What CDC Does

FluVaxView
Communications Resource Center
International Work
Outbreak Investigations

Influenza Types

Seasonal
Pandemic
Avian
Swine
Influenza in Animals

Selecting Viruses for the Seasonal Influenza Vaccine

Español | Other Languages Print

A|) flu vaccine for 2024-2025 will be trivalent (three-component).

Summary

Seasonal influenza (flu) vaccines are designed to protect against the four main groups of flu: Type A and B viruses that research indicates are most likely to spread and cause illness among people during the upcoming flu season. All current U.S. flu vaccines protect against a flu A(H1) virus, a flu A(H3) virus, a flu B/Yamagata lineage virus and a flu B/Victoria lineage virus. Each of these four vaccine virus components are selected based on the following:

- which flu viruses are making people sick prior to the upcoming flu season,
- the extent to which those viruses are spreading prior to the upcoming flu season,
- how well the previous season's vaccines may protect against those flu viruses, and
- the ability of vaccine viruses to provide cross-protection against a range of related flu viruses of the same type or subtype/lineage.

There are currently 144 national influenza centers in over 114 countries that conduct year-round surveillance for flu viruses as part of the World Health Organization (WHO) Global Influenza Surveillance and Response System (GISRS). This involves receiving and testing thousands of flu virus samples from patients. For human seasonal flu surveillance, the laboratories send representative viruses to five* of the seven WHO Collaborating Centers for Influenza, which are located in the following places:

- Atlanta, Georgia, USA (Centers for Disease Control and Prevention, CDC)
- Memphis, Tennessee, USA (St. Jude Children's Research Hospital)
- London, United Kingdom (The Francis Crick Institute)
- Melbourne, Australia (Victoria Infectious Diseases Reference Laboratory)
- Tokyo, Japan (National Institute for Infectious Diseases)
- Beijing, China (National Institute for Viral Disease Control and Prevention)
- Koltsovo, Russian Federation (State Research Center of Virology and Biotechnology "VECTOR," Rospotrebnadzor)

*Note: Two of the WHO Collaborating Centers: the one in Memphis, Tennessee and the one in Koltsovo, Russian Federation only collect flu virus specimens from animals and do not participate in human seasonal flu surveillance.

Twice a year, the WHO organizes a consultation with the Directors of the seven WHO Collaborating Centers, Essential Regulatory Laboratories and representatives of key national laboratories and academies. They review results from surveillance, laboratory, and clinical studies, and the availability of flu vaccine viruses and make recommendations on the composition of flu vaccines. These meetings take place in February for selection of the upcoming Northern Hemisphere's seasonal flu vaccines and in September for the Southern Hemisphere's flu vaccines. The WHO vaccine composition committee, which is comprised of independent technical advisors, i.e., directors of each of the WHO Collaborating Centers and ERLs), meets to present global flu data and recommend specific vaccine viruses for trivalent (three-virus component) and quadrivalent (four-virus component) flu vaccines. Next, each country makes its own decision about which viruses should be included in flu vaccines licensed in their country.

In the United States, the Food and Drug Administration (FDA)'s Vaccines and Related Biological Products Advisory Committee (VRBPAC) makes the final decision about vaccine viruses for domestic flu vaccines. Information about the circulation of flu viruses and available vaccine viruses is summarized and presented to VRBPAC in February or March of each year for the U.S. decision about which viruses to include in the upcoming season's flu vaccine.

Questions & Answers

What is CDC Influenza Division's role in vaccine virus selection?

As one of seven WHO Global Influenza Surveillance and Response System's (GISRS) WHO Collaboration Centers, CDC's Influenza Division receives and tests thousands of influenza viruses from around the world each year and collaborates with other WHO Collaborating Centers and national influenza centers in the annual seasonal vaccine virus selection process for the Northern and Southern hemispheres. CDC plays a major role in identifying and testing the flu viruses that are spreading globally through its global surveillance activities and preparing candidate vaccine viruses (CVVs). The Influenza Division provides this information during the WHO vaccine consultation meetings and participates in discussions regarding which viruses should be recommended by WHO and, in the United States, FDA VRBPAC decisions for inclusion in flu vaccines.

What are the main factors that influence which viruses are selected for use in flu vaccine production each year?

The flu viruses in seasonal flu vaccines are selected each year based on a variety of data, including the following:

- **Epidemiologic data**: Global flu surveillance is conducted year-round by GISRS to determine which flu viruses are circulating in different areas and at different times.
- **Genetic data:** Flu viruses are constantly changing, and all flu viruses undergo genetic changes over time. A flu virus' genome consists of all the genetic information that makes up the virus. CDC conducts genetic characterization of circulating flu viruses to monitor changes in the genomes of these viruses throughout the year. The information CDC collects from studying genetic changes is important because it helps to determine whether vaccines and antiviral drugs will work against circulating flu viruses as well as helping to determine the potential for animal flu viruses to infect humans. A laboratory process called genetic sequencing is performed on flu viruses collected throughout the year to monitor how circulating flu viruses are changing. The process of comparing genetic sequences is called genetic characterization. Learn more: Influenza Virus Genome Sequencing and Genetic Characterization.
- **Antigenic data:** "Antigens" are molecular structures on the surface of viruses that are recognized by the immune system and can trigger an immune response (i.e., production of antibodies). For flu viruses, the major antigens are the virus' surface proteins, hemagglutinin and neuraminidase. The term "antigenic properties" is used to describe the antibody or immune response triggered by the antigens of a particular virus. "Antigenic characterization" refers to the analysis of a virus' antigenic properties to help assess its similarity to another virus. Antigenic characterization relies on testing blood (antisera) of ferrets (with no prior flu infections or vaccinations) after they are infected with a flu virus. Antiserum is blood serum containing antibodies against specific antigen. Ferrets are infected with an influenza virus (such as a vaccine virus) to raise antisera (blood containing antibodies specific to that particular influenza virus). If the vaccine virus-induced antibodies produced by ferrets effectively target and neutralize circulating flu viruses (e.g., A/(H1N1)pdm09), then these viruses are considered to be "antigenically similar" to the vaccine virus. Therefore, it is likely that the current flu type A(H1) vaccine component is capable of providing protection and may not need to be updated. In contrast, if the vaccine-induced antibodies do not effectively target and neutralize currently circulating flu viruses, then the viruses are "antigenically different" or "drifted," and this vaccine component may need to be updated. Because the ferrets whose blood (antisera) is used in antigenic characterization have never been vaccinated or infected with influenza previously, the antibodies they produce are specific to the virus used to raise antibodies. For this reason, antigenic data obtained using ferret antisera are helpful for making early risk assessments of circulating flu viruses and for selecting candidate vaccine viruses (CVVs).
  - Antigenic characterization testing is done separately for each of the four vaccine components in the U.S. seasonal flu vaccine. And the vaccine composition for each component is independently decided. In some seasons, one or more of the components of the flu vaccine may need to be updated.
  - Ferret antisera are also used to qualify new candidate vaccine viruses (CVVs) as antigenically similar to the recommended vaccine virus. A CVV is a flu virus prepared by CDC or public health partners for use by vaccine manufacturers to produce a flu vaccine.
- **Human serology studies:** CDC's Influenza Division uses human serology data to improve the selection of viruses recommended for inclusion in seasonal flu vaccines. Serology is the scientific study of blood to look at the response of the immune system to vaccination or infection with pathogens, like flu viruses. Serology tests, also known as antibody tests, are conducted on a person's blood serum to look for the presence of antibodies. CDC collects blood samples from people of all age groups and from different geographic areas both before and after flu vaccination. Laboratory tests including the hemagglutination inhibition assay (HI test) and microneutralization assay, are commonly used for serology testing. The goal is to measure how well the antibodies elicited from flu vaccination can recognize and neutralize the flu viruses in circulation. If the antibodies produced from vaccination effectively neutralize circulating flu viruses, then it is likely that the current flu vaccine's composition is appropriate and will protect people during the upcoming flu season. This could signal that the flu vaccine's composition does not need to be updated. In contrast, if the antibodies produced from vaccination do not effectively neutralize currently circulating flu viruses, then it is likely that this component will need to be updated. Human serology studies are useful because people have varying levels of pre-existing antibodies from prior infections and vaccinations, and therefore, may respond to vaccines differently from ferrets with no pre-existing antibodies to flu.
- **Evolutionary analysis and data integration:** Flu viruses are assessed in terms of their evolutionary characteristics and fitness advantages and disadvantages that affect their ability to compete against other circulating flu viruses. Flu forecasts are made to anticipate which flu viruses are the most likely to circulate and predominate during the coming season. Flu forecasts are made independently for each of the four distinct flu virus groups.
- **Vaccine effectiveness studies:** Vaccine effectiveness studies are conducted each year to assess how well available flu vaccines are working to protect against circulating flu viruses in real-world conditions. Vaccine effectiveness studies can measure different outcomes, such as how well vaccines work to prevent illness resulting in a doctor's visit, or illness resulting in hospitalization, intensive care unit (ICU) admission, or even death associated with flu. Virus factors and host factors, such as age, underlying medical conditions, history of prior flu illness, and prior flu vaccination, all can affect the benefits received from vaccination. The most important factor that affects the benefits provided by flu vaccines is the degree to which vaccine viruses are antigenically similar to circulating flu viruses. Since all these factors play a role in the benefits provided by flu vaccines, it is important to collect all the different kinds of data described on this page.

Availability of good vaccine candidate viruses: Candidate vaccine viruses (CVVs) must be tested and available in time to allow for manufacturers to produce the large amount of vaccine virus needed to make flu vaccines. CVVs are chosen to protect against the viruses likely to circulate during the upcoming season. There are numerous factors that can make getting a good vaccine virus for vaccine production challenging, including both scientific issues and time issues. For example, CVVs must be prepared and made available to vaccine manufacturers early enough for them to produce vaccine in time for flu season. Historically, vaccine viruses were required by FDA to be isolated and grown in chicken eggs, but now the FDA allows vaccine viruses to be grown in mammalian cell lines, too. Some flu viruses, like flu A(H3N2) viruses grow poorly in eggs, making it challenging to get good CVVs for vaccine production. CVVs grown in eggs can develop changes caused by virus adaptation to eggs and such changes can reduce antigenic similarity of vaccine virus to circulating viruses. Vaccines that use newer technologies, such as cell culture-based or recombinant flu vaccines, are not affected by egg-adapted changes.

In some years certain influenza viruses may not circulate until later in the influenza season, making it difficult to prepare a candidate vaccine virus in time for vaccine production. This can make vaccine virus selection very challenging.

How does CDC determine if the vaccine virus will protect against a circulating virus?

CDC's Flu Division collects and reports information on flu activity in the United States each week. Laboratory studies of circulating flu viruses allow CDC to evaluate the ability of vaccine viruses to target and neutralize circulating flu viruses each season. Genetic characterization can inform decision-making for vaccine virus selection based on similarities between the genomes of vaccine viruses and circulating flu viruses. Antigenic characterization can indicate if circulating viruses have evolved in such a way that the current flu vaccine may not produce an optimal immune response against them. Antigenic characterization plays an important role in early assessments of how well a vaccine may work by looking at how well ferret antibodies can target and neutralize circulating flu viruses. Because the ferrets used in antigenic characterization testing have never been vaccinated or infected with influenza previously, they produce very specific and narrowly focused antibodies. However, one limitation of antigenic characterization data using ferrets antisera is that it does not account for the human experience and how a person's prior flu virus infections and vaccinations can influence the way their immune system responds to current flu vaccines. As a result, CDC also uses human serology studies that involve collecting blood samples from people. As part of these studies, people's antibodies (found in their blood) are tested to determine whether they target and neutralize circulating flu viruses, both before and after vaccination. Such studies better account for the role prior infections and vaccinations play in the human immune response to vaccination. The most direct measure of the protection received from flu vaccination comes from vaccine effectiveness studies. For more information, see Vaccine Effectiveness – How Well Does the Flu Vaccine Work? For more information about CDC's surveillance and to access the weekly reports, visit Flu Activity and Surveillance.

What happens after a recommendation has been made about which viruses should be included in the seasonal flu vaccine?

As soon as recommendations have been made about what viruses should be included in the vaccine, private sector manufacturers begin the process of producing vaccine. In fact, some manufacturers may start growing one or more viruses for use in production of vaccine even before a WHO recommendation or FDA decision is made on the vaccine viruses. This gives manufacturers more time to make vaccine ahead of the season; the more time a manufacturer has to make vaccine, the greater the number of doses that can be produced.

How long does it take to manufacture seasonal flu vaccine?

Currently, it takes at least six months to produce large quantities of flu vaccine. For information about flu vaccine production, see How Influenza (Flu) Vaccines Are Made.

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