Questions and Answers

Recommended composition of influenza virus vaccines for use in the southern hemisphere 2017 influenza season and development of candidate vaccine viruses for pandemic preparedness

29 September 2016

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 143 National Influenza Centres (NICs) in 113 WHO Member States, 6 WHO Collaborating Centres for Influenza (CCs), 4 WHO Essential Regulatory Laboratories (ERLs) and 13 WHO H5 Reference Laboratories.

This network conducts numerous public health activities including assessment of influenza viruses of public health concern, such as viruses with pandemic potential. NICs collect and test more than two millions of clinical specimens annually in recent years 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, risk assessment, 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 and regulatory 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 evaluated and updated frequently because circulating influenza viruses continuously evolve. 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 because approximately 6-8 months are needed to produce and approve vaccines. For countries in equatorial regions, epidemiological considerations influence which recommendation (February or September) individual national and regional authorities consider appropriate.

3. What viruses are recommended by WHO to be included in influenza vaccines for use in the 2017 southern hemisphere influenza season?

WHO recommends that influenza vaccines for use in the 2017 southern hemisphere influenza season contain the following viruses:

– an A/Michigan/45/2015 (H1N1)pdm09-like virus;
– an A/Hong Kong/4801/2014 (H3N2)-like virus; and
– a B/Brisbane/60/2008-like virus.

Among circulating influenza B viruses, there are two distinct lineages. The B/Brisbane/60/2008-like viruses are from the influenza B/Victoria lineage and represent the predominant circulating influenza B virus. Quadrivalent influenza vaccines contain both a B/Victoria lineage and a B/Yamagata lineage vaccine virus. It is recommended that quadrivalent vaccines contain the above three viruses and a B/Phuket/3073/2013-like virus, which represents viruses of the B/Yamagata lineage.

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

Only the influenza A(H1N1)pdm09 vaccine virus recommended for the 2017 southern hemisphere influenza season has been updated compared with the viruses recommended for the 2016 southern hemisphere and those recommended for the northern hemisphere 2016-17 influenza seasons. This updated recommendation is as follows:

- replacement of the A/California/7/2009 (H1N1)pdm09-like virus component with an A/Michigan/45/2015 (H1N1)pdm09-like virus.

All previous WHO recommendations can be found on the WHO Global Influenza Programme website at: http://www.who.int/influenza/vaccines/virus/recommendations/en/

5. Why are there recommendations for vaccines produced in cell culture as well as for vaccines produced in eggs?

Influenza vaccines are made in hens' eggs or in cell culture. Viruses used in egg-based vaccines are isolated and propagated exclusively in hens' eggs while those used in cell culture-based vaccines can be isolated and propagated either in hens' eggs or in an appropriate cell culture system.

6. What is a candidate vaccine virus (CVV)?

A CVV is a virus prepared for potential use in vaccine manufacturing that is antigenically indistinguishable from the virus that has been recommended for use in egg-based or cell culture-based vaccines.

7. How are influenza vaccine recommendations made?

Many different sources of data and information are used to determine the recommended vaccine viruses, including:

- ***Surveillance data from the GISRS network, which includes WHO NICs, WHO CCs, WHO ERLs and WHO H5 Reference Laboratories:***
  Virus surveillance data, complemented with epidemiologic and clinical findings, inform the vaccine virus selection process.

- ***Antigenic characterization of viruses:***
  GISRS laboratories, in particular the WHO CCs, also conduct testing to evaluate the antibody or immune response triggered by the proteins on the surface of influenza viruses. Antigenic cartography is used as a way to visualize relatedness of viruses.

- ***Human serology studies with inactivated influenza virus vaccines:***
  WHO CCs and ERLs use tests to determine how well antibodies from vaccinated people react with recently circulating influenza viruses.

- ***Genetic characterization of viruses:***
  GISRS laboratories conduct testing to compare virus gene sequences of circulating influenza viruses to the sequences of vaccine viruses to determine how genetic changes might influence protection by a given vaccine.

- ***Virus fitness forecasting:***
  Information from modelling studies, based on genetic and antigenic information, is also considered.

- ***Antiviral resistance:***
  GISRS laboratories tested influenza viruses to determine if they have any resistance to the antiviral drugs used to treat influenza infection. This information is taken into consideration when specific viruses are being selected as candidate vaccine viruses.

- ***Vaccine effectiveness:***
  The Global Influenza Vaccine Effectiveness (GIVE) Collaboration, made up of 12 different studies conducted in countries in both the northern and southern hemispheres, provides information on vaccine performance in previous and current influenza seasons.£

- ***Availability of potential vaccine candidates:***
  The vast majority of vaccines produced globally use egg-based manufacturing processes. This requires candidate vaccine viruses which grow well in eggs. These viruses must be available in time to produce the hundreds of millions of doses available for the next influenza season.

These data, and other findings made available by GISRS laboratories, are evaluated during WHO Consultations in February and September of each year. The consultation includes Advisers from WHO CCs and WHO ERLs, as well as observers and 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). Further information about GISRS is available at http://www.who.int/influenza/gisrs_laboratory/en/.

8. Could a B/Yamagata lineage virus still be considered for use as a vaccine component in trivalent vaccines?

Countries or regions of the world that expect B/Yamagata lineage viruses to predominate in 2016-2017 may choose to use a B/Phuket/3073/2013-like virus in their trivalent influenza vaccines. Approval of the composition and formulation of vaccines to be used in each country is the responsibility of national or regional regulatory authorities. Quadrivalent influenza vaccines contain both a B/Yamagata and a B/Victoria lineage vaccine virus, of which a B/Phuket/3073/2013-like virus and a B/Brisbane/60/2008-like virus are currently recommended.

9. 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 2017 southern hemisphere influenza season are listed at:
http://www.who.int/influenza/vaccines/virus/candidates_reagents/2017_south

The availability of high-growth reassortants by type/subtype, including A(H7N9) and A(H5) viruses, and corresponding potency test reagents is posted and updated on the WHO web site**:**
http://www.who.int/influenza/vaccines/virus/en/

10. 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 regulatory 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 the manufacturers and regulatory agencies.
(http://www.who.int/influenza/vaccines/virus/candidates_reagents/home)

11. What vaccine formulation (i.e., recommendation for northern or southern hemisphere influenza season) should countries in equatorial and tropical regions consider for use in vaccines?

Influenza viruses circulate at varying times through the year in equatorial and tropical countries. In selecting which vaccine formulations to use, these countries should consider their surveillance information, in particular epidemiological and virological data to decide when to start vaccination and whether to use the formulation recommended for northern or southern hemisphere influenza season.

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

Influenza viruses circulate widely in some animals and may transmit sporadically to humans resulting in zoonotic infections. As part of an 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 to maintain a bank of potential candidate vaccine 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. Further information about zoonotic influenza candidate vaccine viruses can be found at:
http://www.who.int/influenza/vaccines/virus/characteristics_virus_vaccines/en/

For more information, please contact the WHO Global Influenza Programme at gisrs-whohq@who.int