RECOMMENDATION FOR THE INFLUENZA VACCINE COMPOSITION 2005

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RECOMMENDATIONS

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- A(H1N1) an A/New Caledonia/20/99-like strain
- A(H3N2) an A/Wellington/1/2004-like strain
- B a B/Shanghai/361/2002-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 8 October issue of the *Weekly Epidemiological Record, 2004 79(41):369-376* (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 2004

Between February and September 2004, influenza was reported in Africa, the Americas, Asia, Europe and Oceania. In the Northern Hemisphere outbreaks due to influenza A(H3N2) viruses continued to be reported in several countries in North America, Asia and Europe between February and August 2004. In the southern hemisphere, influenza was relatively mild. Outbreaks due to influenza A(H3N2) viruses were reported in South America between March and July and in New Zealand during August and September. Influenza A(H3N2) viruses predominated in most parts of the world and were responsible for the majority of outbreaks. Influenza A(H1) and B viruses circulated at low levels.

Between 1 January and 22 September 2004, 40 patients with influenza A(H5), of whom 28 died, were reported from Viet Nam and Thailand (http://www.who.int/csr/disease/avian_influenza/country/en/). These cases were associated

with outbreaks of highly pathogenic avian influenza A(H5N1) in poultry. There has been no evidence of human-to-human transmission to date. In March 2004, two human cases of influenza A(H7N3) were associated with outbreaks of avian influenza A(H7N3) in poultry in Bristish Columbia, Canada. There has been no evidence of human-to-human transmission (http://www.who.int/csr/don/2004_04_05/en/).

The Australia WHO Collaborating Centre analysed influenza isolates received from 1 January to 24 September 2004. A(H3N2) was the predominant strain which accounted for 75% (464/621) of isolates while 11% (69/621) were influenza A(H1) and 14% (88/621) were influenza B (Figures 2.1 and Table 2.1, Appendix 2).

1.2 Southern Hemisphere Influenza Activity, March-September 2004

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 throat or nasal 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*, distributed through a printed format or on 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*, distributed through 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)*.

Influenza activity in 2004 was higher than 2002, but lower than 2003. Figure 1 shows weekly consultation rates for influenza-like-illness (ILI) in New Zealand from 2002 to 2004. The consultation rate remained at the baseline level from week 18 to week 35 (the end of August). Then it increased rapidly and peaked in week 38 (in the middle of September) with the consultation rate for ILI at 127/100,000. Influenza activity started to decline from Week 39. Routinely, influenza sentinel surveillance operates from May to September each year. Because of the late peak in 2004, Ministry of Health, public health units, GPs and virology laboratories all agreed to extend this year's sentinel surveillance for another month till the end of October. When weekly consultation rates for ILI from 1992 to 2004 were compared (Figure 2), influenza activity in 2004 is in the low- to middle-range of normal seasonal activity compared with the past 13 years. It is the higher than 1998, 2000, 2002 but lower than 2003, 2001 and other years.

Influenza isolates were reported weekly by sentinel and laboratory-based surveillance (Figure 3). There are two interesting features in influenza activity: 1) The isolation data are similar to the consultation data. The consultation rate peaked in Week 38 while the viral isolation peaked in week 37 (172) and 38 (149). 2) Comparing the viral isolations between sentinel and laboratory-based surveillance, more influenza viruses were identified in laboratory-based surveillance than sentinel surveillance. A total of 579 influenza isolates were reported by sentinel and laboratory-based surveillance. Sentinel surveillance yielded 138 influenza viruses while laboratory-based surveillance yielded 441 influenza viruses. Based on the fact that laboratory-based surveillance is mainly for hospital in-patients and A(H3N2) is associated with more severe disease, it is therefore not surprising that more influenza virus isolations were reported from hospitalised patients.

Figures 4 and 5 show weekly influenza isolates by types in 2004. There are three interesting features: 1) During May to October (Week 18 to 39), influenza AH3N2 was the predominant strain. 2) (H1N1) was not isolated in 2004. 3) Influenza B co-circulated with AH3N2 throughout the winter season in 2004.

During the period January to September 2004, a total of 553 influenza A isolates were identified. Influenza A(H3N2) was the predominant subtype. A total of 245 influenza A(H3N2) were subtyped comprising 90% typed/subtyped isolates and 42% total isolates. Between January and May 2004, 5 virology labs in NZ used antisera against A/Moscow strain supplied by CSL to subtype AH3N2 viruses. After May, antiserum against A/Fujian-like virus was used to subtype AH3N2 viruses. 244 influenza A(H3N2) viruses were subtyped as A/Fujian-like viruses and one virus was subtyped in February by Auckland virology lab as A/Moscow-like virus. This virus would probably be A/Fujian-like virus if Auckland virology laboratory had had A/Fujian antiserum at the time of subtyping.

Since A/Wellington/1/2004-like strain was recommended by WHO as the H3 vaccine component for the southern hemisphere, details of its isolation follow: A/Wellington/1/2004 virus was isolated from a 57 year old New Zealander who went to visit Guangzhou in Southern China. He presented with influenza like illness soon after his return. He was sent to Wellington Hospital's emergency department, specimens were collected on January 26. The specimens were sent to ESR's virology laboratory for viral isolation and characterisation. ESR handled the specimens with extra precautions (BSL 2 facility using BSL 3 practice) since at that time, the WHO had issued a warning of Avian Influenza A(H5N1) in Viet Nam

and Thailand but China had not admitted to Avian Influenza existence in China. In summary, even though this virus was isolated in New Zealand, it actually originated from the Southern part of China.

An interesting influenza A outbreak occurred in a rest home in Hutt Valley, Wellington region, in the middle of September 2004. This rest home offers 58 beds. During the outbreak, 26 residents became ill; attack rate, 45%. Four cases died; all cases had significant medical problems. Vaccination status for 26 residents who developed ILI was as follows: 16 had had flu vaccination (vaccination coverage, 62%), 6 refused vaccinations and remaining 4, unknown vaccination status. In addition, the rest home has approximately 74 staff members, 17 developed ILI during the outbreak. The Ministry of Health released Tamiflu for prophylaxis for residents with onset of symptoms within 48 hours. Tamiflu was also provided for unaffected residents and staff. The outbreak was well under control soon after. The causative agent was A/Fujian-like viruses. They were A/Fujian-low reactors, reduced reactivity (8 fold or greater) against A/Fujian antisera compared with the homologous virus. The vaccine breakthrough could be due to the drifting of A(H3N2) viruses.

Tenty-six influenza B viruses were isolated in 2004. The antisera used for detecting influenza B were B/Sichuan/379/99 and B/Hong Kong/330/2001, supplied by the Australian WHO collaborating centre for influenza. Among 26 influenza B viruses, five typed as B/Sichuan/379/99 like viruses. Another three influenza B viruses were forwarded by the Christchurch virology laboratory to Australian WHO collaborating centre for influenza for further typing and they typed as B/Shanghai/361/2002-like viruses.

Figure 6 shows the percentage of influenza isolates by types, from 1990 to 2004. Influenza A(H3N2) predominated in 2004 (90% of typed/subtyped isolates). A similar pattern was observed in 1994,1996 and 2003.

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. A total of 162 patients (37%) in 0-4 age group and >65 age group yielded influenza viruses in 2004. 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. In 2004, there were 599 influenza A cases reported by LabVise compared with 2,125 cases in 2003. The third form is the laboratory surveillance conducted by WHO collaborating centre for reference and research on influenza. 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 2004 in NSW, July-August in WA and remained the baseline activity throughout the winter in Vic. whilst the tropical influenza activity in Northern Territory peaked in March and July 2004. The national trend indicated reduced activity in 2004 compared with 2003. 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 2004 is not available yet.

A total of 107 influenza isolates from Australia was received for analysis at the Australian WHO Collaborating Centre (Appendix 2) from 1 January to 24 September 2004. 82% (88/107) of isolates were A(H3N2) viruses, antigenically related to A/Fujian-like strain. Two (2%, 2/107) A(H1N1) were isolated, H1 was antigenically similar to A/New Caledonia/20/99-like strain. Seventeen influenza B isolates (16%, 17/107) were analysed, almost all were B/Shanghai/361/2002 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

Between weeks 20 (week starting 10 May) and 32 (week starting 2 August), influenza virus has been isolated from 26 patients attending Viral Watch centres. Of these 25 were influenza A virus, and one influenza B. 24 of the influenza A isolates have been further identified as influenza A H3N2. Patient's ages ranged from three to 46 years (median 21).

In addition a further 12 influenza A isolates (9 of which were further identified as A H3N2) were confirmed in specimens from private pathologists. Specimens were received between weeks 22 and 34. Date of onset/date specimen collected and patient details unknown.

The school absenteeism programme, monitoring approximately 8 000 children at primary and high schools, rose to above the mean (calculated over a five year period), on weeks 26 and 29. However, these were the weeks that winter school holidays started and ended in government schools.

Influenza A(H3N2) were antigenically related A/Fujian/411/02-like strains. Sequence analysis revealed genetic drift from the A/Fujian/411/02 viruses. The phylogenetic analysis of South Africa A(H3N2) viruses indicated that they were very closely related to viruses isolated from Madagascar and Senegal. The only one influenza B (B/Johannesburg/22/04) was antigenically related to the B/Victoria/02/87 lineage (the most recent representative of this lineage is B/HongKong/330/2001). Sequence analysis showed that B/Johannesburg/22/04 was identical to B/Israel/12/04.
(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 continue to circulate world-wide but have been a minor proportion of the A(H1) viruses recently.

The virology laboratories in New Zealand used the kit supplied by the WHO Collaborating Centre for Influenza, Melbourne to analyse influenza A(H1N1) strains. The antiserum used for detecting A(H1) were A/New Caledonia/20/99. No A(H1) viruses were isolated in 2004.

Since January 2004, the WHO Collaborating Centre for Influenza, Melbourne, analysed 69 A(H1) isolates from 8 countries with most coming from an outbreak in the Philippines in June-July. All were A/New Caledonia/20/99-lineage viruses (Table 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. Some “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 groups. One group representing recent A(H1N1) viruses with changes at V169A and W255R, the second group containing the A(H1N2) viruses with changes at V169A and either A219T or H196N. Isolates received at the Australia Centre from February to September 2004 all fell into the first group with some minor differences creating subgroups with changes at R149K or E287G or V317A. Nine 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 around the A/Fujian/156/2000 N1 (Fig. 3.2, Fig. 3.3 in Appendix 4). Furthermore, vaccines containing influenza A/New Caledonia/20/99(H1N1) antigen stimulated post-immunization HA antibodies at titres >40 to the influenza A(H1N1) vaccine virus in the sera of 55% of child, 80% of adult and 61% of elderly vaccinees. For representative recent isolates, the titres and frequencies of antibodies were similar. (WER 78(43), and Table 3.6 and 3.7 in Appendix 5).

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 2005 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 A/Bayern-like strains whereas the converse was not true.

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 2004 winter in New Zealand and Australia, influenza A(H3N2) was by far the predominant subtype.

The WHO Collaborating Centre for Influenza in Melbourne has analysed 464 A(H3N2) isolates from 13 countries since January 2004. These viruses made up the majority (74.7%) of all viruses analysed at the Centre. Some viruses reacted well with ferret antisera raised to A/Wyoming/3/2003 and A/Kumamoto/102/2002 an increasing proportion (41%) of viruses, however, had reduced reactivity (8 fold or greater) with the A/Wyoming/3/2003 antisera compared with that with the homologous virus. The ESR national influenza reference laboratory also detected a significant percentage (78%, 115/148) of A(H3N2) viruses were A/Fujian virus-low reactors. Table 4.1 (Appendix 3) shows the HI titres (fold increased/decreased) obtained with the isolates using ferret sera against A/Panama/2007/99 or A/Wyoming/3/2003 compared with the homologous titres. HI assays in Tables 4.3 to 4.6 (Appendix 3) were performed at the Melbourne Centre. In addition, genetic analysis indicated that three main groups were apparent from the A(H3) HA1 sequencing. One group that contained viruses received at the Centre in 2003 and some earlier 2004 viruses were closely related to the reference strain A/Fujian/411/2002 and the vaccine strain A/Wyoming/3/2003. A second group that contained mostly 2004 viruses had the characteristic S227P change with A/Wellington/1/2004 being broadly representative of this group. A third group contained some of the most recent viruses obtained from New Zealand, Australia and Asia. This group was characterized by amino acid changes at K145N and V226I. Sequence analysis of the N2 NA gene fell into 3 broad groups. One containing the A(H1N2) viruses, another with an N2 like the A/Wyoming/3/2003 and A/Kumamoto/102/2002 strains, and the third group which appeared to have an N2 similar to earlier A(H3) strains such as A/Chile/6416/2001. Unlike 2003 where most viruses had an A/Wyoming/3/2003-like NA, only the 2004 A(H3) viruses from Victoria had this A/Chile-like NA. The rest of the 2004 A(H3) NA sequences falling into a subgroup of the A/Wyoming/3/2003-like NA represented by A/Wellington/1/2004 (Figures 4.2 and 4.3, Tables 4.8 to 4.11 in Appendix 4). Furthermore, vaccines containing influenza A/Wyoming/3/2003 antigens stimulated post-immunization HI antibodies at titres >40 to the vaccine virus in the sera of 95% of adult and 90% of elderly vaccinees. For representative recent isolates, the frequencies of antibodies were somewhat lower; 75% of adult and 73% of elderly vaccinees had HI antibodies at titres>40. Furthermore, the geometric mean postimmunization HI titres were, on average, 58% lower to A/Wellington/1/2004–like viruses than to the vaccine virus. (WER 78(43), and Tables 4.12 and 4.13 in Appendix 5).

In summary, influenza A(H3N2) viruses were associated with outbreaks in many countries. The majority of recent isolates were similar to A/Wellington/1/2004. Current vaccines containing A/Wyoming/3/2003 antigens stimulated anti-HA antibodies that were lower in frequency and titre to A/Wellington/1/2004-like viruses than to the vaccine virus. Based on all epidemiological, antigenic, genetic and serological data, the WHO Consultative Group recommended an A/Wellington/1/2004-like virus as A(H3N2) vaccine component for 2005 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/Sichuan-like strains (B/Shanghai/361/2002 is the current reference strain) continued to be isolated worldwide in 2004. The predominant strains isolated in the region and elsewhere in 2004 have been B/Shanghai/361/2002, although B/HongKong-like viruses have been isolated in outbreaks in Brazil and from sporadic cases in Thailand, Malaysia and Australia and elsewhere.

The WHO Collaborating Centre for Influenza in Melbourne have received 88 influenza B isolates from 10 countries since January 2004 (14.2% of total isolates). The majority of isolates (95.6%) were typed as B/Shanghai/361/2002-like and reacted well with ferret sera raised against egg-grown B viruses of this lineage. B/Hong Kong-like viruses (4.4%) reacted 4-8 fold lower in titres against reference antisera (compared to their homologous titres). Table 5.1 (appendix 3) shows the HI titres (fold increased/decreased) obtained with the isolates using ferret sera against B/Shanghai/361/2002 or B/Hong Kong/330/2001 compared with the homologous titres. HI assays in Tables 5.2 and 5.3 (Appendix 3) were performed at the Melbourne Centre. 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 most closely matched B/Jiangsu/10/2003-like strains or had a further change at V252M as represented by B/Canada/580/2004. The B/Victoria lineage viruses fell mainly into one group, represented by the B/Shangdong/7/97-like viruses. All of B viruses analysed in 2004 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. Sequence analysis of the neuraminidase (NA) gene of all B viruses received in 2003 showed that they had an NA sequence similar to the NA of B/Sichuan/379/99 (Figures 5.2 & 5.3 in Appendix 4). Furthermore, vaccines containing influenza B/Shanghai/361/2002 -like antigens (actual strain B/Jiangsu/10/2003) stimulated post-immunization HI antibodies at titres >40 to the vaccine virus in the sera of 71% of adult and 76% of elderly vaccinees. For representative recent B/Shanghai/361/2002-like isolates, the titres and frequencies of antibodies were similar. For representative recent B/Hong Kong/330/2001-like viruses, the titres and frequencies of antibodies were lower: 27% of adults and 43% of elderly vaccinees had HI titres >40. (WER 78(43), Tables 5.6 to 5.8 in Appendix 5).

In summary, the great majority of recent influenza B isolates are antigenically closely related to B/Shanghai/361/2002 and these viruses became the predominant influenza B viruses. B/Hong Kong/330/2001-like viruses continued to circulate at a lower level. Current vaccines containing influenza B/Shanghai/361/2002 antigen induced anti-HA antibodies to recently isolated viruses, 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 B/Shanghai/361/2002 –like strain. The AIVC accepts this recommendation.

3 SUMMARY

It is recommended that the influenza vaccine formulation for New Zealand in 2005 is:

- A(H1N1) an A/New Caledonia/20/99-like strain
- A(H3N2) an A/Wellington/1/2004-like strain
- B a B/Shanghai/361/2002-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 Canberra on 21-23 September.

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/Wellington/1/2004 (H3N2)	**Reassortant of IVR-139**
B/Shanghai/361/2002	**B/Jiangsu/10/2003**

The SRID reference standard reagents for A/New Caledonia/20/99 (IVR-116) and B/Jiangsu/10/2003 are available from NIBSC (UK). However, the preparation of A/Wellington/1/2004 (IVR-139) reagents is still in progress. It is estimated that A/Wellington/1/2004 (IVR-139) reagents will be available from TGA by the end of November, and it is anticipated that their calibration will be finalised by 13-17 December 2004.

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Australian Influenza Vaccine Committee

Table 1. Influenza Vaccine Recommended Formulations 1990-2005

Formulation Recommendations		A H3N2	A H1N1	B
NZ & WHO*	2004	A/Wellington/1/2004	A/New Caledonia/20/99	B/Shanghai/361/2002
NZ & WHO*	2003	A/Moscow/10/99	A/New Caledonia/20/99	B/Hong Kong/330/2001
NZ & WHO*	2002	A/Moscow/10/99	A/New Caledonia/20/99	B/Sichuan/379/99
NZ & WHO*	2001	A/Moscow/10/99	A/New Caledonia/20/99	B/Sichuan/379/99
NZ	2000	A/Sydney/5/97	A/New Caledonia/20/99	B/Beijing/184/93
WHO*	2000	A/Moscow/10/99	A/New Caledonia/20/99	B/Beijing/184/93
NZ & WHO*	1999	A/Sydney/5/97	A/Beijing/262/95	B/Beijing/184/93
NZ	1998	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	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	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	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	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	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	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	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, 2002, 2003 and 2004

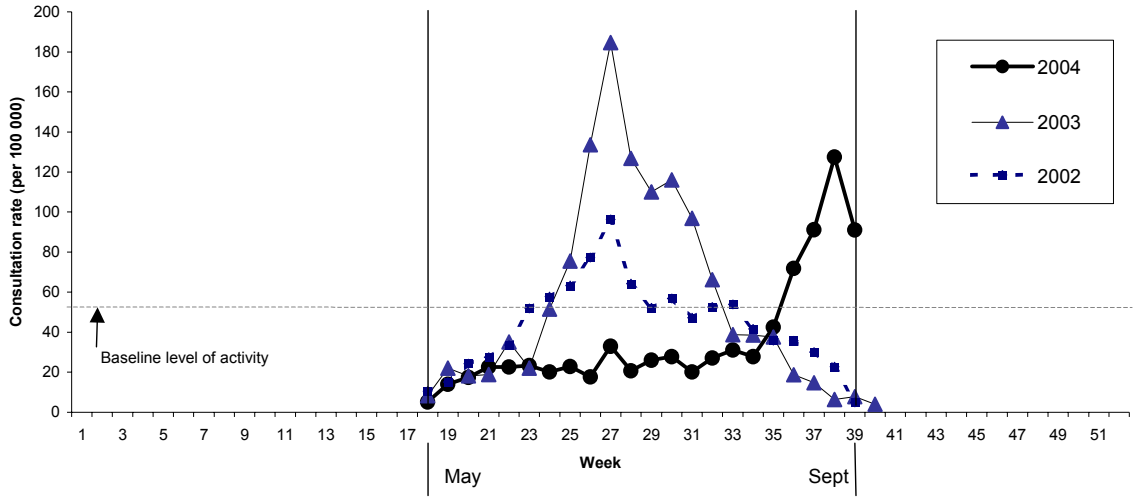


Figure 2. Weekly consultation rates for influenzea-like illness in New Zealand 1992-2004

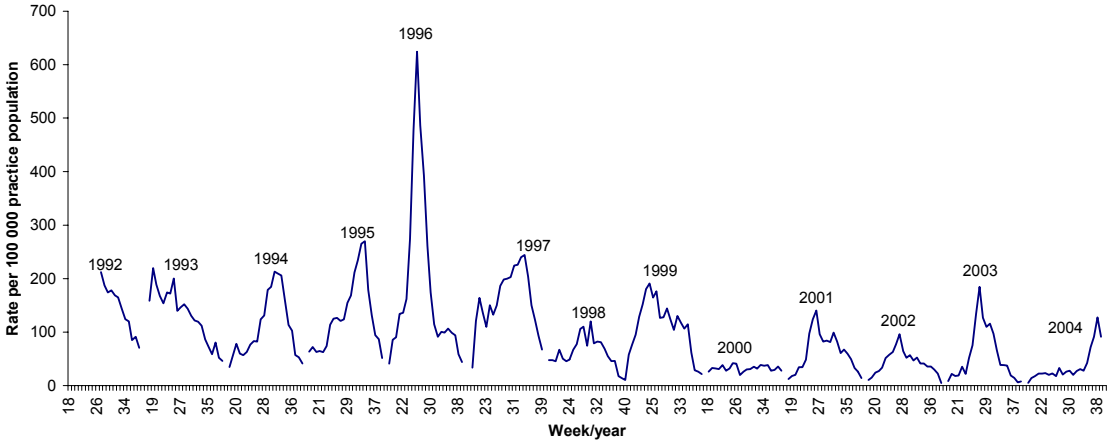


Figure 3. Total Influenza Isolates by Surveillance Type and Week Specimen Taken, 2004

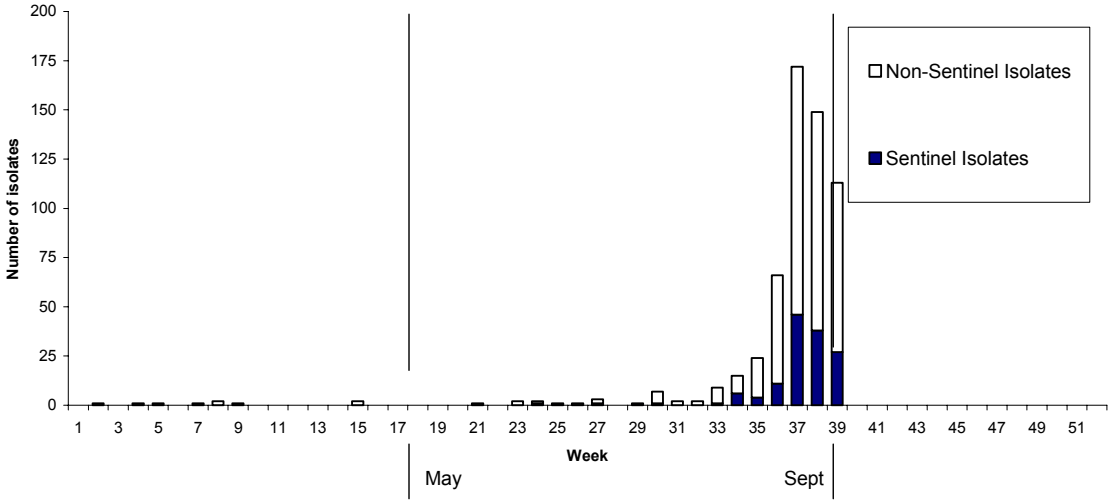


Figure 4. Total Influenza Isolates by Type and Week Specimen Taken, 2004

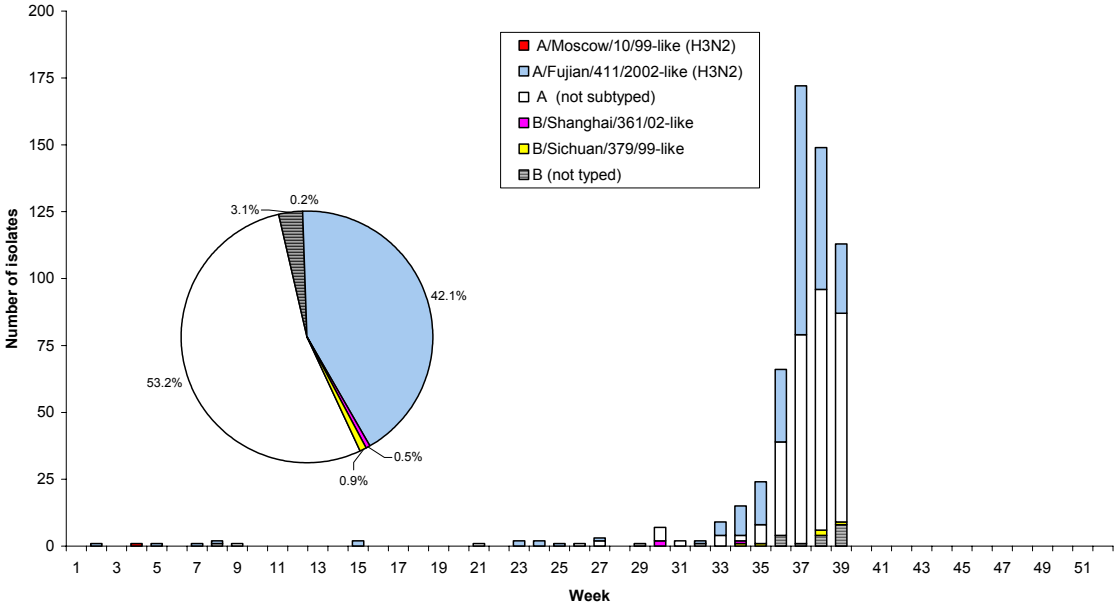


Figure 5. Total Influenza Virus Isolates by Type and Week Specimen Taken, 2004

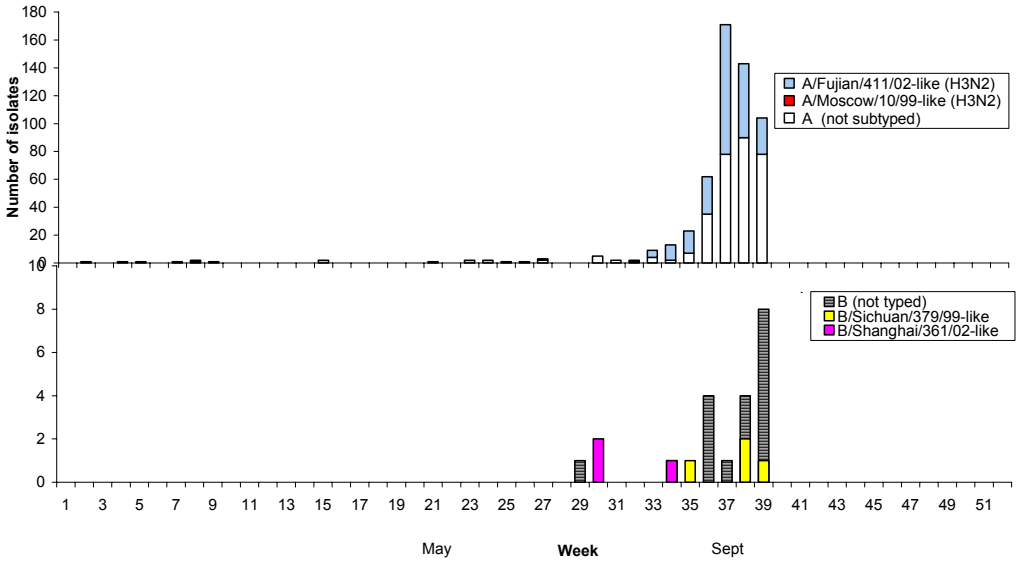
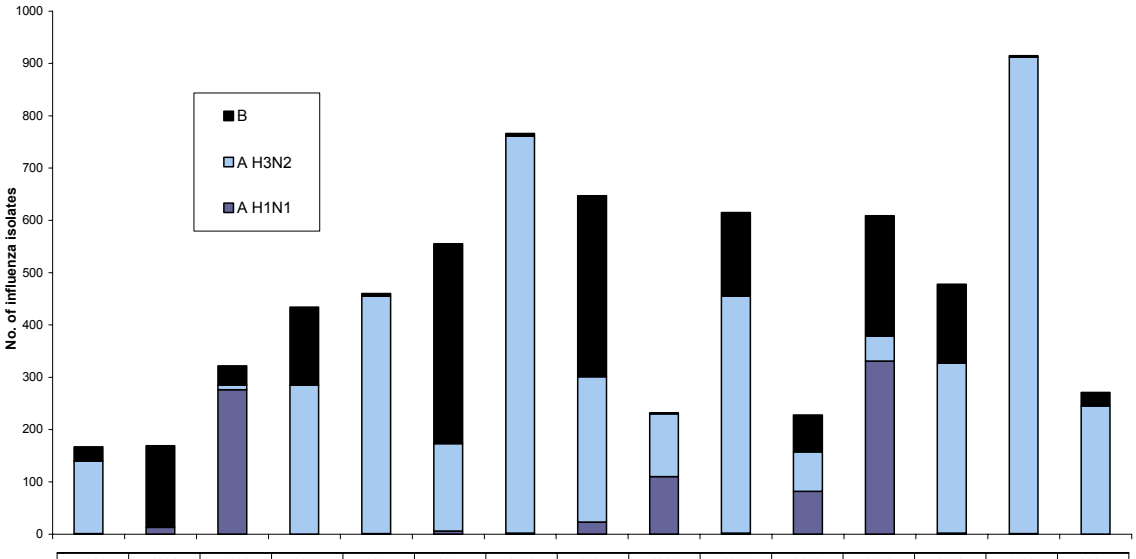
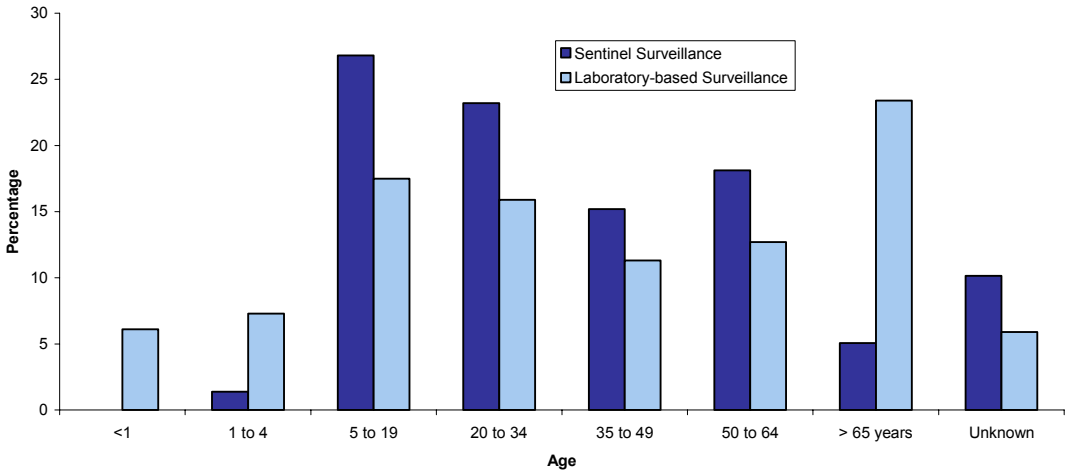


Figure 6. Influenza Isolates by Type, 1990-2004



	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004
B	16%	92%	11%	34%	1%	69%	1%	53%	1%	26%	31%	38%	32%	0%	9.6%
A H3N2	83%	0%	3%	66%	99%	30%	99%	43%	52%	74%	33%	8%	68%	100%	90.4%
A H1N1	1%	8%	86%	0%	0%	1%	0%	4%	47%	0%	36%	54%	0%	0%	0.0%

Figure 7. Comparison of Sentinel and Laboratory-based Surveillance by Age Group, 2004



APPENDIX 1

The 2004 AIVC meeting was convened at 3.30 pm on 5 October 2004 in Canberra, when overseas participants in the teleconference were connected by Telstra.

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 Centre, Melbourne
Prof. Gordon Ada, JCSMR, ANU
Prof. Greg Tannock, RIMT, Melbourne
Dr Mike Catton, VIDRL
Dr Grahame Dickson, DSEB, TGA
Dr John McEwen, DSEB, TGA
*Dr Sue Huang, CDI, ESR, NZ
*Prof. Barry Schoub, National Institute for Communicable Diseases
*Dr Terry Besselaar, National Institute for Communicable Diseases

Observers: Dr Ian Barr, WHO Collaborating Centre for Reference and Research on Influenza
Dr Moira McKinnon, PHD, Health and Ageing
Mr Darryl Mills, CSL Limited
Mr Jeremy Brett, Aventis Pasteur Pty Ltd
Dr Mark Lupi, GlaxoSmithKline Australia Pty Ltd
Mr Tony Wilson-Williams, Solvay Biosciences Pty Ltd
Mrs Margaret Richards, Delpharm Consultants Pty Ltd (for Chiron Behring Gmbh & Co)
Mr George Weber, Chiron Vaccines Australia Pty Ltd (for Evans Vaccines Ltd)
Dr Stephen Pasaribu, Baxter Healthcare Pty Ltd
Mr Peter Louridas, Merck Sharp & Dohme Australia Pty Ltd
*Dr Kathy Coelingh, MedImmune Vaccines Inc.
Dr Larry Kelly, Acting-Director TGAL, TGA
Dr Nick Medveczky, TGAL, TGA
Mr Chris Boswell, TGAL, TGA

* Participating by telephone

APPENDIX 2

ISOLATES RECEIVED FOR ANALYSIS AT THE AUSTRALIAN WHO COLLABORATING CENTRE

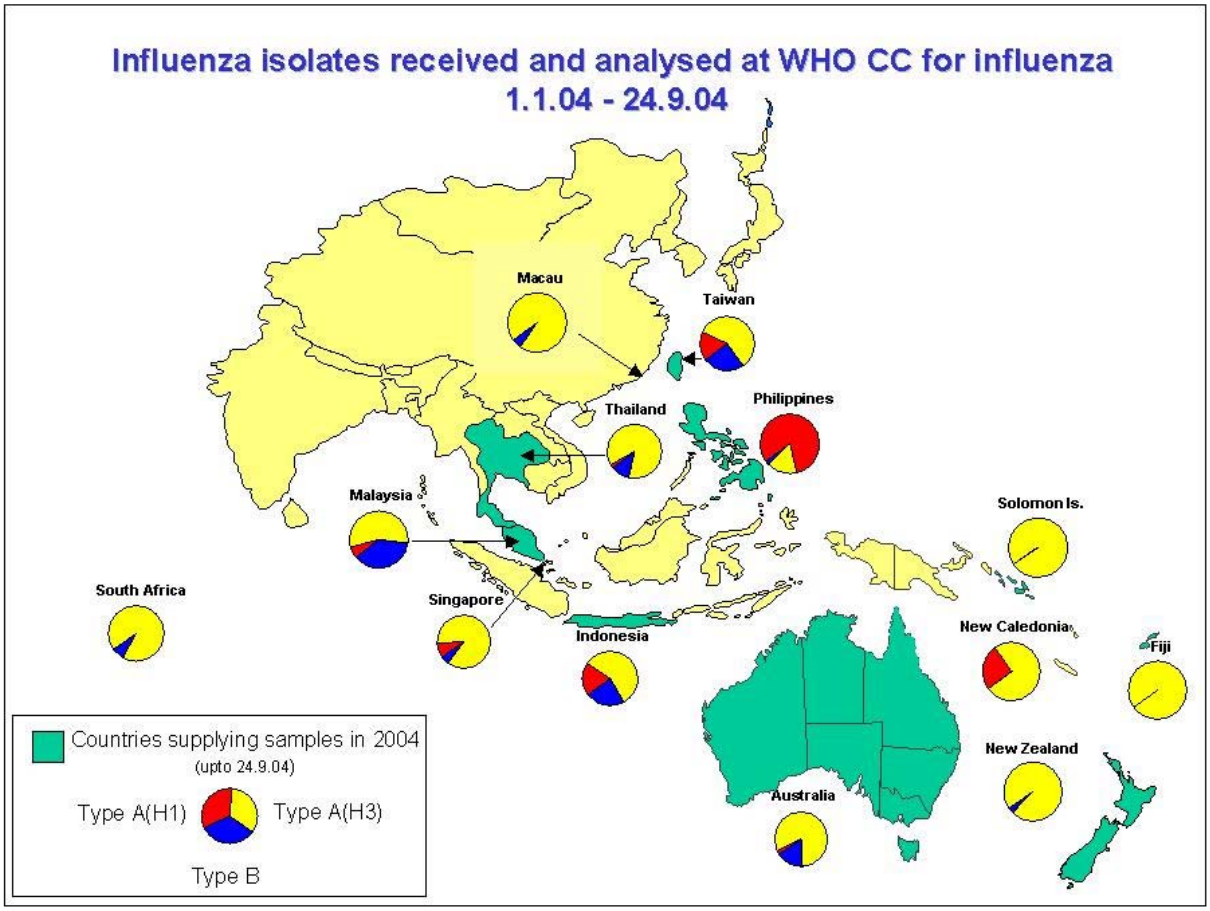
TABLE 2.1

Influenza Isolates Analysed at the Melbourne WHO CC 1/1/2004-24/9/2004

Country	A(H1) + A(H1N1)	A(H1N2)	A(H3N2)	B	TOTAL
Australia	2	0	88	17	**107**
Fiji	0	0	1	0	**1**
Indonesia	11	0	40	17	**68**
Macau	0	0	54	3	**57**
Malaysia	5	0	45	32	**82**
New Caledonia	3	0	9	0	**12**
New Zealand	0	0	125	4	**129**
Philippines	39	0	8	1	**48**
Singapore	5	0	50	3	**58**
Solomon Islands	0	0	3	0	**3**
South Africa	0	0	13	1	**14**
Taiwan	2	0	7	3	**12**
Thailand	2	0	78	10	**90**
Total	**69**	**0**	**464**	**88**	**621**

FIGURE 2.1

Influenza isolates received and analysed at the WHO CC for Influenza (1/1/2004 – 24/9/2004)



APPENDIX 3

ANTIGENIC CHARACTERISATION OF NEW ZEALAND AND AUSTRALIAN INFLUENZA ISOLATES

TABLE 3.1

Summary of HI fold differences in strains tested in Melbourne 1/3 – 24/9/2004

Fold difference compared to homologous ferret sera titres with:	**4-fold higher**	**2-fold higher**	**equal**	**2-fold lower**	**4-fold lower**	**8-fold lower**	**Total isolates**
A/New Caledonia 20/99	0	8	28	17	4	0	57

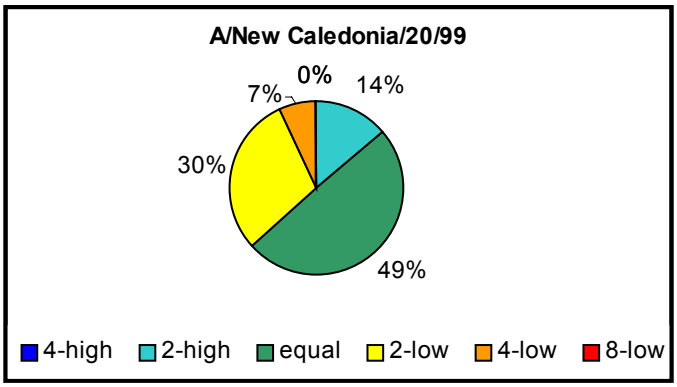


FIGURE 3.1

TABLE 3.2

Haemagglutination-inhibition reactions of influenza A(H1) isolates

Compilation: 26/3, 20/5, 28/7, 10/8, 20/8

WHO Collaborating Centre for Reference & Research on Influenza

Melbourne, Australia

	ANTISERA NO.	F735/13D X,E3 1 BAY/7	F635/13D E7 2 BEIJ/262	F776-13D E3 3 NC/20	F726/14D E3 4 AUCK/65	F739-14D E4 5 FUJI/156	F750-13D EX,E1 6 ENG/51	Human Sera Pool	MA042 (H1) A/TEX/36/92	Passage History	Specimen Date
	REF. Ag										
1	A/BAYERN/7/99	**1280**	20	<20	<20	<20	<20	640	10240	E6	
2	A/BEIJING/262/95	20	**640**	320	320	320	320	640	10240	E7	
3	A/NEW CALEDONIA/20/99	<20	80	**320**	320	640	320	640	10240	E6	
4	A/AUCKLAND/65/2000	<20	40	160	**160**	320	160	160	5120	E3	
5	A/FUJIAN/156/2000	<20	80	320	320	**1280**	160	320	5120	E6	
6	A/ENGLAND/51/2002	<20	160	160	160	160	**320**	320	5120	E3	
	TEST Ag										
1	A/SINGAPORE/11/04	<20	320	640	320	1280	160	1280	10240	MDCK3	25-Feb-04
2	A/TAIWAN/2/2002	<20	40	640	320	640	80	160	5120	P=(X+1)MDCK2	
3	A/MALAYSIA/99/2004	<20	320	640	640	2560	640	1280	>20480	X,MDCK1	19-Jan-04
4	A/BANGKOK/1318/2004	<20	320	640	320	640	160	640	10240	P1,MDCK1	12-Jul-04
5	A/MALAYSIA/1513/04	<20	160	320	160	640	80	640	5120	X,MDCK1	10-Jul-04
6	A/MALAYSIA/1533/04	<20	160	320	320	640	160	640	10240	X,MDCK1	
7	A/SINGAPORE/5/04	<20	160	320	320	640	80	640	5120	MDCK2	27-Jan-04
8	A/SINGAPORE/14/04	<20	160	320	320	640	160	640	10240	MDCK2	31-Mar-04
9	A/SINGAPORE/23/04	<20	160	320	320	640	160	640	10240	MDCK2	25-May-04
10	A/AUCKLAND/2/2002	<20	40	320	320	640	80	160	5120	P=(X+1),MDCK2	
11	A/MALAYSIA/91/2004	<20	320	320	320	640	160	320	5120	X,MDCK1	19-Jan-04
12	A/NEW CALEDONIA/3/2004	<20	160	320	320	640	160	640	10240	MDCKX,MDCK1	19-Apr-04
13	A/NEW CALEDONIA/4/2004	<20	160	320	320	640	80	320	5120	MDCKX,MDCK1	19-Apr-04
14	A/NEW CALEDONIA/9/2004	<20	160	320	160	640	80	320	2560	MDCKX,MDCK1	11-Jun-04
15	A/BANGKOK/1406/2004	<20	160	320	320	640	80	320	5120	P1,MDCK1	03-Aug-04
16	A/MALAYSIA/88/2004	<20	80	160	320	640	320	320	10240	X,MDCK1	19-Jan-04

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TABLE 4.1

Summary of HI fold differences in strains tested in Melbourne 1/3 – 24/9/2004

Fold difference compared to homologous ferret sera titres with:	**4-fold higher**	**2-fold higher**	**equal**	**2-fold lower**	**4-fold lower**	**8-fold lower**	**Total isolates**
A/Wyoming/3/2003	0	5	31	83	125	169	413

FIGURE 4.1

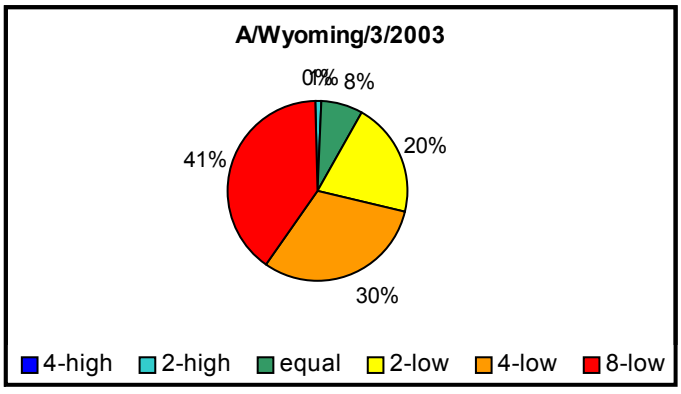

TABLE 4.3

Haemagglutination-Inhibition Reactions of Influenza A(H3N2) Isolates)

19th August & 2nd September 2004

WHO Collaborating Centre for Reference & Research on Influenza

Melbourne, Australia

	ANTISERA NO.	F757/14D E6 1 PAN/2007	F780-13D X/C2,MDCK3 2 FUJ/411	F787-13D SPFCK2,E3 3 WYOM/3	F799-13D MDCKX,MDCK1 4 PHIL/825	F795-14D E7 5 C'CH/28	F807-14D X,MDCK1 6 MALY/1	F809-14D E5 7 MALY/1	F812-13D E5 8 WELL/1	MAb143	Human sera pool 7/27/04	Passage History	Date
	REF. Ag												
1	A/PANAMA/2007/99	**320**	40	40	<40	<40	80	160	80	32	320	E8	
2	A/FUJIAN/411/2002	80	**160**	320	160	80	320	160	320	8	160	C2,MDCK7	
3	A/WYOMING/3/2003	160	640	**1280**	320	320	640	320	640	>512	640	SPFCK2E5	
4	A/PHILIPPINES/825/2003	40	160	640	**320**	160	640	320	640	<4	160	MDCKXMDCK2	
5	A/CHRISTCHURCH/28/2003	80	640	1280	160	**160**	320	160	320	128	160	E8	
6	A/MALAYSIA/1/2004	80	160	320	160	160	**1280**	320	640	32	160	X,MDCK4	
7	A/MALAYSIA/1/2004	80	160	160	80	80	640	**320**	640	4	80	E6	
8	A/WELLINGTON/1/2004	160	320	640	320	160	1280	640	1280	256	640	E4	
	TEST Ag												
1	A/SYDNEY/12/2004	<40	640	2560	1280	320	640	640	1280	8	320	MDCKX,MDCK1	02-Aug-04
2	A/CHRISTCHURCH/23/2004	<40	320	1280	320	160	640	320	1280	8	320	MDCK3	19-Aug-04
3	A/SYDNEY/23/2004	<40	320	1280	640	320	320	320	640	4	320	MDCKX,MDCK1	18-Aug-04
4	A/TAK/1242/2004	80	320	640	320	320	1280	320	1280	32	320	P3,MDCK1	22-May04
5	A/CHANTHABURI/1281/04	80	320	640	320	160	640	320	1280	256	320	P2,MDCK1	14-Jun-04
6	A/NEW CALEDONIA/11/2004	80	320	640	160	160	640	320	640	256	640	MDCK1	12-Jul-04
7	A/SYDNEY/17/2004	<40	320	640	640	320	320	640	1280	4	320	MDCKX,MDCK1	11-Aug-04
8	A/WELLINGTON/2/2004	<40	320	640	640	320	640	640	1280	4	320	MDCK1	20-May-04
9	A/BANGKOK/1333/2004	80	160	320	160	160	640	320	640	128	320	P1,MDCK1	14-Jul-04
10	A/BANGKOK/1407/2004	<40	160	320	160	160	640	320	640	<4	160	P1,MDCK1	03-Aug-04
11	A/NEW CALEDONIA/8/2004	80	160	320	160	160	640	320	640	256	320	MDCK1	10-May04
12	A/UD/1170/2004	80	160	320	80	160	640	320	640	8	160	P2,MDCK1	22-Mar-04
13	A/VICTORIA/106/2004	40	160	320	160	160	1280	320	640	<4	80	MDCK3	14-Jul-04
14	A/MALAYSIA/1366/2004	40	160	320	160	160	1280	320	1280	<4	80	x,MDCK2	10-Jun-04
15	A/PRAJIANBURI/1411/2004	40	160	320	320	320	1280	320	640	4	80	P1,MDCK1	03-Aug-04
16	A/NEW CALEDONIA/7/2004	40	160	160	80	80	640	160	640	4	160	MDCKX,MDCK1	07-May-04
17	A/CHRISTCHURCH/9/2004	<40	40	160	80	40	160	80	160	<4	40	MDCK3	19-Jul-04
28	A/SYDNEY/11/2004	<40	40	160	80	<40	80	<40	160	4	80	MDCKX,MDCK1	28-Jul-04
29	A/OTAGO/1/2004	<40	40	160	80	40	80	<40	160	<4	40	X,MDCK1	10-Aug-04
18	A/JOHANNESBURG/26/2004	80	160	160	160	160	640	80	640	<4	80	X,MDCK2	09-Jul-04
19	A/VICTORIA/117/2004	80	160	160	80	80	320	160	320	4	40	MDCK2	17-Aug-04
20	A/VICTORIA/118/2004	40	160	160	80	80	320	80	320	<4	20	MDCK2	23-Aug-04
21	A/SYDNEY/4/2004	<40	<40	80	40	<40	<40	<40	40	<4	20	MDCKX,MDCK2	18-Jul-04
22	A/JOHANNESBURG/30/2004	40	80	80	80	80	160	40	160	<4	40	X,MDCK2	

TABLE 4.4
Haemagglutination-Inhibition Reactions of Influenza A(H3N2) Isolates

WHO Collaborating Centre for Reference & Research on Influenza
Melbourne, Australia

8th & 14th September 2004

	ANTISERA NO.	F757/14D	F780-13D	F787-13D	F789-13D	F799-13D	F807-14D	F812-13D	F813-13D	Human	MAb143		Date
		E6	X/C2,MDCK3	SPFCK2,E3	XE1	MDCKX,MDCK1	X,MDCK1	E5	MDCK2	sera			
		1	**2**	**3**	**4**	**5**	**7**	**9**	**10**	pool		**Passage**	
	REF. Ag	PAN/2007	FUJ/411	WYOM/3	X147	PHIL/825	MALY/1	WELL/1	VIC/110	7/27/04		**History**	
1	A/PANAMA/2007/99	**160**	<40	<40	<40	<40	40	40	<40	160	<8	E8	
2	A/FUJIAN/411/2002	80	**320**	320	320	160	320	320	160	320	8	C2,MDCK7	
3	A/WYOMING/3/2003	320	2560	**2560**	2560	1280	640	1280	1280	640	64	SPFCK2E5	
4	AX147 (A/WYOMING/3/2003)	320	640	640	**2560**	160	320	640	640	1280	64	XE3	
5	A/PHILIPPINES/825/2003	<40	160	320	320	**320**	320	640	320	160	8	MDCKXMDCK2	
6	A/MALAYSIA/1/2004	160	320	320	320	320	**640**	1280	1280	320	32	X,MDCK4	
7	A/WELLINGTON/1/2004	160	320	640	640	320	640	**1280**	640	320	32	E4	
8	A/VICTORIA/110/2004	40	160	160	160	160	320	640	**640**	160	8	MDCK3	
	TEST Ag												
1	A/AUCKLAND/14/2004	<40	640	1280	640	1280	640	1280	2560	320	16	MDCK1	17-Aug04
2	A/VICTORIA/124/2004	<40	640	1280	640	640	640	1280	2560	320	16	MDCK1	30-Aug04
3	A/AUCKLAND/10/2004	80	320	640	320	160	640	640	640	160	16	MDCKX, MDCK1	15-Aug04
4	A/VICTORIA/120/2004	<40	320	640	320	320	1280	1280	1280	160	16	MDCK1	24-Aug04
5	A/AUCKLAND/8/2004	<40	160	320	320	320	320	640	1280	160	8	MDCKX, MDCK1	10-Aug04
6	A/SINGAPORE/36/2004	40	320	320	160	160	640	640	320	160	<8	C2/C2,MDCK1	
7	A/VICTORIA/123/2004	<40	160	320	320	320	320	640	640	160	8	MDCK1	27-Aug04
8	A/VICTORIA/125/2004	<40	80	160	80	160	320	320	320	80	8	MDCK1	30-Aug04
9	A/MALAYSIA/1665/2004	40	640	1280	1280	640	640	2560	2560	320	16	X,MDCK1	03-Aug04
10	A/MALAYSIA/1722/2004	40	640	1280	1280	1280	640	1280	2560	320	16	X,MDCK1	08-Aug04
11	A/BRISBANE/6/2004	40	320	1280	640	1280	1280	1280	2560	320	8	MDCKX,MDCK1	20-Aug04
13	A/VICTORIA/504/2004	80	640	640	320	320	320	1280	1280	160	8	MDCKX,MDCK1	01-Sep04
14	A/MALAYSIA/1536/2004	160	640	640	320	320	640	640	1280	160	8	X,MDCK1	19-Jul-04
15	A/BRISBANE/5/2004	<40	160	640	320	320	640	640	640	160	8	MDCKX,MDCK1	18-Aug04
16	A/MALAYSIA/1775/2004	160	320	320	160	160	320	640	320	80	16	X,MDCK1	17-Aug04
17	A/MALAYSIA/1821/2004	<40	80	320	160	160	80	640	80	80	8	XMDCK1	25-Aug04
18	A/BRISBANE/7/2004	<40	160	320	160	320	640	640	640	160	8	MDCKX,MDCK1	23-Aug04
19	A/VICTORIA/122/2004	80	320	320	160	320	1280	1280	1280	160	<8	MDCK2	24-Aug04
20	A/AUCKLAND/7/2004	<40	80	160	80	80	80	160	80	80	<8	MDCKX, MDCK2	10-Aug04
21	A/BRISBANE/2/2004	80	160	160	160	160	320	640	640	80	8	MDCKX,MDCK1	02-Sep04
22	A/BRISBANE/3/2004	<40	80	160	160	80	80	320	40	80	8	MDCKX,MDCK1	01-Sep04
23	A/VICTORIA/504/2004	<40	160	160	80	160	320	320	320	40	<8	MDCKX,MDCK1	28-Aug04

TABLE 4.5
Haemagglutination-Inhibition Reactions of Influenza A(H3N2) Isolates

16th September 2004

WHO Collaborating Centre for Reference & Research on Influenza

Melbourne, Australia

ANTISERA NO.	F757/14D	F780-13D	F787-13D	F789-13D	F799-13D	F807-14D	F812-13D	F816-13D	F813-13D	AS 389	Human	Mab 143		
	E6	X/C2,MDCK3	SPFCK2,E3	XE1	MDCKX, MDCK1	X,MDCK1	E5	2ND CLONE	MDCK2		sera pool		Passage	Sample
	PAN/2007	FUJ/411	WYOM/3	X147	PHIL/825	MALY/1	WELL/1	WELL/1	VIC/110	KUM/102	7/27/04		History	Date
REF. Ag	1/40	1/40	1/40	1/40	1/40	1/40	1/40	1/40	1/40	1/20	1/20	1/8		
A/PANAMA/2007/99	**640**	40	40	40	<40	160	160	40	<40	>2560	320	32	E8	
A/FUJIAN/411/2002	40	**80**	160	80	80	160	160	80	40	640	80	8	C2,MDCK7	
A/WYOMING/3/2003 (X147)	640	640	1280	**2560**	160	1280	1280	320	1280	>2560	1280	1024	XE3	
A/PHILIPPINES/825/2003	40	160	320	160	**160**	320	640	160	320	1280	160	<8	MDCKXMDCK2	
A/MALAYSIA/1/2004	160	160	320	160	160	**640**	640	640	640	1280	160	32	X,MDCK4	
A/WELLINGTON/1/2004	160	160	320	640	320	640	**1280**	1280	640	>2560	320	256	E4	
IVR 139 (A/WELL/1/2004)	80	160	320	640	320	320	640	**640**	1280	>2560	320	256	VI 1474	
A/VICTORIA/110/2004	40	160	160	40	80	640	640	320	**640**	320	40	<8	MDCK3	
TEST Ag														
A/AUCKLAND/48/2004	<40	320	1280	640	640	640	1280	640	1280	1280	160	<8	MDCKX,MDCK1	31Aug04
A/AUCKLAND/53/2004	<40	320	1280	320	640	640	1280	640	2560	1280	160	8	MDCKX,MDCK1	01Sep04
A/AUCKLAND/42/2004	<40	320	1280	640	640	640	1280	640	2560	>2560	160	8	MDCKX,MDCK1	25Aug04
A/AUCKLAND/43/2004	<40	160	1280	320	640	640	640	640	1280	1280	160	8	MDCKX,MDCK1	29Aug04
A/AUCKLAND/21/2004	<40	320	1280	640	640	320	640	1280	1280	1280	80	<8	MDCK1	30Aug04
A/AUCKLAND/32/2004	<40	320	1280	640	640	640	1280	640	2560	>2560	320	<8	MDCKX,MDCK1	26Aug04
A/AUCKLAND/38/2004	<40	320	1280	320	640	320	640	640	1280	1280	160	<8	MDCK1	27Aug04
A/AUCKLAND/46/2004	<40	160	640	320	320	320	640	640	1280	1280	160	8	MDCKX,MDCK1	30Aug04
A/AUCKLAND/49/2004	<40	320	640	320	640	640	1280	640	2560	1280	160	<8	MDCKX,MDCK1	31Aug04
A/AUCKLAND/22/2004	<40	320	640	320	320	640	640	1280	1280	1280	160	<8	MDCKX,MDCK1	31Aug04
A/AUCKLAND/24/2004	<40	160	640	320	320	640	640	640	1280	1280	160	8	MDCKX,MDCK1	06Sep04
A/AUCKLAND/25/2004	<40	320	640	320	320	640	1280	640	2560	1280	160	8	MDCKX,MDCK1	09Sep04
A/AUCKLAND/27/2004	<40	320	640	320	640	640	1280	1280	2560	1280	160	8	MDCKX,MDCK1	18Aug04
A/AUCKLAND/28/2004	<40	160	640	320	320	640	640	640	1280	1280	160	<8	MDCKX,MDCK1	20Aug04
A/AUCKLAND/31/2004	<40	320	640	320	320	640	1280	320	2560	1280	160	<8	MDCKX,MDCK1	25Aug04
A/AUCKLAND/34/2004	<40	320	640	320	640	640	1280	1280	2560	1280	160	8	MDCKX,MDCK1	25Aug04
A/AUCKLAND/35/2004	<40	640	640	640	640	640	640	640	2560	1280	160	8	MDCKX,MDCK1	25Aug04
A/AUCKLAND/57/2004	<40	80	320	80	160	320	640	320	640	320	80	8	MDCKX,MDCK1	02Sep04
A/AUCKLAND/23/2004	<40	160	320	160	320	320	320	640	1280	1280	160	<8	MDCKX,MDCK1	31Aug04
A/AUCKLAND/44/2004	<40	80	320	160	160	320	640	640	640	320	160	8	MDCKX,MDCK1	30Aug04
A/AUCKLAND/45/2004	<40	40	160	80	80	160	320	80	320	320	40	<8	MDCKX,MDCK1	30Aug04
A/VICTORIA/505/2004	80	160	160	80	160	640	640	640	640	320	80	8	MDCKX,MDCK1	24Aug04
A/VICTORIA/507/2004	40	80	80	40	80	320	320	320	320	320	40	<8	MDCKX,MDCK1	26Aug04

TABLE 4.6
Haemagglutination-Inhibition Reactions of Influenza A(H3N2) Isolates

29 TH SEPTEMBER 2004 — The WHO Collaborating Centre for Reference and Research on Influenza, Melbourne, Australia

ANTISERA NO.	F757/14D E6 PAN	F780-13D X/C2,MDCK3 FUJ/411	F787-13D SPFCK2,E3 WYOM	F818-13D XE1 X147	F799-13D MDCKX, PHIL	F807-14D X,MDCK1 MALY/1	F812-13D E5 WELL/1	F819-13D IVR139 WELL/1	F813-13D MDCK2 VIC/110	F794-14D E7 C'CH	F791-13D E8 AUCK/6	Human serum pool	**Passage History**	**Sample Date**
REF. Ag	1/40	1/40	1/40	1/40	1/40	1/40	1/40	1/40	1/40		1/20	1/20		
A/PANAMA/2007/99	**640**	<40	<40	80	<40	160	160	160	<40	<40	20	640	E8	
A/FUJIAN/411/2002	<40	**320**	640	320	160	320	320	320	160	80	320	320	C2,MDCK8	
A/WYOMING/3/2003 (X147)	640	1280	1280	**2560**	320	1280	1280	640	1280	320	640	>2560	XE3	
A/PHILIPPINES/825/2003	<40	160	320	320	**320**	640	640	640	320	160	160	160	MDCKXMDCK2	
A/MALAYSIA/1/2004	320	640	1280	640	640	**1280**	1280	1280	1280	320	320	320	X,MDCK5	
A/WELLINGTON/1/2004	160	320	640	640	320	640	**1280**	2560	1280	160	80	320	E4	
A/VICTORIA/110/2004	<40	160	160	80	160	640	640	640	640	**160**	80	80	MDCK3	
A/CHRISTCHURCH/28/2003	160	1280	1280	640	320	320	320	320	160	**320**	160	320	E8	
A/AUCKLAND/6/2003	160	1280	1280	1280	640	640	640	640	1280	**320**	640	640	E8	
Test Antigens														
A/VICTORIA/138/2004	<40	640	2560	640	1280	640	1280	1280	>5120	320	320	320	MDCKX,MDCK1	20-Sep-04
A/BRISBANE/30/2004	<40	320	1280	640	640	640	1280	640	1280	320	160	320	MDCKX,MDCK1	09-Sep-04
A/BANGKOK/1429/2004	<40	640	1280	640	640	640	1280	2560	2560	640	160	320	MDCK2	09-Aug-04
A/PERTH/11/2004	<40	320	640	320	640	640	2560	1280	2560	320	160	160	MDCKX,MDCK1	
A/VICTORIA/127/2004	320	640	640	640	320	1280	1280	1280	1280	320	320	320	MDCK2	09-Jun-04
A/NONTHABURI/1612/2004	<40	320	640	320	640	640	640	640	1280	160	80	160	MDCK2	06-Sep-04
A/DARWIN/3/2004	<40	160	640	320	320	320	640	640	640	160	80	160	MDCK1	13-Sep-04
A/SURIN/1503/2004	160	320	640	640	640	1280	1280	1280	1280	320	160	320	MDCK2	23-Aug-04
A/BANGKOK/1519/2004	<40	160	640	320	320	320	640	320	1280	80	80	160	MDCK2	26-Aug-04
A/BANGKOK/1491/2004	<40	320	640	320	640	640	1280	1280	1280	320	160	160	MDCK2	20-Aug-04
A/DARWIN/4/2004	<40	320	640	320	320	320	640	640	1280	320	160	160	MDCK1	20-Sep-04
A/VICTORIA/129/2004	<40	320	320	160	160	640	640	640	640	320	160	80	MDCK2	08-Sep-04
A/AUCKLAND/41/2004	<40	160	320	320	160	640	640	640	640	160	80	80	MDCKX,MDCK2	10-Aug-04
A/BRISBANE/28/2004	<40	160	320	160	160	320	320	320	320	80	80	80	MDCKX,MDCK1	04-Sep-04
A/BRISBANE/31/2004	<40	160	320	320	320	320	640	640	640	160	80	160	MDCKX,MDCK1	10-Sep-04
A/BRISBANE/34/2004	<40	160	320	320	320	320	640	640	640	80	80	80	MDCKX,MDCK1	10-Sep-04
A/VICTORIA/131/2004	<40	160	320	160	160	320	320	320	640	160	80	80	MDCK2	09-Sep-04
A/BANGKOK/1454/2004	160	320	320	320	320	640	160	160	160	320	160	320	MDCK2	13-Aug-04
A/PRACHINBURI/1665/2004	<40	80	160	160	160	320	320	320	320	80	40	80	MDCK2	11-Sep-04
A/PRACHINBURI/1709/2004	<40	160	160	160	160	640	640	640	640	160	80	160	MDCK2	14-Sep-04
A/BRISBANE/21/2004	<40	160	160	160	160	640	640	320	640	160	80	80	MDCKX,MDCK1	31-Aug-04
A/BRISBANE/36/2004	<40	80	160	160	160	160	320	320	320	80	40	80	MDCKX,MDCK1	14-Sep-04
A/BANGKOK/1417/2004	80	160	160	80	160	640	640	640	320	160	80	80	MDCK3	03-Aug-04
A/CHACHOENGSAO/1422/04	<40	80	160	80	80	320	320	320	320	80	40	80	MDCK2	05-Aug-04

TABLE 5.1

Summary of HI fold differences in strains tested in Melbourne 1/3 – 29/9/2004

Fold difference compared to homologous ferret sera titres with:	**4-fold higher**	**2-fold higher**	**equal**	**2-fold lower**	**4-fold lower**	**8-fold lower**	**Total isolates**
B/Shanghai/361/2002	0	0	15	25	24	1	65
B/Hong Kong/330/2001	0	0	0	0	0	3	3

FIGURE 5.1

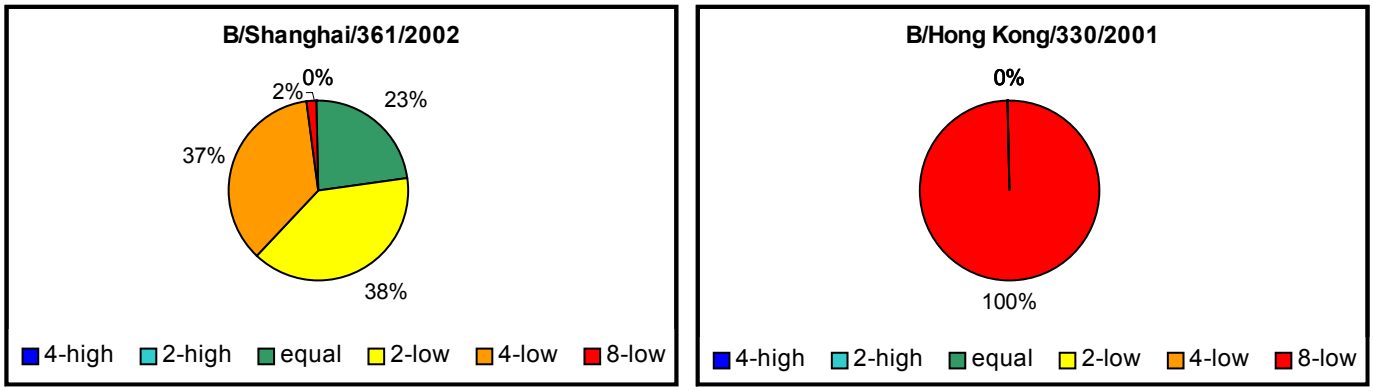

TABLE 5.2
Haemagglutination-inhibition reactions of influenza B isolates

Compilation	WHO Collaborating Centre for Reference & Research on Influenza Melbourne, Australia											
ANTISERA NO.	F639-29D E9 A	F710-21D E4 B	F725-21D E4 C	F748-21D P2,MDCK1 D	F762-21D E9 E	F765-21D E2 F	F628-28D E4 G	F658-21D E9 H	H/SERA POOL S2	(B)	Passage	Specimen
REF. Ag	SHANG/7	AKITA/27	HK/330	BNK/62	HK/1351	BRIS/32	SHEN/654	SICH/379	Feb-03	MA139	History	Date
A B/SHANGDONG/7/97	**160**	640	160	160	>2560	1280	<20	<20	<20	>512	E10	
B B/AKITA/27/2001	160	**1280**	320	80	640	640	<20	<20	<20	>512	E4	
C B/HONG KONG/330/2001	160	1280	**640**	80	640	640	<20	<20	<20	>512	E6	
D B/BANGKOK/62/2002	20	40	20	**160**	320	160	<20	<20	<20	4	P2,MDCK2	
E B/HONG KONG/1351/2001	160	160	160	80	**640**	640	<20	<20	<20	>512	E10	
F B/BRISBANE/32/2002	80	320	160	80	640	**640**	<20	<20	<20	>512	E2	
G B/SHENZHEN/654/99	<20	<20	<20	<20	<20	<20	**640**	160	40	<4	E7	
H B/SICHUAN/379/99	20	<20	<20	<20	20	<20	<20	**1280**	40	<4	E10	
TEST Ag												
B/INDONESIA/19/2003	20	80	20	80	160	80	<20	<20	<20	4	P4,MDCK1	22-Jan-03
B/AUCKLAND/1/2003	<20	80	20	160	320	80	<20	<20	<20	<4	X,MDCK1	18-Feb-03
B/CHANTHABURI/218/2003	<20	<20	<20	<20	20	<20	80	160	40	4	MDCK1	26-Jul-03
B/BANGKOK/227/2003	<20	<20	<20	<20	20	<20	160	320	40	<4	MDCK1	30-Jun-03
B/MALAYSIA/428/2003	<20	<20	<20	<20	20	<20	80	320	80	<4	X,MDCK1	21-Apr-03
B/MALAYSIA/453/2003	<20	<20	<20	<20	20	<20	80	160	40	<4	X,MDCK1	29-Apr-03
B/MALAYSIA/522/2003	<20	<20	<20	<20	20	<20	80	160	40	<4	X,MDCK1	23-May-03
B/TOWNSVILLE/1/2003	<20	<20	<20	<20	20	<20	80	320	80	<4	MDCK2	03-Jul-03

TABLE 5.3
Haemagglutination-inhibition reactions of influenza B isolates

26th August & 2nd September 2004	WHO Collaborating Centre for Reference & Research on Influenza Melbourne, Australia												
ANTISERA NO.	F769-20D	F725-21D	F748-21D	F765-21D	F705-21D	F658-21D	F806-20D	F805-21D	Human				
	E11	E4	P2,MDCK1	E2	E4	E9	E8	E6	Sera		Kit 2004		
	A	**B**	**C**	**D**	**E**	**F**	**G**	**H**	**Pool**	**(B)**		**Passage**	**Specimen**
REF. Ag	SHANG/7	HK/330	BNK/62	BRIS/32	SHEN/654	SICH/379	SHANG/361	B/JIANGSU	2004	MA 045	Vic/504	**History**	**Date**
A B/SHANGDONG/7/97	**640**	160	160	640	<20	<20	<20	<20	160	<160	40	E10	
B B/HONG KONG/330/2001	80	**640**	80	640	<20	<20	<20	<20	160	<160	20	E6	
C B/BANGKOK/62/2002	20	40	**160**	160	<20	<20	<20	<20	80	<160	<20	P2,MDCK3	
D B/BRISBANE/32/2002	80	160	80	**320**	<20	<20	<20	<20	160	<160	20	E3	
E B/SHENZHEN/654/99	<20	<20	<20	<20	**640**	320	320	1280	80	<160	640	E7	
F B/SICHUAN/379/99	<20	<20	<20	20	40	**1280**	640	160	80	2560	640	E13	
G B/SHANGHAI/361/2002	<20	<20	<20	40	80	1280	**640**	160	160	2560	640	E8	
H B/JIANGSU/10/2003	<20	<20	<20	<20	320	160	160	**640**	80	<160	320	E7	
TEST Ag													
1 B/WULUMUQI/26/2004	160	80	80	320	<20	<20	<20	<20	80	<160	20	E6	
2 B/PERTH/6/2004	20	20	160	160	<20	<20	<20	<20	160	<160	<20	MDCKX,MDCK1	25-Aug04
3 B/PERTH/7/2004	20	20	160	160	<20	<20	<20	<20	80	<160	<20	MDCKX,MDCK1	25-Aug04
4 B/SURIN/1587/2004	20	40	160	160	<20	<20	<20	<20	80	<160	<20	MDCK2	04-Sep04
5 B/SURIN/1597/2004	20	<20	160	160	<20	<20	<20	<20	80	<160	<20	MDCK2	04-Sep04
6 B/SURIN/1608/2004	20	20	160	160	<20	<20	<20	<20	80	<160	<20	MDCK3	04-Sep04
7 B/VICTORIA/106/2004	<20	<20	<20	<20	80	160	320	80	80	640	160	MDCK1	07-Sep04
8 B/PERTH/10/2004	<20	<20	<20	<20	80	160	320	80	80	640	160	MDCKX,MDCK1	06-Sep04
9 B/VICTORIA/508/2004	<20	<20	<20	<20	80	320	320	160	80	640	160	MDCKX,MDCK1	10-Sep04
10 A/CHRISTCHURCH/77/2004	<20	<20	<20	<20	80	320	320	160	160	320	320	MDCKX,MDCK1	
11 B/CHRISTCHURCH/33/2004	<20	<20	<20	<20	40	160	160	80	80	320	160	MDCKX,MDCK1	30-Aug04
12 B/CHRISTCHURCH/95/04	<20	<20	<20	<20	40	160	160	80	80	320	160	MDCK1	12-Sep04
13 B/VICTORIA/507/2004	<20	<20	<20	<20	40	160	160	40	40	160	160	MDCKX,MDCK1	08-Sep04
14 B/VICTORIA/105/2004	<20	<20	<20	<20	80	160	160	80	80	320	160	MDCK1	07-Sep04
15 B/BRISBANE/2/2004	<20	<20	<20	<20	80	160	160	80	80	320	160	MDCKX,MDCK1	06-Sep04
16 B/BRISBANE/3/2004	<20	<20	<20	<20	40	160	160	40	40	160	160	MDCKX,MDCK1	07-Sep04
17 B/BRISBANE/4/2004	<20	<20	<20	<20	40	160	160	80	40	320	160	MDCKX,MDCK1	11-Sep04
18 B/CHRISTCHURCH/27/2004	<20	<20	<20	80	160	160	80	80	80	1280	320	MDCKX,MDCK1	27-Aug04
19 B/CHRISTCHURCH/22/2004	<20	<20	<20	<20	40	160	80	80	40	320	160	MDCK1	18-Aug04
20 B/PERTH/8/2004	<20	<20	160	80	<20	<20	<20	<20	80	<160	<20	MDCKX,MDCK1	31-Aug04
21 B/PERTH/12/2004	<20	<20	160	80	<20	<20	<20	<20	80	<160	<20	MDCKX,MDCK1	08-Sep04

APPENDIX 4

GENETIC ANALYSIS OF RECENT INFLUENZA ISOLATES

FIGURE 3.2

Phylogenetic relationships among influenza A(H1) HA1 genes 2003

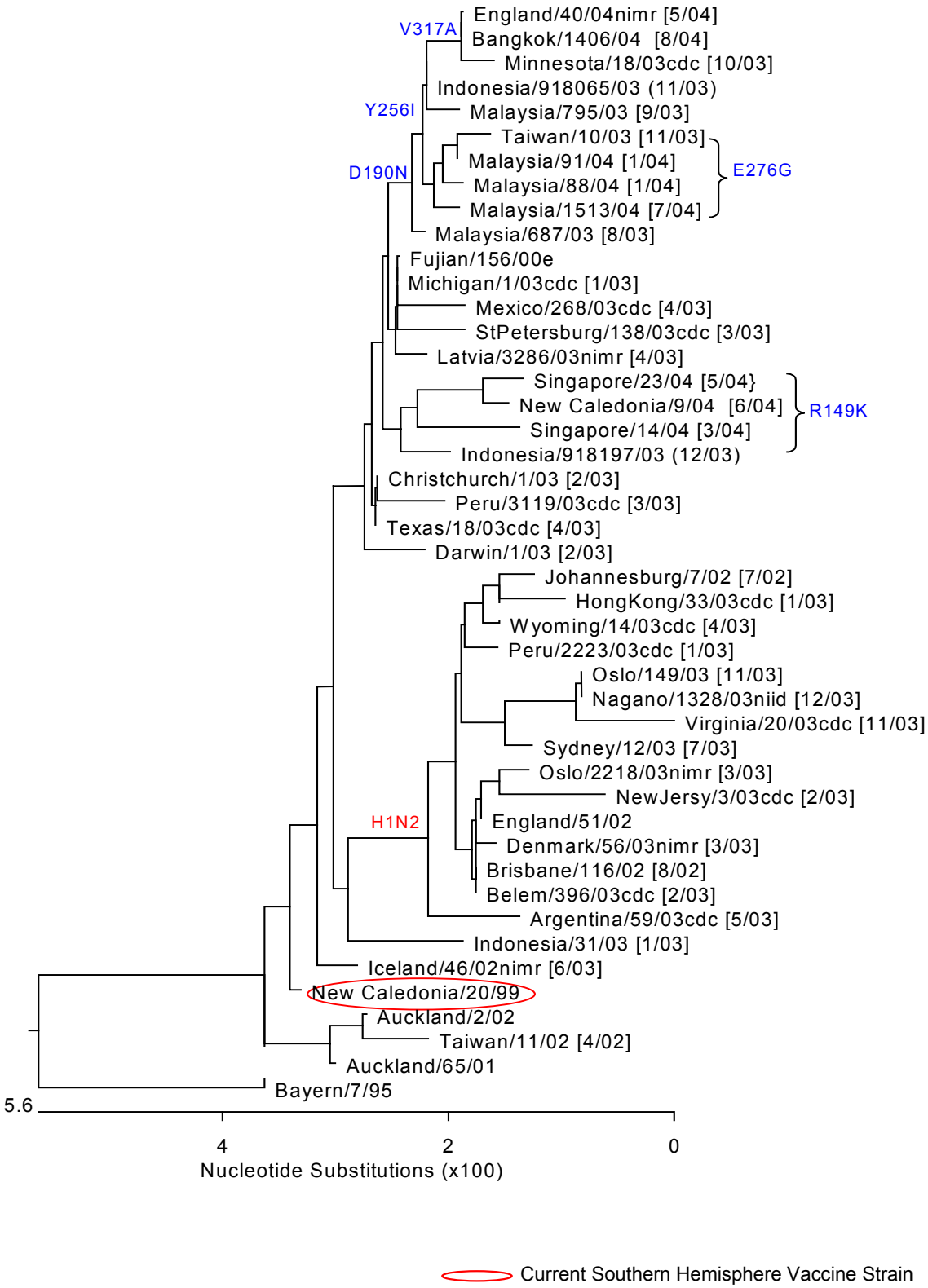

FIGURE 3.3

Phylogenetic relationships among influenza N1 neuraminidase genes 2003

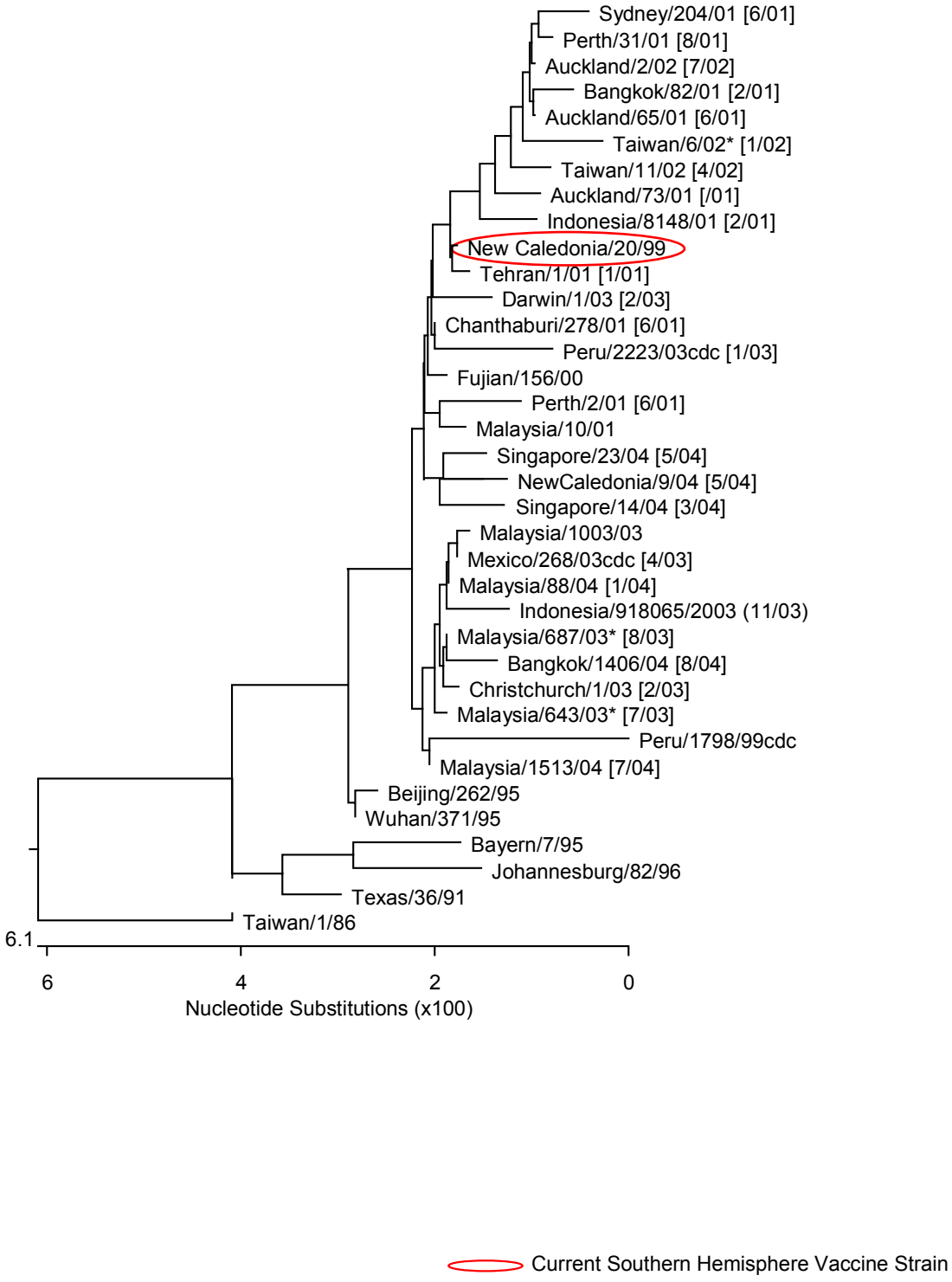

FIGURE 4.2
Phylogenetic relationships among influenza A(H3) HA1 genes 2004

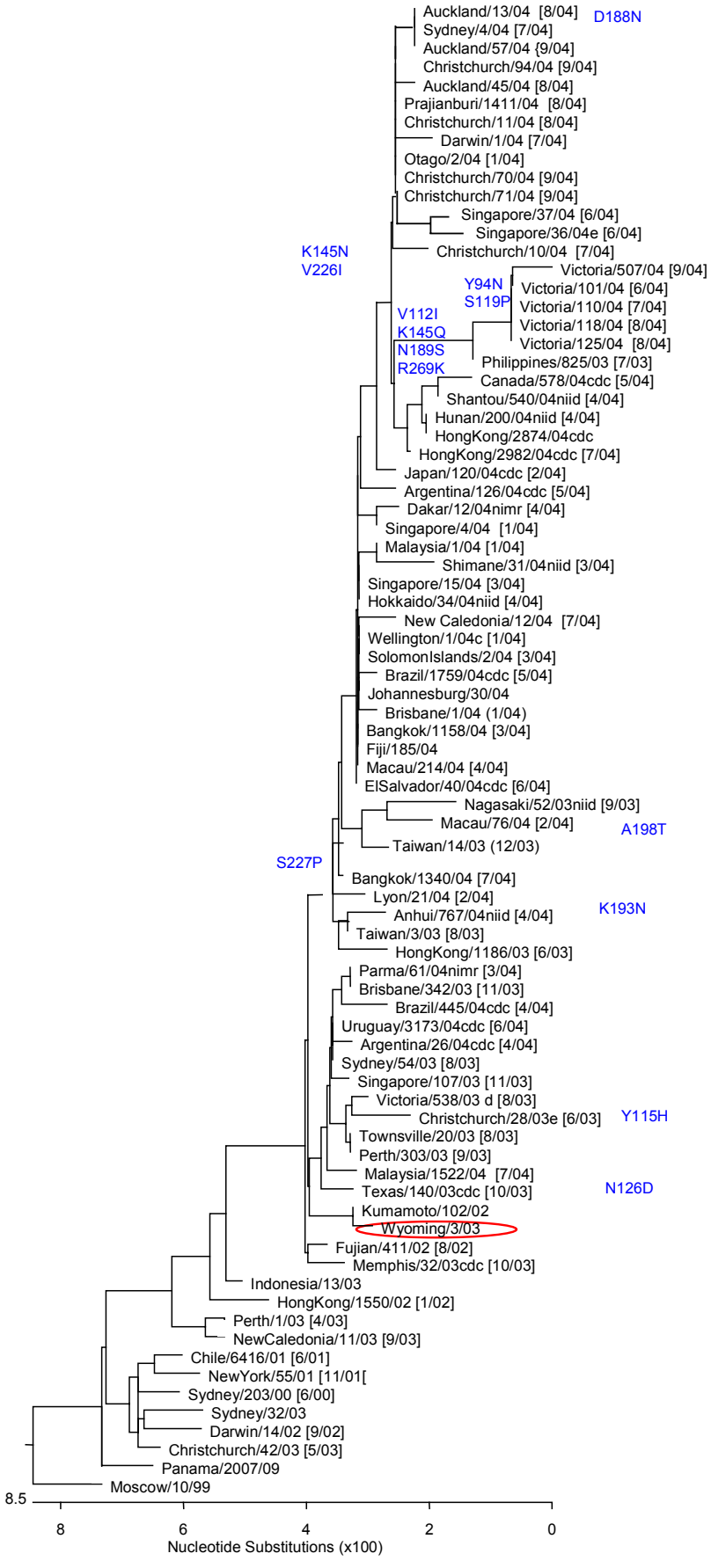

FIGURE 4.3

Phylogenetic relationships among influenza N2 neuraminidase genes 2003

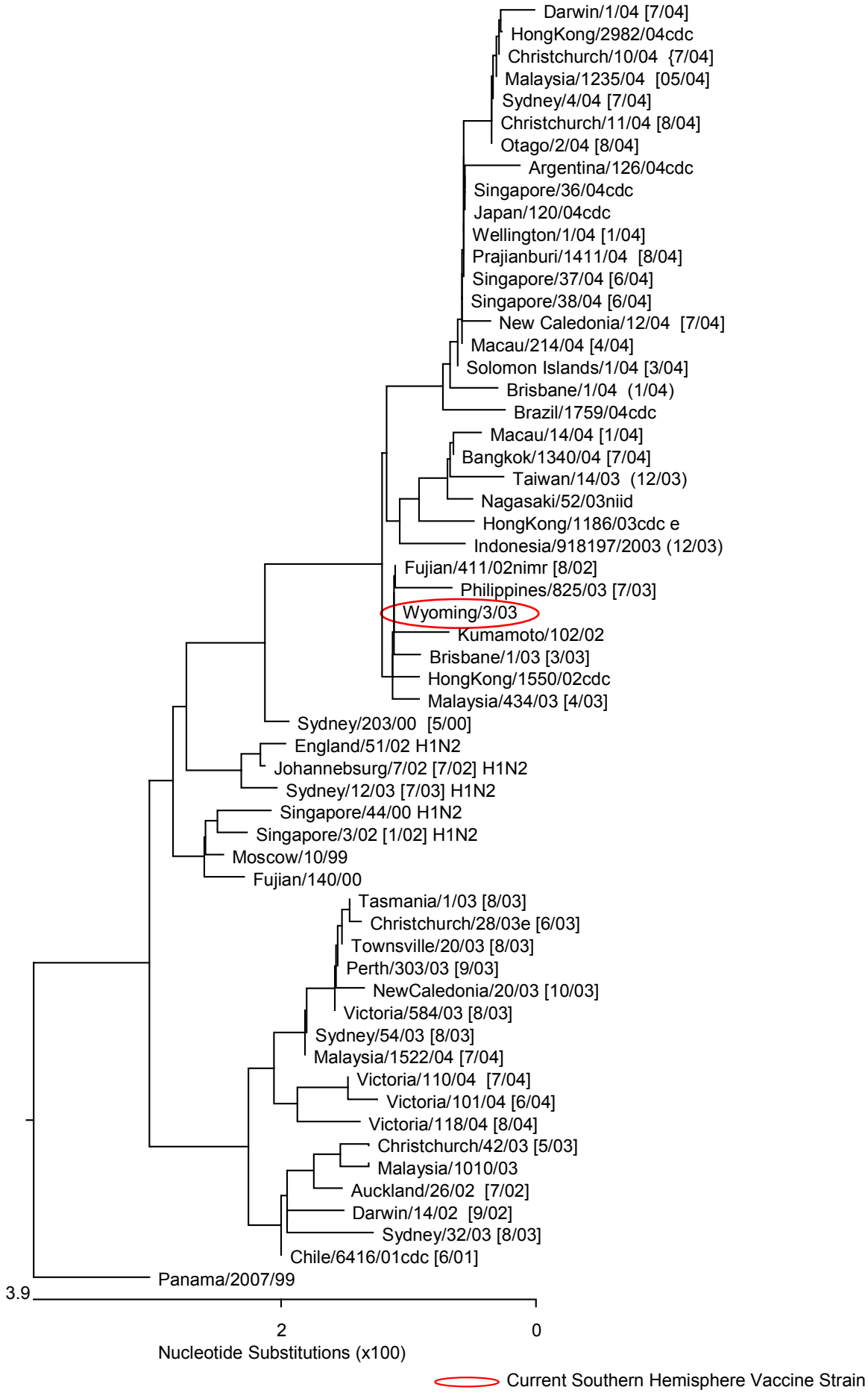

TABLE 4.8
Number of Amino Acid Differences from Consensus H3 HA Sequence

Virus	Number of Amino Acid Differences From Consensus Sequence HA1
A/Kumamoto/102/02	5
A/Wyoming/3/03	6
A/Fujian/411/02	4
A/Uruguay/3173/04	5
A/Anhui/767/04	6
A/Victoria/110/04	7
A/Japan/120/04	1
A/Christchurch/10/04	3
A/Singapore/37/04	4
A/Darwin/1/04	3
A/Christchurch/11/04	1
A/Bangkok/1340/04	2
A/Malaysia/1/04	2
A/Macau/214/04	1
A/Wellington/1/04	1
A/Argentina/126/04	3
A/Canada/578/04	5
A/HongKong/2971/04	2

TABLE 4.9
Influenza A(H3) haemagglutinin HA1 sequence comparison

```
H3
Consensus                 Q K L P G N D N S T A T L C L G H H A V P N G T I V K T I T N D Q I E V T N A T
                          ----------+---------+---------+---------+---------+---------+---------+-
                                    10        20        30        40
                          ----------+---------+---------+---------+---------+---------+---------+-
Kumamoto/102/02niid       . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Wyoming/3/03              . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Fujian/411/02cdc [8/02]   . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Uruguay/3173/04cdc [6/04] . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Anhui/767/04niid [4/04]   . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . D . . . . . . .
Victoria/110/04 [7/04]    . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Japan/120/04cdc [2/04]    . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Christchurch/10/04 [7/04] . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Singapore/37/04 [6/04]    . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Darwin/1/04 [7/04]        . . . . . . . . . . . . . . . . . . . . . . . . . . V . . . . . . . . . .
Christchurch/11/04 [8/04] . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Bangkok/1340/04 [7/04]    . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Malaysia/1/04 [1/04]      . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Macau/214/04 [4/04]       . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Wellington/1/04c [1/04]   . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Argentina/126/04cdc [5/04] . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Canada/578/04cdc          . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
HongKong/2982/04cdc       . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .

Consensus                 E L V Q S S S T G G I C D S P H Q I L D G E N C T L I D A L L G D P Q C D G F Q
                          ----------+---------+---------+---------+---------+---------+---------+-
                                    50        60        70        80
                          ----------+---------+---------+---------+---------+---------+---------+-
Kumamoto/102/02niid       . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Wyoming/3/03              . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Fujian/411/02cdc [8/02]   . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Uruguay/3173/04cdc [6/04] . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Anhui/767/04niid [4/04]   . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Victoria/110/04 [7/04]    . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Japan/120/04cdc [2/04]    . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Christchurch/10/04 [7/04] . . . . . . . . . . . . . N . . . . . . . . . . . . . . . . . . . . . . . .
Singapore/37/04 [6/04]    . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Darwin/1/04 [7/04]        . . . . . . . . . . . . . . . . . . . . . . . . . . . . . M . . . . . . . .
Christchurch/11/04 [8/04] . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Bangkok/1340/04 [7/04]    . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Malaysia/1/04 [1/04]      . . . . N . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Macau/214/04 [4/04]       . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Wellington/1/04c [1/04]   . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Argentina/126/04cdc [5/04] . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Canada/578/04cdc          . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
HongKong/2982/04cdc       . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
```

TABLE 4.9 (Continued)

Influenza A(H3) haemagglutinin HA1 sequence comparison

```
Consensus                 N K K W D L F V E R S K A Y S N C Y P Y D V P D Y A S L R S L V A S S G T L E F
                          ----------+---------+---------+---------+---------+---------+---------+-
                                    90        100       110       120
                          ----------+---------+---------+---------+---------+---------+---------+-
Kumamoto/102/02niid       . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Wyoming/3/03              . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Fujian/411/02cdc [8/02]   . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Uruguay/3173/04cdc [6/04] . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Anhui/767/04niid [4/04]   . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Victoria/110/04 [7/04]    . . . . . . . . . . . . . . H . . . . . . . . . . . . . . . . . I . . . . . .
Japan/120/04cdc [2/04]    . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Christchurch/10/04 [7/04] . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Singapore/37/04 [6/04]    . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Darwin/1/04 [7/04]        . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Christchurch/11/04 [8/04] . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Bangkok/1340/04 [7/04]    . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Malaysia/1/04 [1/04]      . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Macau/214/04 [4/04]       . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Wellington/1/04c [1/04]   . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Argentina/126/04cdc [5/04] . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Canada/578/04cdc          . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
HongKong/2982/04cdc       . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .

Consensus                 N N E S F N W T G V T Q N G T S S A C K R R S N K S F F S R L N W L T H L K F K
                          ----------+---------+---------+---------+---------+---------+---------+-
                                    130       140       150       160
                          ----------+---------+---------+---------+---------+---------+---------+-
Kumamoto/102/02niid       . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . Y .
Wyoming/3/03              . . . . . . . A . . . . . . . . . . . . . . . . . . . . . . . . . . . . Y .
Fujian/411/02cdc [8/02]   . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . Y .
Uruguay/3173/04cdc [6/04] . . . . . D . . . . . . . . . . . . . . . . . . . . . . . . . . . . . Y .
Anhui/767/04niid [4/04]   . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . Y .
Victoria/110/04 [7/04]    . . . . . . . . . . . . . . . . . . . . . . . . Q . . . . . . . . . . . . .
Japan/120/04cdc [2/04]    . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Christchurch/10/04 [7/04] . . . . . . . . . . . . . . . . . . . . . . . . N . . . . . . . . . . . . .
Singapore/37/04 [6/04]    . . . . . . . . . . . . . . . . . . . . . . . . N . . . . . . . . . . . . .
Darwin/1/04 [7/04]        . . . . . . . . . . . . . . . . . . . . . . . . N . . . . . . . . . . . . .
Christchurch/11/04 [8/04] . . . . . . . . . . . . . . . . . . . . . . . . N . . . . . . . . . . . . .
Bangkok/1340/04 [7/04]    . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . Y .
Malaysia/1/04 [1/04]      . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Macau/214/04 [4/04]       . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Wellington/1/04c [1/04]   . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Argentina/126/04cdc [5/04] . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Canada/578/04cdc          . . . . . . . . . . . . . . . . . . . . . . . . N . . . . . . . . . . . . .
HongKong/2982/04cdc       . . . . . . . . . . . . . . . . . . . . . . . . N . . . . . . . . . . . . .

Consensus                 Y P A L N V T M P N N E K F D K L Y I W G V H H P G T D N D Q I S L Y A Q A S G
                          ----------+---------+---------+---------+---------+---------+---------+-
                                    170       180       190       200
                          ----------+---------+---------+---------+---------+---------+---------+-
Kumamoto/102/02niid       . . . . . . . . . . . . . . . . . . . . . . . . V . . S . . . . . . . . . .
Wyoming/3/03              . . . . . . . . . . . . . . . . . . . . . . . . V . . S . . . . . . . . . .
Fujian/411/02cdc [8/02]   . . . . . . . . . . . . . . . . . . . . . . . . . . . S . . . . . . . . . .
Uruguay/3173/04cdc [6/04] . . . . . . . . . . . . . . . . . . . . . . . . . . . S . . . . . . . . . .
Anhui/767/04niid [4/04]   . . . . K . . . . . . . . . . . . . . . . . . . . . . S . . . N . . . . . .
Victoria/110/04 [7/04]    . . . . . . . . . . . . . . . . . . . . . . . . . . . S . . . . . . . . . P .
Japan/120/04cdc [2/04]    . . . . . . . . . . . . . . . . . . . . . . . . V . . . . . . . . . . . . .
Christchurch/10/04 [7/04] . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . P .
Singapore/37/04 [6/04]    . . . . . . . . . . . . . . . . . . . . . . . . V . . . . . . . . . . . . .
Darwin/1/04 [7/04]        . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Christchurch/11/04 [8/04] . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Bangkok/1340/04 [7/04]    . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Malaysia/1/04 [1/04]      . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Macau/214/04 [4/04]       . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Wellington/1/04c [1/04]   . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Argentina/126/04cdc [5/04] . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . P .
Canada/578/04cdc          . . . . . . . . . . . . . N . . . . . . . . . . . . . . . . . . . . . . . .
HongKong/2982/04cdc       . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .

Consensus                 R I T V S T K R S Q Q T V I P N I G S R P R V R D I P S R I S I Y W T I V K P G
                          ----------+---------+---------+---------+---------+---------+---------+-
                                    210       220       230       240
                          ----------+---------+---------+---------+---------+---------+---------+-
Kumamoto/102/02niid       . . . . . . . . . . . . . . . . . . . Y . . . . . . . S . . . . . . . . . .
Wyoming/3/03              . . . . . . . . . . . . . . . . . . . Y . . . . . . . S . . . . . . . . . .
Fujian/411/02cdc [8/02]   . . . . . . . . . . . . . . . . . . . . . . . . . V S . . . . . . . . . . .
Uruguay/3173/04cdc [6/04] . . . . . . . . . . . . . . . . . . . . . . . . . V S . . . . . . . . . . .
Anhui/767/04niid [4/04]   . . . . . . . . . . . . . . . . . . . . . . . . . V . . . . . . . . . . . .
Victoria/110/04 [7/04]    . . . . . . . . . . . . . . . . . . . . . . . . . . S . . . . . . . . . . .
Japan/120/04cdc [2/04]    . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Christchurch/10/04 [7/04] . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Singapore/37/04 [6/04]    . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Darwin/1/04 [7/04]        . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Christchurch/11/04 [8/04] . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Bangkok/1340/04 [7/04]    . . . . . . . . . . . . . . . . . . . . . . . . V . . . . . . . . . . . . .
Malaysia/1/04 [1/04]      . . . . . . . . . . . . . . . . . . . . . . . . V . . . . . . . . . . . . .
Macau/214/04 [4/04]       . . . . . . . . . . . . . . . . . . . . . . . . V . . . . . . . . . . . . .
Wellington/1/04c [1/04]   . . . . . . . . . . . . . . . . . . . . . . . . V . . . . . . . . . . . . .
Argentina/126/04cdc [5/04] . . . . . . . . . . . . . . . . . . . . . . . . V . . . . . . . . . . . . .
Canada/578/04cdc          . . . . . . . . . . . . . . . . . . . . . . . . . S . . . . . . . . . . . .
HongKong/2982/04cdc       . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
```

TABLE 4.9 (Continued)
Influenza A(H3) haemagglutinin HA1 sequence comparison

```
Consensus                 D I L L I N S T G N L I A P R G Y F K I R S G K S S I M R S D A P I G K C N S E
                          ----------+---------+---------+---------+---------+---------+---------+-
                                    250       260       270       280
                          ----------+---------+---------+---------+---------+---------+---------+-
Kumamoto/102/02niid       . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Wyoming/3/03              . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Fujian/411/02cdc [8/02]   . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Uruguay/3173/04cdc [6/04] . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Anhui/767/04niid [4/04]   . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Victoria/110/04 [7/04]    . . . . . . . . . . . . . . . . . . . . . . . . . . . . K . . . . . . . . .
Japan/120/04cdc [2/04]    . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Christchurch/10/04 [7/04] . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Singapore/37/04 [6/04]    . M . . . S . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Darwin/1/04 [7/04]        . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Christchurch/11/04 [8/04] . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Bangkok/1340/04 [7/04]    . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Malaysia/1/04 [1/04]      . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Macau/214/04 [4/04]       . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Wellington/1/04c [1/04]   . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Argentina/126/04cdc [5/04] . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . D . . . . .
Canada/578/04cdc          . . . . . . C . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
HongKong/2982/04cdc       . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .

Consensus                 C I T P N G S I P N D K P F Q N V N R I T Y G A C P R Y V K Q N T L K L A T G M
                          ----------+---------+---------+---------+---------+---------+---------+-
                                    290       300       310       320
                          ----------+---------+---------+---------+---------+---------+---------+-
Kumamoto/102/02niid       . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Wyoming/3/03              . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Fujian/411/02cdc [8/02]   . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Uruguay/3173/04cdc [6/04] . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Anhui/767/04niid [4/04]   . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Victoria/110/04 [7/04]    . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Japan/120/04cdc [2/04]    . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Christchurch/10/04 [7/04] . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Singapore/37/04 [6/04]    . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Darwin/1/04 [7/04]        . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Christchurch/11/04 [8/04] . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Bangkok/1340/04 [7/04]    . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Malaysia/1/04 [1/04]      . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Macau/214/04 [4/04]       . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Wellington/1/04c [1/04]   . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Argentina/126/04cdc [5/04] . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Canada/578/04cdc          . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
HongKong/2982/04cdc       . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .

Consensus                 R N V P E K Q T R
                          -----------------

                          -----------------
Kumamoto/102/02niid       . . . . . . . . .
Wyoming/3/03              . . . . . . . . .
Fujian/411/02cdc [8/02]   . . . . . . . . .
Uruguay/3173/04cdc [6/04] . . . . . . . . .
Anhui/767/04niid [4/04]   . . . . . . . . .
Victoria/110/04 [7/04]    . . . . . . . . .
Japan/120/04cdc [2/04]    . . . . . . . . .
Christchurch/10/04 [7/04] . . . . . . . . .
Singapore/37/04 [6/04]    . . . . . . . . .
Darwin/1/04 [7/04]        . . . . . . . . .
Christchurch/11/04 [8/04] . . . . . . . . .
Bangkok/1340/04 [7/04]    . . . . . . . . .
Malaysia/1/04 [1/04]      . . . . . . . . .
Macau/214/04 [4/04]       . . . . . . . . .
Wellington/1/04c [1/04]   . . . . . . . . .
Argentina/126/04cdc [5/04] . . . . . . . . .
Canada/578/04cdc          . . . . . T . . .
HongKong/2982/04cdc       . . . . . T . . .
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TABLE 4.10
Number of Amino Acid Differences from Consensus N2 Neuraminidase Sequence

Virus	Number of Amino Acid Differences From Consensus Sequence
	N2
A/Wyoming/3/03	3
A/Kumamoto/102/02	5
A/Fujian/411/02	3
A/Macau/214/04	0
A/Christchurch/10/04	1
A/Bangkok/1340/04	5
A/Japan/120/04	0
A/Wellington/1/04	0
A/Singapore/37/04	0
A/Sydney/4/04	1
A/Victoria/110/04	16
A/Malaysia/1522/04	15

TABLE 4.11
Influenza N2 Neuraminidase Sequence Comparison

```
N2
Consensus                 M N P N Q K I I T I G S V S L T I S T I C F F M Q I A I L I T T V T L H F K Q Y
                          ----------+---------+---------+---------+---------+---------+---------+-
                                    10        20        30        40
                          ----------+---------+---------+---------+---------+---------+---------+-
Wyoming/3/03              . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Kumamoto/102/02           . . . . . . . . . . . . . . . . I . . . . . . . . . . . . . . . . . . . . .
Fujian/411/02nimr [8/02]  . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Macau/214/04 [4/04]       . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Christchurch/10/04 {7/04] . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Bangkok/1340/04 [7/04]    . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Japan/120/04cdc           . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Wellington/1/04 [1/04]    . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Singapore/37/04 [6/04]    . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Sydney/4/04 [7/04]        . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Victoria/110/04  [7/04]   . . . . . . . . . . . . A . . . . A . . . . L . . . . . V . . . . . . . . H
Malaysia/1522/04 [7/04]   . . . . . . . . . . . . . . . . A . . . . L . . . . . V . . . . . . . . H

Consensus                 E F N S P P N N Q V M L C E P T I I E R N I T E I V Y L T N T T I E K E I C P K
                          ----------+---------+---------+---------+---------+---------+---------+-
                                    50        60        70        80
                          ----------+---------+---------+---------+---------+---------+---------+-
Wyoming/3/03              . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Kumamoto/102/02           . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Fujian/411/02nimr [8/02]  . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Macau/214/04 [4/04]       . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Christchurch/10/04 {7/04] . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Bangkok/1340/04 [7/04]    . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Japan/120/04cdc           . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Wellington/1/04 [1/04]    . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Singapore/37/04 [6/04]    . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Sydney/4/04 [7/04]        . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Victoria/110/04  [7/04]   . C . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Malaysia/1522/04 [7/04]   . C . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .

Consensus                 L A E Y R N W S K P Q C D I T G F A P F S K D N S I R L S A G G D I W V T R E P
                          ----------+---------+---------+---------+---------+---------+---------+-
                                    90        100       110       120
                          ----------+---------+---------+---------+---------+---------+---------+-
Wyoming/3/03              . . . . . . . . . . . N . . . . . . . . . . . . . . . . . . . . . . . . . .
Kumamoto/102/02           . . . . . . . . . . . N . . . . . . . . . . . . . . . . . . . . . . . . . .
Fujian/411/02nimr [8/02]  . . . . . . . . . . . N . . . . . . . . . . . . . . . . . . . . . . . . . .
Macau/214/04 [4/04]       . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Christchurch/10/04 {7/04] . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Bangkok/1340/04 [7/04]    . . . . . . . . . . . N . . . . . . . . . . . . . . . . . . . . . . . . . .
Japan/120/04cdc           . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Wellington/1/04 [1/04]    . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Singapore/37/04 [6/04]    . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Sydney/4/04 [7/04]        . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Victoria/110/04  [7/04]   . . . . . . . . . . . N . . . . . . . . . . . . . . . . . . . . . . . . . .
Malaysia/1522/04 [7/04]   . . . . . . . . . . . N . . . . . . . . . . . . . . . . . . . . . . . . . .
```

TABLE 4.11 (Continued)
Influenza N2 Neuraminidase Sequence Comparison

```
Consensus                 Y V S C D P D K C Y Q F A L G Q G T T L N N V H S N D T V H D R T P Y R T L L M
                          ----------+---------+---------+---------+---------+---------+---------+-
                                    130       140       150       160
                          ----------+---------+---------+---------+---------+---------+---------+-
Wyoming/3/03              . . . . . .
Kumamoto/102/02           . . . . . .
Fujian/411/02nimr [8/02]  . . . . . .
Macau/214/04 [4/04]       . . . . . .
Christchurch/10/04 {7/04} . . . . . .
Bangkok/1340/04 [7/04]    . . . . . .
Japan/120/04cdc           . . . . . .
Wellington/1/04 [1/04]    . . . . . .
Singapore/37/04 [6/04]    . . . . . .
Sydney/4/04 [7/04]        . . . . . .
Victoria/110/04 [7/04]    . . . . . G . . . . . .
Malaysia/1522/04 [7/04]   . . . . . G . . . . . .

Consensus                 N E L G V P F H L G T K Q V C I A W S S S S C H D G K A W L H V C V T G D D K N
                          ----------+---------+---------+---------+---------+---------+---------+-
                                    170       180       190       200
                          ----------+---------+---------+---------+---------+---------+---------+-
Wyoming/3/03              . . . . . E .
Kumamoto/102/02           . . . . . E .
Fujian/411/02nimr [8/02]  . . . . . E .
Macau/214/04 [4/04]       . . . . . .
Christchurch/10/04 {7/04} . . . . . .
Bangkok/1340/04 [7/04]    . . . . . E .
Japan/120/04cdc           . . . . . .
Wellington/1/04 [1/04]    . . . . . .
Singapore/37/04 [6/04]    . . . . . .
Sydney/4/04 [7/04]        . . . . . .
Victoria/110/04 [7/04]    . . . . . R . . . . . .
Malaysia/1522/04 [7/04]   . . . . . R . . . . . .

Consensus                 A T A S F I Y N G R L V D S I V S W S K K I L R T Q E S E C V C I N G T C T V V
                          ----------+---------+---------+---------+---------+---------+---------+-
                                    210       220       230       240
                          ----------+---------+---------+---------+---------+---------+---------+-
Wyoming/3/03              . . . . . .
Kumamoto/102/02           . . . . . .
Fujian/411/02nimr [8/02]  . . . . . .
Macau/214/04 [4/04]       . . . . . .
Christchurch/10/04 {7/04} . . . . . E . . . . . .
Bangkok/1340/04 [7/04]    . . . . . V . . . . . .
Japan/120/04cdc           . . . . . .
Wellington/1/04 [1/04]    . . . . . .
Singapore/37/04 [6/04]    . . . . . .
Sydney/4/04 [7/04]        . . . . . E . . . . . .
Victoria/110/04 [7/04]    . . . . . G . . . . . .
Malaysia/1522/04 [7/04]   . . . . . G . . . . . .
Consensus                 M T D G S A S G K A D T K I L F I E E G K I V H T S T L S G S A Q H V E E C S C
                          ----------+---------+---------+---------+---------+---------+---------+-
                                    250       260       270       280
                          ----------+---------+---------+---------+---------+---------+---------+-
Wyoming/3/03              . . . . . .
Kumamoto/102/02           . . . . . I . . . . . .
Fujian/411/02nimr [8/02]  . . . . . .
Macau/214/04 [4/04]       . . . . . .
Christchurch/10/04 {7/04} . . . . . .
Bangkok/1340/04 [7/04]    . . . . . .
Japan/120/04cdc           . . . . . .
Wellington/1/04 [1/04]    . . . . . .
Singapore/37/04 [6/04]    . . . . . .
Sydney/4/04 [7/04]        . . . . . .
Victoria/110/04 [7/04]    . . . . . I . I . . . . . .
Malaysia/1522/04 [7/04]   . . . . . I . . . . . .

Consensus                 Y P R Y P G V R C V C R D N W K G S N R P I V D I N I K D Y S I V S S Y V C S G
                          ----------+---------+---------+---------+---------+---------+---------+-
                                    290       300       310       320
                          ----------+---------+---------+---------+---------+---------+---------+-
Wyoming/3/03              . . . . . .
Kumamoto/102/02           . . . . . .
Fujian/411/02nimr [8/02]  . . . . . .
Macau/214/04 [4/04]       . . . . . .
Christchurch/10/04 {7/04} . . . . . .
Bangkok/1340/04 [7/04]    . . . . . .
Japan/120/04cdc           . . . . . .
Wellington/1/04 [1/04]    . . . . . .
Singapore/37/04 [6/04]    . . . . . .
Sydney/4/04 [7/04]        . . . . . .
Victoria/110/04 [7/04]    . . . . . V . . . . . .
Malaysia/1522/04 [7/04]   . . . . . V . . . . . .

Consensus                 L V G D T P R K N D S S S S S H C L D P N N E E G G H G V K G W A F D D G N D V
                          ----------+---------+---------+---------+---------+---------+---------+-
                                    330       340       350       360
                          ----------+---------+---------+---------+---------+---------+---------+-
Wyoming/3/03              . . . . . .
Kumamoto/102/02           . . . . . .
Fujian/411/02nimr [8/02]  . . . . . .
Macau/214/04 [4/04]       . . . . . .
Christchurch/10/04 {7/04} . . . . . .
Bangkok/1340/04 [7/04]    . . . . . .
Japan/120/04cdc           . . . . . .
Wellington/1/04 [1/04]    . . . . . .
Singapore/37/04 [6/04]    . . . . . .
Sydney/4/04 [7/04]        . . . . . .
Victoria/110/04 [7/04]    . . . . . F . . . . . .
Malaysia/1522/04 [7/04]   . . . . . F . . . . . .
```

TABLE 4.11 (Continued)
Influenza N2 Neuraminidase Sequence Comparison

```
Consensus                W M G R T I S E K L R S G Y E T F K V I E G W S N P N S K L Q I N R Q V I V D R
                         ----------------+----------------+----------------+----------------+-
                                         370              380              390              400
                         ----------------+----------------+----------------+----------------+-
Wyoming/3/03             . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Kumamoto/102/02          . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Fujian/411/02nimr [8/02] . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Macau/214/04 [4/04]      . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Christchurch/10/04  {7/04] . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Bangkok/1340/04 [7/04]   . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Japan/120/04cdc          . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Wellington/1/04 [1/04]   . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Singapore/37/04 [6/04]   . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Sydney/4/04 [7/04]       . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Victoria/110/04  [7/04]  . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . E . .
Malaysia/1522/04 [7/04]  . . . . . . . . . . . . . . . . . . . . . . K . . . . . . . . . . E . .

Consensus                G N R S G Y S G I F S V E G K S C I N R C F Y V E L I R G R K E E T E V L W T S
                         ----------------+----------------+----------------+----------------+-
                                         410              420              430              440
                         ----------------+----------------+----------------+----------------+-
Wyoming/3/03             . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . Q . . . . . . . .
Kumamoto/102/02          . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . Q . . . . . . . .
Fujian/411/02nimr [8/02] . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . Q . . . . . . . .
Macau/214/04 [4/04]      . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Christchurch/10/04  {7/04] . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Bangkok/1340/04 [7/04]   . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . N Q . . . . . . . .
Japan/120/04cdc          . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Wellington/1/04 [1/04]   . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Singapore/37/04 [6/04]   . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Sydney/4/04 [7/04]       . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .
Victoria/110/04  [7/04]  . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . W . . .
Malaysia/1522/04 [7/04]  . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . W . . .
1326

Consensus                N S I V V F C G T S G T Y G T G S W P D G A
                         ----------------+----------------+----
                                         450              460
                         ----------------+----------------+----
Wyoming/3/03             . . . . . . . . . . . . . . . . . . . .
Kumamoto/102/02          . . . . . . . . . . . . . . . . . . . .
Fujian/411/02nimr [8/02] . . . . . . . . . . . . . . . . . . . .
Macau/214/04 [4/04]      . . . . . . . . . . . . . . . . . . . .
Christchurch/10/04  {7/04] . . . . . . . . . . . . . . . . . . .
Bangkok/1340/04 [7/04]   . . . . . . . . . . . . . . . . . . . .
Japan/120/04cdc          . . . . . . . . . . . . . . . . . . . .
Wellington/1/04 [1/04]   . . . . . . . . . . . . . . . . . . . .
Singapore/37/04 [6/04]   . . . . . . . . . . . . . . . . . . . .
Sydney/4/04 [7/04]       . . . . . . . . . . . . . . . . . . . .
Victoria/110/04  [7/04]  . . . . . . . . . . . . . . . . . . . .
Malaysia/1522/04 [7/04]  . . . . . . . . . . . . . . . . . . . .
```

FIGURE 5.2

Phylogenetic relationships among influenza B HA1 genes 2004

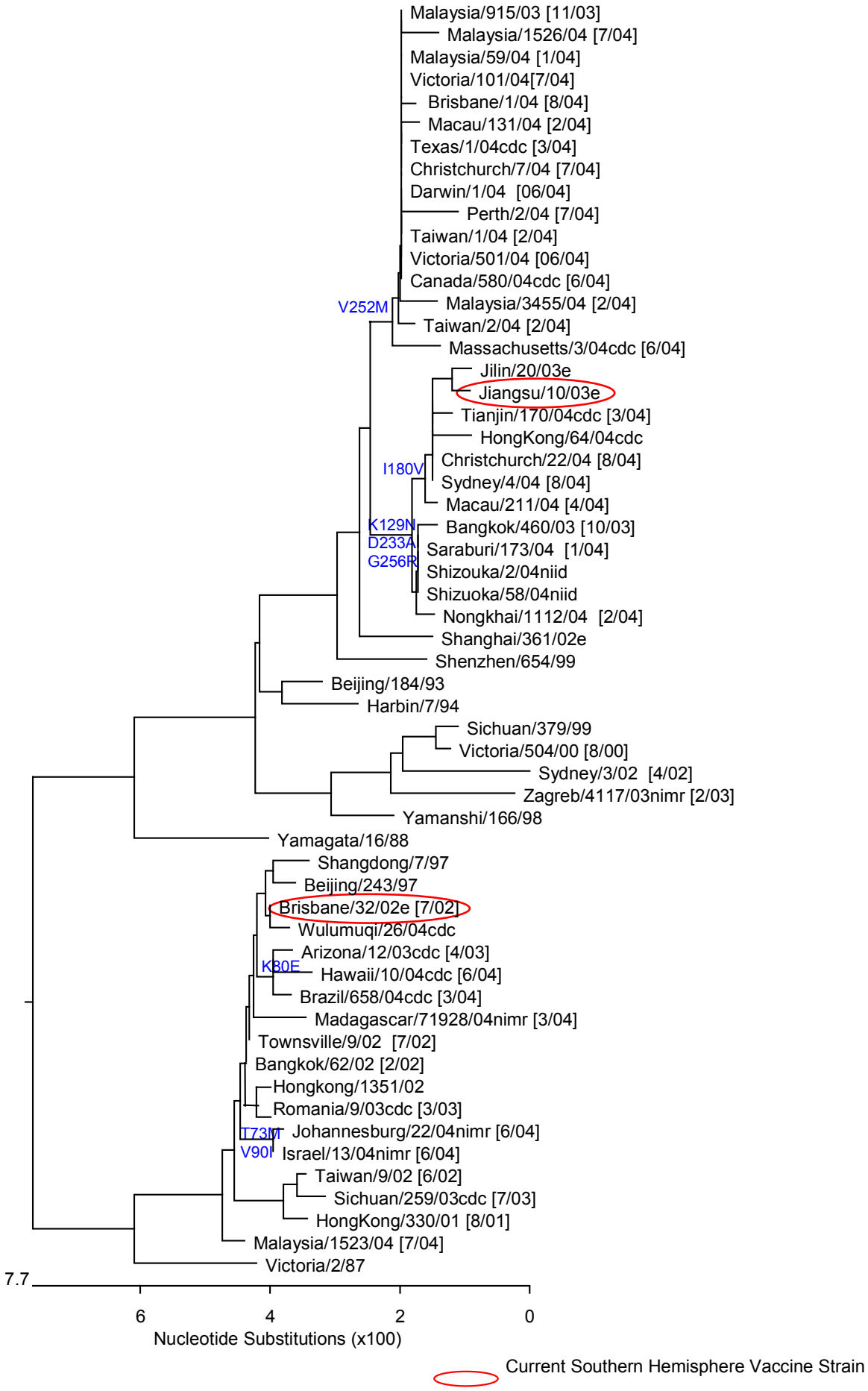

FIGURE 5.3

Phylogenetic relationships among influenza B neuraminidase genes 2004

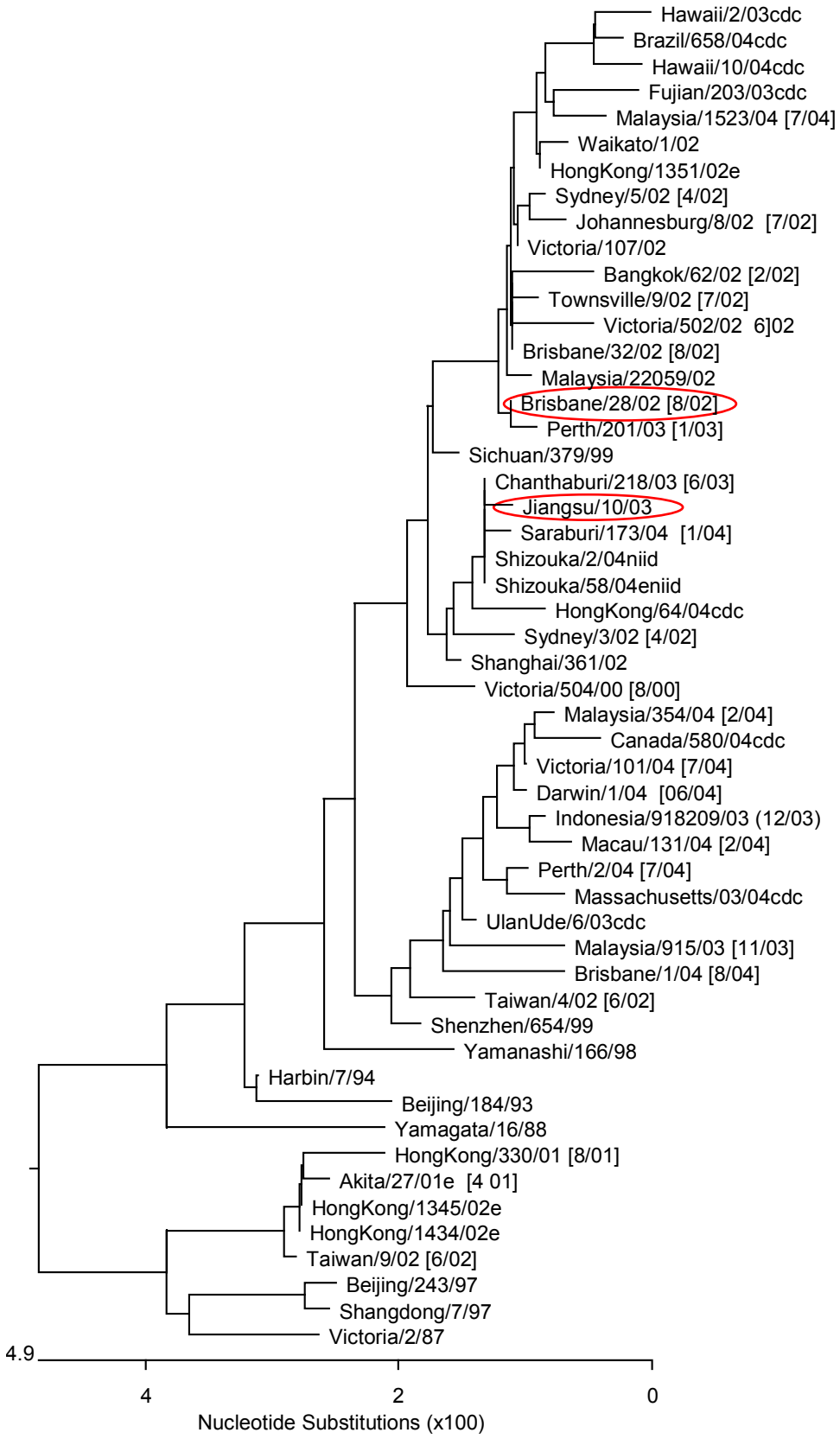

TABLE 5.6

Number of Amino Acid Differences (B/Yamagata/16/88 lineage) from Consensus B HA Sequence

Virus	Number of Amino Acid Differences From Consensus Sequence HA1
B/Malaysia/915/03	1
B/Macau/131/04	2
B/Victoria/101/04	1
B/Brisbane/1/04	2
B/Victoria/501/04	1
B/Shanghai/361/02	5
B/Taiwan/1/04	1
B/Canada/580/04	1
B/Massachusetts/3/04	3
B/HongKong/64/04	6
B/Sydney/4/04	4
B/Jiangsu/10/03	7
B/Saraburi/173/04	3
B/Shizouka/2/04	3
B/Shenzhen/654/99	7

TABLE 5.7

Number of Amino Acid Differences (B/Victoria/2/87 lineage) from Consensus B HA Sequence

Virus	Number of Amino Acid Differences From Consensus Sequence HA1
B/Shangdong/7/97	1
B/ Brisbane/32/2002	1
B/Hawaii/10/04	3
B/Johannesburg/22/04	2
B/Malaysia/1523/04	2

TABLE 5.8

Number of Amino Acid Differences from Consensus B Neuraminidase Sequence

Virus	Number of Amino Acid Differences From Consensus Sequence B NA
B/Hawaii/10/04	8
B/Malaysia/1523/04	7
B/Brisbane/32/02	3
B/Jiangsu/10/03	3
B/Saraburi/173/04	3
B/Shizouka/2/04	2
B/HongKong/64/04	5
B/Shanghai/361/02	2
B/Victoria/101/04	9
B/Malaysia/915/03	9
B/Brisbane/1/04	10

APPENDIX 5

SEROLOGICAL STUDIES OF INFLUENZA VACCINES

Serological Studies

Collaborative assays were performed in 5 laboratories using panels of pre and post immunisation sera from young adults and older adults. Panels were derived from recipients of the 2004 Australian, 2003-2004 European vaccines and the 2002-2003 Japanese vaccine. No serum panel from the USA was received.

Australian H1 vaccine A/New Caledonia/20/99 (H1N1)-like strain

Europe H1 vaccine A/New Caledonia/20/99 (H1N1)-like strain

Japanese H1 vaccine A/New Caledonia/20/99 (H1N1)-like strain

TABLE 3.6
Haemagglutination-inhibition antibody responses
Influenza type A(H1) vaccine component
Young Adults

Population	N	Antigen	Passage History	% Rise	GMT		%≥40		%≥160	
					Pre	Post	Pre	Post	Pre	Post
Australian Younger Adult		A/New Caledonia/20/99	E6	84	8.7	75.5	8	79	0	29
		A/Hong Kong/2637/2004	MDCK5	88	7.55	73.3	4	79	0	29
		A/Singapore/14/2004	E3	92	10.3	123.3	17	96	1	46
British Younger Adult		A/New Caledonia/20/99	E5	79	10.3	123.3	17	88	0	63
		A/Hong Kong/2637/2004	MDCK5	79	9.7	113.1	17	88	0	58
		A/Singapore/14/2004	E3	79	12.6	142.5	17	96	4	67
Japanese Younger Adult		A/New Caledonia/20/99	E6	32	7.2	17.4	12	28	0	8
		A/Hong Kong/2637/2004	MDCK5	28	6.6	13.9	0	24	0	4
		A/Singapore/14/2004	E3	24	9	21.7	16	40	0	12

TABLE 3.7
Haemagglutination-inhibition antibody responses
Influenza Type A(H1) Vaccine Component
Older Adults

Population	N	Antigen	Passage History	% Rise	GMT		%≥40		%≥160	
					Pre	Post	Pre	Post	Pre	Post
Older Adult		A/New Caledonia/20/99	E6	92	5	51.9	0	83	0	17
		A/Hong Kong/2637/2004	MDCK5	92	5.6	50.4	0	88	0	21
		A/Singapore/14/2004	E3	92	5.8	71.3	0	83	0	21
British Younger Adult		A/New Caledonia/20/99	E6	50	8.7	27.5	0	46	0	8
		A/Hong Kong/2637/2004	MDCK5	50	7.3	24.5	0	38	0	8
		A/Singapore/14/2004	E3	50	10.9	41.2	17	67	0	8
Japanese Younger Adult		A/New Caledonia/20/99	E6	17	6.8	12	0	17	0	7
		A/Hong Kong/2637/2004	MDCK5	13	6.2	10	0	10	0	3
		A/Singapore/14/2004	E3	13	7.8	12.6	7	23	0	3

Serological Studies

Collaborative assays were performed in 5 laboratories using panels of pre and post immunisation sera from young adults and older adults. Panels were derived from recipients of the 2004 Australian, 2003-2004 European vaccines and the 2002-2003 Japanese vaccine. No serum panel from the USA was received.

Australian H3 vaccine	A/Fujian/4112002 (H3N2)-like strain (actual strain A/Wyoming/3/2003)
Europe H3 vaccine	A/Fujian/411/2002(H3N2)-like strain (actual strain A/Wyoming/3/2003)
Japanese H3 vaccine	A/Moscow/10/99 (H3N2)-like strain (actual strain A/Panama/2007/99)

TABLE 4.12
Haemagglutination-inhibition antibody responses
Influenza type A(H3N2) vaccine component
Young Adults

Population	N	Antigen	Passage History	% Rise	GMT		%≥40		%≥160	
					Pre	Post	Pre	Post	Pre	Post
Australian Younger Adult		A/Wyoming/3/2003	CK2E5	79	13.3	164.7	21	92	4	67
		A/Malaysia/1/2004	E5	83	8.7	56.6	8	83	0	21
		A/Wellington/1/2004	E4	79	8.4	106.8	8	83	4	50
		A/Victoria/110/2004	MDCK3	50	6.9	22.4	0	38	0	8
		A/Singapore/37/2004	E3	54	6.9	30.0	4	54	0	8
		A/Japan/120/2004	SPFCKE3	92	11.6	226.2	8	79	0	29
British Younger Adult		A/Wyoming/3/2003	CK2E5	58	14.6	71.3	25	83	0	29
		A/Malaysia/1/2004	E5	58	10.6	37.7	8	75	0	4
		A/Wellington/1/2004	E4	50	10.0	38.9	8	25	0	13
		A/Victoria/110/2004	MDCK3	33	7.7	17.8	4	8	0	0
		A/Singapore/37/2004	E3	58	7.5	26.7	8	38	0	4
		A/Japan/120/2004	SPFCKE3	67	15.4	100.8	17	88	0	63
Japanese Younger Adult		A/Wyoming/3/2003	CK2E5	16	9.5	16.0	12	28	0	0
		A/Malaysia/1/2004	E5	4	6.8	8.7	4	4	0	0
		A/Wellington/1/2004	E4	8	7.2	9.0	4	8	0	0
		A/Victoria/110/2004	MDCK3	0	5.3	6.1	0	0	0	0
		A/Singapore/37/2004	E3	4	5.7	6.1	0	4	0	0
		A/Japan/120/2004	SPFCKE3	16	10.9	16.9	12	28	0	8

TABLE 4.13
Haemagglutination-inhibition antibody responses
Influenza type A(H3N2) vaccine component
Older Adults

Population	N	Antigen	Passage History	% Rise	GMT		%≥40		%≥160	
					Pre	Post	Pre	Post	Pre	Post
Australian Older Adult	24	A/Wyoming/3/2003	CK2E5	88	7.9	63.5	4	79	0	33
		A/Malaysia/1/2004	E5	75	8.2	36.7	8	54	0	8
		A/Wellington/1/2004	E4	79	6.5	47.6	0	63	0	29
		A/Victoria/110/2004	MDCK3	42	6.9	18.9	4	29	0	0
		A/Singapore/37/2004	E3	54	5.6	20.6	0	33	0	4
		A/Japan/120/2004	SPFCKE3	96	7.7	89.8	0	83	0	17
European Older Adult	24	A/Wyoming/3/2003	CK2E5	54	15.4	63.5	25	75	4	38
		A/Malaysia/1/2004	E5	58	10.6	40.0	8	67	0	4
		A/Wellington/1/2004	E4	71	9.7	50.4	4	58	4	25
		A/Victoria/110/2004	MDCK3	46	7.3	18.9	0	21	0	0
		A/Singapore/37/2004	E3	75	6.9	30.8	5	50	0	13
		A/Japan/120/2004	SPFCKE3	71	16.8	113.1	0	46	0	8
Japanese Older Adult	25	A/Wyoming/3/2003	CK2E5	13	12.6	24.1	30	43	3	13
		A/Malaysia/1/2004	E5	7	7.8	10.7	7	20	0	0
		A/Wellington/1/2004	E4	3	6.9	9.1	7	10	0	3
		A/Victoria/110/2004	MDCK3	3	6.6	8.3	0	7	0	0
		A/Singapore/37/2004	E3	4	6.9	8.5	7	13	0	0
		A/Japan/120/2004	SPFCKE3	10	11.2	20.0	0	17	0	7

Serological Studies

Collaborative assays were performed in 5 laboratories using panels of pre and post immunisation sera from young adults and older adults. Panels were derived from recipients of the 2004 Australian, 2003-2004 European vaccines and the 2002-2003 Japanese vaccine. No serum panel from the USA was received.

Australian B vaccine B/Hong Kong/330/2001-like strain (actual strain B/Brisbane/32/2002)

Europe B vaccine B/Shanghai/361/2002-like strain (actual strain B/Jiangsu/10/2003)

Japanese B vaccine B/Hong Kong/330/2001-like strain (actual strain B/Shangdong/7/97)

TABLE 5.9

Haemagglutination inhibition antibody responses
Influenza type B vaccine component Young Adults

Population	N	Antigen	Passage History	% Rise	GMT		%≥40		%≥160	
					Pre	Post	Pre	Post	Pre	Post
Australian Younger Adult	24	B/Jiangsu/10/2003	E7	67	14.1	50.4	46	79	21	58
		B/Brisbane/32/2002	E3	83	18.9	174.4	25	96	8	67
		B/Victoria/501/2004	E5	75	23.1	106.8	46	96	4	46
		B/Wulumuqi/26/04	E6	88	19.4	190.2	25	96	17	67
European Younger Adult	24	B/Jiangsu/10/2003	E7	96	9.2	146.7	17	63	4	8
		B/Brisbane/32/2002	E3	46	13.3	36.7	25	54	8	13
		B/Victoria/501/2004	E5	79	11.2	71.3	25	67	0	33
		B/Wulumuqi/26/04	E6	21	12.2	25.9	25	38	8	13
Japanese Younger Adult	25	B/Jiangsu/10/2003	E7	0	5.6	7.2	60	68	0	12
		B/Brisbane/32/2002	E3	20	19.5	37.8	44	72	0	4
		B/Victoria/501/2004	E5	16	17.9	26.4	44	56	0	0
		B/Wulumuqi/26/04	E6	20	17.9	34.8	44	68	0	4

TABLE 5.10

Haemagglutination inhibition antibody responses
Influenza type B vaccine component Older Adults

Population	N	Antigen	Passage History	% Rise	GMT		%≥40		%≥160	
					Pre	Post	Pre	Post	Pre	Post
Australian Older Adult	24	B/Jiangsu/10/2003	E7	71	10.0	41.2	54	88	13	46
		B/Brisbane/32/2002	E3	96	14.6	195.8	17	96	0	67
		B/Victoria/501/2004	E5	63	15.4	51.9	21	67	0	21
		B/Wulumuqi/26/04	E6	96	14.1	179.5	8	96	0	71
European Older Adult	24	B/Jiangsu/10/2003	E7	100	8.2	109.9	21	54	0	13
		B/Brisbane/32/2002	E3	13	18.3	34.6	38	50	17	17
		B/Victoria/501/2004	E5	75	9.4	43.6	4	63	0	21
		B/Wulumuqi/26/04	E6	17	15.9	26.7	33	46	13	13
Japanese Older Adult	30	B/Jiangsu/10/2003	E7	3	6.9	7.9	23	27	10	10
		B/Brisbane/32/2002	E3	13	21.4	33.2	37	57	10	20
		B/Victoria/501/2004	E5	3	8.7	11.0	13	23	0	7
		B/Wulumuqi/26/04	E6	10	17.8	27.0	27	47	7	10

APPENDIX 6

WHO RECOMMENDATION FOR INFLUENZA VACCINES IN 2004

Weekly epidemiological record
Relevé épidémiologique hebdomadaire

8 OCTOBER 2004, 79th YEAR / 8 OCTOBRE 2004, 79e ANNÉE
No. 41, **2004**, **79**, 369–376
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Recommended composition of influenza virus vaccines for use in the 2005 influenza season

This recommendation relates to the composition of vaccines for the forthcoming winter in the southern hemisphere (May–October 2005). A recommendation will be made in February 2005 which relates to vaccines that will be used for the winter in the northern hemisphere (November 2005–April 2006). Epidemiological considerations will influence which recommendation (September 2004 or February 2005) is more appropriate for countries in equatorial regions.

Influenza activity February–September 2004

Between February and September 2004, influenza activity was reported in Africa, the Americas, Asia, Europe and Oceania. In the northern hemisphere, outbreaks caused by influenza A(H3N2) viruses continued to be reported in several countries in North America, Asia and Europe between February and August. In the southern hemisphere, influenza activity was relatively mild. Outbreaks caused by influenza A(H3N2) viruses were reported in South America between March and July and in New Zealand during August and September.

Influenza A(H3N2) viruses predominated in most parts of the world and were responsible for the majority of outbreaks. Influenza A(H1) and B viruses circulated at low levels.

Influenza A(H1N1) and A(H1N2)

Outbreaks caused by influenza A(H1N1) and A(H1N2) viruses were reported in the United Kingdom in May, and in the Philippines in June and July, respectively.

Composition recommandée des vaccins antigrippaux pour la saison 2005

La présente recommandation s'applique à la composition des vaccins pour le prochain hiver dans l'hémisphère austral (mai-octobre 2005). Une recommandation relative aux vaccins à utiliser pendant l'hiver dans l'hémisphère boréal (novembre 2005-avril 2006) sera formulée en février 2005. La recommandation la mieux adaptée (de septembre 2004 ou de février 2005) aux pays des régions équatoriales s'appuiera sur les données épidémiologiques.

Activité grippale, février-septembre 2005

Entre février et septembre 2004, une activité grippale a été signalée en Afrique, dans les Amériques, en Asie, en Europe et en Océanie. Dans l'hémisphère boréal, des flambées de grippe dues au virus A(H3N2) ont encore été déclarées dans plusieurs pays d'Amérique du Nord, d'Asie et d'Europe entre février et août. Dans l'hémisphère austral, l'activité grippale a été relativement modérée. Entre mai et septembre 2003, des flambées dues au virus A ont été signalées en Afrique, en Amérique du Sud et en Océanie. Entre mars et juillet, des flambées causées par le virus A(H3N2) se sont déclarées en Amérique du Sud, et d'août à septembre en Nouvelle-Zélande.

Le virus grippal A(H3N2) a prédominé pratiquement partout dans le monde et a été responsable de la majorité des flambées. Les virus grippaux A(H1) et B ont circulés à de faibles niveaux.

Virus grippaux A(H1N1) et A(H1N2)

Des flambées de grippe A(H1N1) et A(H1N2) ont été signalées, en mai au Royaume-Uni, et aux Philippines en juin et en juillet, respectivement.

Influenza A(H1N1) viruses and A(H1) viruses for which the neuraminidase was not characterized were also isolated in Africa (Morocco), the Americas (Canada, Mexico, Peru and the United States), Asia (China, Hong Kong Special Administrative Region (Hong Kong SAR), Japan, Malaysia, Saudi Arabia, Singapore and Thailand), Europe (France, Italy, Luxembourg, Russian Federation and Sweden) and Oceania (Australia and New Caledonia).

A few influenza A(H1N2) viruses were isolated in the Americas (Canada) and in Europe (Italy, Norway and Sweden).

Influenza A(H3N2)

Between February and September, outbreaks caused by influenza A(H3N2) viruses were reported in the Americas (Argentina, Brazil, Canada, Chile and Paraguay), Asia (China (Province of Taiwan), Hong Kong SAR, Japan and the Republic of Korea), Europe (Germany, Italy, Latvia, Russian Federation and Ukraine) and Oceania (New Zealand).

Influenza A(H3N2) viruses were also isolated in Africa (Madagascar, Morocco, Senegal and South Africa), the Americas (Ecuador, El Salvador, Guyana, Mexico, Peru, the United States and Uruguay), Asia (Cambodia, China; China, Macao Special Administrative Region (Macao SAR), Guam, Malaysia, Nepal, Qatar, Singapore, Thailand and Viet Nam), Europe (Austria, Croatia, Czech Republic, Denmark, France, Greece, Iceland, Ireland, Israel, Poland, Serbia and Montenegro, Slovakia, Sweden, Switzerland, Turkey and the United Kingdom) and Oceania (Australia, Fiji, New Caledonia and Solomon Islands).

Influenza B

An outbreak caused by influenza B viruses was reported in Brazil during June and July.

Influenza B viruses were also isolated in Africa (Egypt, Madagascar and South Africa), the Americas (Argentina, Canada, Chile, Colombia, Mexico, Peru, the United States and Uruguay), Asia (China; China (Province of Taiwan), Hong Kong SAR, Macao SAR, Japan, the Republic of Korea, Malaysia, the Philippines, Saudi Arabia, Singapore and Thailand), Europe (Denmark, France, Israel, Italy, Kazakhstan, Norway, Russian Federation, Sweden, Turkey and the United Kingdom) and Oceania (Australia, New Caledonia and New Zealand).

Influenza A(H5N1) and A(H7N3)

Between 1 January and 22 September 2004, 40 patients with influenza A(H5), of whom 28 died, were reported from Viet Nam and Thailand.[1] These cases were associated with outbreaks of highly pathogenic avian influenza A(H5N1) in poultry. There has been no evidence of human-to-human transmission to date.

In March 2004, 2 human cases of influenza A(H7N3) were associated with outbreaks of avian influenza A(H7N3) in poultry in British Columbia, Canada. There has been no evidence of human-to-human transmission.[2]

[1] See http://www.who.int/csr/disease/avian_influenza/country/en/

[2] See http://www.who.int/csr/don/2004_04_05/en/

Des virus grippaux A(H1N1) et A(H1N2) chez lesquels la neuraminidase n'a pas été caractérisée ont également été isolés en Afrique (Maroc), dans les Amériques (Canada, États-Unis, Mexique et Pérou), en Asie (Arabie saoudite, Hong Kong, Région administrative spéciale de la Chine (Hong Kong RAS), Japon, Malaisie, Singapour et Thaïlande), en Europe (Fédération de Russie, France, Italie Luxembourg, et Suède) ainsi qu'en Océanie (Australie et Nouvelle-Calédonie).

Quelques virus grippaux A(H1N2) ont été isolés dans les Amériques (Canada) et en Europe (Italie, Norvège et Suède).

Virus grippal A(H3N2)

Entre février et septembre 2004, des flambées dues au virus grippal A(H3N2) ont été signalées dans les Amériques (Argentine, Brésil, Canada, Chili et Paraguay), en Asie (Chine (Province de Taiwan), Hong Kong RAS, Japon et République de Corée), en Europe (Allemagne, Fédération de Russie, Italie, Lettonie et Ukraine) ainsi qu'en Océanie (Nouvelle-Zélande).

Des virus grippaux A(H3N2) ont également été isolés en Afrique (Afrique du Sud, Madagascar, Maroc et Sénégal), dans les Amériques (Équateur, El Salvador, États-Unis, Guyana, Mexique Pérou et Uruguay), en Asie (Cambodge, Chine, Guam, Macao Région administrative spéciale de la Chine (Macao RAS), Malaisie, Népal, Qatar, Singapour, Thaïlande et Viet Nam), en Europe (Autriche, Bélarus, Croatie, Danemark, France, Grèce, Irlande, Islande, Israël, Lettonie, Pologne, République tchèque, Royaume-Uni, Serbie et Monténégro, Slovaquie, Suède, Suisse et Turquie) ainsi qu'en Océanie (Australie, Fidji, Îles Salomon et Nouvelle-Calédonie).

Virus grippal B

Une flambée due au virus grippal B a été signalée au Brésil entre juin et juillet 2004.

Des virus grippaux B ont également été isolés en Afrique (Afrique du Sud, Égypte et Madagascar), dans les Amériques (Argentine, Canada, Chili, Colombie, États-Unis, Mexique, Pérou et Uruguay), en Asie (Arabie saoudite, Chine; Chine (Province de Taiwan), Hong Kong RAS, Japon, Macao RAS, Malaisie, Philippines, République de Corée, Singapour et Thaïlande), en Europe (Danemark, Fédération de Russie, France, Israël, Italie, Kazakhstan, Norvège, Suède, Royaume-Uni et Turquie) ainsi qu'en Océanie (Australie, Nouvelle-Calédonie et Nouvelle-Zélande).

Virus grippaux A(H5N1) et A(H7N3)

Entre le 1er janvier et le 22 septembre 2004, parmi les 40 patients souffrant de grippe A(H5N1) signalés par la Thaïlande et le Viet Nam, 28 sont décédés.[1] Ces cas ont été associées avec des flambées de grippe aviaire H5N1 hautement pathogène affectant la volaille. A ce jour, il n'existe aucune preuve de transmission inter-humaine.

En mars 2004, en Colombie Britannique (Canada), 2 cas de grippe humaine A(H7N3) ont été associés à des flambées de grippe aviaire A(H7N3) affectant les volailles. Il n'existe aucune preuve de transmission inter-humaine.[2]

[1] Voir http://www.who.int/csr/disease/avian_influenza/country/en/

[2] Voir http://www.who.int/csr/don/2004_04_05/fr/index.html

Antigenic characteristics of recent isolates

Influenza A(H1N1) and A(H1N2) viruses

In haemagglutination-inhibition (HI) tests with postinfection ferret sera, the majority of influenza A(H1) viruses were closely related to A/New Caledonia/20/99.

Influenza A(H3N2) viruses

In HI tests with postinfection ferret sera, influenza A(H3N2) viruses were heterogeneous. While many viruses were closely related to the A/Fujian/411/2002 and A/Wyoming/3/2003 reference viruses, an increasing proportion of recent isolates was distinguishable from A/Wyoming/3/2003 and more closely related to A/Wellington/1/2004 (*Table 1*).

Influenza B viruses

In HI tests with postinfection ferret sera, the majority (84%) of recent influenza B viruses were closely related to the prototype vaccine strain B/Shanghai/361/2002 (B/Yamagata/16/88 lineage), while the remainder were more closely related to B/Hong Kong/330/2001 (B/Victoria/2/87 lineage).

Studies with inactivated influenza virus vaccines

Antibodies to haemagglutinin (HA) were measured by HI tests in panels of selected sera of vaccinees who had received trivalent inactivated vaccines containing the antigens of A/New Caledonia/20/99(H1N1), A/Wyoming/3/2003(H3N2) and B/Jiangsu/10/2003, administered in doses of 15 μg of each HA.

Vaccines containing influenza A/New Caledonia/20/99(H1N1) antigen stimulated postimmunization HA antibodies at titres ≥40 to the influenza A(H1N1) vaccine virus in the sera of 55% of child, 80% of adult and 61% of elderly vaccinees. For representative recent isolates the titres and frequencies of antibodies were similar.

Vaccines containing influenza A/Wyoming/3/2003(H3N2) antigen stimulated postimmunization HA antibodies at titres ≥40 to the vaccine virus in the sera of 95% of adult and 90% of elderly vaccinees. For representative recent isolates, the frequencies of antibodies were somewhat lower: 75% of adult and 73% of elderly vaccinees had HA antibodies at

Caractéristiques antigéniques des isolements récents

Virus grippaux A(H1N1) et A(H1N2)

Les tests d'inhibition de l'hémagglutination (IH) réalisés au moyen de sérums de furet postinfection ont montré que la plupart des virus grippaux A(H1N1) et A(H1N2) étaient très proches de la souche A/New Caledonia/20/99.

Virus grippaux A(H3N2)

Dans les épreuves d'inhibition de l'hémagglutination réalisées au moyen de sérums de furet postinfection, les virus grippaux A(H3N2) se sont révélés hétérogènes. Si de nombreux virus étaient très proches des virus de référence A/Fujian411/2002 et A/Wyoming/3/2003, une proportion croissante d'isolements récents pouvait être distinguée de A/Wyoming/3/2003 et étroitement reliée à la souche A/Wellington/1/2004 (*Tableau 1*).

Virus grippaux B

Les épreuves d'inhibition de l'hémagglutination réalisées au moyen de sérums de furet postinfection ont montré que la plupart des virus grippaux B récents (84%) étaient étroitement apparentés à la souche du vaccin prototype B/Shanghai/361/2002 (lignée B/Yamagata/16/88) alors que ceux restants étaient très proches de la souche B/Hong Kong/330/2001 (lignée B/Victoria/2/87).

Étude des vaccins antigrippaux à virus inactivé

Le titre en anticorps anti-hémagglutinine (HA) a été déterminé par inhibition de l'hémagglutination sur des batteries de sérums sélectionnées provenant de sujets ayant reçu un vaccin trivalent inactivé comportant les antigènes des virus A/New Caledonia/20/99(H1N1), A/Wyoming/3/2003(H3N2) and B/Jiangsu/10/2003 à la dose de 15 μg de chacune des hémagglutinines.

Les vaccins comportant l'antigène du virus grippal A/New Caledonia/20/99(H1N1) ont suscité la formation d'anticorps IH anti-virus vaccinal A(H1N1) de titre ≥40 chez 55% des enfants, 80% des adultes et 61% des personnes âgées. Concernant les isolements récents représentatifs, les fréquences et les titres des anticorps étaient comparables.

Les vaccins comportant l'antigène du virus grippal /Wyoming/3/2003(H3N2) ont suscité la formation d'anticorps IH anti-virus vaccinal de titre ≥40 chez 95% des adultes et 90% des personnes âgées. Concernant les isolements récents représentatifs, les fréquences des anticorps étaient légèrement plus faibles; parmi les vaccinés, 75% des adultes et 73% des personnes âgées avaient un titre en

Table 1 **Results of haemagglutination-inhibition tests of influenza A(H3) viruses with postinfection ferret sera**
Tableau 1 **Résultats des tests d'inhibition de l'hémagglutination réalisés au moyen de sérum de furet postinfection pour les virus grippaux A (H3)**

Antigens	A/Wyoming/3/2003	A/Wellington/1/2004
A/Wyoming/3/2003	**1280**	640
A/Wellington/1/2004	320	**640**
Recent isolates		
A/Thailand/1406/2004	1280	640
A/Paraguay/76/2004	1280	160
A/Sendai/14/2004	640	1280
A/Shantou/1132/2004	320	1280
A/Victoria/505/2004	160	640
A/Kitakyushi/2/2004	160	640
A/Johannesburg/26/2004	160	640
A/Paraguay/226/2004	160	320

titres ≥40. Furthermore, the average geometric mean postimmunization HI titres were 58% lower to A/Wellington/1/2004-like viruses than to the vaccine virus.

Vaccines containing influenza B/Jiangsu/10/2003 (B/Shanghai/361/2002-like) antigen stimulated postimmunization HI antibodies at titres ≥40 to the vaccine virus in the sera of 71% of adult and 76% of elderly vaccinees. For representative recent B/Shanghai/316/2002-like isolates, the frequencies of antibodies were similar, although the postimmunization HI titres to some viruses were lower than to the vaccine virus. For representative recent B/Hong Kong/330/2001-like viruses (B/Victoria/2/87 lineage), the frequencies of antibodies were lower: 27% of adult and 43% of elderly vaccinees had HI titres ≥40. Furthermore, the average geometric mean postimmunization HI titres were 72% lower for adults and the elderly to B/Hong Kong/330/2001-like viruses than to the vaccine virus.

Recommended composition of influenza virus vaccines for use in the 2005 influenza season

During the period February to September 2004, influenza A(H1N1), A(H3N2) and B viruses circulated in many parts of the world.

Influenza A(H1N1) viruses were isolated from sporadic cases in many countries; two countries reported outbreaks. In HI tests, most isolates were antigenically similar to A/New Caledonia/20/99. 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.

Influenza A(H3N2) viruses were associated with outbreaks in many countries. While the majority of isolates were similar to A/Fujian/411/2002, an increasing proportion of recent isolates was distinguishable from the A/Wyoming/3/2003 vaccine virus and more closely related to A/Wellington/1/2004. Current vaccines containing A/Wyoming/3/2003 antigen stimulated HA antibodies that were lower in frequency and titre to A/Wellington/1/2004-like viruses than to the vaccine virus.

Influenza B activity occurred in many countries with only one outbreak being reported. The majority of recent isolates were antigenically similar to B/Shanghai/361/2002. Current vaccines containing influenza B/Shanghai/361/2002-like antigen stimulated postimmunization HI antibodies at titres ≥40 to the vaccine virus in the sera of 71% of adult and 76% of elderly vaccinees.

It is recommended that vaccines to be used in the 2005 season (southern hemisphere winter) contain the following:

— an A/New Caledonia/20/99(H1N1)-like virus;

— an A/Wellington/1/2004(H3N2)-like virus;

— a B/Shanghai/361/2002-like virus[a]

[a] Currently used vaccine viruses include B/Shanghai/361/2002, B/Jilin/20/2003 and B/Jiangsu/10/2003

Il est donc recommandé que les vaccins à utiliser au cours de la saison 2005 (hiver austral) comportent les souches suivantes:

— un virus analogue à A/New Caledonia/20/99(H1N1);

— un virus analogue à A/Wellington/1/2004 (H3N2)[a];

— un virus analogue à B/Shanghai/361/2002.

[a] Parmi les virus vaccinaux actuellement utilisés figurent: B/Shanghai/361/2002, B/Jilin/20/2003 et B/Jiangsu/10/2003

Les vaccins comportant les antigènes des virus B/Jiangsu/10/2003 (analogue au virus B/Shanghai/361/2002) ont suscité la formation d'anticorps IH anti-virus vaccinal de titre ≥40 chez 71% des adultes et 76% des personnes âgées. Concernant les isolements représentatifs récents, analogues à la souche B/Shanghai/361/2002, les fréquences et les titres des anticorps étaient comparables. Concernant les virus récents représentatifs analogues à la souche B/Hong Kong/330/2001 (lignée B/Victoria/2/87), les fréquences étaient plus faibles parmi les vaccinés; 27% des adultes et 43% des personnes âgées avaient un titre IH ≥40. En outre, après vaccination, le titre moyen géométrique des anticorps IH dirigés contre les virus représentatifs apparentés à B/Hong Kong/330/2001 était en moyenne inférieur de 72% chez les adultes et les personnes âgées à celui des anticorps dirigés contre le virus vaccinal.

Recommandations pour la composition des vaccins antigrippaux destiné à la saison de grippe 2005

De février à septembre 2004, les virus grippaux A(H1N1), A(H1N2), A(H3N2) et B ont circulé dans de nombreuses parties du monde.

Les virus A(H1N1) ont été isolés chez des cas sporadiques dans de nombreux pays; seuls deux pays ont signalé une flambée. Les tests IH ont montré que la plupart des isolements appartenant à ce sous-type étaient antigéniquement similaires à la souche A/New Caledonia/20/99. Les vaccins actuels comportant l'antigène A/New Caledonia/20/99 ont suscité la formation d'anticorps anti-HA dirigés contre les isolements récents de virus grippal A(H1N1), d'une fréquence et d'un titre comparables à ceux des anticorps dirigés contre le virus vaccinal.

Les virus grippaux A(H3N2) ont été associés à des flambées dans de nombreux pays. Si la plupart des isolements récents sont comparables au virus A/Fujian/411/2002, une proportion croissante d'isolements récents pouvait être distinguée de A/Wyoming/3/2003 et étroitement reliée à la souche A/Wellington/1/2004. Les vaccins actuels comportant l'antigène du virus grippal A/Wyoming/3/2003 ont suscité la formation d'anticorps anti-HA dirigés contre les virus analogues au virus A/Wellington/1/2004, d'un titre et d'une fréquence inférieurs à ceux des anticorps dirigés contre le virus vaccinal.

Le virus grippal B a été actif dans de nombreux pays mais une seule flambée a été signalée. La plupart des isolements récents étaient antigéniquement comparables à la souche B/Shanghai/361/2002. Les vaccins actuels comportant les antigènes des anticorps IH ≥40. D'autre part, le titre moyen géométrique des anticorps IH dirigés contre les virus analogues au virus A/Wellington/1/2004 après vaccination était en moyenne inférieur de 58% à celui des anticorps dirigés contre le virus vaccinal.

hai/361/2002-like antigen stimulated HA antibodies to recent B/Shanghai/361/2002-like isolates that were of similar titre and frequency to those against the vaccine virus.

As in previous years, the national control authorities should approve the specific vaccine viruses used in each country. National public health authorities are responsible for recommendations regarding the use of the vaccine. WHO has published recommendations on the prevention of influenza.[3]

Most of the population is likely to have been infected with influenza A(H1N1), influenza A(H3N2) and influenza B viruses. As a consequence, 1 dose of inactivated influenza vaccine should be immunogenic for individuals of all ages except young children. Previously unimmunized children should receive 2 doses of inactivated vaccine with an interval between doses of at least 4 weeks.

Reagents for use in the laboratory standardization of inactivated vaccine may be obtained from: Immunology (Vaccines), Therapeutic Goods Administration Laboratories, P.O. Box 100, Woden ACT, 2606 Australia (fax: +61 2 6232 8564, web site http://www.health.gov.au/tga); Division of Virology, National Institute for Biological Standards and Control, Blanche Lane, South Mimms, Potters Bar, Hertfordshire, EN6 3QG, England (fax: +44 1707 646 730, e-mail: enquiries@nibsc.ac.uk, web site http://www.nibsc.ac.cn); or Division of Viral Products, Center for Biologics Evaluation and Research, Food and Drug Administration,1401 Rockville Pike, Rockville, MD 20892, United States (fax: +1 301 402 51 28).

Requests for reference strains for antigenic analysis should be addressed to the WHO Collaborating Centre for Reference and Research on Influenza, 45 Poplar Road, Parkville, Victoria 3052, Australia (fax: +61 3 9389 1881, web site: http://www.influenzacentre.org); the WHO Collaborating Centre for Reference and Research on Influenza, National Institute of Infectious Diseases, Gakuen 4-7-1, Musashi-Murayama, Tokyo 208-0011, Japan (fax: +81 42 5610812 or +81 42 5652498, web site http://www.nih.go.jp/niid/index-e.html); the WHO Collaborating Center for Surveillance, Epidemiology and Control of Influenza, Centers for Disease Control and Prevention, 1600 Clifton Road, Mail stop G16, Atlanta, GA 30333, United States (fax: +1 404 639 23 34, web site: http://www.cdc.gov/flu/); or the WHO Collaborating Centre for Reference and Research on Influenza, National Institute for Medical Research, The Ridgeway, Mill Hill, London NW7 1AA, England (fax: +44 2089 064 477).

Updated epidemiological information is available on WHO's web site at http://www.who.int/influenza. ■

[3] See No. 33, 2003, pp. 290–293.

virus grippaux B/Shanghai/361/2002 ont suscité la formation d'anticorps anti-HA dirigés contre des virus analogues au virus B/Shanghai/361/2002 récemment isolés, d'une fréquence et d'un titre et comparables à ceux des anticorps dirigés conte le virus vaccinal.

Comme les années précédentes, les virus vaccinaux utilisés dans chaque pays devront être approuvés par les autorités nationales de contrôle. Les recommandations relatives à l'usage du vaccin sont du ressort des autorités nationales de santé publique. L'OMS a publié des recommandations sur la prévention de la grippe.[3]

La plus grande partie de la population a probablement été infectée par les virus grippaux A(H1N1), A(H3N2), et B. Par conséquent, une dose unique de vaccin antigrippal inactivé devrait être immuno-gène quel que soit l'âge, sauf chez le jeune enfant. Les enfants qui n'ont pas encore été vaccinés recevront 2 doses de vaccin inactivé, administrées à au moins 4 semaines d'intervalle.

Les réactifs nécessaires à la standardisation au laboratoire du vaccin inactivé peuvent être obtenus auprès des organismes suivants: Immunology (Vaccines), Therapeutic Goods Administration Laboratories, P.O. Box 100, Woden ACT, Australie (télécopie: +61 2 62 32 8564, site Web: http://www.health.gov.au/tga); Division of Virology, National Institute for Biological Standards and Control, Blanche Lane, South Mimms, Potters Bar, Hertfordshire, EN6 3QG, Royaume-Uni (télécopie: +44 17 07 64 6730, e-mail: enquiries@nibsc.ac.uk, site Web: http://nibsc.ac.cn); Division of Viral Products, Center for Biologics Evaluation and Research, Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20892, Etats-Unis (télécopie: +1 301 402 51 28).

Les souches de référence nécessaires à l'analyse antigénique peuvent être obtenues en s'adressant aux Centres collaborateurs OMS de référence et de recherche pour la grippe: WHO Collaborating Centre for Reference and Research on Influenza, 45 Poplar Road, Parkville, Victoria 3052, Australie (télécopie: +61 3 93 89 18 81; site Web: http://www.influenzacentre.org); WHO Collaborating Centre for Reference and Research on Influenza, National Institute of Infectious Diseases, Gakuen 4-7-1, Musashi-Murayama, Tokyo 208-0011, Japon (télécopie: +81 42 5610812 ou +81 42 5652498, site Web: http://www.nih.go.jp/niid/index-e.html); WHO Collaborating Center for Surveillance, Epidemiology and Control of Influenza, Centers for Disease Control and Prevention, 1600 Clifton Road, Mail stop G16, Atlanta, GA 30333, Etats-Unis (télécopie: +1 404 639 23 34), site Web: http://www.cdc.gov.flu); ou WHO Collaborating Centre for Reference and Research on Influenza, National Institute for Medical Research, The Ridgeway, Mill Hill, Londres NW7 1AA, Royaume-Uni (télécopie: +44 208 906 44 77).

Des données épidémiologiques à jour sont consultables sur le site Web de l'OMS: http://www.who.int/influenza. ■

[3] Voir N° 33 2003, pp.290-293.

Human African trypanosomiasis: emergency action in southern Sudan

Background

Human African trypanosomiasis (HAT), also known as sleeping sickness, remains a significant public health problem in sub-Saharan African countries. During the last century, although Sudan suffered a series of successive HAT outbreaks, the disease was nearly eliminated in the 1960s as a result of a systematic diagnosis and treatment programme. Recently, however, there has been a resurgence of the disease

Trypanosomiase humaine africaine: action d'urgence au Soudan méridional

Historique

La trypanosomiase humaine africaine (THA) – ou maladie du sommeil – reste un problème de santé publique significatif dans les pays d'Afrique subsaharienne. Au cours du siècle dernier, plusieurs flambées successives ont touché le Soudan, mais la maladie a pratiquement été éliminée au cours des années 60, suite à un programme systématique de diagnostic et de traitement. Récemment, on a toutefois constaté une résurgence de la maladie à la suite de la guerre

as a result of the civil war, displacement of population and the collapse of the health system.

HAT situation in Sudan

Endemic HAT foci are located in the southern part of the country, along the borders with the Democratic Republic of Congo, the Central African Republic and Uganda.

In 1997, International Medical Care began active case detection, diagnosis and treatment of patients in Tambura and Ezo counties. The programme continued until September 2000 when another nongovernmental organization, CARE International, took over the HAT activities for approximately 1 year. Since mid-2001, there has been no organization supporting HAT activities in Tambura and Ezo counties on a regular basis.

In December 2003, a WHO team conducted an evaluation mission with the objective of assessing the HAT situation as well as the status of the health system in the two counties. Based on the results of the mission, which confirmed the re-emergence of HAT, WHO initiated emergency action to respond to the disease situation, for a period of 6 months.

Objectives of the emergency action

The emergency action started in June 2004, 6 months after the evaluation mission, with the main objective of decreasing the mortality and morbidity caused by HAT in Tambura and Ezo counties. A further objective was to increase the capacity of the health authorities (at the local level and at the central level, the south Sudan health authorities) regarding HAT control.

Three sites were selected for the interventions: Tambura hospital, Source Yubu primary health care (PHC) centre in Tambura county and Ezo PHC centre.

Rehabilitating health centres and establishing drug supply

In order to provide care in an adequate environment, the first task of the WHO-directed international and local team was the rehabilitation of the laboratory in all three facilities and the rehabilitation of the wards in Tambura hospital. In addition to carrying out minors repairs, as well as painting and cleaning, necessary medical equipment was provided for diagnosis and disease staging of all patients in the three sites. Beds, mattresses, bednets and blankets were also procured for the hospital.

HAT drugs are provided by WHO in the framework of an agreement signed in 2001 by WHO and Aventis Pharma, to provide HAT drugs free of charge for Africa. Based on the predicted disease situation in the two counties, the appropriate quantity of drugs required was procured. In addition, general drugs and equipment were provided for supportive treatments and therapies.

All drugs and equipment were procured from Kampala, Uganda. As Kampala is more than 1000 km from the intervention area, this added many logistical problems to the emergency action.

Training of national staff

The field team includes WHO and national staff. The WHO staff consists of 1 team leader (medical doctor), 2 medical assistants, 1 nurse and 1 driver. They will be based in the field throughout the 6-month programme. During June

civile, des déplacements de population et de l'écroulement du système de santé.

La situation au Soudan

Les foyers d'endémie trypanosomienne sont situés dans le sud du pays, le long de la frontière avec l'Ouganda, la République centrafricaine et la République démocratique du Congo.

En 1997, *International Medical Care* a entrepris des activités de dépistage actif, de diagnostic et de traitement dans les comtés de Tambura et d'Ezo. Le programme s'est poursuivi jusqu'en septembre 2000 et une autre organisation non gouvernementale, CARE International a ensuite pris le relais pendant une année environ. Depuis mi-2001, aucune organisation n'appuie de façon régulière les activités de lutte antitrypanosomienne dans les comtés de Tambura et d'Ezo.

En décembre 2003, une équipe de l'OMS a entrepris une mission d'évaluation visant à faire le point de la situation et à vérifier l'état du système de santé dans les deux comtés. Sur la base des résultats de la mission, qui ont confirmé la réapparition de la trypanosomiase, l'OMS a pris des mesures d'urgence pour répondre à la situation pendant une période de 6 mois.

Objectifs du plan d'urgence

Les mesures d'urgence ont commencé en juin 2004, 6 mois après la mission d'évaluation avec pour principal objectif de réduire la mortalité et la morbidité trypanosomiennes dans les comtés de Tambura et d'Ezo. Un autre objectif consistait à accroître la capacité des autorités sanitaires (au niveau local et au niveau central, les autorités sanitaires du Soudan méridional) concernant la lutte antitrypanosomienne.

Trois sites ont été retenus pour les interventions: l'hôpital de Tambura, le centre de soins de santé primaires de Source Yubu (comté de Tambura) et le centre de soins de santé primaires d'Ezo.

Remise en état des centres de santé et mise en place de l'approvisionnement en médicaments

Pour apporter des soins dans un environnement satisfaisant, il s'agissait d'abord pour l'équipe, tant internationale que locale, dirigée par l'OMS d'assurer la remise en état du laboratoire dans les trois installations ainsi que celle des salles de l'hôpital de Tambura. Il a fallu procéder à des réparations mineures, ainsi qu'à des travaux de peinture et de nettoyage, et le matériel médical nécessaire a été fourni pour le diagnostic et la détermination du stade de la maladie chez tous les patients dans les trois sites. Des lits, des matelas, des moustiquaires et des couvertures ont également été achetés pour l'hôpital.

Dans le cadre d'un accord signé en 2001 par l'OMS et Aventis Pharma, les antitrypanosomiens doivent être fournis gratuitement en Afrique par l'OMS. Sur la base des prévisions concernant la maladie dans les deux comtés, les quantités voulues de médicaments ont été achetées. En outre, des fournitures et des médicaments généraux ont été fournis pour les traitements d'appoint.

L'ensemble des médicaments et du matériel ont été achetés à Kampala en Ouganda. Kampala étant situé à plus de 1000 km de la zone d'intervention, de nombreux problèmes logistiques ont dû être surmontés.

Formation de personnel national

L'équipe de terrain est composée de personnel de l'OMS et de personnel national. Elle est constituée d'un chef d'équipe (médecin), de 2 assistants médicaux, d'un(e) infirmier(ère) et d'un chauffeur et sera basée sur le terrain pendant les 6 mois du programme. En juin

2004, 1 laboratory technician and 1 logistician were also on site to facilitate the implementation of the programme.

A total of 52 national (local) staff, who were already working at the three sites, have been recruited to run the programme: 5 medical assistants, 17 nurses and nurse-assistants, 8 laboratory technicians and laboratory assistants, 1 pharmacist, 1 cold-chain technician, 1 registration clerk, 1 food monitor and 18 non-medical staff (cleaners, watchman, etc.).

A refresher training session was organized at the beginning of the emergency action. The first objective of the training was to provide the national staff with the skills required for routine laboratory diagnosis, staging tools and techniques, and patient follow-up methods. The second objective was to train the health-care providers in the appropriate treatment modalities for all patients. Data collection, record keeping and dissemination of data for monthly and final reports were also discussed and methodologies decided.

Treatment of patients

At Tambura hospital, all persons suspected of having HAT are serologically screened, diagnosed and staged, and the appropriate treatment for stage one and stage two of the disease is provided.

At the Ezo and Source Yubu facilities, only diagnosis, staging and treatment of stage 1 of the disease is provided. All patients with stage 2 of the disease are transferred to Tambura hospital. One car was procured by WHO for the transport of patients between the health facilities.

Currently, only diagnosis of the disease is carried out in the three facilities: systematic screening of the population cannot be done for the time being.

Control, treatment and follow-up activities

As at the end of August 2004, the team screened about 5550 people and found 134 cases. Of these, 86 were in stage 1 and 39 in stage 2 of the disease. The number of relapses was 9. In the three sites, 92 patients undergoing treatment were regarded as "old" HAT cases.

Agreements within WHO and with other organizations

An agreement was established between WHO and the Sudanese authorities, including the south Sudan health autorities and the appropriate county authorities in Tambura and Ezo counties, to facilitate capacity building of national staff, to promote sustainability of the programme.

Other neglected diseases programmes of WHO's Communicable Disease Control, Prevention and Eradication department have supported the HAT action thus building an integrated action. The neglected diseases include leprosy, Buruli ulcer, schistosomiasis and intestinal parasites, lymphatic filariasis and guinea-worm disease. The WHO Complex Emergencies team also helped with the training of national staff.

As part of the integrated action, other drugs, medical material and training and advocacy documents were sent to Tambura hospital. After national staff have been trained in these neglected diseases, decisions will be made for each disease on the appropriate or additional action to be taken in Tambura and Ezo counties.

2004, un technicien de laboratoire et un logisticien étaient également sur place pour faciliter la mise en œuvre du programme.

Au total, 52 membres du personnel national (local), qui travaillaient déjà sur les trois sites, ont été recrutés pour gérer le programme: 5 assistants médicaux, 17 infirmiers(ères) et assistants(es) infirmiers(ères), 8 techniciens de laboratoire et assistants de laboratoire, 1 pharmacien, 1 technicien de la chaîne du froid, 1 commis, 1 chargé de restauration et 18 agents non médicaux (chargés de tâches comme le nettoyage, le gardiennage, etc.).

Une séance de recyclage a été organisée au début de l'intervention d'urgence. Le premier objectif de la formation était de doter le personnel national des compétences requises pour procéder au diagnostic de routine en laboratoire, d'outils et de techniques pour la détermination des stades de la maladie et de méthodes de suivi des patients. Le deuxième objectif était de former les dispensateurs de soins de santé aux modalités de traitement appropriées pour tous les patients. La collecte des données, la tenue des dossiers et la diffusion des données destinées aux rapports mensuels et au rapport final ont également été évoquées et des méthodologies arrêtées.

Traitement des patients

A l'hôpital de Tambura, toutes les personnes présumées atteintes de THA font l'objet d'un dépistage sérologique, d'un diagnostic et d'une détermination du stade de la maladie et reçoivent un traitement approprié pour la phase un ou la phase deux de la maladie.

Dans les centres de Ezo et Source Yubu, seuls sont assurés le diagnostic, la détermination du stade et le traitement du stade 1 de la maladie. Tous les malades au stade 2 sont transférés à l'hôpital de Tambura. L'OMS a acheté une voiture pour le transport des patients entre les centres de santé.

Actuellement, seul le diagnostic de la maladie est organisé dans les trois établissements: le dépistage systématique de la population ne peut avoir lieu pour l'intant.

Activités de lutte, traitement et suivi

Fin août 2004, l'équipe avait examiné près de 5550 personnes et dépisté 134 cas. Là dessus, 86 malades étaient au stade 1 et 39 au stade 2 de la maladie. Les rechutes étaient au nombre de 9. Dans les trois sites, 92 malades en traitement étaient considérés comme des cas «anciens» de maladie du sommeil.

Accords au sein de l'OMS et avec d'autres organisations

Un accord a été conclu entre l'OMS et les autorités soudanaises, y compris les autorités sanitaires du Soudan méridional et les autorités compétentes des comtés de Tambura et Ezo pour faciliter le développement du potentiel du personnel national, afin de permettre une pérennisation du programme.

D'autres programmes du Département Maladies transmissibles, prévention, lutte et éradication, dirigés contre des maladies négligées, ont soutenu l'action maladie du sommeil, ce qui a permis de mettre sur pied une action intégrée. Parmi ces maladies négligées figurent la lèpre, l'ulcère de Buruli, la schistosomiase et les parasitoses intestinales, la filariose lymphatique et la dracunculose. L'équipe OMS chargée des situations d'urgence complexes a également contribué à la formation du personnel national.

Dans le cadre de l'action intégrée, des médicaments, du matériel médical, ainsi que des matériels de formation et de sensibilisation ont été envoyés à l'hôpital de Tambura. Une fois que le personnel national aura été formé à la prise en charge de ces maladies négligées, des décisions seront prises quant aux mesures supplémentaires éventuelles à appliquer pour chaque maladie dans les comtés de Tambura et d'Ezo.

WHO requested the collaboration of other United Nations organizations, such as UNICEF and the World Food Programme (WFP), as well as that of nongovernmental organizations. The WFP was requested to provide food for inpatients (stage-2 patients) throughout the 6-month programme and UNICEF was asked to provide nutritional support for outpatients (stage-1 patients). UNICEF also was requested to provide the necessary cold-chain equipment and a technician for the programme.

Handover of the project

The emergency action is scheduled to end at the beginning of December 2004. A major concern of WHO and the health authorities is the handover of the project after the 6-month period. WHO and the south Sudan health authorities have made efforts to involve other partners working on HAT control. After negotiations, it is likely that Médecins Sans Frontières-Spain will assume responsibility for the project, starting in December 2004. A final decision on this will be taken shortly. ■

L'OMS a demandé la collaboration d'autres organisations des Nations Unies, telles que l'UNICEF et le Programme alimentaire mondial (PAM), ainsi que celle d'organisations non gouvernementales. Le PAM a été invité à fournir des denrées alimentaires pour les patients hospitalisés (malades de stade 2) pendant la durée du programme de 6 mois, et l'UNICEF a été invité à fournir un soutien nutritionnel aux patients ambulatoires (malades de stade 1). L'UNICEF a également été prié de fournir le matériel de chaîne du froid nécessaire ainsi qu'un technicien pour le programme.

Reprise du projet

L'action d'urgence doit prendre fin début décembre 2004. L'une des principales préoccupations de l'OMS et des autorités sanitaires concerne la reprise du projet au terme de la période de 6 mois. L'OMS et les autorités sanitaires du Soudan méridional se sont efforcées de mobiliser d'autres partenaires pour lutter contre la trypanosomiase. Après négociations, il est vraisemblable que Médecins Sans Frontières – Espagne assumera la responsabilité du projet, à partir de décembre 2004. Une décision finale sur ce point sera prise prochainement. ■

Influenza

Except in Canada, where an increasing influenza activity was reported, activity remained low in most parts of the world in weeks 36–39.

Australia.[1] Influenza activity remained low since week 36; only one localized outbreak was reported during week 37.

Canada.[1] An increasing influenza activity was noted in eastern Ontario. Four outbreaks associated with influenza A/Fujian/411/2002(H3N2) virus were reported in long-term care facilities during weeks 36–39.

Hong Kong Special Administrative Region of China.[1] Influenza activity remained moderate during weeks 36–39. There was an increase in the number of influenza B viruses detected, although the majority of the viruses isolated were influenza A(H3N2).

Thailand.[1] During weeks 36–39, influenza A(H1), A(H3N2) and B viruses co-circulated at low levels.

Other reports. During weeks 36–39, low influenza activity mainly caused by A(H3N2) viruses was reported from Argentina,[1] Chile,[1] Japan, Madagascar,[1] New Caledonia,[1] Norway,[2] Peru,[3] Thailand and Uruguay.[1]

[1] See No. 37, 2004, pp. 339–340.

[2] See No. 24, 2004, p. 228.

[3] See No. 30, 2004, p. 279.

Grippe

L'activité grippale est restée faible pratiquement partout dans le monde au cours des semaines 36-39, sauf au Canada, où l'on a signalé une activité grippale croissante.

Australie.[1] L'activité grippale est restée faible depuis la semaine 36; seule une flambée localisée a été signalée pendant la semaine 37.

Canada.[1] On a enregistré une activité grippale croissante dans l'est de l'Ontario. Quatre flambées associées au virus grippal A/Fujian/411/2002(H3N2) ont été signalées dans des établissements médicaux pour longs séjours au cours des semaines 36-39.

Hong Kong, Région administrative spéciale de la China.[1] L'activité grippale est restée modérée au cours des semaines 36-39. Le nombre des virus grippaux B dépistés a augmenté bien que la plupart des virus isolés soient de type A(H3N2).

Thaïlande.[1] Des virus grippaux de type A(H1), A(H3N2) et B ont co-circulé à faible niveau pendant les semaines 36-39.

Autres rapports.. Au cours des semaines 36-39, seule une faible activité grippale essentiellement due au virus A(H3N2) a été signalé par l'Argentine,[1] le Chili,[1] le Japon, Madagascar,[1] la Norvège,[2] la Nouvelle-Calédonie,[1] le Pérou,[3] la Thaïlande et l'Uruguay.[1]

[1] Voir N° 37, 2004, pp. 339-340.

[2] Voir N° 24, 2004, p. 228.

[3] Voir N° 30, 2004, p. 279.

CORRIGENDUM, TO No. 40, 2004 / RECTIFICATIF AU N° 40, 2004

Please read as follows (changes shown in ***bold italics***), under Philippines, table 4, p. 364.

Prière de lire comme suit (changements indiqués en ***gras italique***), sous Philippes, tableau 4, p. 364.

Table 4 (continued) – Tableau 4 (suite)

		Kyauktan	2001	4.4	445	3	64.7	98.4	93.8	–	4.0	257	9.1
Philippines	Nauhan	Naujan[1]	***2000***	***12.6***	ND	4	92.8	95.0	98.0	97.0	0	ND	100.0

INTERNATIONAL HEALTH REGULATIONS / RÈGLEMENT SANITAIRE INTERNATIONAL

Notifications of diseases received from 1 to 7 October 2004 / Notifications de maladies reçues du 1 au 7 octobre 2004

Cholera / Choléra

	Cases / Deaths Cas / Décès
Africa / Afrique	
Guinea / Guinée	6-26.IX
.....	193 9