Recommended composition of influenza virus vaccines for use in the 2004 influenza season

This recommendation relates to the composition of vaccines for the forthcoming winter in the southern hemisphere (May-October 2004). A recommendation will be made in February 2004 which relates to vaccines that will be used for the winter in the northern hemisphere (November 2004 - April 2005). Epidemiological considerations will influence which recommendation (September or February) is more appropriate for countries in equatorial regions.

Influenza activity February–September 2003

Between February and September 2003, influenza was reported in Africa, the Americas, Asia, Europe and Oceania. In the northern hemisphere outbreaks due to influenza A(H3N2) and B viruses continued to be reported in several countries in North America and Europe between February and April 2003(See *Weekly Epidemiological Record* Vol. No: 9 2003, pp 58-62). In the southern hemisphere, between May and September 2003, outbreaks due to influenza A viruses were reported in Africa, Oceania and South America. Widespread outbreaks associated with influenza A(H3N2) occurred in Argentina, Australia and New Zealand; no outbreaks due to influenza B viruses were reported.

In addition, 2 human influenza A(H5N1) infections were reported in Hong Kong SAR China in February 2003 (Influenza A(H5N1) in Hong Kong Special Administrative Region of China – Update 2) and over 80 influenza A(H7N7) infections were associated with severe outbreaks in poultry in the Netherlands in March 2003.

Influenza A(H1N1) and A(H1N2)

Influenza A(H1N1) outbreaks were reported in the Americas (Argentina and the United States) and Europe (Russian Federation and Ukraine).

Influenza A(H1N1) viruses and those for which the neuraminidase was not characterized were also isolated in Africa (Senegal and South Africa), the Americas (Canada, Chile, Guyana, Mexico, Peru and Uruguay), Asia (China, Hong Kong SAR China, India, Malaysia and Singapore), Europe (Croatia, Finland, France, Germany, Greece, Hungary, Iceland, Israel, Italy, Latvia, the Netherlands, Norway, Poland, Portugal, Romania, Serbia and Montenegro, Slovakia, Spain, Sweden, Switzerland and the United Kingdom) and Oceania (Australia and New Zealand).

Local activity due to influenza A(H1N2) viruses was reported in Brazil. Sporadic cases of Influenza A(H1N2) infection were also reported in Africa (Senegal and South Africa), the Americas (Argentina, Chile, Canada, Guyana, Trinidad and Tobago, the United States and Uruguay), Europe (Denmark, Finland, France, Germany, Italy, Norway, Serbia and Montenegro, Slovakia and Switzerland) and Oceania (Australia).

Influenza A(H3N2)

Between February and September 2003, outbreaks due to influenza A(H3N2) viruses were reported in Africa (South Africa and Zambia), the Americas (Argentina, Chile, El Salvador, Paraguay, the United States and Uruguay), Asia (Japan), Europe (Albania, Bulgaria, Denmark, Germany, Israel, Italy, Latvia, Poland, Russian Federation, Slovakia, Switzerland and Ukraine) and Oceania (Australia, New Caledonia and New Zealand).

Influenza A(H3N2) viruses were also isolated in Africa (Egypt, Madagascar and Senegal), the Americas (Brazil, Canada, Guyana, Mexico and Peru), Asia (Bangladesh, China, Hong Kong SAR China, India, Indonesia, Malaysia, Philippines, Saudi Arabia, Singapore, Taiwan Province of China and Thailand), Europe (Austria, Belarus, Czech Republic, Finland, France, Greece, Hungary, Iceland, the Netherlands, Norway, Portugal, Romania, Serbia and Montenegro, Spain, Sweden and the United Kingdom) and Oceania (Guam).

Influenza B

Between February and September 2003, outbreaks due to influenza B were reported in the Americas (Canada and the United States) and Europe (Finland, France, Greece, Iceland, Israel and Spain). Influenza B viruses were also isolated in Africa (Egypt, Morocco, South Africa and Tunisia), the Americas (Argentina, Brazil, Ecuador, Guyana, Mexico, Peru and Uruguay), Asia (Bangladesh, China, Hong Kong SAR China, Indonesia, Japan, Malaysia, Singapore and Thailand), Europe (Albania, Austria, Belarus, Bulgaria, Croatia, Czech Republic, Denmark, Germany, Hungary, Italy, Latvia, the Netherlands, Norway, Poland, Portugal, Romania, Russian Federation, Serbia and Montenegro, Slovakia, Sweden, Switzerland, Turkey, Ukraine and the United Kingdom) and Oceania (Australia and New Zealand).

Antigenic characteristics of recent isolates

Influenza A(H1N1) and A(H1N2) viruses

In haemagglutination-inhibition (HI) tests with postinfection ferret sera, the majority of influenza A(H1N1) and A(H1N2) viruses were closely related to A/New Caledonia/20/99. The neuraminidases of H1N2 viruses were closely related to those of contemporary H3N2 viruses.

Influenza A(H3N2) viruses

In HI tests with postinfection ferret sera, whereas many influenza A(H3N2) viruses were closely related to A/Moscow/10/99 and A/Panama/2007/99, the majority of recent isolates were closely related to A/Fujian/411/2002 (See *Weekly Epidemiological Record* Vol. No: 9 2003, pp 58-62) .

Influenza B viruses

In HI tests with postinfection ferret sera, the majority of influenza B viruses were related to B/Hong Kong/330/2001. Influenza B/Sichuan/379/99-like viruses were isolated infrequently.

The majority of recent B/Hong Kong/330/2001-like viruses were reassortants which possessed neuraminidases that were closely related to those of B/Sichuan/379/99-like viruses and are represented by B/Brisbane/32/2002.

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/Panama/2007/99(H3N2) and either B/Shandong/7/97 or B/Hong Kong/1434/2002 administered in doses of 15ug of each haemagglutinin.

Vaccines containing influenza A/New Caledonia/20/99(H1N1) antigens stimulated postimmunization HI antibodies at titres ≥40 to the influenza A(H1N1) vaccine virus in the sera of 76% of adult and 52% of elderly vaccinees. For representative recent isolates, including H1N2 isolates, the titres and frequencies of antibodies were similar.

Vaccines containing influenza A/Panama/2007/99(H3N2) antigens stimulated postimmunization HI antibodies at titres ≥40 to the vaccine virus in the sera of 85% of adult and 80% of elderly vaccinees. For representative recent isolates, the frequencies of antibodies were somewhat lower; 76% of adult and 72% of elderly vaccinees had HI antibodies at titres ≥. Furthermore, the geometric mean postimmunization HI titres were, on average, 41% lower to A/Fujian/411/2002–like viruses than to the vaccine virus.

Vaccines containing influenza B/Hong Kong/330/2001-like antigens, stimulated postimmunization HI antibodies at titres ≥40 to the vaccine virus in the sera of 68% of adult and 58% of elderly vaccinees. For representative recent B/Hong Kong/330/2001-like isolates, the titres and frequencies of antibodies were similar. For representative recent B/Sichuan/379/99-like viruses the titres were lower; 49% of adult and 37% of elderly vaccinees had HI titres ≥40.

Recommendations for the composition of influenza virus vaccines.

During the period February 2003 to September 2003, influenza A(H1N1), A(H1N2), A(H3N2) and B viruses circulated in many parts of the world.

Influenza A(H1N1) and A(H1N2) viruses caused outbreaks in some countries in the Americas and Europe. In HI tests most isolates of both subtypes were antigenically similar to A/New Caledonia/20/99. Current vaccines containing A/New Caledonia/20/99 antigens stimulated anti HA antibodies against recent A(H1N1) and A(H1N2) influenza isolates, which were of similar titre and frequency to those against the vaccine virus.

Influenza A(H3N2) viruses were associated with outbreaks in many countries. The majority of recent isolates were similar to A/Fujian/411/2002. Current vaccines containing A/Panama/2007/99 antigens stimulated anti HA antibodies which were lower in frequency and titre to A/Fujian/411/2002 –like viruses than to the vaccine virus. Whereas the A/Fujian/411/2002 reference virus was isolated in cell culture, A/Kumamoto/102/2002 and A/Wyoming/3/2003 are A/Fujian/411/2002–like egg isolates and may be considered as candidate vaccine viruses.

Influenza B viruses caused outbreaks in the Americas and Europe and were isolated in most regions of the world. The majority of isolates were antigenically similar to B/Hong

Kong/330/2001; B/Sichuan/379/99-like viruses continued to circulate at a low level. The majority of B/Hong Kong/330/2001 – like viruses were reassortants which possessed neuramindases that were closely related to those of B/Sichuan/379/99-like viruses and are represented by B/Brisbane/32/2002. Current vaccines containing influenza B/Hong Kong/1434/2001 or B/Shandong/7/97 antigens induced anti HA antibodies to recently isolated B/Hong Kong/330/2001–like viruses, which were of similar titre and frequency to those against the vaccine virus.

Consequently, it is recommended that vaccines to be used in the 2004 season (southern hemisphere winter) contain the following:

- an A/New Caledonia/20/99(H1N1) -like virus
- an A/Fujian/411/2002(H3N2) - like virus*
- a B/Hong Kong/330/2001-like virus**

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* A/Kumamoto/102/2002 and A/Wyoming/3/2003 are egg-grown A/Fujian/411/2002-like viruses.
**Currently used vaccine viruses include B/Shandong/7/97, B/Hong Kong/330/2001, B/Hong Kong/1434/2002. B/Brisbane/32/2002 is also available as a vaccine virus.

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 (See *Weekly Epidemiological Record* Vol. No. 35, 2000, pp. 281-288) .

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 62 32 8564,
website: 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
United Kingdom
Fax: +44 17 07 64 6730,
email: enquiries@nibsc.ac.uk

Division of Viral Products, Center for Biologics Evaluation and Research
Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20892
United States of America
Fax: +1 301 402 51 28

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 93 89 18 81
website: http//www.influenzacentre.org

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 5610812 or +81 42 5652498

WHO Collaborating Center for Surveillance, Epidemiology and Control of Influenza
Centers for Disease Control and Prevention,
1600 Clifton Road, Mail stop G16, Atlanta, Georgia 30333,
United States of America
Fax: +1 404 639 23 34

WHO Collaborating Centre for Reference and Research on Influenza, at the National Institute for Medical Research,
The Ridgeway, Mill Hill, London NW7 1AA
United Kingdom
Fax: +44 208 906.4477

Updated epidemiological information is available on the WHO's websiteand the geographical information system, FluNet