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

This recommendation relates to the composition of vaccines for the forthcoming winter in the southern hemisphere (May–October 2008). A recommendation will be made in February 2008 relating to vaccines that will be used for winter in the northern hemisphere (November 2008–April 2009). Epidemiological considerations will influence which recommendation (September 2007 or February 2008) is more appropriate for countries in equatorial regions.

Influenza activity, February–September 2007

Between February and September 2007, influenza activity was reported in Africa, the Americas, Asia, Europe and Oceania. In some countries influenza activity was higher than in recent years for example in Argentina and Australia .

In the northern hemisphere, influenza continued to cause outbreaks in Asia, Europe and North America. In the United States, A(H1N1) viruses predominated, while in Canada and Europe A(H3N2) viruses predominated. Influenza A(H1N1) and B viruses co-circulated with A(H3N2) viruses in several countries in Asia, Eastern Europe and the Middle-East. Influenza activity declined in April, except in the Russian Federation, where activity continued through June, and in China Hong Kong Special Administrative Region (Hong Kong SAR), where outbreaks due to A(H3N2) viruses occurred in July.

In the southern hemisphere, influenza activity began in April in South America, increased in May, remained high through July and declined in August. In Oceania and South Africa activity started in June, peaked in July to August and declined in September. Influenza A(H3N2) and B viruses co-circulated and caused outbreaks in South America, while in Oceania, A(H3N2) and A(H1N1) viruses co-circulated and caused outbreaks in Australia. Outbreaks due to A(H1N1) viruses were reported in New Zealand in July, and in South Africa in August.

Influenza A(H1N1)

Outbreaks caused by influenza A(H1N1) viruses were reported in Africa (South Africa), the Americas (Mexico and the United States of America), Europe (Russian Federation and Ukraine) and Oceania (Australia and New Zealand).

Influenza A(H1N1) viruses were also reported in Africa (Madagascar, Mauritius, Senegal and Tunisia), the Americas (Brazil, Canada, Chile, El Salvador, Honduras and Peru), Asia (Bangladesh, China, China Hong Kong SAR, China (Province of Taiwan), India, Iran, Japan, Malaysia, Mongolia, Republic of Korea, Singapore, Sri Lanka, Thailand and

Viet Nam) and Europe (Belarus, Croatia, Czech Republic, Denmark, Finland, France, Georgia, Germany, Greece, Iceland, Italy, Kazakhstan, Latvia, Norway, Poland, Romania, Slovenia, Spain, Sweden, Switzerland and the United Kingdom of Great Britain and Northern Ireland).

Influenza A(H3N2)

Outbreaks caused by influenza A(H3N2) viruses were reported in Africa (Egypt), the Americas (Argentina, Brazil, Canada, Chile, Dominican Republic and Mexico), Asia (China Hong Kong SAR, China (Province of Taiwan), Japan, Mongolia, and Thailand), Europe (Austria, Belarus, Bulgaria, Croatia, Czech Republic, Denmark, Finland, Germany, Greece, Iceland, Latvia, Luxemburg, Norway, Russian Federation, Spain, Sweden, Switzerland and the United Kingdom of Great Britain and Northern Ireland) and Oceania (Australia).

Influenza A(H3N2) viruses were also reported in Africa (Madagascar, Mauritius, Morocco, South Africa, Tunisia and Uganda), the Americas (Peru, the United States of America and Uruguay), Asia (Bangladesh, China, Iran, Nepal, Philippines, Republic of Korea, Singapore, Sri Lanka and Viet Nam), Europe (France, Georgia, Italy, Kazakhstan, Poland, Portugal, Romania, Serbia, Slovenia, Turkey and Ukraine) and Oceania (New Caledonia and New Zealand).

Influenza B

Outbreaks associated with influenza B viruses were reported in Africa (Egypt), the Americas (Brazil and Chile), Asia (Afghanistan, China Hong Kong SAR, China (Province of Taiwan), Japan and Mongolia) and Europe (Belarus, Kazakhstan, Romania and Russian Federation).

Influenza B viruses were also reported in Africa (Madagascar, Mauritius, Senegal, South Africa, Tunisia and Uganda), the Americas (Argentina, Canada, Mexico, Panama, Peru, the United States of America and Uruguay), Asia (Bangladesh, China, India, Iran, Mongolia, Philippines, Republic of Korea, Singapore, Sri Lanka, Thailand and Viet Nam), Europe (Albania, Austria, Bulgaria, Czech Republic, Finland, France, Georgia, Germany, Greece, Italy, Latvia, Luxemburg, Norway, Portugal, Serbia, Slovenia, Spain, Sweden, Switzerland, Turkey, Ukraine and the United Kingdom of Great Britain and Northern Ireland) and Oceania (Australia and New Zealand).

Influenza A(H5N1)

Between February and 19 September 2007, 58 confirmed human cases with 36 deaths from influenza A(H5N1) were reported to WHO from Cambodia, China, Egypt, Indonesia, Lao People's Democratic Republic, Nigeria and Viet Nam. Since November 2003, a total of 328 human cases with 200 deaths have been confirmed from 12 countries. The WHO influenza pandemic preparedness level remains unchanged at Phase 3. So far, there has been no evidence of sustained human-to-human transmission. The current status

of the development of candidate A(H5N1) vaccine viruses and guidance for national authorities and vaccine companies on the selection of candidate viruses for use in vaccine development are available at: http://www.who.int/csr/disease/avian_influenza/guidelines/h5n1virus/en/index.html .

Antigenic characteristics of recent isolates

Influenza A(H1N1) viruses

In haemagglutination-inhibition (HI) tests with postinfection ferret sera, the proportion of A(H1N1) viruses that were antigenically distinguishable from A/New Caledonia/20/99 and closely related to A/Solomon Islands/3/2006[i] continued to increase, and A/Solomon Islands/3/2006-like viruses were predominant among recent isolates.

Influenza A(H3N2) viruses

In HI tests with postinfection ferret sera, some influenza A(H3N2) viruses were antigenically similar to the vaccine viruses A/Wisconsin/67/2005 and A/Hiroshima/52/2005. However, the majority of recent A(H3N2) viruses was distinguishable from the vaccine viruses and was closely related to the A/Perth/27/2007 and A/Brisbane/10/2007 viruses.

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

	Postinfection ferret sera		
	A/Wisconsin/67/2005	A/Perth/27/2007	A/Brisbane/10/2007
Antigens			
A/Wisconsin/67/2005	**1280**	640	640
A/Perth/27/2007*	160	**320**	640
A/Brisbane/10/2007	1280	1280	**640**
Recent isolates –			
A/Victoria/566/2007	640	640	640
A/Cambodia/31/2006	640	640	640
A/Brisbane/92/2007	80	640	640
A/Santiago/6881/2007	<40	320	320
A/Johannesburg/93/2007	80	320	320
A/Maryland/702/2007	40	320	320
A/Capetown/97/2007	160	640	640

* MDCK cell isolate

Influenza B viruses

Influenza B viruses of both the B/Victoria/2/87 and the B/Yamagata/16/88 lineages continued to circulate. The proportion of the B/Yamagata/16/88 lineage viruses has increased and were predominant among recent isolates, particularly in Australia, Chile, China Hong Kong SAR, New Zealand and some Asian countries.

In HI tests with postinfection ferret antisera, the majority of viruses of the B/Victoria/2/87 lineage was closely related to the vaccine virus B/Malaysia/2506/2004. Most 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 B/Florida/4/2006 and B/Brisbane/3/2007.

Table 2
Results of haemagglutination-inhibition tests of influenza B viruses with postinfection ferret sera

	Postinfection ferret sera			
	B/Malaysia/2506/2004	B/Jiangsu/10/2003	B/Florida/4/2006	B/Brisbane/3/2007
Antigens				
B/Malaysia/2506/2004	**1280**	<20	<20	<20
B/Jiangsu/10/2003	<20	**1280**	320	320
B/Florida/4/2006	40	<20	**640**	640
B/Brisbane/3/2007	20	<20	320	**320**
Recent isolates –				
B/Hong Kong/121/2007	640	<20	<20	<20
B/Malaysia/683/2007	640	<20	<20	<20
B/Johannesburg/75/2007	640	<20	<20	<20
B/Malaysia/890/2007	<20	ND	320	160
B/Christchurch/2/2007	20	ND	640	320
B/Shizuoka/109/2007	<20	160	1280	320
B/Mauritius/481/2007	20	80	1280	ND
B/Victoria/504/2007	20	40	640	320
B/Santiago/6336/2007	<20	ND	640	ND
B/Johannesburg/1197/2007	<20	80	640	320

ND: not determined

Resistance to M2 inhibitors

Resistance to amantadine and rimantadine remained high among influenza A(H3N2) viruses globally, notably among viruses genetically related to A/Brisbane/10/2007. Resistance among A(H1N1) viruses also persisted but the proportion of resistant viruses

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/Solomon Islands/3/2006 (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 4 panels of sera, 3 of which were selected for the presence of postimmunization antibody to the vaccine viruses. In addition, a fifth panel of sera from vaccinated paediatric subjects was tested.

Vaccines containing influenza A/Solomon Islands/3/2006 (H1N1) antigen stimulated HA antibodies at titres ≥40 to the vaccine virus in the sera of 100% of adults and 88% of elderly people. Although the average postimmunization geometric mean HI titres were 76% lower to recent isolates compared to the vaccine virus, the proportions of sera with titres ≥40 were similar to those against 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 100% of children, 92% of adults and 88% of elderly people. When the sera were tested against recent isolates, the corresponding proportions were somewhat lower; 85% of children, 59% of adults, 40% of elderly people. Furthermore, the average postimmunization geometric mean HI titres were lower to recent isolates than to the vaccine virus (reductions: children 33%; adults 47%; elderly 60%).

Immunization with vaccines containing influenza B/Malaysia/2506/2004 antigen stimulated HA antibodies at titres ≥40 to the vaccine virus in the sera of 59% of children, 75% of adults and 70% of elderly people. In adults and elderly people, the corresponding proportions were similar for recent B/Malaysia/2506/2004-like viruses (B/Victoria/2/87 lineage) and recent B/Yamagata/16/88 lineage viruses. In children, the proportions were similar for the vaccine viruses and recent B/Malaysia/2506/2004-like isolates but were somewhat lower (22%) for recent B/Yamagata/16/88 lineage isolates. In children, adults and elderly, the average postimmunization geometric mean HI titres to recent B/Malaysia/2506/2004-like viruses were similar to those to the vaccine virus but titres to recent B/Yamagata/16/88 lineage viruses were somewhat reduced (reductions: children 52%; adults 47%; elderly 34%).

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

During the period February to September 2007 influenza A(H1N1), A(H3N2) and B viruses circulated in many parts of the world.

Outbreaks caused by influenza A(H1N1) viruses were reported in several countries. In HI tests, the majority of recent viruses were antigenically similar to A/Solomon Islands/3/2006. Influenza A (H1N2) viruses were not reported. Similar proportions of vaccinees receiving vaccines containing A/Solomon Islands/3/2006 antigen had antibody with titres of ≥40 to the vaccine virus and recent isolates.

Influenza A(H3N2) viruses were associated with outbreaks in many countries. While some isolates were antigenically similar to the vaccine virus, A/Wisconsin/67/2005, the majority of recent isolates were distinguishable from the vaccine virus and antigenically similar to A/Brisbane/10/2007. 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.

Influenza B outbreaks were reported in several countries. Viruses of both B/Victoria/2/87 and B/Yamagata/16/88 lineages were reported in many countries but occurred in different proportions. Recently B/Yamagata/16/88 lineage viruses predominated in Australia, Chile, China Hong Kong SAR, New Zealand and some Asian countries. For the B/Victoria/2/87 lineage viruses the majority of recent isolates were antigenically similar to B/Malaysia/2506/2004. Most of the recent B/Yamagata/16/88 lineage viruses were antigenically similar to B/Florida/4/2006. Current vaccines containing B/Malaysia/2506/2004 antigen stimulated HA antibodies that were similar in titre to recently isolated B/Malaysia/2506/2004-like viruses but were somewhat lower in titre to recently isolated B/Yamagata/16/88 lineage viruses.

It is recommended that vaccines to be used in the 2008 season (southern hemisphere winter) contain the following:
— an A/Solomon Islands/3/2006 (H1N1)-like virus*;
— an A/Brisbane/10/2007 (H3N2)-like virus;
— a B/Florida/4/2006-like virus.
***A/Solomon Islands/3/2006 is a current vaccine virus**

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[ii].

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 of at least 4 weeks between doses.

Vaccine viruses (including reassortants) and reagents and for use in the laboratory standardization of inactivated vaccine may be obtained from: Immunobiology Section, 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, England EN6 3QG (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 or +1 301 480 9748).

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, England NW7 1AA (fax: +44 208 906 4477).

Updated epidemiological information is available on WHO's web site at Http://www.who.int/csr/disease/influenza

[i] http://www.who.int/wer/2007/wer8209/en/index.html
[ii] http://www.who.int/docstore/wer/pdf/2002/wer7728.pdf