Recommended composition of influenza virus vaccines for use in the 2006–2007 influenza season

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

Influenza activity October 2005–January 2006

Between October 2005 and January 2006, influenza was reported in Africa, the Americas, Asia, Europe and Oceania. In general, influenza activity was low compared with the same period in recent years.[1] In North America and Asia, influenza activity began in October and increased in December in some countries, while in Europe, activity remained low throughout the period.

Influenza A(H1) viruses circulated at a low level and were responsible for one outbreak in Africa.

Influenza A(H3N2) viruses predominated in North America and Asia and caused outbreaks.

Influenza B viruses circulated at low levels in many countries; they were the predominant viruses in some European countries.

Influenza A(H1)

Between October 2005 and January 2006, an influenza A(H1) outbreak was reported in Africa (Tunisia).

Influenza A(H1N1) viruses and A(H1) viruses, for which the neuraminidase subtype was not identified, were also isolated in Africa (Egypt and Madagascar), the Americas (Brazil, Mexico and the United States), Asia (China, Hong Kong Special Administrative Region of China (Hong Kong SAR), Japan, Kuwait, Mongolia, Republic of Korea, Qatar, Taiwan Province of China and Thailand), Europe (France, Germany, Iran, Israel, Norway, Portugal, Russian Federation, Sweden, Switzerland, Turkey and the United Kingdom) and Oceania (Australia and New Zealand). No influenza A(H1N2) viruses were reported.

Influenza A(H3N2)

Between October 2005 and January 2006, outbreaks caused by influenza A(H3N2) viruses were reported in the Americas (Canada and the United States), and Asia (Japan).

Influenza A(H3N2) viruses were also isolated in Africa (Madagascar, South Africa and Tunisia), the Americas (Argentina, Brazil and Mexico), Asia (China, Hong Kong SAR, Kuwait, Malaysia, Mongolia, Republic of Korea, Taiwan Province of China and Thailand), Europe (Denmark, Finland, France, Greece, Iceland, Ireland, Israel, Italy, Latvia, Norway, Russian Federation, Slovenia, Sweden, Turkey and the United Kingdom) and Oceania (Australia, New Caledonia and New Zealand).

Influenza B

[1] http://www.who.int/wer/en/

Outbreaks caused by influenza B viruses were not reported between October 2005 and January 2006.

Influenza B viruses were isolated in Africa (Madagascar, Morocco, South Africa and Tunisia), the Americas (Argentina, Brazil, Canada, Chile, Colombia, Honduras, Mexico, Peru and the United States), Asia (Hong Kong SAR, Japan, Kuwait, Philippines and Thailand), Europe (Belarus, Denmark, France, Greece, Iran, Israel, Latvia, Norway, Portugal, Russian Federation, Slovenia, Sweden, Switzerland, Turkey and the United Kingdom) and Oceania (Australia and New Zealand).

Influenza A(H5N1)

Between October 2005 and 13 February 2006, 49 human cases of influenza A(H5N1) were associated with outbreaks of highly pathogenic avian influenza A(H5N1) in poultry in China, Indonesia, Iraq, Thailand and Turkey. Since December 2003, a total of 165 human cases have been confirmed from 7 countries (http://www.who.int/csr/disease/avian_influenza/country/en/). The WHO influenza pandemic preparedness level remains unchanged at Phase 3 (http://www.who.int/csr/disease/avian_influenza/phase/en/index.html). So far there has been no evidence of sustained human-to-human transmission.

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. Although a genetic variant emerged during 2004 and has become more prevalent in recent months, viruses in this genetic group were antigenically indistinguishable from A/New Caledonia/20/99-like viruses.

Influenza A(H3N2) viruses
In HI tests with postinfection ferret sera, many influenza A(H3N2) viruses were closely related to the reference virus, A/California/7/2004. However, an increasing proportion were antigenically more closely related to A/Wisconsin/67/2005 (Table 1).

Table 1 **Results of haemagglutination-inhibition tests of influenza A(H3N2) viruses with postinfection ferret sera**

Antigens	A/California/7/2004	A/New York/55/2004	A/Wisconsin/67/2005
A/California/7/2004	**1280**	320	640
A/New York/55/2004	640	**320**	640
A/Wisconsin/67/2005	320	160	**1280**
Recent isolates			
A/Anhui/544/2005	640	320	320
A/Georgia/1/2005	640	160	640
A/Ishikawa/1/2006	640	320	320
A/Ulan Bator/1806/2005	160	80	640
A/Guam/963/2005	160	80	640
A/Taiwan/567/2005	320	160	1280
A/Mexico/2014/2005	320	160	1280
A/Oregon/14/2005	320	160	1280
A/Hiroshima/52/2005	320	160	1280

Influenza B viruses

Influenza B viruses of both the B/Victoria/2/87 and B/Yamagata/16/88 lineages continued to circulate. While the relative proportions of viruses of the two lineages varied in different countries over time, in recent months viruses of the B/Victoria/2/87 lineage have predominated.

In HI tests with postinfection ferret antisera, viruses of the B/Victoria/2/87 lineage were closely related to the vaccine virus B/Malaysia/2506/2004. Many of the B/Yamagata/16/88 lineage viruses were distinguishable from the vaccine viruses B/Shanghai/361/2002 and B/Jiangsu/10/2003 and were more closely related to reference viruses such as B/Florida/7/2004 and B/Egypt/144/2005.

Studies with inactivated influenza virus vaccines

Antibodies to haemagglutinin (HA) were measured by HI tests in panels of sera from people 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 mcg of each HA. Cross-reactions of postimmunization antibody to recent isolates were examined in 5 panels of sera 3 of which were selected for postimmunization antibody ›40 to the vaccine virus.

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 children, 75% of adults and 62% of elderly people who had been vaccinated. In children, adults, and elderly people, the postimmunization average geometric mean HI titres and proportions of titres ›40 to recent isolates were similar.

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 86% of children, 79% of adults and 77% of elderly people who had been vaccinated. In adults and elderly people, the postimmunization average geometric mean HI titres and proportions of titres ›40 to recent isolates were similar, but in children only 55% had titres ›40 to recent isolates. Furthermore, the average postimmunization geometric mean HI titre to recent A/Wisconsin/67/2005-like viruses was 55% lower for children, 42% lower for adults and 43% lower for elderly people than to the vaccine virus.

Vaccines containing influenza B/Shanghai/361/2002-like antigens stimulated postimmunization HA antibodies at titres ›40 to the vaccine virus in the sera of 56% of children, 74% of adults and 73% of elderly people who had been vaccinated. In adults and elderly people, the proportions with titres ›40 were similar for representative recent B/Shanghai/361/2002-like (B/Yamagata/16/88 lineage) viruses, but in children only 36% had titres ›40 to recent B/Shanghai/361/2002-like isolates. For representative recent B/Malaysia/2506/2004-like viruses (B/Victoria/2/87 lineage), the proportions with titres ›40 were lower: 4% of children, 39% of adults and 44% of elderly people who had been vaccinated. Furthermore, the average postimmunization geometric mean HI titre to recent B/Malaysia/2506/2004-like viruses was 85% lower for children, 64% lower for adults and 49% lower for elderly people than to the vaccine virus.

Recommended composition of influenza virus vaccines for use in the 2006–2007 influenza season

During the period October 2005 to January 2006, 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; only one country reported an outbreak. In HI tests, most isolates were antigenically similar to A/New Caledonia/20/99. Influenza A(H1N2)

viruses were not reported. Current vaccines containing A/New Caledonia/20/99 antigens stimulated HA antibodies that were similar in titre to recent influenza A(H1N1) viruses and to the vaccine virus.

Influenza A(H3N2) viruses were associated with outbreaks in several countries. Many recent isolates were antigenically similar to the current reference virus, A/California/7/2004, but an increasing proportion of recent viruses was more closely related to A/Wisconsin/67/2005. Current vaccines containing A/New York/55/2004 antigens stimulated HA antibodies that were lower in titre to A/Wisconsin/67/2005-like viruses than to the vaccine virus.

No outbreaks of influenza B were reported, although low levels of activity were reported in many countries. The majority of recent isolates were antigenically similar to B/Malaysia/2506/2004. Vaccines containing influenza B/Shanghai/361/2002-like antigens stimulated HA antibodies that were similar in titre to recent B/Shanghai/361/2002-like viruses but were lower in titre to recent B/Malaysia/2506/2004-like viruses.

It is recommended that vaccines to be used in the 2006-7 season (northern hemisphere winter) contain the following:
— an A/New Caledonia/20/99(H1N1)-like virus;
— an A/Wisconsin/67/2005 (H3N2)-like virus[a];
— a B/Malaysia/2506/2004-like virus[b]

Candidate vaccine viruses include:
[a] A/Wisconsin/67/2005 (H3N2) and A/Hiroshima/52/2005
[b] B/Malaysia/2506/2004 virus and B/Ohio/1/2005

As in previous years, national control authorities should approve the specific vaccine viruses used in each country. National public health authorities are responsible for making recommendations regarding the use of the vaccine.

WHO has published recommendations on the prevention of influenza.[2] 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.tga.gov.au); Division of Virology, National Institute for Biological Standards and Control, Blanche Lane, South Mimms, Potters Bar, Hertfordshire, EN6 3QG, England (fax: +44 1707 641050, 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/indexe.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 .

[2] See No. 33, 2003, pp. 290–293.