

# Prevention and Control of Seasonal Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices (ACIP)—United States, 2021-22

## Summary of Recommendations

For additional information: *MMWR Recomm Rep* 2021;70(No. RR-5), at <https://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/flu.html>. This document is available in HTML format at <https://www.cdc.gov/flu/professionals/acip/summary/summary-recommendations.htm>.

### GROUPS RECOMMENDED FOR VACCINATION

- Routine annual influenza vaccination is recommended for all persons aged  $\geq 6$  months who do not have contraindications.
- If vaccine supply is limited, see priority groups for vaccination in the ACIP statement.

### TIMING OF VACCINATION

- Vaccine should be ideally administered by the end of October, but should continue to be offered as long as influenza viruses are circulating locally and unexpired vaccine is available.
- Some children aged 6 months through 8 years require 2 doses of influenza vaccine (**Figure**, this page). These children should receive their first dose as soon as possible after vaccine becomes available, and the second dose  $\geq 4$  weeks later.
- Children needing 1 dose can be vaccinated soon after vaccine becomes available.
- Vaccination soon after vaccine is available may also be considered for pregnant persons in their third trimester.
- For non-pregnant adults, vaccination in July and August should be avoided, even if vaccine is available during these months, unless there is concern that later vaccination might not be possible.

### APPROVED AGES AND DOSE VOLUMES

- Approved dose volumes vary by age and product. An age-appropriate vaccine should be used at an appropriate dose.
- Intramuscular influenza vaccines (IIV4s and RIV4) and their approved ages and dose volumes are:

Vaccine	Approved Ages	Dose volume
Afluria Quadrivalent	6 through 35 months $\geq 3$ years	0.25 mL 0.5 mL
Fluarix Quadrivalent	$\geq 6$ months	0.5 mL
FluLaval Quadrivalent	$\geq 6$ months	0.5 mL
Fluzone Quadrivalent	6 through 35 months $\geq 3$ years	0.25 mL or 0.5 mL 0.5 mL
Flucelvax Quadrivalent	$\geq 2$ years	0.5 mL
Flublok Quadrivalent	$\geq 18$ years	0.5 mL
Fluzone High-Dose Quadrivalent	$\geq 65$ years	0.7 mL
Fluad Quadrivalent	$\geq 65$ years	0.5 mL

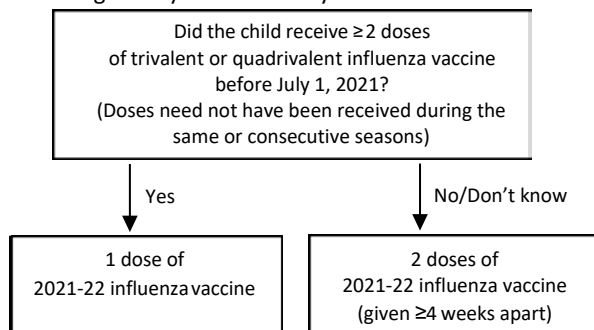
- If a dose less than the necessary volume is administered and the error is discovered immediately (before the recipient has left the vaccination setting), administer the remaining additional volume needed. Alternatively, if it is difficult to measure the remaining needed volume, or if the error is discovered later (after the recipient has left the vaccination setting), administer a repeat full dose.
- Healthy non-pregnant persons aged 2 through 49 years may alternatively receive 0.2 mL of LAIV4, 0.1 mL per nostril, using the supplied intranasal sprayer (**Table 3**, page 4)

### INFLUENZA VACCINATION IN PREGNANCY

- Persons who are pregnant or who might be pregnant during the influenza season should receive influenza vaccine.
- Any age-appropriate IIV4 or RIV4 may be given in any trimester.
- LAIV4 should not be used during pregnancy but can be used postpartum.

### NUMBER OF DOSES FOR AGES 6 MONTHS THROUGH 8 YEARS

- Determine the number of doses needed based on child's age at time of first dose of 2021–22 influenza vaccine and number of doses of influenza vaccine received in previous seasons (**Figure**).
  - Children in this age group who previously received  $\geq 2$  doses of trivalent or quadrivalent influenza vaccine  $\geq 4$  weeks apart before July 1, 2021 need 1 dose of 2021-22 influenza vaccine. The two previous doses need not have been received in the same or consecutive influenza seasons.
  - Children in this age group who have not previously received  $\geq 2$  doses of trivalent or quadrivalent influenza vaccine  $\geq 4$  weeks apart before July 1, 2021 or whose vaccination history is unknown need 2 doses of 2021-22 influenza vaccine, given  $\geq 4$  weeks apart.
- For children aged 8 years who require 2 doses, both doses should be administered even if the child turns age 9 years between dose 1 and dose 2.
- Persons aged  $\geq 9$  years need only one dose.



### ADULTS AGED $\geq 65$ YEARS

- Persons aged  $\geq 65$  years may receive any age-appropriate IIV4 or RIV4. Vaccination should not be delayed to find a particular product if an appropriate one is already available.
- Data support greater benefit of HD-IIV3, RIV4, or aIIV3 relative to standard-dose unadjuvanted IIVs in this age group, but comparisons of these vaccines with one another are limited.
- HD-IIV3, the most well studied, was more effective than IIV3 in a large two-season randomized trial. However, HD-IIV3 and aIIV3 have been replaced by HD-IIV4 and aIIV4. Data comparing benefits of these newer formulations to standard-dose unadjuvanted IIV4s are limited.

### VACCINATION OF PERSONS WITH COVID-19

- Persons in isolation for COVID-19 or in quarantine for known or suspected exposures should not be vaccinated if vaccination will pose an exposure risk to others in the vaccination setting.
- For persons who are moderately or severely ill, vaccination should be deferred until they have recovered. Moderate or severe acute illness with or without fever is a general precaution to vaccination.
- Persons who are mildly ill may be vaccinated; alternatively, vaccination may be deferred until recovery to avoid confusing COVID-19 illness symptoms with post-vaccination reactions.

### PERSONS WITH CHRONIC MEDICAL CONDITIONS

- LAIV4 is not recommended for persons with some chronic medical conditions (**Table 3**, page 4).

### IMMUNOCOMPROMISED PERSONS

- Immunocompromised persons should receive an age-appropriate IIV4 or RIV4. LAIV4 should not be used.
- Immune response might be reduced or minimal in persons on certain medications, chemotherapy, or transplant regimens.
- Timing influenza vaccination relative to a specified period before or after interventions that compromise immunity may be appropriate. The Infectious Diseases Society of America (IDSA) has published guidance concerning the timing of vaccination in relation to such interventions (see **Further Information**, this page).

### CAREGIVERS AND CONTACTS OF HIGH-RISK PERSONS

- Caregivers and contacts (including those of immunosuppressed persons) may receive any age-appropriate IIV4 or RIV4.
- LAIV4 may be given to caregivers and contacts of persons who are not severely immunocompromised (i.e., who do not require a protected environment).
- Health care personnel or hospital visitors who receive LAIV4 should avoid providing care for severely immunosuppressed persons who require a protected environment for 7 days after vaccination.

### PERSONS WITH EGG ALLERGY

- Persons who have experienced only hives after exposure to egg may receive any licensed, recommended influenza vaccine appropriate for their age and health status (i.e., IIV4, RIV4, or LAIV4).
- Persons reporting symptoms other than hives after exposure to egg (such as angioedema, respiratory distress, lightheadedness, or recurrent emesis; or who required epinephrine or another emergency medical intervention) may also receive any licensed, recommended influenza vaccine that is otherwise appropriate.
  - If a vaccine other than cclIV4 or RIV4 is selected, it should be administered in an inpatient or outpatient medical setting, supervised by a health care provider who can recognize and manage severe allergic reactions.

### PREVIOUS SEVERE ALLERGIC REACTIONS TO INFLUENZA VACCINES

- Previous severe allergic reaction (e.g., anaphylaxis) to any influenza vaccine (any egg-based IIV, cclIV, RIV, or LAIV of any valency) is a contraindication to all egg-based IIV4s and LAIV4.
- Previous severe allergic reaction to cclIV of any valency or to any component of cclIV4 is a contraindication to cclIV4. Previous severe allergic reaction to any other influenza vaccine (any egg-based IIV, RIV, or LAIV of any valency) is a precaution to cclIV4.
- Previous severe allergic reaction to RIV of any valency or any component of RIV4 is a contraindication to RIV4. Previous severe allergic reaction to any other influenza vaccine (any egg-based IIV, cclIV, or LAIV of any valency) is a precaution to RIV4.
- Each vaccine is also contraindicated for those with a history of severe allergic reaction to any component of that vaccine (other than egg).
- See **Table 3** and **Table 4** on page 4 for more information.

### VACCINATION ISSUES FOR TRAVELERS

- Travelers who wish to reduce risk for influenza should consider vaccination, preferably  $\geq 2$  weeks before departure.
- Persons at higher risk for complications of influenza who were not vaccinated during the preceding fall or winter should consider influenza vaccination before departure, if planning to travel to the tropics, with organized tourist groups, on cruise ships, or to the Southern Hemisphere during April-September.
- Southern Hemisphere influenza vaccines might differ in viral composition from Northern Hemisphere formulations.
- Vaccination with Southern Hemisphere influenza vaccine prior to Southern Hemisphere travel may be reasonable; however, these formulations are generally not available in the U.S.

### VACCINATION AND INFLUENZA ANTIVIRAL MEDICATIONS

- IIV4 and RIV4 may be administered to persons receiving influenza antiviral medications.
- Influenza antivirals might reduce effectiveness of LAIV4, if given before or after LAIV4. Persons who receive influenza antivirals during the following periods should be revaccinated with an age-appropriate IIV4 or RIV4 (intervals may be longer in conditions where medication clearance is delayed):

Influenza Antiviral	Estimated window for potential LAIV interference (based upon half-life reported in package insert)
Oseltamivir and Zanamivir	48 hours before to 2 weeks after LAIV4
Peramivir	5 days before to 2 weeks after LAIV4
Baloxavir	17 days before to 2 weeks after LAIV4

### ADMINISTRATION OF INFLUENZA VACCINES WITH OTHER VACCINES

- IIV4s and RIV4 may be administered concurrently or sequentially with other live or inactivated vaccines.
- Providers should refer to current CDC/ACIP recommendations and guidance for the use of COVID-19 vaccines for up to date information on administration of these vaccines with other vaccines.
- Injectable vaccines given simultaneously should be administered at separate anatomic sites.
- LAIV4 may be administered simultaneously with other inactivated or live vaccines. If not given simultaneously, then  $\geq 4$  weeks should pass between administration of LAIV4 and another live vaccine.
- Immunogenicity and safety of simultaneous or sequential administration of two vaccines containing non-aluminum adjuvants has not yet been evaluated.

### VACCINE ADVERSE EVENT REPORTING SYSTEM (VAERS)

- VAERS is the national vaccine safety monitoring system co-managed by CDC and FDA which serves as an early warning system to detect possible safety problems with U.S. vaccines.
- Health care providers are required to report to VAERS any adverse event listed by the vaccine manufacturer as a contraindication to further doses of vaccine and adverse events listed here: [https://vaers.hhs.gov/docs/VAERS Table of Reportable Events Following Vaccination.pdf](https://vaers.hhs.gov/docs/VAERS_Table_of_Reportable_Events_Following_Vaccination.pdf)
- For information on how to report to VAERS, go the VAERS website at <https://vaers.hhs.gov>

### FURTHER INFORMATION

#### **CDC Influenza Information (for more, call 800-232-4636)**

- General influenza page: [www.cdc.gov/flu](http://www.cdc.gov/flu)
- FluView (weekly U.S. surveillance): [www.cdc.gov/flu/weekly](http://www.cdc.gov/flu/weekly)
- Influenza Antiviral Guidance: <https://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm>
- COVID-19 vaccination recommendations: <https://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/covid-19.html>
- Vaccine Storage and Handling Toolkit: <https://www.cdc.gov/vaccines/hcp/admin/storage/toolkit/index.html>

#### **American Academy of Pediatrics (AAP) Guidance:**

<https://redbook.solutions.aap.org/selfserve/sspage.aspx?selfservecontid=influenza-resources>

#### **IDSA Guidance for vaccination of immunocompromised hosts:**

<https://academic.oup.com/cid/article/58/3/e44/336537>

#### **Manufacturer package inserts for U.S.-licensed vaccines:**

<https://www.fda.gov/vaccines-blood-biologics/vaccines/vaccines-licensed-use-united-states>

## Available Influenza Vaccines, Age indications, and Administration: 2021-22 Influenza Season

**Table 1: Inactivated Influenza Vaccines (IIV4s) and Recombinant Influenza Vaccine (RIV4)**

Trade name Manufacturer	Available presentations	Approved age indications	Volume per dose by age group
<b>Quadrivalent IIVs (IIV4s)—Standard-dose—Egg-based (15 µg HA per virus component in 0.5 mL; 7.5 µg HA per virus component in 0.25 mL)</b>			
Afluria Quadrivalent <i>Seqirus</i>	0.25 mL prefilled syringe 0.5 mL prefilled syringe 5.0 mL multidose vial*	6 through 35 mos ≥3 yrs ≥6 mos (needle/syringe) 18 through 64 yrs (jet injector)	6 through 35 mos—0.25 mL ≥3 yrs—0.5 mL
Fluarix Quadrivalent <i>GlaxoSmithKline</i>	0.5 mL prefilled syringe	≥6 mos	≥6 mos—0.5 mL
FluLaval Quadrivalent <i>GlaxoSmithKline</i>	0.5 mL prefilled syringe	≥6 mos	≥6 mos—0.5 mL
Fluzone Quadrivalent <i>Sanofi Pasteur</i>	0.5 mL prefilled syringe 0.5 mL single-dose vial 5.0 mL multidose vial*	≥6 mos ≥6 mos ≥6 mos	6 through 35 mos—0.25 mL <b>or</b> 0.5 mL ≥3 yrs—0.5 mL
<b>Quadrivalent IIV (ccIIV4)—Standard-dose—Cell culture-based (15 µg HA per virus component in 0.5 mL)</b>			
Flucelvax Quadrivalent <i>Seqirus</i>	0.5 mL prefilled syringe 5.0 mL multidose vial*	≥2 yrs ≥2 yrs	≥2 yrs—0.5 mL
<b>Quadrivalent IIV (HD-IIV4)—High-dose—Egg-based (60 µg HA per virus component in 0.7 mL)</b>			
Fluzone High-Dose Quadrivalent <i>Sanofi Pasteur</i>	0.7 mL prefilled syringe	≥65 yrs	≥65 yrs—0.7 mL
<b>Adjuvanted quadrivalent IIV4 (aiIIV4)—Standard-dose with MF59 adjuvant—Egg-based (15 µg HA per virus component in 0.5 mL)</b>			
Fluad Quadrivalent <i>Seqirus</i>	0.5 mL prefilled syringe	≥65 yrs	≥65 yrs—0.5 mL
<b>Quadrivalent RIV (RIV4)—Recombinant HA (45 µg HA per virus component in 0.5 mL)</b>			
Flublok Quadrivalent <i>Sanofi Pasteur</i>	0.5 mL prefilled syringe	≥18 yrs	≥18 yrs—0.5 mL

\*Contains thimerosal as a preservative agent.

### Administration of IIV4s and RIV4

- IIVs and RIV4 are administered intramuscularly (IM). For adults and older children, the deltoid is the preferred site. For infants and younger children, the anterolateral thigh is the preferred site. Detailed guidance for administration sites and needle length is available in the Best Practice Guidelines of the Advisory Committee on Immunization Practices (ACIP) at <https://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/index.html>
- Afluria Quadrivalent is licensed for IM administration via the Pharmajet Stratis jet injector for ages 18 through 64 years only.
- RIV4 is licensed for persons aged ≥18 years and should not be used for children and adolescents aged <18 years.

**Table 2: Live Attenuated Influenza Vaccine (LAIV4)**

Trade name Manufacturer	Available presentations	Approved age indication	Volume per dose
<b>Quadrivalent LAIV (LAIV4)—Egg-based (contains 10<sup>6.5-7.5</sup> fluorescent focus units/0.2 mL)</b>			
FluMist Quadrivalent <i>AstraZeneca</i>	0.2 mL prefilled single-use intranasal sprayer	2 through 49 yrs	0.1 mL each nostril (0.2 mL total)

### Administration of LAIV4

- LAIV4 is administered intranasally using the supplied prefilled, single-use sprayer containing 0.2 mL of vaccine.
  - Half of the total sprayer contents is sprayed into the first nostril while the recipient is in the upright position.
  - The attached divider clip is removed and the second half of the dose administered into the other nostril.
- If the vaccine recipient sneezes immediately after administration, the dose should not be repeated.
- If nasal congestion is present that might interfere with delivery of the vaccine to the nasopharyngeal mucosa, deferral should be considered, or another age-appropriate vaccine should be administered

**Table 3: Influenza Vaccine Contraindications and Precautions**

<b>Egg-based IIV4s</b>	<p><b>Contraindications:</b></p> <ul style="list-style-type: none"> <li>History of severe allergic reaction (e.g., anaphylaxis) to any component of the vaccine (other than egg), or to a previous dose of any influenza vaccine (any egg-based IIV, cclIV, RIV, or LAIV of any valency).</li> </ul> <p><b>Precautions:</b></p> <ul style="list-style-type: none"> <li>Moderate or severe acute illness with or without fever.</li> <li>History of Guillain-Barré syndrome within 6 weeks of receipt of influenza vaccine.</li> </ul>
<b>cclIV4</b>	<p><b>Contraindications:</b></p> <ul style="list-style-type: none"> <li>History of severe allergic reaction (e.g., anaphylaxis) to cclIV of any valency, or to any component of cclIV4.</li> </ul> <p><b>Precautions:</b></p> <ul style="list-style-type: none"> <li>Moderate or severe acute illness with or without fever.</li> <li>History of Guillain-Barré syndrome within 6 weeks of receipt of influenza vaccine.</li> <li>History of severe allergic reaction to a previous dose of any other influenza vaccine (any egg-based IIV, RIV, or LAIV of any valency).</li> </ul>
<b>RIV4</b>	<p><b>Contraindications:</b></p> <ul style="list-style-type: none"> <li>History of severe allergic reaction (e.g., anaphylaxis) to RIV of any valency, or to any component of RIV4</li> </ul> <p><b>Precautions:</b></p> <ul style="list-style-type: none"> <li>Moderate or severe acute illness with or without fever</li> <li>History of Guillain-Barré syndrome within 6 weeks of receipt of influenza vaccine</li> <li>History of severe allergic reaction to a previous dose of any other influenza vaccine (any egg-based IIV, cclIV, or LAIV of any valency).</li> </ul>
<b>LAIV4</b>	<p><b>Contraindications:</b></p> <ul style="list-style-type: none"> <li>History of severe allergic reaction (e.g., anaphylaxis) to any component of the vaccine (other than egg) or to a previous dose of any influenza vaccine (i.e., any egg-based IIV, cclIV, RIV, or LAIV of any valency).</li> <li>Concomitant aspirin or salicylate-containing therapy in children and adolescents</li> <li>Children aged 2 through 4 years who have received a diagnosis of asthma or whose parents or caregivers report that a health care provider has told them during the preceding 12 months that their child had wheezing or asthma or whose medical record indicates a wheezing episode has occurred during the preceding 12 months</li> <li>Children and adults who are immunocompromised due to any cause, including but not limited to medications, congenital or acquired immunodeficiency states, HIV infection, anatomic asplenia, or functional asplenia (e.g., due to sickle-cell anemia)</li> <li>Close contacts and caregivers of severely immunosuppressed persons who require a protected environment</li> <li>Pregnancy</li> <li>Persons with active communication between the CSF and the oropharynx, nasopharynx, nose, or ear or any other cranial CSF leak</li> <li>Persons with cochlear implants (due to potential for CSF leak, which might exist for some period of time after implantation. Providers might consider consultation with a specialist concerning risk of persistent CSF leak if an age-appropriate inactivated or recombinant vaccine cannot be used).</li> <li>Receipt of influenza antiviral medication within the previous 48 hours for oseltamivir and zanamivir, 5 days for peramivir, and 17 days for baloxavir (see <b>Vaccination and influenza antiviral medications</b>, page 2, for additional guidance).</li> </ul> <p><b>Precautions:</b></p> <ul style="list-style-type: none"> <li>Moderate or severe acute illness with or without fever</li> <li>History of Guillain-Barré syndrome within 6 weeks of receipt of influenza vaccine</li> <li>Asthma in persons aged <math>\geq 5</math> years</li> <li>Other underlying medical conditions that might predispose to complications from influenza (e.g., chronic pulmonary, cardiovascular [except isolated hypertension], renal, hepatic, neurologic, hematologic, or metabolic disorders [including diabetes mellitus])</li> </ul>

**Table 4: Contraindications and Precautions for Persons with a History of Severe Allergic Reaction to an Influenza Vaccine**

Vaccine (of any valency) associated with previous severe allergic reaction (e.g., anaphylaxis)	Available 2021–22 influenza vaccines		
	Egg-based IIV4s and LAIV4	cclIV4	RIV4
Any egg-based IIV or LAIV	Contraindication*	Precaution†	Precaution†
Any cclIV	Contraindication*	Contraindication*	Precaution†
Any RIV	Contraindication*	Precaution†	Contraindication*
Unknown influenza vaccine	Allergist consultation recommended		

\*When a contraindication is present, a vaccine should not be administered. In addition to the contraindications based on history of severe allergic reaction to influenza vaccines noted in the Table, each individual influenza vaccine is contraindicated for persons who have had a severe allergic reaction (e.g., anaphylaxis) to any component of that vaccine. Vaccine components can be found in package inserts. Although a history of severe allergic reaction (e.g., anaphylaxis) to egg is a labeled contraindication to the use of egg-based IIV4s and LAIV4, ACIP makes an exception for allergy to egg (see **Persons with Egg Allergy**, page 2).

†When a precaution is present, vaccination should generally be deferred but might be indicated if the benefit of protection from the vaccine outweighs the risk for an adverse reaction. Providers can consider using the following vaccines in these instances; however, vaccination should occur in an inpatient or outpatient medical setting with supervision by a health care provider who is able to recognize and manage severe allergic reactions: 1) for persons with a history of severe allergic reaction (e.g., anaphylaxis) to any egg-based IIV or LAIV of any valency, the provider can consider administering cclIV4 or RIV4; 2) for persons with a history of severe allergic reaction (e.g., anaphylaxis) to any cclIV of any valency, the provider can consider administering RIV4; and 3) for persons with a history of severe allergic reaction (e.g., anaphylaxis) to any RIV of any valency, the provider can consider administering cclIV4. Providers can also consider consulting with an allergist to help determine which vaccine component is responsible for the allergic reaction.

**VACCINE ABBREVIATIONS****Main influenza vaccine types:**

- IIV = Inactivated Influenza Vaccine
- RIV = Recombinant Influenza Vaccine
- LAIV = Live Attenuated Influenza Vaccine

**Numerals after letters indicate valency (the number of influenza viruses represented):**

- 4 for quadrivalent vaccines
- 3 for trivalent vaccines

**Prefixes are sometimes used to refer specifically to certain IIVs:**

- a for adjuvanted IIV (e.g., aIIV4)
- cc for cell culture-based IIV (e.g., ccIIV4)
- HD for high-dose IIV (e.g., HD-IIV4)
- SD for standard-dose IIV (e.g., SD-IIV4)