Questions and Answers

Recommended composition of influenza virus vaccines for use in the northern hemisphere 2015-16 influenza season and development of candidate vaccine viruses for pandemic preparedness

February 2015

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 142 National Influenza Centres (NICs) in 112 WHO Member States, 6 WHO Collaborating Centers for Influenza (CCs), 4 WHO Essential Regulatory Laboratories (ERLs) and 13 WHO H5 Reference Laboratories.

This network conducts numerous public health activities including warning and assessment of influenza viruses of public health concern, such as viruses with pandemic potential. NICs collect and test clinical specimens from patients and share representative influenza viruses with the WHO CCs for detailed analysis, and for making recommendations for vaccine composition. 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 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. As it takes

approximately 6-8 months to produce influenza vaccines using egg-based manufacturing processes, 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 2015-16 northern hemisphere influenza season?

WHO recommends that influenza vaccines for use in the 2015-16 northern hemisphere influenza season contain the following viruses:

– an A/California/7/2009 (H1N1)pdm09-like virus
– an A/Switzerland/9715293/2013 (H3N2)-like virus
– a B/Phuket/3073/2013-like virus.

It is recommended that quadrivalent vaccines containing two influenza B viruses contain the above three viruses and a B/Brisbane/60/2008-like virus.

4. Are the vaccine viruses in this recommendation different from those in previous recommendations?

The vaccine viruses recommended for the 2015-16 northern hemisphere influenza season are the same as those used for the 2015 southern hemisphere.

5. How was the vaccine recommendation made for the 2015-16 northern hemisphere influenza season?

Many different sources of information and factors were used to determine the recommended 2015-16 northern hemisphere vaccine viruses, including:

- **Surveillance data from the GISRS network, which includes NICs, WHO CCs, WHO ERLs and WHO H5 Reference Laboratories:**
  Laboratory testing at these designated laboratories identified the different influenza viruses that were circulating and predominant around the globe. These virological data, complemented with epidemiologic and clinical findings, inform the vaccine virus selection process.
- **Genetic characterization of viruses:**
  GISRS laboratories conducted testing to compare genetic sequences of circulating seasonal and zoonotic influenza viruses to determine how related influenza viruses are to one another and current vaccine viruses, how they are evolving, and how genetic changes might influence protection by a given vaccine.
- **Antigenic characterization of viruses:**
  GISRS laboratories, in particular the WHO CCs, also conducted testing to evaluate the antibody or immune response triggered by the proteins on the surface of influenza viruses. The most common of these tests is the haemagglutination inhibition assay, which works by measuring how well antibodies bind to (and thus inactivate) influenza viruses. Other tests used to see how well a particular virus might work as a vaccine candidate include microneutralization assays, plaque reduction neutralization tests,

and serological tests of blood collected from humans that have been immunized with influenza vaccine.

- **Antiviral resistance:**
  GISRS laboratories tested influenza viruses to determine if they have any resistance to the antiviral drugs used to treat influenza infection, such as oseltamivir, zanamivir, peramivir, and laninamivir.
- **Vaccine effectiveness:**
  The Global Influenza Vaccine Effectiveness (GIVE) Collaboration, made up of 17 different study partners, provided information on vaccine effectiveness for northern and southern hemisphere seasons.
- **Availability of potential vaccine candidates:**
  The vast majority of vaccines produced globally use egg-based manufacturing processes. This often requires 6 to 8 months in order to produce the hundreds of millions of doses available for the northern hemisphere season. Selection of potential vaccine candidates also considers the availability of adequate egg-grown viruses and/or virus reassortants used by vaccine manufacturers in order to produce large quantities of vaccine.

These data, and other findings made available by GISRS laboratories, were evaluated during a WHO Consultation from 23 to 25 February 2015. The consultation included nine advisers from WHO CCs and WHO ERLs, and was observed by 26 other experts from WHO CCs, WHO ERLs, WHO H5 Reference Laboratories, NICs, the University of Cambridge and the OIE/FAO Network of expertise on animal influenza (OFFLU).

Based on the findings presented at the consultation meeting, including hundreds of antigenic and genetic test results comparing multiple circulating viruses, potential candidate vaccine viruses, and current vaccine viruses, no changes to the vaccine composition were made from the southern hemisphere influenza season made in September 2014.

With regard to the H3N2 component of the vaccine, this decision was based on the best available data by 25 February 2015. These data indicate that subsets of two clades of H3N2 (3C.2a and 3C.3a) viruses were responsible for the majority of H3N2 infections globally. Epidemiologic and virological data suggested that 3C.2a viruses were emerging as the season progressed to be more predominant in many countries especially in Europe and North America. 3C.3a viruses were circulating and predominant in China, parts of Asia and Africa. The recommended vaccine virus for the 2015 southern hemisphere influenza season, A/Switzerland/9715293/2013, is a 3C.3a virus. In consideration of an available 3C.2a vaccine candidate virus, antigenic data were limited and insufficient for a recommendation. Antigenic testing using antisera raised against A/Switzerland/9715293/2013 (H3N2)-like viruses covered most 3C.2a viruses. This indicates that the vaccine containing A/Switzerland/9715293/2013 (H3N2)-like virus is expected to protect against the majority of 3C.2a viruses.

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 for quadrivalent vaccines, B/Brisbane/60/2008-like viruses continue to be the most appropriate 4th component. In addition, countries or regions of the world that expect B/Victoria lineage viruses to predominate in 2015-16 may choose to use a B/Brisbane/60/2008-like virus in their trivalent influenza vaccines. Approval of the

composition and formulation of vaccines that will be used in each country is the responsibility of national or regional authorities.

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

The WHO recommended candidate vaccine viruses for vaccine development and production for the 2015-16 northern hemisphere influenza season are listed at:
http://www.who.int/influenza/vaccines/virus/candidates_reagents/2015_16_north

The availability of high-growth reassortants by type/subtype, including A(H7N9) and A(H5N1) viruses, and corresponding potency test reagents is posted and updated on the WHO GISRS web site**:** http://www.who.int/influenza/vaccines/virus/en/

8. What happens after the WHO recommendations are made?

Approval of the composition and formulation of vaccines that will be used in each country is the responsibility of national or regional authorities. It is the responsibility of the vaccine manufacturer to obtain the appropriate candidate vaccine viruses and to obtain approval from the local regulatory agency. WHO publishes and updates a list of candidate vaccine viruses for selection by manufacturers and regulatory agencies.
(http://www.who.int/influenza/vaccines/virus/candidates_reagents/2015_16_north)

9. Why does GISRS continue to update the list of available candidate vaccine viruses for pandemic preparedness?

Influenza viruses evolve in animals and may transmit sporadically to humans resulting in zoonotic infections. As part of influenza pandemic preparedness program, the WHO GISRS in collaboration with animal health partners analyses a range of zoonotic and potentially pandemic influenza viruses as they emerge, and develops relevant candidate vaccine viruses as a first step in the production of influenza vaccines. The selection and development of a zoonotic candidate vaccine virus is done for the purposes of having a bank of potential viruses suitable for the immediate development of vaccines, for example during a pandemic, and also to assist those who may want to make pilot lots of vaccines, conduct clinical trials, or perform other pandemic preparedness tasks. The decision to use these materials for vaccine development should be based on an assessment of the public health risk and needs in consultation with national regulatory and public health authorities.

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