Questions and Answers

Recommended composition of influenza virus vaccines for use in the northern hemisphere 2012-2013 influenza season

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 137 National Influenza Centres (NICs) in 107 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 2012-2013 northern hemisphere influenza season?

WHO recommends that influenza vaccines for use in the 2012-2013 northern hemisphere influenza season contain the following viruses:

- 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.

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

This recommendation changed two components of vaccines from those for the 2012 southern hemisphere and 2011-2012 northern hemisphere influenza seasons, which contained the following:

- an A/California/7/2009 (H1N1)pdm09-like virus;
- an A/Perth/16/2009 (H3N2)-like virus; and
- a B/Brisbane/60/2008-like virus.

5. Why was there a recommendation by WHO to change the A(H3N2) component from an A/Perth/16/2009-like to an A/Victoria/361/2011-like virus?

While many viruses circulating since September 2011 were closely related to A/Perth/16/2009, an increasing proportion of the most recent viruses showed reduced reactivity with ferret antisera raised against A/Perth/16/2009 but showed higher titres with sera raised against more recently circulating A(H3N2) viruses. The HA genes of recent viruses fell into two phylogenetic groups represented by A/Victoria/361/2011 (genetic group 3) and A/Brisbane/299/2011 (genetic group 6), with the majority falling within genetic group 3.

Human serology studies using serum panels from groups vaccinated with trivalent vaccines containing A/Perth/16/2009-like antigens also detected reduced reactivity with some of the currently circulating A(H3N2) viruses.

Based on the above analysis, an A/Victoria/361/2011-like virus was recommended for use in vaccines for 2012-2013 northern hemisphere influenza season.

6. **Why was there a recommendation by WHO to change the influenza B component from a B/Brisbane/60/2008-like virus (B/Victoria lineage) to a B/Wisconsin/1/2010-like virus (B/Yamagata lineage)?**

Influenza B viruses of both the B/Victoria/2/87 and the B/Yamagata/16/88 lineages co-circulated in many parts of the world. The recommendation for the influenza B virus component of the vaccine has often been challenging as it is uncertain which lineage of influenza B virus will predominate in the forthcoming season.

The previous vaccine virus, B/Brisbane/60/2008, belongs to the B/Victoria/2/87 lineage and the new vaccine virus, B/Wisconsin/1/2010, belongs to the B/Yamagata/16/88 lineage.

While both lineages of influenza B viruses have co-circulated in the past few years, B/Victoria/2/87 lineage viruses have predominated over B/Yamagata/16/88 lineage viruses. However, in the past few months, the two lineages were observed in similar proportions in many countries, indicating an increase in the prevalence of viruses of the B/Yamagata/16/88 lineage relative to viruses of the B/Victoria/2/87 lineage, although the number of viruses collected so far was relatively small.

The majority of recent viruses of the B/Yamagata/16/88 lineage were antigenically similar to B/Wisconsin/1/2010-like reference viruses and the HA gene sequences of the majority of B/Yamagata/16/88 lineage viruses clustered in a single genetic clade.

Based on the above analysis and knowledge accumulated through monitoring and analysing influenza B viruses of two lineages in the past, the WHO's expert group recommended that the influenza B component of the vaccines for 2012-2013 northern hemisphere season should be a B/Yamagata/16/88 lineage virus and antigenically similar to B/Wisconsin/1/2010.

7. **Could a B/Victoria/2/87 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/2/87 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 2012-2013 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.

8. **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/

9. **How do the recommendations for the 2012-2013 northern hemisphere influenza season relate to the previous WHO recommendation for vaccines for the upcoming 2012 southern hemisphere season?**

To date, the majority of circulating influenza A and B viruses are antigenically similar to the vaccine viruses recommended for the southern hemisphere in 2012. Importantly, vaccines containing A/Perth/16/2009-like viruses can be expected to provide to some extent cross-protection against A/Victoria/361/2011-like viruses. Vaccines containing B/Victoria/2/87 lineage viruses also provide some cross-protection of adult, but not paediatric, populations against B/Yamagata/16/88 lineage viruses.

10. **How was the WHO recommendation made for the composition of influenza virus vaccines for the 2012-2013 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 December 2011 and February 2012, respectively, to review the virus characterization data generated in WHO Collaborating Centres (WHO CCs) and WHO Essential Regulatory Laboratories (WHO ERLs) of GISRS, along with surveillance information from National Influenza Centres (NICs) of GISRS and antigenic cartographic analysis by Cambridge University.

From 20 - 22 February 2012, a WHO Consultation took place with 9 Advisers from WHO CCs and WHO ERLs of GISRS. The Consultation was observed by 20 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. In addition to seasonal influenza, the consultation also covered avian influenza, including A(H5N1) and A(H9N2), and variant influenza viruses e.g. A(H3N2)v, 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.

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