World Health Organization

Questions and Answers

Recommended composition of influenza virus vaccines for use in the southern hemisphere 2020 influenza season and development of candidate vaccine viruses for pandemic preparedness

27 September 2019

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

GISRS is a global system of public health institutions coordinated by WHO, currently consisting of 142 National Influenza Centres (NICs) in 115 WHO Member States, 6 WHO Collaborating Centres for Influenza (CCs), 4 WHO Essential Regulatory Laboratories (ERLs) and 13 WHO H5 Reference Laboratories.

GISRS monitors the evolution of influenza viruses of public health concern, including seasonal, zoonotic and potential pandemic viruses, and recommends and implements risk assessment and response measures. So far in 2019, NICs collected and tested almost three million clinical specimens and shared more than 8000 representative influenza viruses with the WHO CCs for further analyses. Virus characterization and other analyses, complemented with other available epidemiological and disease information, form the evidence base for public health decisions on epidemic response and pandemic preparedness including seasonal vaccine virus selection and zoonotic influenza candidate vaccine virus development. GISRS 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 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 regularly because circulating influenza viruses continuously evolve. Recommendations are usually made in February for the following influenza season in the northern hemisphere and in September for the following influenza season in the southern hemisphere. This timeframe is decided by the fact that approximately 6-8 months are needed to produce and approve manufactured vaccines.

3. How are influenza vaccine recommendations made?

Data and information from the GISRS network, which includes NICs, WHO CCs, WHO ERLs and WHO H5 Reference Laboratories, and from other sources are used to determine the recommended vaccine viruses, including:

- ***Surveillance data:***
  Virus surveillance data from the GISRS network, complemented with epidemiologic and clinical findings inform the vaccine virus selection process.

- ***Antigenic characterization of viruses:***
  GISRS laboratories, in particular the WHO CCs, 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 WHO ERLs test 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 identify genetic changes that might influence protection conferred by a given vaccine.

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

- ***Antiviral resistance:***
  GISRS laboratories test 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 selected as CVVs.

- ***Vaccine effectiveness:***
  The Global Influenza Vaccine Effectiveness (GIVE) Collaboration, made up of 18 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 Candidate Vaccine Viruses (CVVs):***
  The vast majority of vaccines produced globally use egg-based manufacturing processes. This requires CVVs which grow well in eggs. These viruses must be available in order to produce egg-based vaccines and make those vaccines available in time for the next influenza season. Separate recommendations are made for CVVs used in cell-based manufacturing. Influenza vaccines using recombinant technology do not require CVVs for manufacturing.

These data, and other findings made available by GISRS, are evaluated during WHO Consultations usually in February and September of each year. The Consultation includes experts from WHO CCs, WHO ERLs, WHO H5 Reference Laboratories, NICs, the OIE/FAO Network of expertise on animal influenza (OFFLU), academic institutions, and other national and regional institutions. Further information about GISRS is available at http://www.who.int/influenza/gisrs_laboratory/en/.

4. What viruses are recommended by WHO to be included in influenza vaccines for use in the 2020 southern hemisphere influenza season?

WHO recommends that quadrivalent influenza vaccines for use in the 2020 southern hemisphere influenza season contain the following:

- an A/Brisbane/02/2018 (H1N1)pdm09-like virus;
- an A/South Australia/34/2019 (H3N2)-like virus;
- a B/Washington/02/2019-like virus; and
- a B/Phuket/3073/2013-like virus.

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5. Are the vaccine viruses in this recommendation different from those in the previous northern hemisphere recommendations announced in February-March 2019?

There have been the following updates to the vaccine recommendations:

- replacement of the A/Kansas/14/2017 (H3N2)-like virus with an A/South Australia/34/2019 (H3N2)-like virus; and
- replacement of the B/Colorado/06/2017-like virus with a B/Washington/02/2019-like virus

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

6. Is the vaccine composition for the 2019-2020 northern hemisphere influenza season still appropriate?

The influenza A(H1N1)pdm09 and B/Yamagata lineage virus components have not changed. The 2020 southern hemisphere vaccine will contain an update to address recent changes in circulating influenza A(H3N2) and B/Victoria lineage viruses. Changes to vaccine components are made based on the best available data at the time of the WHO vaccine composition meeting. It is challenging to predict which viruses will be circulating in the forthcoming seasons and whether the chosen vaccine components will optimally cover the circulating influenza viruses.

7. What is the difference between quadrivalent and trivalent vaccines?

Quadrivalent vaccines include two subtypes of influenza A viruses (an A(H1N1)pdm09 virus and an A(H3N2) virus) and two lineages of influenza B viruses (a B/Victoria lineage virus and a B/Yamagata lineage virus). Trivalent vaccines include two subtypes of influenza A viruses (an A(H1N1)pdm09 virus and an A(H3N2) virus) and one type B virus.

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

Influenza viruses circulate at varying times through the year in tropical and sub-tropical countries. In selecting which vaccine formulation 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 the northern or southern hemisphere influenza season. WHO has developed guidance to support countries in tropical and sub-tropical regions in choosing between the northern or southern hemisphere formulations (http://www.who.int/influenza/vaccines/tropics/en/).

9. What are candidate vaccine viruses (CVVs)?

A CVV is a virus prepared for potential use in vaccine manufacturing that is antigenically similar to the virus that has been recommended for use in vaccines.

10. What CVVs are available for use in influenza vaccines?

The WHO recommended CVVs for vaccine development and production for the 2020 southern hemisphere influenza season are listed at:
www.who.int/influenza/vaccines/virus/candidates_reagents/2020_south/en/

The availability of CVVs by type/subtype, including zoonotic viruses, and corresponding potency test reagents is posted and updated on the WHO web site:
http://www.who.int/influenza/vaccines/virus/en/

11. Why does GISRS continue to update the list of available CVVs 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 evolve and develops relevant CVVs as a first step in the production of some influenza vaccines. The selection and development of a zoonotic CVV is done to maintain a bank of 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 the assessment of public health risk and needs in consultation with national regulatory and public health authorities.

12. 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 manufacturers to obtain the appropriate CVVs and to obtain approval from the local regulatory agencies. WHO publishes and updates a list of CVVs for selection by the manufacturers and regulatory agencies.
(http://www.who.int/influenza/vaccines/virus/candidates_reagents/home)

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