Recommended composition of influenza virus vaccines for use in the 2007–2008 influenza season

This recommendation relates to the composition of vaccines for the forthcoming influenza season in the northern hemisphere (November 2007 to April 2008). A recommendation will be made in September 2007 relating to vaccines that will be used for the influenza season in the southern hemisphere (May to October 2008). For countries in equatorial regions epidemiological considerations will influence which recommendation (February or September) individual National Authorities consider more appropriate.

Influenza activity, September 2006–January 2007

Between September 2006 and January 2007, influenza activity was reported in Africa, the Americas, Asia, Europe and Oceania. In general, activity was low compared with the same period in recent years[1]. In the southern hemisphere, mild influenza activity continued in September and declined in October, except in Madagascar, where an influenza A(H3N2) outbreak was reported in October. In the northern hemisphere, influenza activity began in November, which was late when compared with previous years. Influenza activity increased in December in North America and also in January in Europe.

Influenza A(H1N1) viruses circulated sporadically in South America, predominated in the United States of America and were associated with outbreaks. Influenza A(H3N2) viruses predominated in Canada and Europe and were associated with outbreaks in some countries. In most countries influenza B viruses circulated at low levels throughout the period.

Influenza A(H1N1)

Between September 2006 and January 2007, an influenza A(H1N1) outbreak was reported in the Americas (the United States).

Influenza A(H1N1) viruses and A(H1) viruses, for which the neuraminidase subtype was not identified, were also isolated in Africa (Madagascar, Morocco and Tunisia), the Americas (Argentina, Brazil, Canada, Chile, Costa Rica and Mexico), Asia (China; China, Hong Kong Special Administrative Region (Hong Kong SAR); China (Province of Taiwan); Islamic Republic of Iran; Japan; Malaysia; Mongolia; Thailand and Viet Nam), Europe (Belgium, Bulgaria, Croatia, France, Germany, Ireland, Italy, Netherlands, Norway, Russian Federation, Serbia, Slovenia, Sweden, Switzerland and the United Kingdom of Great Britain and Northern Ireland) and Oceania (New Zealand). No influenza A(H1N2) viruses were reported.

Influenza A(H3N2)

Between September 2006 and January 2007, outbreaks caused by influenza A(H3N2) viruses were reported in Africa (Madagascar), the Americas (Canada) and Europe (Czech Republic, Greece, Israel, Luxemburg, Norway and Sweden).

Influenza A(H3N2) viruses were also isolated in Africa (Algeria, Egypt, Kenya, Morocco, Senegal and Tunisia), the Americas (Argentina, Brazil, Chile, Costa Rica, El Salvador, Guyana, Honduras, Mexico and the United States), Asia (Bangladesh; China; China, Hong Kong SAR; China (Province of Taiwan); Islamic Republic of Iran; Japan; Malaysia; Philippines; Republic of Korea; Singapore; Sri Lanka and Thailand), Europe (Belgium, Bulgaria, Croatia, Denmark, Finland, France, Germany, Ireland, Italy, Latvia, Netherlands, Portugal, Romania, Russian Federation, Serbia, Slovakia, Slovenia, Spain, Switzerland and the United Kingdom) and Oceania (Australia, Cook Islands, Fiji, New Caledonia and New Zealand).

Influenza B

Outbreaks caused by influenza B viruses were not reported between September 2006 and January 2007.

Influenza B viruses were isolated in Africa (Madagascar and Tunisia), the Americas (Argentina, Brazil, Canada, Chile, Colombia, Mexico, Paraguay, Peru and the United States), Asia (Bangladesh; China; China, Hong Kong SAR; China (Province of Taiwan); Indonesia; Islamic Republic of Iran; Japan; Thailand and Viet Nam), Europe (Bulgaria, Greece,

[1] http://www.who.int/wer/2006/wer8142/en/index.html

Israel, Italy, Netherlands, Norway, Portugal, Romania, Russian Federation, Sweden, Switzerland and the United Kingdom) and Oceania (Australia, Cook Islands and Solomon Islands).

Influenza A(H5N1)

Between September 2006 and 13 February 2007, 31 human cases of influenza A(H5N1) were confirmed in China, Egypt, Indonesia, Iraq, Nigeria and Thailand. Many of these cases were associated with outbreaks of highly pathogenic avian influenza A(H5N1) in poultry. Since December 2003, a total of 272 human cases have been confirmed from 11 countries[2]. The WHO influenza pandemic preparedness level remains unchanged at Phase 3[3]. 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, many influenza A(H1N1) viruses were closely related to the vaccine virus A/New Caledonia/20/99. However, an increasing proportion of viruses was antigenically distinguishable from the vaccine strain and more closely related to A/Fukishima/141/2006, A/Hong Kong 2652/2006 and A/Solomon Islands/3/2006 (Table 1).

Table 1 **Results of haemagglutination-inhibition tests of influenza A(H1N1) viruses with postinfection ferret sera**

Antigens	A/New Caledonia/20/99	A/Solomon Islands/3/2006	A/Hong Kong/2652/2006	A/Fukishima/141/ 2006
A/New Caledonia/20/99	**640**	80	80	320
A/Solomon Islands/3/2006	40	**320**	320	640
A/Hong Kong/2652/2006	40	320	**640**	2560
A/Fukishima/141/2006	160	320	640	**2560**
Recent isolates				
A/Canada/1204/2006	640	80	80	nd[a]
A/Kentucky/15/2006	640	80	80	nd
A/Madagascar/2649/2006	320	<40	40	80
A/Morocco/229/2006	320	40	40	80
A/Fujian-G/1387/2006	20	640	320	nd
A/Maryland/9/2006	40	320	640	nd
A/Norway/2287/2006	<40	160	320	1280
A/Parma/11/2006	<40	320	640	1280
A/Taiwan/785/2006	40	160	160	nd
A/Thailand/695/2006	40	320	640	nd

[a] nd, not determined

[2] http://www.who.int/csr/disease/avian_influenza/country/cases_table_2007_02_06/en/index.html
[3] http://www.who.int/csr/disease/avian_influenza/phase/en/index.html

Influenza A(H3N2) viruses

In HI tests with postinfection ferret sera, many influenza A(H3N2) viruses were closely related to the vaccine viruses, A/Wisconsin/67/2005 and A/Hiroshima/52/2005. An increasing proportion of recent isolates was distinguishable both antigenically and genetically from the vaccine strains; however, antigenic analysis did not reveal the emergence of a sufficiently well characterized antigenically variant group.

Influenza B viruses

Influenza B viruses of both the B/Victoria/2/87 and the B/Yamagata/16/88 lineages continued to circulate. Most of the viruses belonged to the B/Victoria/2/87 lineage.

In HI tests with postinfection ferret antisera, the majority of 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 previous 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, B/Egypt/144/2005 and B/Michigan/2/2006.

Resistance to M2 inhibitors

Resistance to amantadine and rimantadine remains high among influenza A(H3N2) viruses globally. Resistance among A(H1N1) viruses also occurred but the proportion varied from country to country. Resistance in both subtypes was predominantly associated with a serine to asparagine change in residue 31 of the M2 ion channel protein.

Studies with inactivated influenza virus vaccines

Antibodies to haemagglutinin (HA) were measured by HI tests in panels of sera from adults who had received trivalent inactivated vaccines containing the antigens of A/New Caledonia/20/99 (H1N1), B/Malaysia/2506/2004 and either A/Hiroshima/52/2005 or A/Wisconsin/67/2005 (H3N2), administered in doses of 15 μg of each HA. Cross-reactions of postimmunization antibody to recent isolates were examined in 5 panels of sera, 4 of which were selected for the presence of postimmunization antibody to the vaccine viruses. In addition one panel of sera from vaccinated paediatric subjects was tested for cross-reactions of postimmunization antibody to recent isolates.

Vaccines containing influenza A/New Caledonia/20/99 (H1N1) antigen stimulated HA antibodies at titres ≥40 to the influenza A(H1N1) vaccine virus in the sera of 59% of children, 68% of adults and 53% of elderly people. When the sera were tested against recent isolates, the frequencies were somewhat lower: 26% of children, 52% of adults and 39% of elderly people. Furthermore, the average postimmunization geometric mean HI titres were 47% lower to A/Solomon Islands/3/2006-like viruses than to the vaccine virus.

Vaccines containing influenza A/Wisconsin/67/2005 (H3N2)-like antigens stimulated HA antibodies at titres ≥40 to the vaccine virus in the sera of 62% of children, 83% of adults and 88% of elderly people. When the sera were tested against recent isolates, the frequencies were somewhat lower; 34% of children, 58% of adults, 54% of elderly people. Furthermore for adults and the elderly the average postimmunization geometric mean HI titres were lower to recent isolates than to the vaccine virus.

Immunization with vaccines containing influenza B/Malaysia/2506/2004 antigen stimulated HA antibodies at titres ≥40 to the vaccine virus in the sera of 32% of children, 74% of adults and 73% of elderly people. In adults and elderly people, the average postimmunization geometric mean HI titres and proportions of titres ≥40 to recent B/Malaysia/2506/2004-like isolates (B/Victoria/2/87 lineage) were similar.

Recommended composition of influenza virus vaccines for use in the 2007–2008 influenza season

During the period October 2006 to January 2007, 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. Many isolates were antigenically similar to the current reference virus, A/New Caledonia/20/99, but an increasing proportion of recent viruses was more closely

related to A/Solomon Islands/3/2006. Current vaccines containing A/New Caledonia/20/99 antigens stimulated HA antibodies that were lower in titre to A/Solomon Islands/3/2006 than to the vaccine virus.

Influenza A(H3N2) viruses were associated with outbreaks in several countries. Many isolates were antigenically similar to the current reference virus, A/Wisconsin/67/2005, but an increasing proportion of recent viruses showed antigenic differences from the vaccine virus. Current vaccines containing A/Wisconsin/67/2005 or A/Hiroshima/52/2005 antigens stimulated HA antibodies that were lower in titre and frequency to recent isolates than to the vaccine virus. While there was genetic variation, the absence of a sufficiently well characterized antigenically variant group including the lack of corresponding egg isolates precluded the selection of a new vaccine candidate in time for the 2007–2008 influenza season.

No outbreaks of influenza B were reported, although low levels of activity were recorded in many countries. In HI tests, most isolates were antigenically similar to B/Malaysia/2506/2004. Current vaccines containing B/Malaysia/2506/2004 antigens stimulated HA antibodies that were similar in titre to recent influenza B viruses and to the vaccine virus.

It is recommended that vaccines to be used in the 2007-8 season (northern hemisphere winter) contain the following:

— an A/Solomon Islands/3/2006 (H1N1)-like virus;
— an A/Wisconsin/67/2005 (H3N2)-like virus[a];
— a B/Malaysia/2506/2004-like virus

Vaccine viruses include:
a A/Wisconsin/67/2005 (H3N2) and A/Hiroshima/52/2005

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[4]. 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: Immunobiology, 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: +1 301 496 1810). 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 0080, 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.

[4] http://www.who.int/docstore/wer/pdf/2002/wer7728.pdf