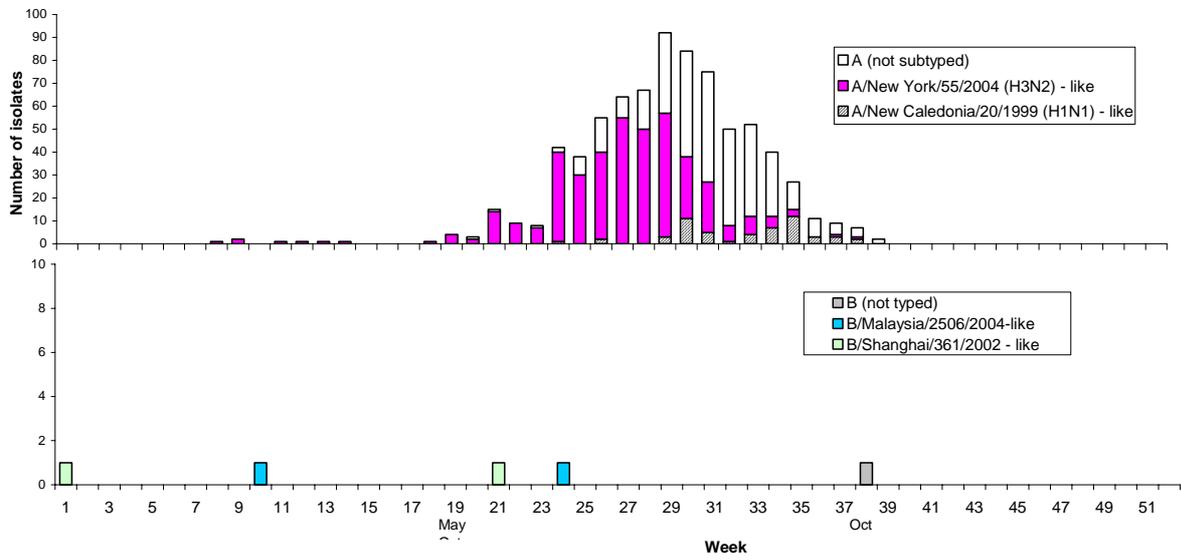


Figure 6. Influenza Isolates by Type, 1990-2006

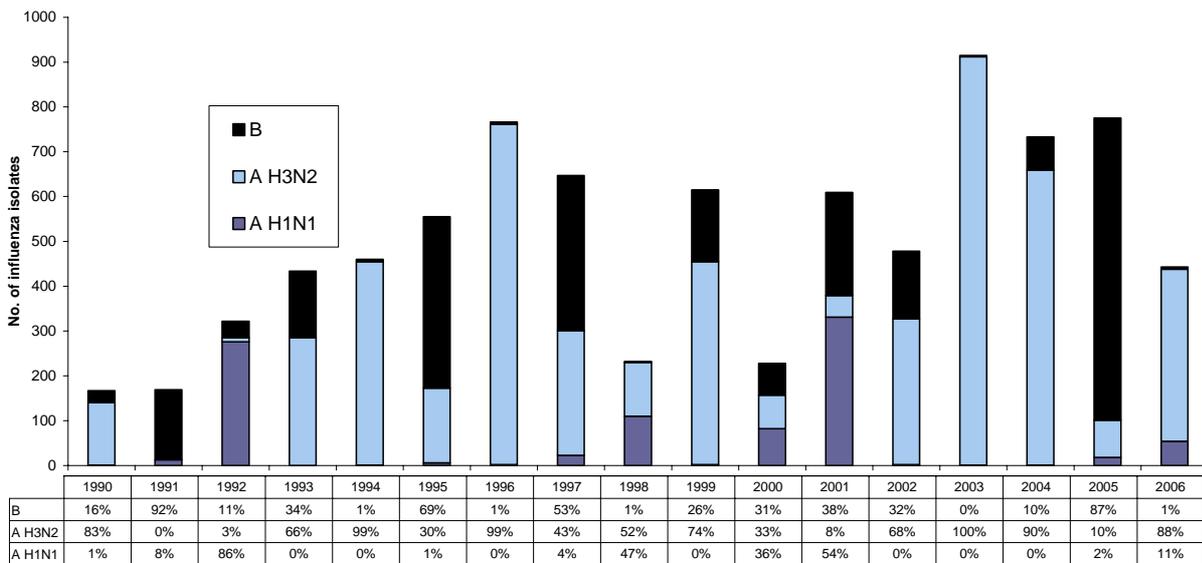


Figure 7. Comparison of Sentinel and Laboratory-based Surveillance by Age Group, 2006

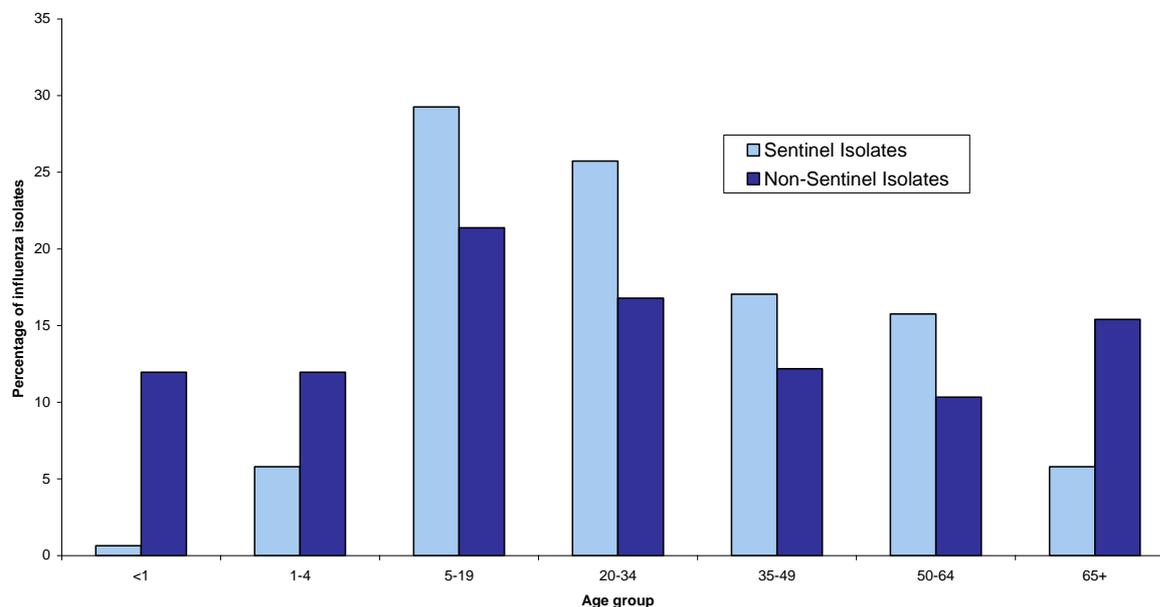


Table 3. Vaccine Breakthrough Cases by Age Groups, 2006

Age Group	Influenza A not subtyped	A/New Caledonia/20/99 (H1N1) - like	A/New York/55/2004 (H3N2) - like	Subtotal
5-19 yrs	1		0	1
20-34 yrs	1	1	2	4
35-49 yrs	1		3	4
50-64 yrs	2		8	10
65 + yrs	1	1	5	7
Subtotal	6	2	18	26

APPENDIX 1

The Australia Influenza Vaccine Committee (AIVC) meeting was convened at 1:30 pm on 4 October 2006 in 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 (2006)

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

Members:

Prof Ian Gust, WHO Collaborating Centre for Reference and Research on Influenza
Dr Ian Barr, WHO Collaborating Centre for Reference and Research on Influenza
Prof Gordon Ada, JCSMR
Prof Greg Tannock, RMIT
Dr Mike Catton, VIDRL
Dr Heath Kelly, VIDRL
Dr Dominic Dwyer, ICPMR
Dr David Smith, UWA
Dr Rohan Hammett, PMA, TGA
Dr Grahame Dickson, DSEB, TGA
Dr Moira McKinnon, HPPB, OHP, DoHA
Mr Alan Hampson, Interflu Pty Ltd
Dr Sue Huang, CDI, ESR, NZ
*Dr Terry Besselaar, National Institute for Communicable Diseases, SA

Observers:

Mr Darren Moulton, CSL Ltd
Mr Sandro Cirianni, CSL Ltd
Mr Ivan Jasenko, CSL Ltd
Dr Catherine Gerdil, Sanofi Pasteur
Mr Philippe Laurent, Sanofi Pasteur
Mr Jeremy Brett, Sanofi Pasteur
Dr Mark Lupi, GlaxoSmithKline Australia Pty Ltd
Mr Tony Wilson-Williams, Solvay Biosciences Pty Ltd
Mr George Weber, Chiron Vaccines Australia Pty Ltd
Dr Stephen Pasaribu, Baxter
*Dr Kathy Coelingh, MedImmune Vaccines Inc., USA
*Dr Vilma Savy, National Influenza Center, Argentina
Dr Larry Kelly, Director TGAL, TGA
Dr Paul Roche, SB, OHP, DoHA
Dr Nick Medveczky, 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 IN 2006**