

Questions and Answers

Recommended composition of influenza virus vaccines for use in the northern hemisphere 2024-2025 influenza season and development of candidate vaccine viruses for pandemic preparedness

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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 151 National Influenza Centres (NICs), 7 WHO Collaborating Centres for Influenza (CCs), 4 WHO Essential Regulatory Laboratories (ERLs) and 12 WHO H5 Reference Laboratories in 129 WHO Member States. The GISRS laboratories function year-round under WHO [Terms of Reference](#), sharing surveillance findings and virus materials in a timely fashion to inform risk assessment and mitigation measures including updates of seasonal influenza virus vaccines.

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. Virus characterizations are combined with other available epidemiologic and disease information to 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 (CVV) 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 virus vaccines for the next influenza season and for pandemic preparedness. In contrast to many other vaccines, the viruses in influenza virus vaccines need to be evaluated and updated regularly because circulating influenza viruses evolve continuously. 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. The recommendation dates are chosen to provide approximately 6-8 months for the production, regulatory approval and distribution of the manufactured vaccines.

For pandemic preparedness, CVV development is considered at least twice a year. The decisions are based on continuous surveillance for zoonotic events (human infection with an influenza virus normally restricted to a non-human host) and influenza activity in animals.

3. What are candidate vaccine viruses (CVVs)?

Haemagglutinin (HA) is the primary antigen in influenza virus vaccines. A CVV is a virus prepared for potential use in vaccine manufacturing that possesses an HA which WHO CCs have determined to be antigenically similar to the virus that has been recommended for use in vaccines.

4. How are influenza virus 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 make vaccine virus recommendations. This includes:

- ***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 WHO CCs, use post-infection ferret antisera and pooled post-vaccination human sera to evaluate antibody reactivity with the surface proteins (antigens) of circulating and vaccine influenza viruses. Antigenic cartography is used to visualize relatedness of viruses based on the data provided by WHO CCs.
- ***Human serology studies with 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 gene sequencing to compare the sequences of circulating influenza viruses with those of vaccine viruses to identify genetic changes that might influence protection conferred by a given vaccine.
- ***Virus fitness forecasting:***
Virus fitness relates to the likelihood of any emerging groups of viruses becoming more prevalent in coming months. Information from modelling studies, based on genetic sequences available in databases and antigenic information provided by the WHO CCs is considered.
- ***Antiviral susceptibility:***
GISRS laboratories analyse influenza viruses to determine if they remain susceptible to the antiviral drugs approved for treatment of influenza infections. 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 many different studies conducted in countries in both the northern and southern hemispheres, provides information on vaccine performance in previous influenza seasons and interim reports on the current season.
- ***Availability of CVVs:***
CVVs are essential for production of vaccines in a timely manner for the next influenza season. Most vaccines produced globally use egg-based manufacturing processes which require CVVs that replicate well in eggs while cell-based vaccines require CVVs that replicate well in cell culture. Separate recommendations are made for egg- and cell-based CVVs because of the differing replication and manufacturing processes. Influenza virus vaccines comprised of recombinant influenza protein antigens do not require CVVs for manufacturing.

These data, and other findings made available by GISRS, are evaluated during WHO Consultations usually held in February and September of each year. The consultations include experts from WHO CCs, WHO ERLs, WHO H5 Reference Laboratories, NICs, the WOAHA/FAO Network of expertise on animal influenza (OFFLU), academic institutions, and other national and regional institutions. Further information about GISRS is available on the [WHO website](#).

5. Which viruses are recommended by WHO to be included in influenza virus vaccines for use in the 2024-2025 northern hemisphere influenza season?

WHO recommends that vaccines for use in the 2024-2025 northern hemisphere influenza season contain the following:

Egg-based vaccines

- an A/Victoria/4897/2022 (H1N1)pdm09-like virus;
- an A/Thailand/8/2022 (H3N2)-like virus; and
- a B/Austria/1359417/2021 (B/Victoria lineage)-like virus.

Cell culture- or recombinant-based vaccines

- an A/Wisconsin/67/2022 (H1N1)pdm09-like virus;
- an A/Massachusetts/18/2022 (H3N2)-like virus; and
- a B/Austria/1359417/2021 (B/Victoria lineage)-like virus

For countries that still use quadrivalent egg- or cell culture-based or recombinant vaccines with two influenza B components, the B/Yamagata lineage component remains unchanged from previous recommendations:

- a B/Phuket/3073/2013 (B/Yamagata lineage)-like virus.

6. What does the term “-like virus” mean in the vaccine composition recommendation?

Recommended vaccine viruses are representative of the antigenic group of viruses anticipated to circulate widely in the forthcoming influenza season. Often multiple CVVs are available which possess HA antigens from other viruses that are antigenically similar to the recommended vaccine viruses. The term “-like virus” is included to allow for the use of these other CVVs for vaccine manufacturing.

7. Why are different viruses sometimes recommended for egg- and cell-based vaccines?

Influenza viruses may not replicate equally well in the egg- and cell-based vaccine production systems. Therefore, different viruses with similar antigenic properties are sometimes recommended for the two production systems.

The use of cell-based vaccine virus sequences is recommended for recombinant protein or other relevant platforms of influenza virus vaccine production.

8. Are the vaccine viruses in this recommendation different from those in the previous northern hemisphere recommendations announced in February 2023?

The following updates to the vaccine have been recommended:

For the A(H3N2) vaccine component, replacement of the A/Darwin/6/2021-like virus with A/Massachusetts/18/2022-like virus for cell culture-based or recombinant vaccines and A/Darwin/9/2021-like virus with A/Thailand/8/2022-like virus for egg-based vaccines.

Previous and present WHO influenza virus vaccine composition recommendations can be found on the WHO Global Influenza Programme [website](#).

9. Are the vaccine viruses in this recommendation different from those in the southern hemisphere recommendations announced in September 2023?

The viruses recommended for production of 2024-2025 northern hemisphere vaccines are the same as the recommendation for the 2024 southern hemisphere vaccine.

10. Why is a B/Yamagata lineage vaccine component no longer needed?

There have been no confirmed naturally occurring B/Yamagata lineage virus detections after March 2020. Further to the [WHO September 2023 recommendation](#), it remains the opinion of the WHO influenza vaccine composition advisory committee that the B/Yamagata lineage antigen should be excluded from influenza vaccines as it is no longer needed. National or regional authorities should make decisions regarding the transition to trivalent influenza vaccines in their jurisdictions.

11. What is the difference between quadrivalent and trivalent influenza virus vaccines?

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

12. Who recommends, approves, and advises on influenza virus vaccine composition and use?

The WHO influenza vaccine composition advisory committee recommends which viruses should be used to make influenza virus vaccines. In each country, national or regional authorities approve the composition and formulation of vaccines (including trivalent or quadrivalent) and develop policy for the use of influenza virus vaccines in their jurisdictions.

13. How is GISRS monitoring for B/Yamagata-lineage viruses?

The WHO GISRS conducts year-round surveillance for influenza viruses. Clinical specimens are submitted to National Influenza Centres (NICs) of GISRS and are tested for influenza and potentially other respiratory viruses of public health importance. NICs perform lineage determination on a subset or all B viruses detected. In addition, representative influenza viruses (clinical specimens and/or virus isolates) are shipped to a WHO Collaborating Centre (CC) of GISRS for advanced antigenic and genetic characterization.

In recent years, each [FluNet](#) report of a B/Yamagata lineage virus detection has been followed up. After March 2020, there have been no naturally circulating B/Yamagata lineage viruses confirmed by a WHO CC or a NIC.

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

WHO has developed [guidance](#) to support countries in tropical and subtropical regions in choosing between the northern and southern hemisphere formulations. These countries should consider their epidemiologic and virologic surveillance data in selecting which vaccine formulation to use and deciding when to start vaccination.

15. Which CVVs are available for use in influenza virus vaccines?

The WHO recommended CVVs for vaccine development and production for the 2024 southern hemisphere influenza season are listed on the [WHO website](#).

The available CVVs, including those for pandemic preparedness purposes ([zoonotic viruses](#)), and corresponding potency test reagents are posted by type/subtype and updated on the [WHO website](#).

16. 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. Human infections with influenza viruses from birds and pigs continue to be detected and these viruses remain a public health threat. As such, GISRS continues to update the list of available CVVs for pandemic preparedness purposes and conducts risk assessments when zoonotic events are identified. The [influenza monthly risk assessment summaries](#) are published on the WHO website.

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 influenza virus vaccines. The selection and development of CVVs against zoonotic/potentially pandemic strains 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.

17. 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 or protein sequences and to obtain approval for their use from the relevant regulatory agencies. WHO publishes and updates a [list](#) of recommended CVVs and sequence accession numbers.

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