



PARENTS PACK

MONTHLY UPDATES ABOUT
VACCINES ACROSS THE LIFESPAN

Flu vaccine: What's in the vial?

November 2022

Most of us are supposed to get a flu vaccine every year. Unfortunately, some of us don't actually get it. Although the reasons vary, in some cases the lack of follow-through comes down to not knowing or understanding what is in the vaccine vial. For example, some people with egg allergies mistakenly think they can't get the influenza vaccine because it contains eggs. Others are concerned that the influenza vaccine contains a mercury-based chemical, called thimerosal, even though most influenza vaccines no longer contain this ingredient and when it is included, the amount has been found to be safe. So, this month, we thought it might help to offer more details about what is — and is not — in flu vaccines.

Flu vaccines: What's in the vial?

Vaccines, including those for influenza, typically contain up to five categories of ingredients, but not all vaccines contain all five categories. So, let's take a look at each category when it comes to influenza vaccines.

Antigens: Antigens are the active ingredient of the vaccine to which we make an immune response. When it comes to influenza vaccines, two aspects of the antigen are worth considering:

1. Which four influenza viruses does the vaccine protect against?
2. Which presentation, or part of influenza virus, is used in a particular product?

Which four influenza vaccines does the vaccine protect against?

Most of us are familiar with the fact that influenza vaccines change annually to better match the strains of the virus predicted to circulate in our communities. All approved influenza vaccines protect against two influenza A viruses and two influenza B viruses. How well the vaccine viruses match the circulating viruses is critical to the overall effectiveness of influenza vaccines in any given season.

Regardless of which influenza vaccine you receive, it will include components of four influenza viruses.

Which presentation of influenza virus is used?

Most influenza vaccines contain whole influenza viruses; however, only one version, FluMist®, contains virus that can still replicate weakly after the vaccine is administered. The other whole virus versions — Afluria®, Fluarix®, FluLaval®, Fluzone®, and Flucelvax® — all contain viruses that have been rendered incapable of replicating through chemical disruption of the outer membrane of the virus. In the case of Flucelvax, additional purification steps remove some proteins found inside of the virus. For this reason, Flucelvax is sometimes referred to as a “subunit” vaccine, whereas the other inactivated influenza vaccines are referred to as “split virus” vaccines because of the disrupted surface of the virus.

Two influenza vaccines contain only proteins from the surface of influenza virus:

1. Fludac® contains two surface proteins, known as hemagglutinin and neuraminidase. These are the two proteins used to identify different types of influenza viruses.
2. Flublok®, made using recombinant DNA technology, only contains the hemagglutinin protein.

The form of virus used and how the vaccine is made are closely related. You can find more detailed descriptions of the process of making different types of influenza vaccines in our Q&A, “Influenza: What you should know.”

Importantly, regardless of the presentation of the virus, none of the influenza vaccines can cause someone to become ill with influenza.

Adjuvants: An adjuvant is added to some vaccines to enhance the recipient's immune response to the vaccine. The only flu vaccine that contains an adjuvant is Fludac, which includes an adjuvant known as MF59. None of the influenza vaccines contain aluminum salts, the most common adjuvant used in vaccines.

Stabilizers: One important part of creating a vaccine is making sure that it remains stable during shipping and storage, so it works the way it is supposed to when administered. This is the role of stabilizers. Typical stabilizers include salts and other chemicals that maintain the integrity of the antigen. Because stabilizers are present in low quantities, they generally do not present any safety issues, but one stabilizer that can cause concerns is gelatin, as some people have gelatin-related allergies. The only influenza vaccine that contains gelatin is FluMist.

Preservatives: Like stabilizers, preservatives ensure that vaccine integrity is maintained in the time between when the vaccine is made and when it is administered. Whereas stabilizers keep what's supposed to be in the vial stable, preservatives keep what shouldn't be in the vial out. For example, if a vial contains multiple vaccine doses, bacteria on the rubber cap could inadvertently get into the vial on the tip of a needle being used to draw up the vaccine dose. While bacteria wouldn't be a problem for the recipient of that dose, without preservatives, it may begin to reproduce in the vial, so the next dose not only contains the antigen but also the germ.

The preservative that many people have heard of is thimerosal, a mercury-containing chemical, long dogged with unfounded safety concerns. Given the history of concerns about thimerosal, most vaccines no longer include it. To eliminate the need for thimerosal, manufacturers started making most vaccines in single-dose vials. However, a small number of influenza vaccines can still be ordered in multi-dose vials and, therefore, still contain thimerosal, including some (but not all) supplies of Afluria, Fluzone, and Flucelvax.

To find out more about thimerosal and the studies looking at its safety, check the “Vaccine Ingredients – Thimerosal” page of our website.

Importantly, if the choice is to receive a flu vaccine with thimerosal or wait for another version, it is safer to get the thimerosal-containing vaccine for three reasons:

1. **The quantities contained in the vaccine have been shown not to be harmful.**
2. **It takes about two weeks after vaccination to develop immunity, during which time, you could become ill with the virus.**
3. **Some people who delay never go back to get the vaccine.**



TRIVIA CORNER

Who should get the influenza vaccine?

- a) Everyone 5 years of age and older
- b) Just infants less than 1 year old
- c) Only adults who may be at increased risk of complications from influenza
- d) Everyone 6 months of age and older

Flu vaccine: What's in the vial? [cont.]

Residual manufacturing byproducts: The antigens in vaccines are from biological systems, which means vaccines cannot be made simply by mixing together a series of ingredients, such as we do when we bake a cake or even as manufacturers of medications like ibuprofen or antacids are able to do. As a result, the “ingredients” needed to make a vaccine are often more complex, and although most are removed completely or almost completely, residual amounts may remain in the vaccine vial. These must be listed, even though oftentimes the amounts are so miniscule that they would either not retain their potential impact or be recognizable by our bodies if isolated from the final product. Examples from influenza vaccines (and which vaccines they are found in) include the following:

- **Antibiotics** – neomycin sulfate (Afluria, Fluad), polymyxin B (Afluria), gentamicin sulfate (Fluarix, FluMist), kanamycin (Fluad)
- **Antifungals** – sodium deoxycholate (Fluarix, Flulaval)
- **Nonhuman cell debris** – canine kidney cells (Fluclavax); baculovirus and fall armyworm cell proteins (Flublok)
- **Nonhuman DNA** – canine kidney cell DNA (Fluclavax); baculovirus and fall armyworm DNA (Flublok)
- **Egg protein or ovalbumin** (Afluria, Fluarix, Flulaval, FluMist, Fluad)
- **Formaldehyde** (Fluarix, FluLaval, Fluzone, Fluad)
- **Hydrocortisone** (Afluria, Fluarix, Fluad)
- **Polysorbate** (FluLaval, Flublok)

Despite the low levels of egg protein in some influenza vaccines, people with egg allergies can get vaccinated against influenza. If affected, individuals can check if an egg-free version is available, but if not, they can get any version. Regardless, people with egg allergies should plan to remain at the vaccination site for 30 minutes after receiving influenza vaccine on the remote chance that they experience a reaction.

Flu vaccines: What's NOT in the vial?

Sometimes as important as what is in the vial, is what is not in the vial.

The following ingredients are not contained in any influenza vaccines distributed in the U.S.:

- Fetal cells
- Human DNA
- Blood products
- Soy
- Gluten
- Microchips
- COVID-19 antigens, including genes, proteins, or whole virus particles — While combination COVID-19 and influenza vaccines have been discussed, and at least one version was tested in small numbers of people, no company has submitted a request for approval of this type of product at this time. Further, a company cannot make a change to an existing vaccine without submitting a request to change it. For the revised vaccine to be approved, the company needs to provide data showing it is as safe and effective as the older version.

The only influenza vaccine that contains an ingredient of porcine origin is FluMist (gelatin).

Although people with latex allergies sometimes need to avoid vaccines with latex-based packaging, this is not a concern for influenza vaccines as no influenza vaccine currently distributed in the U.S. has natural rubber latex in the packaging.

Summary

Hopefully, by having a better sense of what is in influenza vaccines and what is not, some people who have previously been hesitant to protect themselves against influenza will be more comfortable to do so.

For links to referenced resources, visit the online version of the Feature Article, bit.ly/3hg8m8c.

Trivia Answer

The correct answer is D. The influenza vaccine is recommended for everyone 6 months of age and older. Because influenza viruses change frequently, people should receive a dose of influenza vaccine every year.

Subscribe to our newsletter

If you're interested in receiving our free email newsletter, visit our website: www.vaccine.chop.edu/parents to sign up. If you have a question about vaccines, visit the Vaccine Education Center website: www.vaccine.chop.edu.

Send us your comments

If you have any comments about this newsletter or suggestions about how we can make our program more helpful, please send them to contactPACK@chop.edu.