Ask the Experts

The Immunization Action Coalition extends thanks to our experts, medical officers Andrew T. Kroger, MD, MPH; Candice L. Robinson, MD, MPH; Raymond A. Strikas, MD, MPH, FACP, FIDSA; and nurse educators Donna L. Weaver, RN, MN, and JoEllen Wolicki, BSN, RN, all with the National Center for Immunization and Respiratory Diseases at the Centers for Disease Control and Prevention (CDC).

Influenza vaccines

What's new in the 2017–18 influenza vaccine recommendations?

The 2017–18 ACIP influenza vaccine recommendations were published on August 25, 2017, and are available online at www.cdc.gov/mmwr/volumes/66/rr/pdfs/rr6602.pdf. The new guidance

- Describes the vaccine composition for this season (a change in the A/H1N1 component);
- Discusses recent FDA licensure and labelling changes including
  - approval of Afluria Quadrivalent (Seqirus) and Flublok Quadrivalent (Protein Sciences);
  - expansion of the age indication for FluLaval Quadrivalent (GSK) to age 6 months and older (previously licensed for people 3 years and older);
  - expansion of the age indication for Afluria (Seqirus) to include persons 5 years and older (previously recommended for persons 9 years and older); and
- Recommends that live attenuated influenza vaccine (LAIV, FluMist; AstraZeneca) not be used during the 2017–18 season.

Which influenza vaccines will be available during the 2017–18 influenza season?

Multiple manufacturers are producing influenza vaccine for the U.S. market for the 2017–18 season. Inactivated vaccines will be produced using egg-based, cell culture–based, and recombinant technologies. Some of the inactivated influenza vaccines will be quadrivalent (containing four strains of influenza virus) rather than trivalent (three strains). LAIV may be available but is not recommended for use during the 2017–18 season. A complete listing of influenza vaccine products is available from the Immunization Action Coalition (IAC) at www.immunize.org/catg.d/p4072.pdf.

Who is recommended to be vaccinated against influenza?

ACIP recommends annual vaccination for all people ages 6 months and older who do not have a contraindication to the vaccine.

When should influenza vaccine be given?

You can begin administering vaccine as soon as it becomes available. Optimally, vaccination should occur before onset of influenza activity in the community. Healthcare providers should offer vaccination by the end of October, if possible, and vaccination activity should continue through the fall and winter months, as long as influenza virus is circulating in the community. Early vaccination of children younger than age 9 years who need 2 doses of vaccine can be helpful in assuring routine second doses are given before the influenza season begins.

When administering influenza vaccine, is giving patients a VIS mandatory or is it only "recommended"?

Giving patients an influenza Vaccine Information Statement (VIS) is mandatory under the National Childhood Vaccine Injury Act of 1986. The VIS must be given to all adults as well as to parents or guardians of children prior to vaccination. Two VISs are available, one for LAIV (although LAIV is not recommended to be used during the 2017–18 season) and one for inactivated influenza vaccine (IIV). Each can be found at www.immunize.org/vis along with many translations. The influenza VIS has been modified so that it does not need to be replaced each year. The 2015–16 influenza VIS (used for the past two years) should be used during the 2017–18 season.

Which influenza vaccines can we give to children?

Among the injectable inactivated influenza vaccines, both Fluzone (Sanofi Pasteur) and FluLaval are approved by the FDA for use in children ages 6 through 35 months. There are several inactivated influenza vaccines that can be given to children age 3 years or older.

Please provide details about the use of FluLaval influenza vaccine in children younger than 3 years.

On November 18, 2016, the FDA approved an extension of the age range of quadrivalent FluLaval IIV to include children 6 through 35 months of age. FluLaval was previously approved for people 3 years of age and older. The approval of the extended age range for FluLaval was based on a study showing an equivalent ("non-inferior") response compared to children who received the Fluzone pediatric dosage. The vaccine is supplied for this indication in manufacturer-filled syringes and multi-dose vials. The dosage approved for children 6 through 35 months of age is 0.5 mL – the same dosage as for people 3 years of age and older.

Which children younger than age 9 years will need 2 doses of influenza vaccine in this influenza season?

Children age 6 months through 8 years should receive a second dose 4 weeks or more after the first dose 1) if they are receiving influenza vaccine for the first time, 2) if they did not receive a total of at least two doses of trivalent or quadrivalent influenza vaccine before July 1, 2017, or 3) if their vaccination history is unknown. The two doses need not have been received during the same season or consecutive seasons. IAC's handout titled "Guide for Determining the Number of Doses of Influenza Vaccine to Give to Children Ages 6 Months Through 8 Years" provides guidance on this issue; it is available at www.immunize.org/catg.d/p3093.pdf.

Can a child 6 through 35 months of age who needs 2 doses of influenza vaccine this season receive one each of Fluzone and FluLaval vaccine?

Yes. Both Fluzone (0.25 mL dose) and FluLaval (0.5 mL dose) are approved by the FDA for use in children 6 through 35 months of age.

If a child receives Fluzone vaccine (0.25 mL) at age 34 or 35 months for the first time and then returns for the second dose at age 37 months, should we give another 0.25 mL dose of Fluzone or should we give the 0.5 mL dose that is indicated for age 3 and older?

The child should always receive the dose appropriate for his or her age at the time of the clinic visit; at age 37 months that would be 0.5 mL.

A 1-year-old was inadvertently given a 0.25 mL dose of FluLaval rather than the recommended 0.5 mL dose. What should we do?

If the error is discovered while the child is still in the office, you can administer the other "half" of the FluLaval dose. If the error is discovered later, the dose should not be counted, and then the child should be recalled to the office and given a full age-appropriate repeat dose, either a 0.5 mL dose of FluLaval or a 0.25 mL dose of Fluzone.

Is influenza vaccine recommended for pregnant women?

Yes. It is especially important to vaccinate pregnant women because of their increased risk for influenza-related complications. An increased risk of severe influenza infection was also observed in postpartum women (those who delivered within the previous 2 weeks) during the 2009–10 H1N1 pandemic. Vaccination can occur in any trimester, including the first. Only inactivated vaccine should be given to pregnant women.

I heard that a recent study suggested an increase in miscarriage among women who received inactivated influenza vaccine. Please provide details.

A CDC-funded study found that women who had been vaccinated early in pregnancy with an influenza vaccine containing the pandemic H1N1 (H1N1pdm09) component and who also had been vaccinated the prior season with an H1N1pdm09-containing influenza vaccine had an increased risk of spontaneous abortion (miscarriage) in the 28

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days after vaccination. This study does not quantify the risk of miscarriage and does not prove that influenza vaccine was the cause of the miscarriage. Earlier studies have not found a link between influenza vaccination and miscarriage. There is an ongoing investigation to study this issue further among women who were pregnant and eligible to receive influenza vaccine during the 2012–13 through 2014–15 influenza seasons. Results are anticipated in late 2018 or 2019.

CDC and ACIP have not changed the recommendation for influenza vaccination of pregnant women. It is recommended that pregnant women receive influenza vaccine during any trimester of their pregnancy because influenza poses a danger to pregnant women and the vaccine can prevent influenza in pregnant women.

Please tell me about Fluad, the new influenza vaccine for people age 65 years and older.

In November 2015, FDA licensed Fluad (Seqirus), a trivalent, MF59-adjuvanted inactivated influenza vaccine, for people age 65 years and older. Fluad is the first adjuvanted influenza vaccine marketed in the U.S. An adjuvant is a substance added to a vaccine to increase its immunogenicity. The MF59 adjuvant is based on squalene, an oil that occurs naturally in many plants and animals. Fluad has been used in Europe since 1997 and is approved in 38 other countries. In contrast to Fluzone High-Dose (Sanofi Pasteur), Fluad is a standard-dose vaccine, containing 15 mcg of hemagglutinin per dose.

A study published in 2014 found that the injectable vaccine Fluzone High-Dose protects people 65 years and older better than standard-dose Fluzone. Does ACIP preferentially recommend use of Fluzone High-Dose for all people age 65 years and older?

Aging decreases the body's ability to develop a good immune response after getting influenza vaccine, which places older people at greater risk of severe illness from influenza. A higher dose of antigen in the vaccine should give older people a better immune response and therefore provide better protection against influenza. However, despite published evidence of better protection from Fluzone High-Dose when compared to standard-dose Fluzone (*N Engl J Med* 2014; 371:635–45), ACIP has not stated a preference for this vaccine for people age 65 years and older.

May Fluzone High-Dose or Fluad be administered to patients younger than age 65 years?

No. Fluzone High-Dose and Fluad are licensed only for people age 65 years and older and are not recommended for younger people.

What is the latest ACIP guidance on influenza vaccination and egg allergy?

ACIP revised its guidance on vaccination of people with egg allergy for the 2016–17 season. This guidance did not change for the 2017–18 season. ACIP recommends that people with a history of egg allergy who have experienced only hives after exposure to egg should receive any inactivated influenza vaccine without specific precautions (except a 15-minute observation period for syncope). People who report having had an anaphylactic reaction to egg (more severe than hives) may also receive any age-appropriate influenza vaccine. The vaccine for those individuals should be administered in a medical setting (such as a physician office or health department clinic). Vaccine administration should be supervised by a healthcare provider who is able to recognize and manage severe allergic conditions. Although not specifically recommended by ACIP, providers may prefer to administer an egg-free recombinant vaccine (Flublok; Protein Sciences) for people age 18 years and older with severe egg allergy.

A previous severe allergic reaction to influenza vaccine, regardless of the component suspected to be responsible for the reaction, is a contraindication to future receipt of the vaccine. For a complete list of vaccine components (i.e., excipients and culture media) used in the production of the vaccine, check the package insert (at www.immunize.org/package inserts) or go to www.cdc.gov/vaccines/pubs/pinkbook/downloads/appendices/B/excipient-table-2.pdf.

For more details about giving influenza vaccine to people with a history of egg allergy, see www.cdc.gov/mmwr/volumes/66/rr/pdfs/rr6602.pdf, pages 10–12. You also may find the IAC handout "Influenza Vaccination of People with a History of Egg Allergy" helpful (see www.immunize.org/catg.d/p3094.pdf).

Should staff at drive-through influenza vaccination clinics encourage drivers to park and wait for 15 minutes after vaccination to make sure they don't have a syncopal (fainting) episode?

Yes. Syncope has been reported following vaccination. It is prudent for all persons to be observed for syncope for at least 15 minutes after vaccination.

When removing both pediatric (0.25 mL) and adult (0.5 mL) doses from a multi-dose vial of Fluzone, we can get more than 10 doses from the 5.0 mL vial. Can we continue to remove doses from the vial until it is empty?

No. Only the number of doses indicated in the manufacturer's package insert should be withdrawn from the vial. For a 5.0 mL vial of Fluzone this is 10 doses. After the maximum number of doses has been withdrawn, the vial should be discarded, even if there is vaccine remaining in the vial and the expiration date has not been reached.

We inadvertently administered intradermal influenza vaccine to a patient who is outside the recommended age range of 18 through 64 years. What should we do now?

Because people younger than age 12 years or older than 65 years are more likely to have skin that is too thin for proper intradermal administration, a dose of Fluzone ID (Sanofi Pasteur) given to a person in these age ranges should be considered invalid, and the patient should be revaccinated. For people age 12 through 17 years, the dose can be counted as valid on the presumption that their skin thickness is similar to someone 18 through 64 years of age.

How should influenza vaccines be stored?

Both IIV and LAIV should be refrigerated at 2° to 8°C (36° to 46°F). Neither vaccine should be frozen.

Some of my patients refuse influenza vaccination because they insist they "got the flu" after receiving the injectable vaccine in the past. What can I tell them?

There are several reasons why this misconception persists:

- Less than 1% of people who are vaccinated with the injectable vaccine develop flu-like symptoms, such as mild fever and muscle aches, after vaccination. These side effects are not the same as having influenza, but people confuse the symptoms.
- Protective immunity doesn't develop until 1–2 weeks after vaccination. Some people who get vaccinated later in the season (December or later) may be infected with influenza virus shortly afterward. These late vaccinees develop influenza because they were exposed to someone with the virus before they became immune. It is not the result of the vaccination.

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- For many people, "the flu" is any illness with fever and cold symptoms or gastrointestinal symptoms. If they get any viral illness, they may blame it on flu vaccine or think they got "the flu" despite being vaccinated. Influenza vaccine only protects against certain influenza viruses, not all viruses.
- Influenza vaccine is not 100% effective, especially in older persons.

For more information on this topic, go to: www.cdc.gov/flu/professionals/vaccination/effectivenessqa.htm.

Does ACIP recommend one influenza product over another for pregnant women?
Pregnant women can receive any inactivated or recombinant influenza vaccine. They should not be given LAIV (FluMist).

If quadrivalent vaccine includes one additional strain, why isn't it preferred for use over trivalent vaccines?
Two different types of influenza B virus are likely to cause disease during an influenza season, but trivalent influenza vaccines contain only one type of influenza B virus. The quadrivalent vaccine includes both types of B virus. While quadrivalent vaccines may eventually replace trivalent vaccines, during the current season, the quantity of quadrivalent vaccine available may be limited. Consequently, ACIP does not express a preference for use of one type of influenza vaccine over another type (that is, quadrivalent over trivalent) for those for whom more than one type of vaccine is indicated and available.

Sometimes patients age 65 years and older who have received the standard-dose influenza vaccine hear about the high-dose (Fluzone High-Dose) or adjuvanted vaccine (Fluad) and want to receive that, too. Is this okay to administer?
No. ACIP does not recommend that anyone receive more than one dose of influenza vaccine in a season except for certain children age 6 months through 8 years for whom two doses are recommended.

The influenza VIS states that giving pneumococcal conjugate vaccine and inactivated influenza vaccine simultaneously may increase the risk of febrile seizures. Can we continue to give these two vaccines at the same time?
Yes, you can. Some, but not all studies, have reported increased rates of febrile seizures among children, especially those age 12 through 23 months, who received simultaneous vaccination with IIV and pneumococcal conjugate vaccine (PCV13; Pfizer), when compared with children who received these vaccines separately. However, because of the risks associated with delaying either of these vaccines, ACIP does not recommend administering them at separate visits or deviating from the recommended vaccine schedule in any way.

Febrile seizures, occurring in 2% to 5%, of all children, are not uncommon, and they are generally benign. Healthcare providers should be prepared to answer parents' questions about febrile seizures and fever when discussing vaccinations. Here is a helpful CDC resource: www.cdc.gov/vaccinesafety/Concerns/FebrileSeizures.html.

The pneumococcal conjugate vaccine (PCV13) package insert says that in adults, antibody responses to PCV13 were diminished when given with inactivated influenza vaccine. Does this mean we should not give PCV13 and influenza vaccine at the same visit?
The available data have been interpreted that any changes in antibody response to either of the vaccines' components were clinically insignificant. The antibody response was only lowered for three components, and ONLY in patients younger than 65 years of age. In this age group, if PCV13 is recommended, it means there is a high risk of invasive pneumococcal disease for those unvaccinated. If PCV13 and influenza vaccine are both indicated and recommended, they should be administered at the same visit. See the PCV13 ACIP recommendations at www.cdc.gov/mmwr/pdf/wk/mm6337.pdf, page 824.

Some of our patients believe that they have had reactions to influenza vaccine in the past and request the dose to be split into 2 doses administered on different days. Is this an acceptable practice?
This is definitely not an acceptable practice. Doses of influenza vaccine (or any other vaccine) should never be split into "half doses." If a "half dose" is administered, it should not be accepted as a valid dose and should be repeated as soon as possible with a full age-appropriate dose.

Is it acceptable to draw up vaccine into syringes at the beginning of the day? If it isn't, how much in advance can this be done?
CDC discourages the practice of prefilling vaccine into syringes for several reasons, including

- The increased possibility of administration and dosing errors,
- The increased risk of inappropriate storage,
- The probability of bacterial contamination since the syringe will not contain a bacteriostatic agent, and
- The probability of reducing the vaccine's potency over time because of its interaction with the plastic syringe components.

Prefilling vaccine into syringes also violates basic medication administration guidelines, which state that an individual should administer only those medications he or she has prepared and drawn up.

Although pre-drawing vaccine is discouraged, a limited amount of vaccine may be pre-drawn in a mass-immunization clinic setting under the following conditions:

- Only a single type of vaccine (for example, influenza) is administered at the mass-immunization clinic setting,
- Vaccine is not drawn up in advance of its arrival at the mass-vaccination clinic site,
- These pre-drawn syringes are stored at temperatures appropriate for the vaccine they hold,
- No more than 1 vial or 10 doses (whichever is greater) is drawn into syringes, and
- Clinic staff monitor patient flow carefully and avoid drawing up unnecessary doses or delaying administration of pre-drawn doses.
- At the end of the clinic day, any remaining vaccine in syringes prefilled by staff should be discarded.

Ask the Experts

About IAC's Question of the Week

Each week, *IAC Express* highlights a new, topical, or important-to-reiterate Q&A. This feature is a cooperative venture between IAC and CDC. William L. Atkinson, MD, MPH, IAC's associate director for immunization education, chooses a new Q&A to feature every week from a set of Q&As prepared by experts at CDC's National Center for Immunization and Respiratory Diseases.

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