

# **Recommended composition of influenza virus vaccines for use in the 2007 influenza season**

**September 2006**

This recommendation relates to the composition of vaccines for the forthcoming winter in the southern hemisphere (May–October 2007). A recommendation will be made in February 2007 relating to vaccines that will be used for winter in the northern hemisphere (November 2007–April 2008). Epidemiological considerations will influence which recommendation (September 2006 or February 2007) is more appropriate for countries in equatorial regions.

## **Influenza activity February–September 2006**

Between February and September 2006, 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.<sup>1</sup>

In the northern hemisphere, influenza activity continued in North America and Asia declining in April, except in Hong Kong Special Administrative Region (SAR) of China, where outbreaks occurred from March to July. In Europe, activity increased in February, quickly reached a peak and declined in April. In North America and some Eastern European countries influenza A(H3N2) viruses predominated and caused outbreaks, while in other European countries influenza B viruses predominated. In Asia influenza A(H1N1), A(H3N2) and B viruses co-circulated.

In the southern hemisphere, influenza activity began in April. Overall activity was mild to low. In South America, influenza A(H1N1) viruses predominated but circulated locally and were responsible for an outbreak in Brazil. Whilst outbreaks due to influenza A(H3N2) occurred in New Zealand and South Africa, activity elsewhere in Africa and Oceania was low.

## **Influenza A(H1N1)**

Outbreaks caused by influenza A(H1N1) viruses were reported in Africa (Egypt), the Americas (Brazil), Asia (Hong Kong SAR, Japan and Thailand) and Europe (Spain).

Influenza A(H1N1) viruses were also isolated in Africa (Algeria, Madagascar, Senegal, South Africa and Tunisia), the Americas (Argentina, Canada, Chile, Peru, the United States, Uruguay and Venezuela), Asia (Bangladesh, China, Macau SAR, Province of Taiwan, India, Indonesia, Malaysia, the Philippines, the Republic of Korea and Singapore), Europe (Croatia, Czech Republic, Denmark, Finland, France, Germany, Iceland, Iran, Israel, Italy, Latvia, Luxemburg, Norway, Poland, Portugal, the Republic of Serbia, Romania, the Russian Federation, Slovenia, Sweden, Switzerland, Turkey, Ukraine and the United Kingdom) and Oceania (Australia, New Caledonia, New Zealand and the Solomon Islands).

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<sup>1</sup> <http://www.who.int/wer/2006/wer8110.pdf>

## **Influenza A(H3N2)**

Between February and September, outbreaks caused by influenza A(H3N2) viruses were reported in Africa (Egypt and South Africa), the Americas (Canada and the United States), Asia (Japan), Europe (Kazakhstan, the Russian Federation and Slovenia) and Oceania (New Zealand).

Influenza A(H3N2) viruses were also isolated in Africa (Madagascar and Tunisia), the Americas (Argentina, Brazil, Chile, Guatemala, Peru and Venezuela), Asia (China, Hong Kong SAR, India, Indonesia, Malaysia, Nepal, Province of Taiwan, the Philippines, the Republic of Korea, Singapore and Thailand), Europe (Austria, Croatia, Czech Republic, Denmark, Finland, France, Germany, Greece, Iceland, Iran, Israel, Italy, Latvia, Luxemburg, Norway, Poland, Portugal, Romania, Slovakia, Spain, Sweden, Switzerland, Turkey, Ukraine and the United Kingdom) and Oceania (Australia and New Caledonia).

## **Influenza B**

Between February and September, outbreaks due to influenza B viruses were reported in Africa (Egypt), the Americas (the United States), Asia (China, Hong Kong SAR, Republic of Korea and Uzbekistan) and Europe (Denmark, France, Germany, Iceland, Kazakhstan, Kyrgyzstan, Israel, Latvia, Luxemburg, Norway, Spain, Sweden, Switzerland and Ukraine).

Influenza B viruses were also isolated in Africa (South Africa and Tunisia), the Americas (Argentina, Brazil, Canada, Chile, Guatemala, Mexico, Panama, Peru, Surinam, Trinidad-Tobago, Uruguay and Venezuela), Asia (Macau SAR, Province of Taiwan, India, Indonesia, Japan, Malaysia, the Philippines, Singapore, Sri Lanka and Thailand), Europe (Austria, Belarus, Belgium, Czech Republic, Finland, Greece, Iran, Italy, Poland, Portugal, the Republic of Serbia, Romania, the Russian Federation, Slovenia, Turkey and the United Kingdom) and Oceania (Australia, Guam, New Caledonia, New Zealand and Saipan)

## **Influenza A(H5N1)**

Between February and 19 September 2006, 87 confirmed human cases with 59 deaths of influenza A(H5N1) were reported to WHO from Azerbaijan, Cambodia, China, Djibouti, Egypt, Indonesia, Iraq and Thailand. Since November 2003, a total of 247 human cases have been confirmed from 10 countries.<sup>2</sup> The WHO influenza pandemic preparedness level remains unchanged at Phase 3.<sup>3</sup> So far, there has been no evidence of sustained human-to-human transmission.

The current status of the development of new candidate H5N1 vaccine viruses and guidance for national authorities and vaccine companies on the selection of candidate viruses for use in vaccine development could be found on WHO web at:

[http://www.who.int/csr/disease/avian\\_influenza/guidelines/h5n1virus2006\\_08\\_18/en/index.html](http://www.who.int/csr/disease/avian_influenza/guidelines/h5n1virus2006_08_18/en/index.html)

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<sup>2</sup> [http://www.who.int/csr/disease/avian\\_influenza/en/index.html](http://www.who.int/csr/disease/avian_influenza/en/index.html)

<sup>3</sup> [http://www.who.int/csr/disease/avian\\_influenza/phase/en/](http://www.who.int/csr/disease/avian_influenza/phase/en/)

## **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 the vaccine virus A/New Caledonia/20/99. A genetic variant which emerged during 2004 has become more prevalent in recent months. The majority of 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, the majority of influenza A(H3N2) viruses were closely related to the vaccine viruses, A/Wisconsin/67/2005 and A/Hiroshima/52/2005.<sup>4</sup>

### **Influenza B viruses**

Influenza B viruses of both the B/Victoria/2/87 and the B/Yamagata/16/88 lineages continued to circulate. During this period, viruses of the B/Victoria/2/87 lineage made up the vast majority of isolates.

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 and B/Egypt/144/2005.

### **Antiviral resistance**

Resistance to amantadine and rimantadine has continued to increase among influenza A viruses. The majority of recent influenza A(H3N2) viruses were resistant to these drugs. Resistance among influenza A(H1N1) viruses has emerged worldwide and has increased in recent months. Resistance among both subtypes is predominately 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 people 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.

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<sup>4</sup> <http://www.who.int/wer/2006/wer8109/en/index.html>

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 55% of children, 75% of adults and 62% of elderly people. In children and adults the proportions of titres  $\geq 40$  to recent isolates were similar but only 38% of elderly people had titres  $\geq 40$  to recent isolates. The average postimmunization geometric mean HI titres to recent isolates were not significantly different from those to the vaccine virus.

Vaccines containing influenza A/Wisconsin/67/2005(H3N2)-like antigens stimulated postimmunization HA antibodies at titres  $\geq 40$  to the vaccine virus in the sera of 89% of adults and 85% of elderly people. For representative recent isolates, the proportions with titres  $\geq 40$  were somewhat lower; 69% of adult, 71% of elderly people. For adults and the elderly the average postimmunization geometric mean HI titres to recent isolates were somewhat lower.

Immunization with vaccines containing influenza B/Malaysia/2506/2004 antigen stimulated postimmunization HA antibodies at titres  $\geq 40$  to the vaccine virus in the sera of 81% of adults and 75% of elderly people. In adults and elderly people, the postimmunization average geometric mean HI titres and proportions of titres  $\geq 40$  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 influenza season**

During the period February to September 2006, influenza A(H1N1), A(H3N2) and B viruses circulated in many parts of the world.

Influenza A(H1N1) viruses were associated with outbreaks in Africa (Egypt), the Americas (Brazil), Asia (Hong Kong SAR, China, Japan and Thailand) and Europe (Spain). In HI tests, the majority of 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 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. Most recent isolates were antigenically similar to the vaccine viruses A/Wisconsin/67/2005 and A/Hiroshima/52/2005. Current vaccines containing the A/Wisconsin/67/2005(H3N2) antigen stimulated HA antibodies against recent influenza A(H3N2) isolates that were somewhat lower in titre and frequency than to the vaccine virus.

Influenza B outbreaks were reported in many countries in Asia and Europe, and in Egypt and the United States. The majority of recent isolates were antigenically similar to B/Malaysia/2506/2004 (B/Victoria/2/87 lineage). 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.

**It is recommended that vaccines to be used in the 2007 season (southern hemisphere winter) contain the following:**

- an A/New Caledonia/20/99(H1N1)-like virus,
- an A/Wisconsin/67/2005(H3N2)-like virus,<sup>a</sup>
- a B/Malaysia/2506/2004-like virus

<sup>a</sup> The currently used vaccine viruses are A/Wisconsin/67/2005 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.<sup>5</sup>

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](mailto: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 2089064477).

Updated epidemiological information is available on WHO's web site at <http://www.who.int/csr/disease/influenza/update/en/index.html>

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<sup>5</sup> <http://www.who.int/docstore/wer/pdf/2002/wer7747.pdf>