

**RECOMMENDATION FOR INFLUENZA
VACCINE COMPOSITION 2006**

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VACCINE COMPOSITION 2006**

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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 6 October 2005 to consult on the influenza vaccine composition for 2006. The recommended composition was:

- A(H1N1) an A/New Caledonia/20/99-like strain
- A(H3N2) an A/California/ 7/2004 - like strain
- B a B/Malaysia/2506/2004 - like strain

RECOMMENDATION FOR INFLUENZA VACCINE COMPOSITION FOR 2006

The Australian Influenza Vaccine Committee (AIVC), with a New Zealand representative (Appendix 1), met on 6 October 2005 to consult on the influenza vaccine composition for 2006. The recommended composition (Table 1) was:

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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 7 October issue of the *Weekly Epidemiological Record*, 2005 80(40):341-352 (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 2005

Between February and September 2005, influenza activity was reported in Africa, the Americas, Asia, Europe and Oceania.

In the northern hemisphere, influenza A(H3N2) viruses predominated and caused most outbreaks, including a severe and long lasting outbreak in Hong Kong Special Administrative Region (SAR) China during March to June. Influenza B viruses circulated widely and caused outbreaks in several countries in Africa, Asia and Eastern Europe. Influenza A(H1N1) viruses circulated to a lesser extent and caused outbreaks in a few countries in Eastern Europe and central Asia between February and April.

In the southern hemisphere, influenza activity began in April and increased during May in

Oceania, and during June in South America. In Oceania and South America influenza A(H3N2) and B viruses co-circulated and caused several outbreaks, including an epidemic of influenza B in New Zealand. Influenza A(H1N1) viruses circulated at low levels in some countries and a single outbreak was reported in South Africa.

Between 16 December 2004 and 14 September 2005, 68 patients with influenza A(H5N1), of whom 25 died, were reported from Cambodia, Indonesia and Vietnam (http://www.who.int/csr/disease/avian_influenza/updates/en/). These cases were associated with outbreaks of highly pathogenic avian influenza A(H5N1) in poultry. So far there has been no evidence of sustained human-to-human transmission and the WHO influenza pandemic preparedness level remains as Phase 3 (http://www.who.int/csr/resources/publications/influenza/WHO_CDS_CSR_GIP_2005_5/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 29 September 2004. Influenza B was the predominant strain which accounted for 46.1% (855/1853) of isolates while 45.9% (850/1853) were influenza A(H3N2) and 8% (148/1853) were influenza A(H1N1) (Figures 2.1 and Table 2.1, Appendix 2).

1.2 Southern Hemisphere Influenza Activity, March-September 2005

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", from May through September each year. Based on the population and geographic distribution, about 80 voluntary sentinel general practitioners throughout the country are recruited in 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 ESR. This allows the measurement of the incidence and distribution of influenza. In addition, each sentinel practice provides 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 ESR virology laboratory 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 ESR Virology Laboratory. 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 April 2005, one month earlier than the usual start date in May. This was due to issues related to the vaccine, Vaxigrip, supplied by Sanofi-Pasteur. At the end of February 2005, the Ministry of Health's medicine regulatory body, Medsafe, was notified that one of three vaccine components, A/Wellington/1/2004 (H3N2), contains only 10 micrograms per dose rather than the 15 micrograms per dose required. To source alternative vaccine suppliers with full-strength vaccine, the 2005 vaccination programme was delayed from March to mid-April. As a result, Ministry of Health requested the early start of sentinel influenza surveillance in order to monitor influenza activity closely.

Influenza activity in 2005 is higher than that observed in 2004 and similar to that observed in 2003. Figure 1 shows weekly consultation rates for influenza-like-illness (ILI) in New Zealand from 2003 to 2005. The consultation rate remained at the baseline level from week 14 to week 19 (April and early May). Then it increased rapidly and peaked in week 25 (at the end of June) with the consultation rate for flu-like illness at 174/100,000. Influenza activity started to decline and reached baseline level in week 30 (at the end of July). Since then, it has remained at the baseline level. When weekly consultation rates for ILI from 1992 to 2005 were compared (Figure 2), influenza activity in 2005 is at the middle-to-high level. In particular, comparison of data for the last 6 years (2000 to 2005) indicates that influenza activity in 2005 is second only to 2003.

Influenza isolates were reported weekly by sentinel and laboratory-based surveillance (Figure 3). There are two interesting features about influenza activity in 2005: 1) The isolation data are similar to the consultation data. The consultation rate peaked in Week 25 while the viral isolation peaked in week 26 (112) and 27 (112). 2) A greater proportion of influenza viruses were isolated from sentinel surveillance in 2005 (33%) than in 2004 (24%). A total of 826 influenza isolates was reported by sentinel and laboratory-based surveillance in 2005 with sentinel surveillance yielding 276 (33%, 276/826) influenza viruses and laboratory-based surveillance yielding 550 (67%, 550/826) influenza viruses, whereas only 138 (24%, 138/579) influenza viruses were detected from sentinel surveillance and 441 (76%, 441/579) from laboratory-based surveillance in 2004. The increase in the proportion of influenza isolates resulting from sentinel surveillance could reflect wide-spread community outbreaks of influenza in 2005.

Figures 4 and 5 show weekly influenza isolates by type in 2005. A total of 826 influenza viruses was isolated in 2005 from Week 1 to Week 37. Overall, influenza B was the predominant strain with 733 isolates. Two lineages of B co-circulated with more B/HongKong/330/2001-like viruses (530) than B/Shanghai/361/2002-like viruses (117). Influenza A/California/7/2004 (AH3N2)-like strain (63) co-circulated with influenza B throughout the season. There were only five influenza A/New Caledonia (H1N1)-like strain

isolations in 2005. Unlike the usual temporal distribution pattern observed in the past when influenza A predominates first followed by influenza B, a reversal of this pattern was observed in that influenza B predominated during the period from week 21 (at the end of May) to week 31 (at the beginning of August), followed by influenza A predominance in the late season from week 32 onwards. A total of 683 influenza B viruses was isolated from the 10 week period, week 21 to 31, consisting of 93% (683/733) total influenza B isolates in 2005.

Figure 6 shows the percentage of influenza isolates by type from 1990 to 2005. This year has been the largest influenza B outbreak ever recorded since influenza surveillance began in 1992 with 92% of typed and subtyped isolates as influenza B. The second and third largest influenza B outbreaks occurred in 1995 and 1997.

New Zealand experienced an influenza B epidemic in school age children in the North Island in 2005. Influenza B isolations in the 5-19 age group were 4 to 6 times higher than those observed in 1995 and 1997 (Figure 7). In addition, consultation rates for influenza-like illness were the highest in the under-19 age group and comprised >50% of all consultations for ILI. Furthermore, the epidemic has been associated with significant morbidity, as illustrated by reports in the media of significant school absenteeism. In some schools, particularly in Wellington and Auckland regions, the school absenteeism rate reached more than 20% in June. One Wellington school was closed due to a high rate of respiratory illness.

During this epidemic, three children died from complications from influenza B/HongKong/330/2001 infections:

- A 7 year-old boy who developed Reye syndrome. This child was on aspirin for another condition.
- An otherwise healthy 16 year-old boy who developed *Staphylococcus aureus* pneumonia and septicemia.
- An otherwise healthy 11 year-old boy who developed *Staphylococcus aureus* pneumonia and septicemia.

The viral isolates from two of three fatal cases were sent to the Melbourne WHOCC for detailed analysis. The antigenic and genetic sequence analysis of hemagglutinin (HA) and neurominidase (NA) did not indicate any remarkable changes. There are several explanations with this finding:

- Three fatal cases all derived from complications from influenza infections, two with secondary bacterial infections and one with Reye's syndrome due to aspirin treatment. Hence the effect of the viral infection was probably potentiated and the outcome was unlikely to be solely due to some particular characteristic of the virus itself.
- There is a growing awareness that severe, sometimes fatal influenza infections may occur in normal children and adolescents (CDC. Severe morbidity and mortality associated with influenza in children and young adults---Michigan, 2003. MMWR 2003;52:837--40.).
- The basis for pathogenicity of influenza virus in humans remains poorly defined, particularly for influenza B. It is likely that genes other than HA and NA are involved in the pathogenicity of influenza B viruses. For example, in influenza A, animal experiments suggest that a number of genes may contribute, sometimes involving a single point mutation in one of the polymerase genes.

Due to vaccine breakthrough and/or failure observed in 2004 (see Influenza Annual Report in 2004), the issue of surveying influenza vaccine breakthrough/failure was raised by health professionals around the country. Wide consultations were conducted among virology laboratories, influenza coordinators in Public Health Units, Medical Officers of Health, general practitioners and practice nurses in the Wellington region, nearly 100% consensus was obtained. 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 was included: has patient been vaccinated against influenza in the same year as the onset of ILI?

Influenza vaccination history provides the following important information:

- Virologically, an influenza virus isolated from a vaccinated person is extremely valuable. Full antigenic and genetic characterisation of the isolate could indicate the trend in antigenic drift of the virus. It aids the selection of a vaccine strain.
- Epidemiologically, it gives some indications in terms of the trend of vaccine failure/breakthrough. Sentinel surveillance provides relative constant pools of ILI patients. Over a few years, the baseline data for vaccine breakthrough/failure can be built. Any deviations from the baseline event can then be detected.

Results: 272 out of 958 ILI cases (28%) had information on vaccination history. Among them, 25 had influenza vaccination in the same year as the onset of ILI and 247 had none. There were 3 vaccinated patients whose specimens yielded influenza viruses (2 with influenza B/HongKong/330/2001-like viruses and 1 with B/Shanghai/361/2002-like virus). The antigenic analysis for B/Shanghai/361/2002-like virus isolated from the 23-year old vaccinee showed no drifting trend, i.e., the virus had the same titre compared with the homologous virus.

On 11 July 2005, an outbreak of influenza A at Metlifecare Coastal Villas in Paraparaumu was notified to Regional Public Health (RPH). The Coastal Villas is a 630-resident village with a 30-bed long-term care facility (LTCF, largely dementia cases) looked after by 30 staff. The outbreak was confined to the LTCF.

RPH interviewed 2 ill staff, and 5 ill residents whose illness history were provided by nurses as residents were too ill and/or dementia. These showed that symptoms were mainly respiratory and indicative of influenza. Nasopharyngeal swabs were obtained from 3 residents (subsequently 2 more swabs were obtained) and sent to ESR Virology Laboratory. The causal agent was identified as Influenza A/California/7/2004 (H3N2) like – low reactor.

During the outbreak 11 residents and 7 staff became ill with influenza. Among them, two cases were laboratory-confirmed as influenza. One resident died of a complicating pneumonia. Duration of illness ranged from 2+ to 6+ days, with a median of 4+days. The first case was a staff member, an outlier with onset of symptoms on 25 June 2005. The next case was a resident with onset of symptoms on 5 July 2005. The last case was a resident with onset of symptoms on 13 July 2005. All resident cases were housed in one wing of the LTCF, apart from 1 case who mixed with other residents in the lounge.

RPH advised on use of Tamiflu as treatment for residents and prophylaxis for residents and staff. None of staff members was treated with Tamiflu due to rapid recovery but 22 staff members received Tamiflu as a prophylaxis. Four ill residents were treated with Tamiflu; 9 well residents were given Tamiflu as a prophylaxis. The remaining was not treated being either post-illness or having refused the anti-viral drug. RPH also collected influenza vaccination histories. 20% of vaccinated residents became ill.

Figure 8 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. A total of 137 patients (17%, 137/826) in 0-4 age group and >65 age group yielded influenza viruses in 2005. This may reflect the disease burden on these two age groups.

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 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. 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). ASPREN consists of ~120 general practices from New South Wales, 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 peaked during August 2005 in NSW, July-August in Western Australia, July in Victoria and August in Queensland, whilst the tropical influenza activity in Northern Territory peaked in March, June and September 2005. The national trend indicated increased activity in 2005 compared with 2004. Furthermore, Australia post conducts absenteeism data 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 for 2005 is similar to ASPREN data with increased absenteeism during the winter.

A total of 778 influenza isolates from Australia was received for analysis at the Melbourne WHOCC (Appendix 2) from 1 January to 24 September 2004. 72% (556/778) of isolates were A(H3N2) viruses, antigenically related to A/California-like strain. 56 (7%, 56/778) A(H1N1) viruses were isolated and H1 was antigenically similar to A/New Caledonia/20/99-like strain. 165 influenza B viruses (21%, 165/778) were isolated with co-circulation of B/HongKong and B/Shanghai lineage viruses.

(Abridged from a report by Dr Moira McKinnon, Department of Health and Ageing, Australia and a report by Alan Hampson, WHO Collaborating Centre for Influenza, Melbourne.)

1.2.3 South Africa

Influenza activity during the South African 2005 winter season was monitored mainly in Johannesburg and surrounding areas where the active viral watch system has been strengthened this year to include over sixty participating centres. Five influenza B virus isolates were also sent from the National Influenza Centre in Cape Town for further characterisation.

Both subtypes of influenza A and B viruses circulated during the season but the predominant virus subtype isolated was A(H1N1). The first influenza isolation of the season was made from a specimen collected in Johannesburg on 20 April (week 16), and was identified as

influenza A(H1N1) and the last isolation of the season was made from a specimen collected on 13 September (week 37) and was identified as influenza A(H3N2). School absenteeism remained below the mean rate plus two standard deviations during the winter season.

A total of 581 influenza isolations were made i.e. 468 influenza A virus and 113 influenza B. Of the influenza A isolates, 319 were identified as A/Caledonia/20/99-like (H1N1), 127 as A/California/7/04-like (H3N2) and 22 were untyped. The majority of the influenza B isolates was identified as B/Hong Kong/333/01-like while a low percentage was B/Shanghai/361/02-like.

Sequence analysis of the HA1 subunit revealed the H1 viruses isolated during the season showed some 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 Johannesburg exhibited the common amino acid changes relative to the A/Wellington/1/04 vaccine strain at residues 193 (N-S), 226 (V-I) and 246 (S-N). All the viruses sequenced also showed a substitution at 145 (K-S or K-N). The phylogenetic tree was constructed for the HA1 subunit of representative South African 2005 influenza B viruses from both the B/Victoria/2/87 and B/Yamagata/16/88 genetic lineages. The amino acid residue changes relative to the B/Hong Kong/330/01 strain were observed at positions 80 (K-I), 116 (R-H), 121 (N-T), 164 (E-D), 177 (V-I), 190 (V-I) and 197 (S-N). In the B/Shanghai-like viruses, substitutions were seen at residues 37 (I-T), 40 (H-Y), 131 (L-P), 197 (D-N) and 252 (V-M).

Influenza activity in South Africa during both the 2004 and 2005 winter seasons was mild but the strains that circulated differed. The majority of viruses isolated in 2004 were influenza A H3N2 and no H1N1 virus isolates were made. In contrast, influenza A H1N1 viruses were the predominant subtype in 2005, while influenza B viruses of both genetic lineages were detected as well as influenza A H3N2 viruses. The antigenic and genetic drift seen in many of the South African H3N2 viruses differs a little from many of the H3N2 strains isolated in other countries where reduced reactivity with the A/California/7/04-like antisera was not consistently found.

(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 the predominant subtype is A(H1N1) again.

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 only five influenza A/New Caledonia (H1N1)-like virus isolations in New Zealand in 2005.

Since January 2005, the Melbourne WHOCC has analysed 148 A(H1) isolates from 7 countries with most coming from Macau. All were A/New Caledonia/20/99-lineage viruses (Tables 3.1 & 3.2, Figure 3.1 in Appendix 3). Most viruses reacted well with A/New Caledonia/20/99 ferret antisera and post-vaccination human serum pools. Very few “low reactors” (4 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 representing the majority of A(H1N1) viruses with one having an A317 (eg A/Macau/227/2005) and the other having V317 (eg A/Victoria/504/05). This was similar to viruses isolated in 2004. Eleven neuraminidase (N1) genes were sequenced. Some genetic drift has been seen from 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/Macau/227/2005 and A/Victoria/504/05 (Figures 3.2 & 3.3, Tables 3.4 & 3.5 in Appendix 3). Furthermore, vaccines containing influenza A/New Caledonia/20/99(H1N1) antigen stimulated post-immunisation HA antibodies at titres ≥ 40 to the influenza A(H1N1) vaccine virus in the sera of 37% of child, 68% of adult and 52% of elderly vaccinees. In adults and elderly people, the post-immunisation average geometric mean HA titres and proportions of titres ≥ 40 to recent isolates, the titres and frequencies of antibodies were similar. For children, however, the average geometric mean HA titres were 88% lower, and only 5% of children developed titres ≥ 40 . (WER 80(40), and Tables 3.6 and 3.7 in Appendix 3).

The epidemiological, antigenic, genetic and serological data indicated that there was no evidence of a need to change the vaccine strain from an A/New Caledonia/20/99-like virus. Two factors still remain true for recommendation of A/New Caledonia/20/99-like virus for year 2006 vaccine formulation:

- Increasing incidence of viruses of this type, and
- The demonstration that, in humans, vaccines containing viruses of this lineage induce similar antibody responses against both the homologous virus and recent A(H1N1) influenza isolates.

2.2 Influenza A H3N2

Influenza A(H3N2) has been frequently 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 2005 winter in Australia, influenza A(H3N2) was the predominant subtype.

The Melbourne WHOCC has analysed 850 A(H3N2) isolates from 12 countries since January 2005. These viruses made up the majority (45.9%) of all viruses analysed at the Centre. Some viruses reacted well with ferret antisera raised to A/Wellington/1/2004 and A/California/7/2004. A significant proportion of viruses had reduced reactivity (8 fold or greater) with both antisera (A/Wellington - 24% and A/California - 27%) (Figure 4.1 in Appendix 4). The ESR national influenza reference laboratory also detected a significant percentage (96%, 26/27) of A(H3N2) viruses that were A/California/7/2004-low reactors. Tables 4.1 and 4.2 (Appendix 3) show the HI titres (fold increased/decreased) obtained with the isolates using ferret sera against A/Wellington/1/2004 or A/California/7/2004 compared with the homologous titres. In addition, genetic analysis indicated that three main groups were apparent from the A(H3) HA1 sequencing. One group contained viruses similar to the A/California/7/2004 reference strain isolated mainly in early 2005. Group 2 viruses had the characteristic changes at S193F and D225N and these viruses were considered mostly “low reactors” in HI assays (eg A/Macau/577/2005). Viruses obtained from Australian, Southeast Asia and Macau fell into this group. Group 3 viruses had characteristic changes V112I and K173E (eg A/Thailand/220/2005). A number of the Australian isolates formed a sub-branch with a D188Y change (eg A/Darwin/5/2005). Two smaller clades with changes N145S or Y94H (plus others) also had a small number of 2005 isolates. Sequence analysis of the N2 NA gene fell into 3 major groups reflecting a similar division as the HA1 phylogenetic tree. (Figures 4.2 and 4.3, Tables 4.6 & 4.7 in Appendix 4). Furthermore, vaccines containing influenza A/New York/55/2004 (H3N2) antigens stimulated post-immunisation HI antibodies at titres ≥ 40 to the vaccine virus in the sera of 96% of adult and 67% of elderly vaccinees. In adults and elderly people, the post-immunisation average geometric mean HA titres and proportion of titres ≥ 40 to recent isolates were similar (WER 80(40), and Tables 4.8 and 4.9 in Appendix 4).

In summary, influenza A(H3N2) viruses were associated with outbreaks in many countries. The majority of recent isolates were antigenically similar to A/California/7/2004. Current vaccines containing A/New York/55/2005 (H3N2) antigen stimulated anti-HA antibodies against recent influenza A(H3N2) 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 Consultative Group recommended an A/California/7/2004-like virus as A(H3N2) vaccine component for 2006 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/Sichuan/379/99) 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/HongKong/330/2001). For reasons not wholly understood, these remained geographically restricted to Asia until 2001. In 2002 the B/HongKong/330/2001-like strains were the predominant viruses worldwide.

Both recent B/Victoria-like strains (B/Hong Kong/330/2001 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 2005. Varying proportions of the two lineages were seen in many countries with B/HongKong lineage predominating in some countries such as New Zealand and B/Shanghai –lineage viruses predominating in others.

855 influenza B isolates were received in 2005 at the Melbourne Centre from 13 countries (46.1% of total isolates) (Figure 5.1 in Appendix 5). The majority of isolates (65.1%) were typed as B/HongKong/330/2001-like but reacted poorly to ferret sera raised against egg-grown B viruses of this lineage. The remaining 34.9% of B viruses typed as B/Shanghai/361/2002-like reacting well with ferret sera raised against viruses of this lineage. Table 5.1 (appendix 5) shows 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. Most 2005 isolates had the S208P change (eg B/Florida/7/2004) and a number also had a P108N change (eg B/Brisbane/5/2005). The B/Victoria lineage viruses showed further drift from the previous reference viruses B/HongKong/330/2001 and B/Brisbane/32/2002. All B viruses analysed in 2005 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 (Figures 5.2, 5.3, 5.4, & 5.5, Tables 5.4, 5.5 & 5.6 in Appendix 5). Furthermore, vaccines containing influenza B/Shanghai/361/2002-like antigens (actual strain B/Jiangsu/10/2003) stimulated post-immunisation HI antibodies at titres ≥ 40 to the vaccine virus in the sera of 13% of children, 96% of adults and 67% of elderly vaccinees. For representative recent B/Shanghai/361/2002-like isolates, the proportions of titres ≥ 40 were similar. For representative recent B/Malaysia/2506/2004-like viruses, the proportions of titres ≥ 40 were lower: 0% of children, 47% of adults and 36% of elderly people who has been vaccinated. Furthermore, the average post-immunisation geometric mean HA titre to recent B/Malaysia/2506/2004-like viruses was 55% lower for children, 58% lower for adults and 52% lower for elderly people than to the vaccine virus (WER 80(40), Tables 5.7 to 5.8 in Appendix 5).

In summary, influenza B viruses circulated widely and caused outbreaks in several countries, including an epidemic in New Zealand. Viruses of both B/Shanghai/361/2002 lineage and B/HongKong/330/2001 lineage were prevalent in many countries but occurred in different proportions. Whereas many isolates were antigenically similar to B/Shanghai-lineage, an increasing proportion of B/HongKong/330/2001 lineage viruses was identified in many countries. The majority of recent isolates were antigenically similar to B/Malaysia/2506/2004 (B/HongKong/330/2001 lineage). Current vaccines containing B/Shanghai/361/2002-like antigens stimulated HA antibodies that were lower in frequency and titre to B/Malaysia/2506/2004-like viruses than to the vaccine virus. 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 2006 is:

- A(H1N1) an A/New Caledonia/20/99-like strain
- A(H3N2) an A/California/7/2004-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 Malta on 15 September 2005.

The Committee agreed to adopt the September WHO recommendations. The influenza vaccine components for year 2005 season should contain the following:

A/New Caledonia/20/99 (H1N1)	Reassortant of IVR-116
A/California/7/2004 (H3N2)	Reassortant of NYMC X-157
B/Malaysia/2506/2004	B/Malaysia/2506/2004

The SRID reference standard reagents for A/New Caledonia/20/99 (IVR-116) and A/New York/55/2004 (NYMC X-157) are available from NIBSC (UK). However, the preparation of B/Malaysia/2506/2004 reagents is still in progress. It is estimated that B/Malaysia/2506/2004 reagents will be available from TGA by the end of November, and it is anticipated that their calibration will be finalised by 1 December 2005.

4 ACKNOWLEDGEMENTS

Virus Laboratory, Communicable Disease Programme, ESR

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Virus Laboratories in Auckland, Waikato, Christchurch and Dunedin Hospitals

Participants in the ESR 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 1990-2006

Formulation Recommendations		Vaccine used for	A H3N2	A H1N1	B
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, 2003, 2004 and 2005

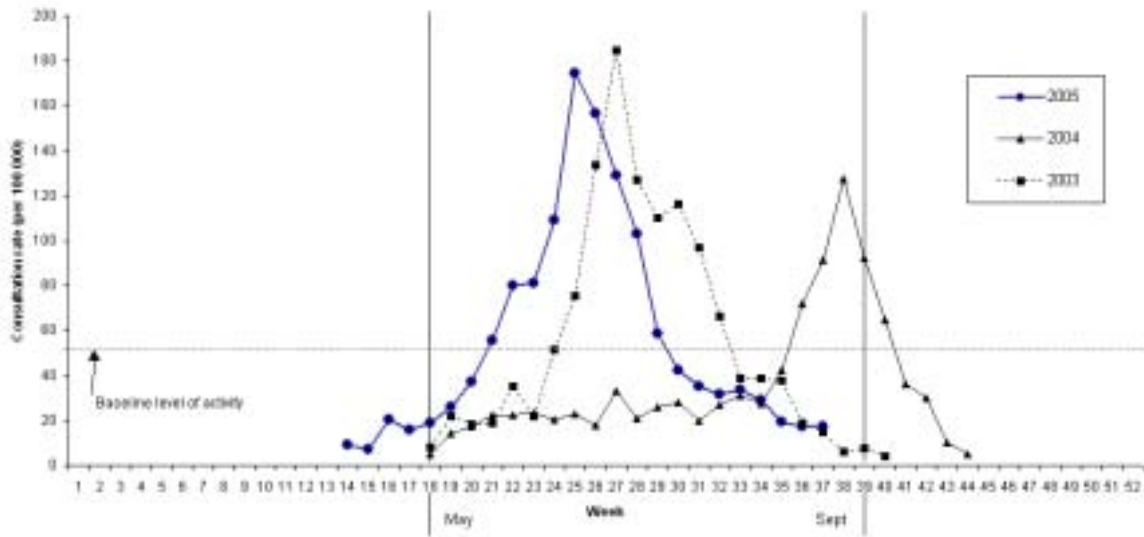


Figure 2. Weekly Consultation Rates for Influenza-like Illness in New Zealand 1992-2005

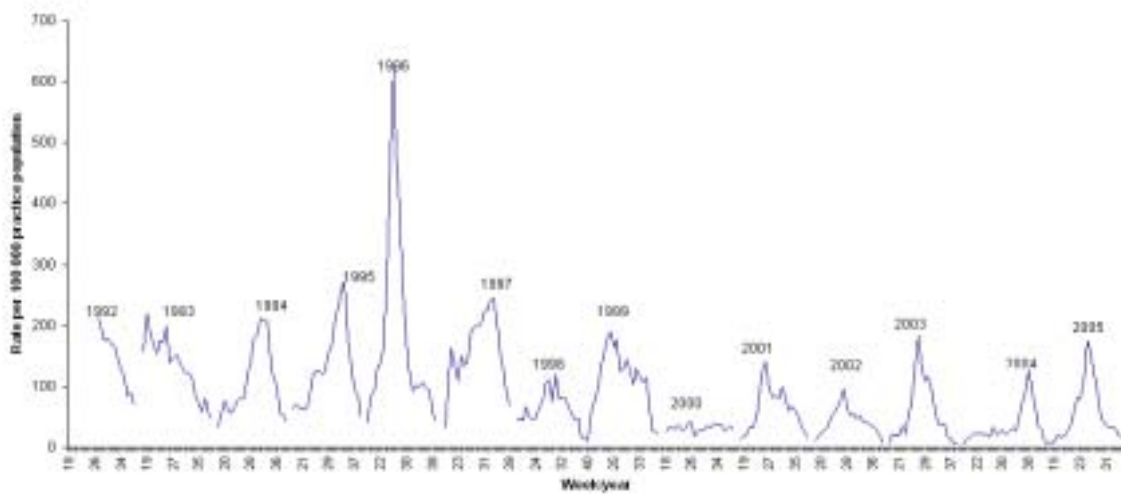


Figure 3. Total Influenza Isolates by Surveillance Type and Week Specimen Taken, 2005

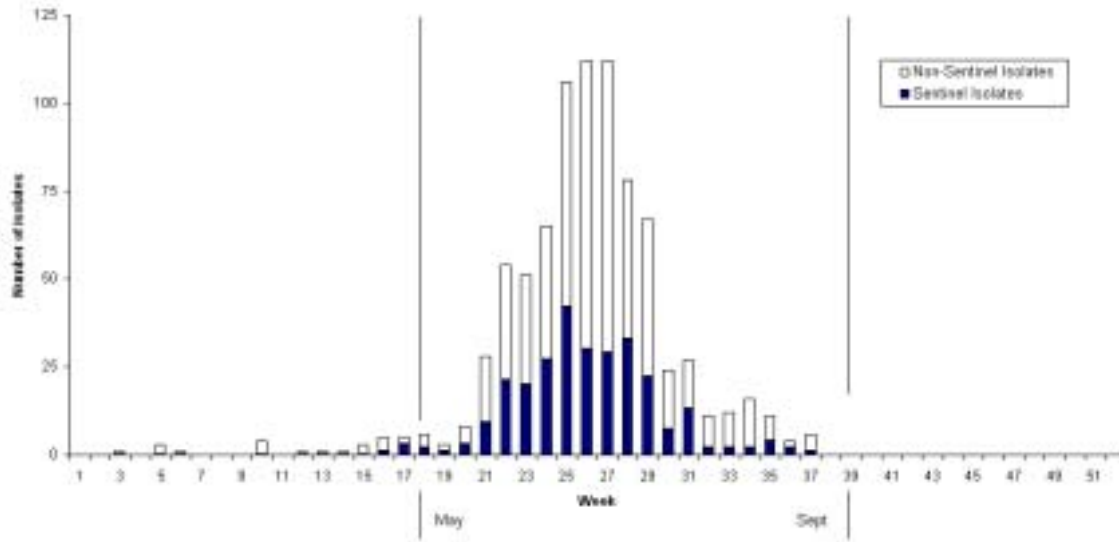


Figure 4. Total Influenza Isolates by Type and Week Specimen Taken, 2005

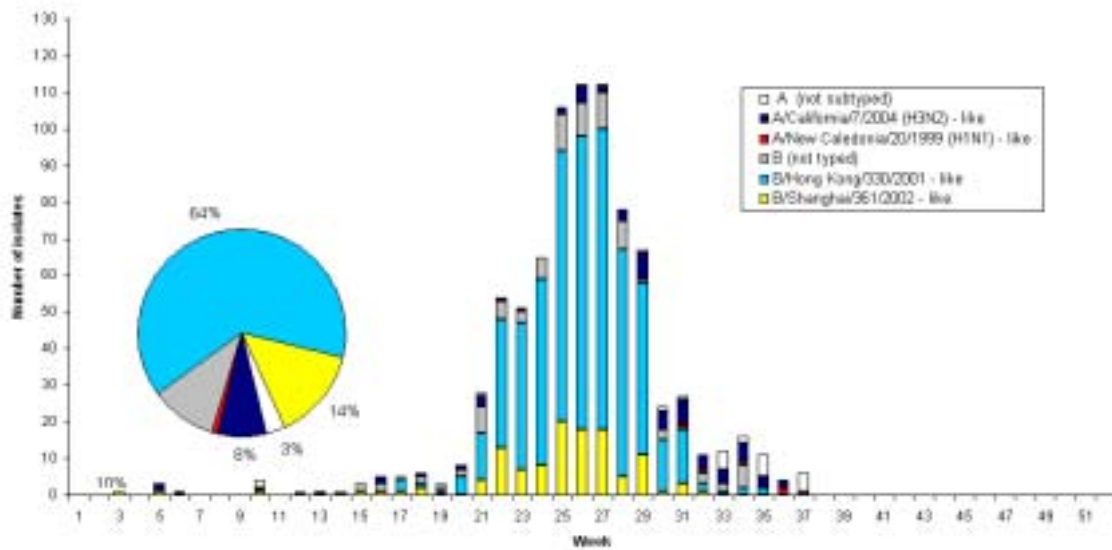


Figure 5. Total Influenza Virus Isolates by Type and Week Specimen Taken, 2005

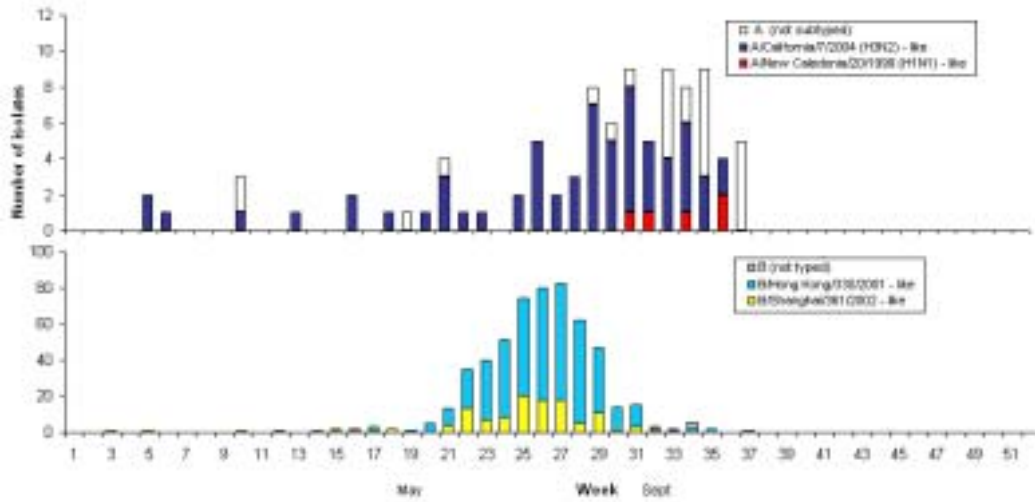


Figure 6. Influenza Isolates by Type, 1990-2005

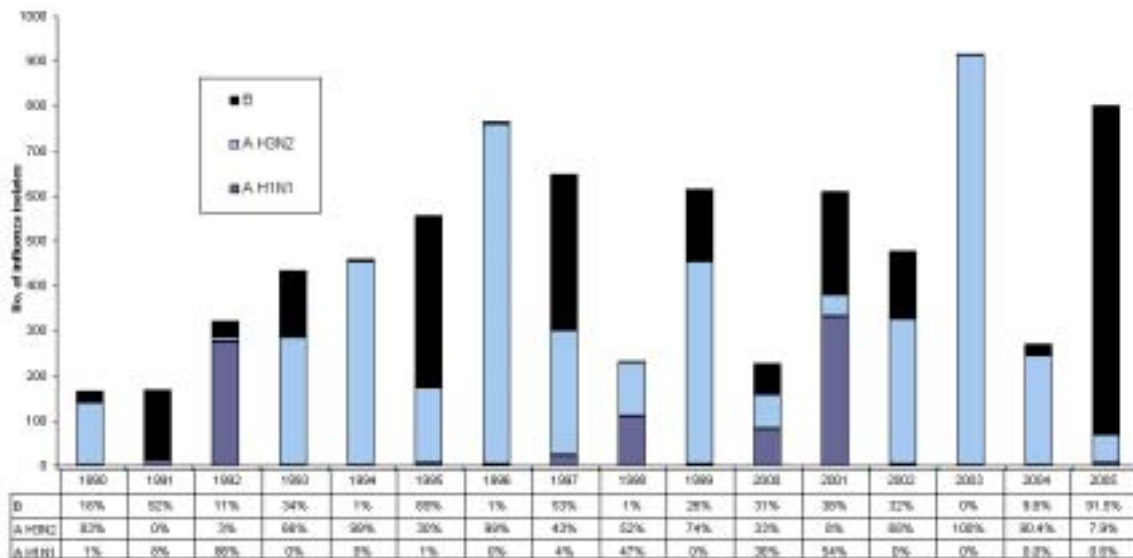


Figure 7. Influenza B Isolates by Age Group by Year, 1992-2005

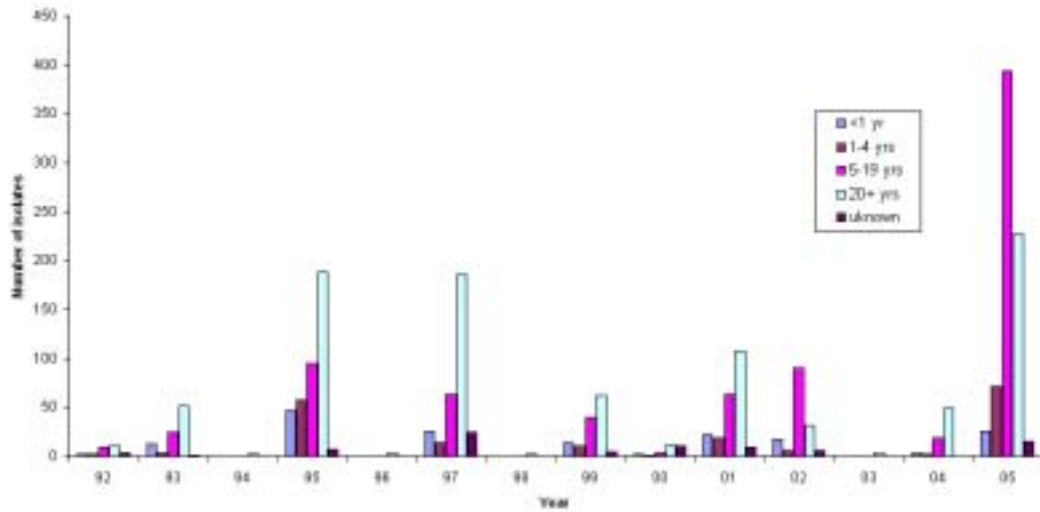
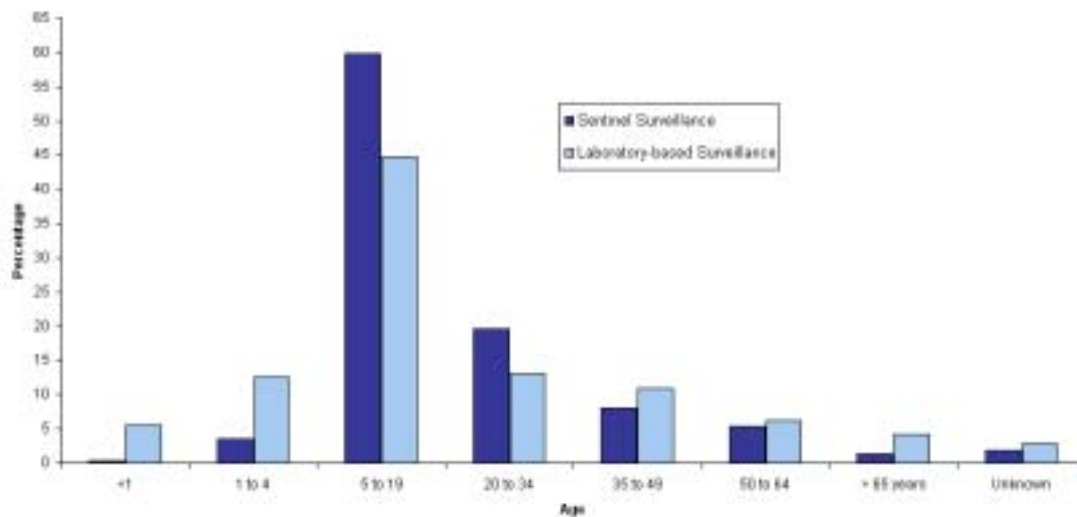


Figure 8. Comparison of Sentinel and Laboratory-based Surveillance by Age Group, 2005



APPENDIX 1

The 2005 AIVC meeting was convened at 3.30 pm on 6 October 2005 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 (2004)

Chairperson: Dr Gary Grohmann, TGAL, TGA

Secretary: Ms Thérèse Marengo, TGAL, TGA

Members: Mr Alan Hampson, Deputy Director, WHO Collaborating Centre, Melbourne
Prof Ian Gust, WHO Collaborating Centre, Melbourne
Dr Ian Barr, WHO Collaborating Centre, Melbourne
Prof. Gordon Ada, JCSMR, ANU
Prof. Greg Tannock, RIMT, Melbourne
Dr Mike Catton, VIDRL
Dr Grahame Dickson, DSEB, TGA
Dr Moira McKinnon, PHD, Health and Ageing
Dr Sue Huang, CDI, ESR, NZ
*Prof. Barry Schoub, National Institute for Communicable Diseases, SA
*Dr Terry Besselaar, National Institute for Communicable Diseases, SA

Observers: Mr William Cracknell, CSL Limited
Mr Jeremy Brett, Sanofi Pasteur
Ms Alicia Ham, 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 David Sarson, Delpharm Consultants Pty Ltd (for Chiron)
*Dr Kathy Coelingh, MedImmune Vaccines Inc.
Dr Jenean Spencer, PHD, Health and Ageing
Dr Larry Kelly, Director TGAL, TGA
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 2005**