Questions and Answers

Recommended composition of influenza virus vaccines for use in the northern hemisphere 2013-2014 influenza season

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1. What is the WHO Global Influenza Surveillance and Response System(GISRS)?

GISRS is a global public health laboratory network coordinated by WHO, currently consisting of 140 National Influenza Centres (NICs) in 110 member states, 6 WHO Collaborating Centers for Influenza (CCs), 4 WHO Essential Regulatory Laboratories (ERLs) and 12 WHO H5 Reference Laboratories.

This network conducts numerous public health activities including warning and assessment relating to influenza viruses of concern, such as potential pandemic viruses, and the collection and testing by the NICs of clinical specimens from patients as well as the further testing and characterization of representative influenza virus isolates by WHO CCs and WHO ERLs. This network also provides guidance to countries and support for activities such as training, outbreak response, development of diagnostic tests, testing for antiviral drug resistance and scientific interpretation of important findings.

2. **What is the purpose of the WHO's recommendations on the composition of influenza virus vaccines?**

These WHO recommendations provide a guide to national public health authorities and vaccine manufacturers for the development and production of influenza vaccines for the next influenza season. In contrast to many other vaccines, the viruses in influenza vaccines have to be updated frequently because circulating influenza viruses continuously evolve. Because it takes 6-9 months for manufacturers to produce influenza vaccines, recommendations are made in September for the following influenza season in the southern hemisphere and in February for the following influenza season in the northern hemisphere.

3. **What viruses are recommended by WHO to be included in influenza vaccines for use in the 2013-2014 northern hemisphere influenza season?**

WHO recommends that influenza vaccines for use in the 2013-2014 northern hemisphere influenza season contain the following viruses:

- an A/California/7/2009 (H1N1)pdm09-like virus [a];
- an A(H3N2) virus antigenically like the cell-propagated prototype virus A/Victoria/361/2011b [b *]; and
- a B/Massachusetts/2/2012-like virus (B/Yamagata lineage).

It is recommended that quadrivalent vaccines containing two influenza B viruses contain the above three viruses and a B/Brisbane/60/2008-like virus [c] (B/Victoria lineage).

[a] A/Christchurch/16/2010 is an A/California/7/2009-like virus;
[b] A/Texas/50/2012 is an A(H3N2) virus antigenically like the cell-propagated prototype virus A/Victoria/361/2011;
[c] B/Brisbane/33/2008 is a B/Brisbane/60/2008-like virus.

* It is recommended that A/Texas/50/2012 is used as the A(H3N2) vaccine component because of antigenic changes in earlier A/Victoria/361/2011-like vaccine viruses (such as IVR 165) resulting from adaptation to propagation in eggs.

4. **Is this recommendation different from those for previous seasons?**

This recommendation changed the B component of vaccines from those for the 2013 southern hemisphere and 2012-2013 northern hemisphere influenza seasons, which contained the following:

- an A/California/7/2009 (H1N1)pdm09-like virus;
- an A/Victoria/361/2011 (H3N2)-like virus; and
- a B/Wisconsin/1/2010-like virus (B/Yamagata lineage).

5. **Why was there a recommendation by WHO to change the influenza B component from a B/Wisconsin/1/2010-like virus (B/Yamagata lineage) to a B/Massachusetts/2/2012-like virus (B/Yamagata lineage)?**

Influenza B viruses of the B/Victoria/2/87 and the B/Yamagata/16/88 lineages have continued to co-circulate in many parts of the world. Viruses of the B/Victoria/2/87 lineage were prevalent in some countries, and B/Yamagata/16/88 lineage viruses have continued to increase in proportion becoming dominant in many countries.

The HA gene sequences of B/Victoria/2/87 lineage viruses predominantly belonged to the B/Brisbane/60/2008 genetic clade and were antigenically closely related to the B/Victoria lineage vaccine virus B/Brisbane/60/2008.

The HA genes of most viruses of the B/Yamagata/16/88 lineage fell within genetic clades 2 or 3, with the proportion of viruses in clade 2 markedly increased in many areas during this period. Many viruses in clade 2 (represented by B/Massachusetts/2/2012) were antigenically distinct from those in clade 3 (represented by B/Wisconsin/1/2010).

Based on the above analysis and knowledge accumulated through monitoring and analysing influenza B viruses in the past, the WHO expert group recommended that the influenza B component of the vaccines for 2013-2014 northern hemisphere season should be a B/Yamagata/16/88 lineage virus and antigenically similar to B/Massachusetts/2/2012.

6. **Could a B/Victoria lineage virus still be considered for use as a vaccine component?**

For those considering the use of both a B/Yamagata and a B/Victoria lineage vaccine virus, e.g. for quadrivalent vaccines containing two influenza B viruses, B/Brisbane/60/2008-like viruses continue to be the most appropriate 4th component. In addition, countries and regions of the world that expect B/Victoria lineage viruses to predominate in the northern hemisphere winter of 2013-2014 may continue to use a B/Brisbane/60/2008-like virus in their influenza virus vaccines.

As always, national or regional authorities approve the composition and formulation of vaccines that will be used in each country.

7. **Have the antigenic characteristics of the circulating A(H3N2) viruses changed since the last recommendation?**

No, most of the circulating viruses have remained antigenically like the cell-propagated A/Victoria/361/2011 virus.

8. **Has the virus to be used as the A(H3N2) component of the vaccine been replaced?**

Yes, the WHO expert group has recommended a change in the virus used as an A/Victoria/361/2011-like virus. This change is required because the A/Victoria/361/2011 egg propagated vaccine virus has antigenic changes compared with the cell-propagated A/Victoria/361/2011 virus. By contrast, both the cell- and egg-propagated A/Texas/50/2012

viruses are antigenically like the A/Victoria/361/2011 cell-propagated virus. Thus, the WHO's expert group recommends the A/Victoria/361/2011-like vaccine virus be A/Texas/50/2012.

9. **What candidate vaccine viruses (high-growth reassortants) are available for use in influenza vaccines?**

The availability of high-growth reassortants by type/subtype and corresponding potency reagents is updated on the WHO GISRS website**:**
http://www.who.int/influenza/vaccines/virus/en/

The WHO recommended candidate virus for vaccine development and production for 2013-2014 are available at
http://www.who.int/influenza/vaccines/virus/candidates_reagents/home **.**

10. **How was the WHO recommendation made for the composition of influenza virus vaccines for the 2013-2014 northern hemisphere influenza season?**

The recommendation was made based on the continuous surveillance conducted by the WHO Global Influenza Surveillance and Response System (GISRS).

Two teleconferences were conducted in January 2013 and February 2013, respectively, to review the virus characterization data generated in WHO Collaborating Centres (WHO CCs) and WHO Essential Regulatory Laboratories (WHO ERLs) of GISR[1], along with surveillance information from National Influenza Centres (NICs) of GISRS and antigenic cartographic analysis by Cambridge University.

From 18 to 20 February 2013, a WHO Consultation took place with 9 Advisers from WHO CCs and WHO ERLs of GISRS. The Consultation was observed by 18 other experts from WHO CCs, WHO ERLs, WHO H5 Reference Laboratories, NICs, Cambridge University and OFFLU.

The consultation was conducted to finalize analyses of characterization of influenza viruses that have been shared with WHO through GISRS, complemented with vaccine serological study results and with available epidemiological and clinical information, as well as preliminary vaccine effectiveness estimates. In addition to seasonal influenza, the consultation also covered avian influenza, including A(H5N1), A(H7N3), A(H9N2), and variant influenza viruses e.g. A(H3N2)v, some of which are infecting humans sporadically and for which either developmental or commercial vaccines are being made. Based on all relevant considerations, the Advisers provided a recommendation to WHO.

For more information, please contact GISRS-WHOHQ@who.int.

[1] http://www.who.int/influenza/gisrs_laboratory/collaborating_centres/list/en/index.html