Recommended composition of influenza virus vaccines for use in the 2006 influenza season

This recommendation relates to the composition of vaccines for the forthcoming winter in the southern hemisphere (May–October 2006). A recommendation will be made in February 2006 which relates to vaccines that will be used for the winter in the northern hemisphere (November 2006–April 2007). Epidemiological considerations will influence which recommendation (September 2005 or February 2006) is more appropriate for countries in equatorial regions.

Influenza activity February–September 2005

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

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

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

Influenza A(H1)

Outbreaks caused by influenza A(H1N1) viruses were reported in Africa (South Africa), Asia (Oman) and Europe (Bulgaria, Greece and Russian Federation).

Influenza A(H1N1) viruses were also isolated in Africa (Algeria and Tunisia), the Americas (Mexico, Paraguay, Peru and the United States), Asia (Hong Kong SAR China, Indonesia, Japan, Macau SAR China, Malaysia, the Republic of Korea, Saudi Arabia, Taiwan Province of China, Thailand and Turkey), Europe (Austria, Belgium, Croatia, Czech Republic, Denmark, Finland, France, Germany, Iran, Israel, Italy, Latvia, Norway, Poland, Portugal, Romania, Serbia and Montenegro, Slovakia, Slovenia, Sweden, Switzerland, Turkey, Ukraine and the United Kingdom) and Oceania (Australia).

Over recent influenza seasons the prevalence of influenza A(H1N2) viruses has declined. Only a single influenza A(H1N2) virus was reported, from Switzerland, in 2005.

Influenza A(H3N2)

Between February and September, outbreaks caused by influenza A(H3N2) viruses were reported in Africa (Egypt), the Americas (Argentina, Canada, Chile, Panama and the United States), Asia (Hong Kong SAR China, Japan and the Republic of Korea), Europe (Belarus, Belgium, Denmark,

Finland, France, Germany, Iceland, Italy, Latvia, Norway, Poland, Portugal, Romania, Russian Federation, Sweden, Switzerland and Ukraine) and Oceania (Australia).

Influenza A(H3N2) viruses were also isolated in Africa (Algeria, Madagascar, Reunion, South Africa and Tunisia), the Americas (Brazil, El Salvador, Guyana, Martinique, Mexico, Peru and Venezuela), Asia (Macau SAR China, Indonesia, Malaysia, Philippines, Saudi Arabia, Singapore, Taiwan Province of China, Thailand and Vietnam), Europe (Austria, Bulgaria, Czech Republic, Greece, Iran, Iraq, Ireland, Israel, Kyrgyzstan, Serbia and Montenegro, Slovakia, Slovenia, Spain and the United Kingdom) and Oceania (Guam and New Zealand).

Influenza B

Between February and September, outbreaks due to influenza B viruses were reported in Africa (Egypt), the Americas (Argentina and Brazil), Asia (Japan, Oman and Taiwan Province of China), Europe (Belarus, Latvia, Norway, Russian Federation, Slovenia and Ukraine) and Oceania (New Zealand).

Influenza B viruses were also isolated in Africa (Algeria, Madagascar, Morocco, Reunion, Senegal and South Africa), the Americas (Canada, Chile, Colombia, Guyana, Mexico, Paraguay, Peru, the United States and Uruguay), Asia (Hong Kong SAR China, India, Indonesia, Macau SAR China, Malaysia, Nepal, Philippines, the Republic of Korea, Saudi Arabia, Singapore and Thailand), Europe (Albania, Belgium, Croatia, Czech Republic, Denmark, Finland, France, Germany, Greece, Iceland, Iran, Ireland, Israel, Italy, Poland, Portugal, Romania, Serbia and Montenegro, Slovakia, Spain, Sweden, Switzerland, Turkey and the United Kingdom) and Oceania (Australia and New Caledonia).

Influenza A(H5N1)

Between 16 December 2004 and 14 September 2005, 68 patients with influenza A(H5N1), of whom 25 died, were reported from Cambodia, Indonesia and Vietnam (http://www.who.int/csr/disease/avian_influenza/updates/en/). These cases were associated with outbreaks of highly pathogenic avian influenza A(H5N1) in poultry. So far there has been no evidence of sustained human-to-human transmission and the WHO influenza pandemic preparedness level remains as Phase 3 (http://www.who.int/csr/resources/publications/influenza/WHO_CDS_CSR_GIP_2005_5/en/index.html).

Antigenic characteristics of recent isolates

Influenza A(H1N1) viruses

In haemagglutination-inhibition (HI) tests with postinfection ferret sera, the majority of influenza A(H1N1) viruses were closely related to A/New Caledonia/20/99.

Influenza A(H3N2) viruses

In HI tests with postinfection ferret sera, the majority of influenza A(H3N2) viruses were closely related to A/California/7/2004. A small proportion of isolates was distinguishable from A/California/7/2004; however, antigenic and genetic analyses did not reveal the emergence of a clearly definable antigenic variant.

Influenza B viruses

Overall the numbers of B/Victoria/2/87 lineage viruses and B/Yamagata/16/88 lineage viruses were similar; however, the relative proportions of viruses of the two lineages varied in different countries. In recent months, an increasing proportion of influenza B isolates were of the B/Victoria/2/87 lineage.

In HI tests with postinfection ferret antisera, viruses of the B/Yamagata/16/88 lineage were closely related to the prototype vaccine strain B/Shanghai/361/2002. Most B/Victoria/2/87 lineage viruses were distinguishable from the prototype vaccine strain B/Hong Kong/330/2001 and the vaccine virus B/Brisbane/32/2002 and were closely related to B/Malaysia/2506/2004 (see Table 1).

Table 1 **Results of haemagglutination-inhibition tests of influenza B viruses with postinfection ferret sera**

	B/HK/330/2001[1]	B/Brisbane/32/2002[1]	B/Malaysia/2506/2004[1]	B/Shanghai/361/2002[2]
Antigens				
B/Hong Kong/330/2001	**320**	160	160	<20
B/Brisbane/32/2002	320	**640**	640	<20
B/Malaysia/2506/2004	160	160	**640**	<20
B/Shanghai/361/2002	<20	40	20	**1280**
Recent isolates				
B/Waikato/14/2005	<20	40	320	<20
B/Philippines/371/2005	<20	40	320	<20
B/Johannesburg/501/2005	20	40	320	<20
B/South Australia/16/2005	40	40	320	<20
B/Malaysia/634/2005	80	160	640	<20
B/Singapore/1/2005	<20	80	320	<20
B/Macau/231/2005	<20	80	320	<20
B/New Caledonia/1/2005	<20	<20	<20	640
B/Auckland/103/2005	<20	<20	<20	640

[1] B/Victoria/2/87 lineage
[2] B/Yamagata/16/88 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/New York/55/2004(H3N2) and either B/Shanghai/361/2002 or 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 $\geq$40 to the influenza A(H1N1) vaccine virus in the sera of 37% of child, 68% of adult and 52% of elderly vaccinees. In adult and elderly vaccinees, the postimmunization average geometric mean HA titres (GMT) and proportions of titres $\geq$40 to recent isolates were similar. For children, however, the average GMT was 88% lower, and only 5% of children developed titres $\geq$40.

Vaccines containing influenza A/New York/55/2004(H3N2) antigen stimulated postimmunization HA antibodies at titres ≥40 to the vaccine virus in the sera of 96% of adult and 67% of elderly vaccinees. In adult and elderly vaccinees, the postimmunization average GMT and proportions of titres ≥40 to recent isolates were similar.

Vaccines containing influenza B/Shanghai/361/2002-like antigens stimulated postimmunization HA antibodies at titres ≥40 to the vaccine virus in the sera of 13% of child, 96% of adult and 67% of elderly vaccinees. For representative recent B/Shanghai/361/2002-like (B/Yamagata/16/88 lineage) viruses, the proportions of titres ≥40 were similar. For representative recent B/Malaysia/2506/2004-like viruses (B/Victoria/2/87 lineage), the proportions of titres ≥40 were lower: 0% of child, 47% of adult and 36% of elderly vaccinees. Furthermore, the average postimmunization GMT to recent B/Malaysia/2506/2004-like viruses was 55% lower for children, 58% lower for adults and 52% lower for the elderly than to the vaccine virus.

Recommended composition of influenza virus vaccines for use in the 2006 influenza season

During the period February to September 2005, influenza A(H1N1), A(H3N2) and B viruses circulated in many parts of the world.

Influenza A(H1N1) viruses were associated with outbreaks in several countries. 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 widespread outbreaks in several countries. The majority of recent isolates were antigenically similar to A/California/7/2004. Current vaccines containing A/New York/55/2004(H3N2) antigen stimulated HA antibodies against recent influenza A(H3N2) isolates, which were of similar titre and frequency to those against the vaccine virus.

Influenza B viruses circulated widely and caused outbreaks in several countries, including an epidemic in New Zealand. Viruses of both B/Yamagata/16/88- and B/Victoria/2/87- lineages were prevalent in many countries but occurred in different proportions. Whereas many isolates were antigenically similar to B/Shanghai/361/2002 (B/Yamagata/16/88 lineage), an increasing proportion of B/Victoria/2/87-lineage viruses was identified in many countries. The majority of recent isolates were antigenically similar to B/Malaysia/2506/2004 (B/Victoria/2/87 lineage). Current vaccines containing B/Shanghai/361/2002-like antigens (B/Yamagata/16/88 lineage) stimulated HA antibodies that were lower in frequency and titre to B/Malaysia/2506/2004-like viruses than to the vaccine virus.

It is recommended that vaccines to be used in the 2006 season (southern hemisphere winter) contain the following:
— an A/New Caledonia/20/99(H1N1)-like virus;
— an A/California/7/2004(H3N2)-like virus[a];
— a B/Malaysia/2506/2004-like virus

[a] The currently used vaccine virus is A/New York/55/2004

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.uk); 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 5128).

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 42 561 0812 or +81 42 565 2498, 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 2334, 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.