



WG Considerations and Proposed Influenza Vaccine Recommendations, 2021-22

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Overview

2021–22 ACIP Influenza Statement

- Core recommendation (unchanged):
 - Annual influenza vaccination is recommended for all persons aged 6 months and older who do not have contraindications.
- Updates:
 - Influenza vaccines expected to be available for the 2021-22 season
 - U.S. influenza vaccine viral composition for the 2021-22 season
 - Change in age indication for Flucelvax Quadrivalent from ≥ 4 years to ≥ 2 years
 - Several changes to Timing of Vaccination language
 - Co-administration of influenza and COVID-19 vaccines
 - Contraindications and precautions concerning persons with previous severe allergic reaction to influenza vaccines or their components

Available Influenza Vaccines, 2021-22

Influenza Vaccines Expected to be Available by Age Indication, United States, 2021–22 Influenza Season

Vaccine type		0 through 6 months	6 through 23 months	2 through 17 years	18 through 49 years	50 through 64 years	≥65 years	
IIV4s	Standard-dose, unadjuvanted inactivated (IIV4)	Not approved for age group	Egg-based Afluria Quadrivalent Fluarix Quadrivalent FluLaval Quadrivalent Fluzone Quadrivalent					
	Cell culture-based inactivated (IIV4)	Not approved for age group			Not egg-based Flucelvax Quadrivalent			
	Adjuvanted inactivated (aIIV4)	Not approved for age group						Egg-based Fluad Quadrivalent
	High-dose inactivated (HD-IIV4)	Not approved for age group						Egg-based Fluzone High-Dose Quadrivalent
RIV4	Recombinant (RIV4)	Not approved for age group			Not egg-based Flublok Quadrivalent			
LAIV4	Live attenuated (LAIV4)	Not approved for age group			Egg-based FluMist Quadrivalent		Not approved for age group	

IIV4=quadrivalent inactivated influenza vaccine **RIV4**=quadrivalent recombinant influenza vaccine **LAIV4**=quadrivalent live attenuated influenza vaccine



Not approved for age group



Egg-based



Not egg-based

All vaccines expected for 2021-22 are quadrivalent (i.e., contain hemagglutinin derived from four viruses: one influenza A(H1N1), one influenza A(H3N2), one influenza B/Victoria and one influenza B/Yamagata.

2021-22 Influenza Vaccine Composition

2021–22 Influenza Vaccine Composition

- ***Egg-based IIV4s and LAIV4:***
 - An A/Victoria/2570/2019 (H1N1)pdm09-like virus; ^{UPDATED}
 - An A/Cambodia/e0826360/2020 (H3N2)-like virus; ^{UPDATED}
 - A B/Washington/02/2019 (Victoria lineage)-like virus; and
 - A B/Phuket/3073/2013 (Yamagata lineage)-like virus.
- ***Cell-culture-based IIV4 and RIV4:***
 - An A/Wisconsin/588/2019 (H1N1)pdm09-like virus; ^{UPDATED}
 - An A/Cambodia/e0826360/2020 (H3N2)-like virus; ^{UPDATED}
 - A B/Washington/02/2019 (Victoria lineage)-like virus; and
 - A B/Phuket/3073/2013 (Yamagata lineage)-like virus.

Change in Age Indication for Flucelvax Quadrivalent (ccIV4)

Change in Age Indication for Flucelvax Quadrivalent

Cell culture-based inactivated influenza vaccine (ccIIV4).

- Previously licensed for ages ≥ 4 years; approved in March 2021 for ages ≥ 2 years.
- Change supported by randomized trial conducted among 4,514 children aged ≥ 2 through < 18 years over three influenza seasons: (Southern Hemisphere 2017 and Northern Hemisphere 2017-18 and 2018-19).
- Randomized 1:1 to receive ccIIV4 or meningococcal serogroup ACWY conjugate vaccine.
- Overall vaccine efficacy 54.6% (95%CI 45.7, 62.1) against RT-PCR or culture) influenza-associated CDC-defined influenza-like illness.
- Vaccine efficacy 62.7% (95%CI 38.1, 80.8) for matched strains.
- Data presented to ACIP in October, 2020.
- New age indication reflected in text and in Table 1.

Co-Administration of Influenza Vaccines with COVID-19 Vaccines

Co-administration of Influenza Vaccines with COVID-19 Vaccines

- **Section on co-administration of influenza vaccines with other vaccines updated to reflect availability of COVID-19 vaccines.**
- **Considerations discussed:**
 - Potential for increased reactogenicity, particularly with influenza vaccines that might be more likely to cause local or systemic reactions.
 - Greater frequency of reactogenicity with adjuvanted and high-dose inactivated vaccines compared with standard-dose, unadjuvanted inactivated vaccines in some studies.
 - These vaccines approved only for ages 65+ in the U.S.
 - Importance of not missing opportunities for vaccination.
- **Language consistent with most current COVID-19 vaccination guidance.**
- **Refers providers to most recent guidance for any updated information.**

Co-administration of Influenza Vaccines with COVID-19 Vaccines

- From the *“Interim Clinical Considerations for Use of COVID-19 Vaccines Currently Authorized in the United States”*
 - *“COVID-19 vaccines were previously recommended to be administered alone, with a minimum interval of 14 days before or after administration of any other vaccines. This was out of an abundance of caution and not due to any known safety or immunogenicity concerns. However, substantial data have now been collected regarding the safety of COVID-19 vaccine currently authorized by FDA for use under EUA...COVID-19 vaccines and other vaccines **may now be administered without regard to timing.**”*
 - *“Administer the COVID-19 vaccines and vaccines that may be more likely to cause a local reaction (e.g., tetanus-toxoid-containing and adjuvanted vaccines) in different limbs, if possible.”*

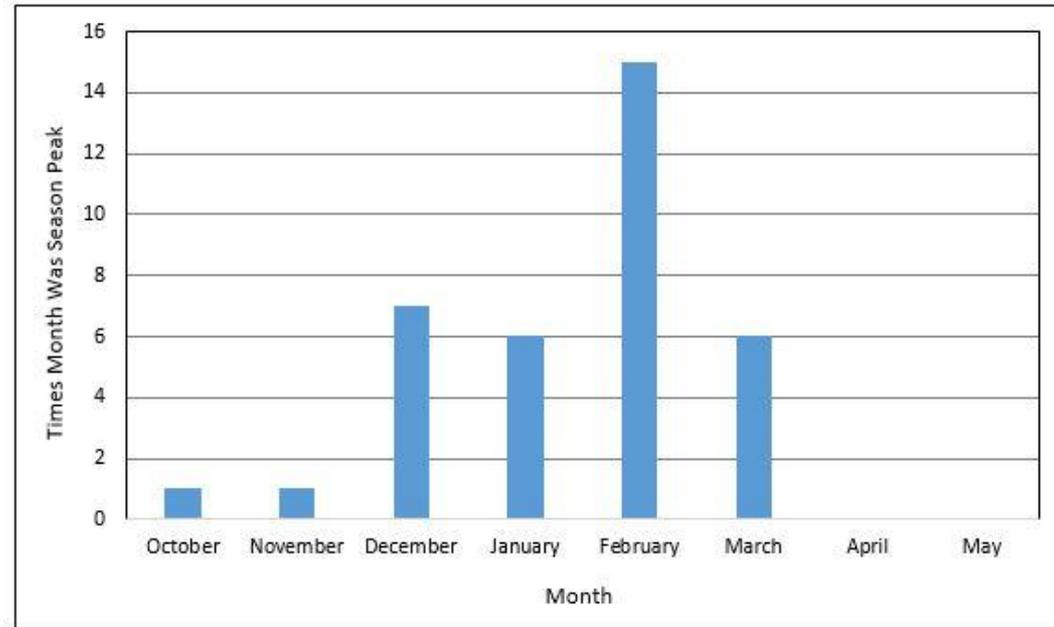
Co-administration of Influenza Vaccines with COVID-19 Vaccines

- **Proposed Language for 2021-22 Influenza Statement**
 - *Current guidance concerning administration of COVID-19 vaccines with other vaccines (<https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html>) indicates that these vaccine may be given with other vaccines, including influenza vaccines. No data are currently available concerning coadministration of currently authorized COVID-19 vaccines and influenza vaccines. Providers should be aware of the potential for increased reactogenicity with coadministration, and should consult CDC guidance at the referenced link for updated guidance as more information becomes available. If coadministered, COVID-19 vaccines and vaccines that might be more likely to cause a local reaction (e.g., aIIV4 or HD-IIV4) should be administered in different limbs, if possible.*

Timing of Vaccination

Timing of Influenza Seasons

- Timing of the onset and peak of influenza activity varies from season to season
- Timing of activity onset can also vary geographically
- In the United States, localized areas of increased activity occur as early as October
- Over the 36 seasons between 1982-83 and 2017-18, peak activity occurred in:¹



- December 7 (19%) seasons
- January 6 (17%) seasons
- February 15 (42%) seasons
- March 6 (19%) seasons

1--<https://www.cdc.gov/flu/about/season/flu-season.htm>

Waning of Protection Following Vaccination

- Current 2020-21 statement contains a discussion of evidence for waning protection following vaccination
 - Declines in influenza vaccine effectiveness over the course of the season have been observed in many observational studies.
 - Appears to be more pronounced among older adults
 - Less evidence for waning among children

Timing of Influenza Vaccination--Background

- Vaccination has been recommended to be offered by the end of October, and to continue as long as influenza viruses are circulating locally
- Language has included recommendation that July and August are probably too early for vaccination in most influenza seasons, particularly for older adults.
 - Exception made for those children ages 6 months through 8 years who require two doses for the season, for whom receipt of the first dose is recommended as soon as possible after vaccine is available (since doses must be ≥ 4 weeks apart).

Timing of Influenza Vaccination—Work Group Considerations

- WG discussed recent literature concerning waning of immunity to influenza vaccines.
- Other considerations discussed included
 - Protection of infants during first months of life (since there is are licensed influenza vaccines for children under age 6 months).
 - Avoiding missed opportunities for vaccination
- Language contains several changes concerning timing of vaccination for children, persons in the third trimester of pregnancy, and adults.

Timing of Influenza Vaccination—Proposed Language: Children

- Similar to previous:

*“Children aged 6 months through 8 years who require 2 doses should receive their first dose as soon as possible after the vaccine becomes available to allow the second dose (which must be administered ≥ 4 weeks later) to be received **ideally** by the end of October.”*

- New:

*“Children of any age who require only one dose for the season should also **ideally** be vaccinated by the end of October; vaccination of these children may occur as soon as vaccine is available, as there is less evidence to suggest that early vaccination is associated with waning immunity among children as compared with adults.”*

Timing of Influenza Vaccination—Proposed Language: Pregnant Persons in Third Trimester

- New:

“Vaccination soon after vaccine becomes available may also be considered for pregnant persons during the third trimester, as vaccination of pregnant persons has been shown to reduce risk of influenza illness of their infants during the first months of life¹⁻⁴ (a period during which they be too young to receive influenza vaccine)”

1-Madhi et al N Engl J Med. 2014 Sep 4;371(10):918-31.

2-Tapia et al Lancet Infect Dis. 2016 Sep;16(9):1026-35.

3-Steinhoff et al Lancet Infect Dis. 2017 Sep;17(9):981-9.

4-Eick et al Arch Pediatr Adolesc Med. 2011 Feb;165(2):104-11.

Timing of Influenza Vaccination—Proposed Language: Non-Pregnant Adults

- New

“For non-pregnant adults, influenza vaccination during July and August should be avoided unless there is concern that later vaccination might not be possible.”

Influenza Vaccine Contraindications and Precautions—Allergic Reactions to Influenza Vaccines or their Components

Allergic Reactions to Influenza Vaccines--Background

- Vaccines (including influenza vaccines) include multiple components that can potentially trigger severe allergic reactions (e.g., anaphylaxis)
- Serious allergic reactions to influenza vaccine are rare
 - In one Vaccine Safety Datalink (VSD) study¹ the estimated rates of post-vaccination anaphylaxis among cases that involved administration of a single vaccine.¹
 - 1.31 cases per million doses for all vaccines
 - 1.35 cases per million doses for IIV3

Allergic Reactions to Influenza Vaccines--Background

- It can be difficult to know the component responsible for a severe allergic reaction.
- ACIP General Best Practices:
 - *“Referral of the individual to an allergist for evaluation is usually indicated to possibly determine the component responsible, before making decisions regarding administration of the additional doses of the same vaccine or other vaccines that have the same components.”*

1--<https://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/downloads/general-recs.pdf>

Allergic Reactions to Influenza Vaccines--Background

Current (2020-21) language (from egg allergy section)

“A previous severe allergic reaction to influenza vaccine, regardless of the component suspected of being responsible for the reaction, is a contraindication to future receipt of the vaccine.”

Package insert contraindications language for egg-based IIVs

- History of severe allergic reaction (e.g. anaphylaxis) to any component of the vaccine (including egg protein), or after a previous dose of any influenza vaccine.

Allergic Reactions to Influenza Vaccines--Background

- Package insert contraindications language for RIV4 (Flublok Quadrivalent) and cIIIV4 (Flucelvax Quadrivalent):
 - History of severe allergic reactions (e.g., anaphylaxis) to any component of the vaccine.
- In the current statement, Table 2 (Contraindications and Precautions):
 - All IIVs (including cIIIV4):
 - "History of severe allergic reaction to any component of the vaccine, or to a previous dose of any influenza vaccine"
 - RIV4:
 - Reflects the package insert language: "History of severe allergic reaction to any component of the vaccine"

Allergic Reactions to Influenza Vaccines--Considerations

- Consistency and simplicity of recommendations
- Harmonization with influenza vaccine package inserts
- Relative compositions of currently available influenza vaccines
- Extending vaccination to those who have had a severe allergic reaction to influenza vaccine, if an alternative vaccine can be received safely
- Potential need for allergy/immunology consultation

Allergic Reactions to Influenza Vaccines--Considerations

- Woo et al analyses of Vaccine Adverse Event Reporting System (VAERS) data
 - Evaluated reports of cases of severe allergic reactions following recombinant influenza vaccine (RIV) ^{1, 2}
- Limitations of VAERS:
 - Passive surveillance
 - Potential for reporting bias
 - Inconsistent data quality and completeness
 - Generally cannot assess causality

Woo et al, Clin Infect Dis 2015;60(5):777-780

Woo et al, Vaccine 2017;35:5618-5621

Allergic Reactions to Influenza Vaccines--Considerations

- Woo et al analyses of Vaccine Adverse Event Reporting System (VAERS) data
 - Evaluated reports of cases of severe allergic reactions following recombinant influenza vaccine (RIV)
 - Egg-free, without antibiotics, gelatin, or preservatives
 - Noted cases of allergic reactions, some meeting Brighton criteria for anaphylaxis, some among persons who had reported a history of allergic reaction to egg or to a previous dose of influenza vaccine.
- Authors note that the occurrence of such reactions might reflect an underlying predisposition to atopy which might lead to reactions following any vaccine, rather than to indicate a relationship to the components of a specific vaccine.

Proposed Contraindication and Precautions—Table 2

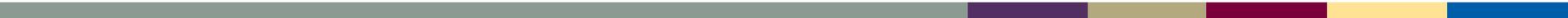
Vaccine Type	Contraindications	Precautions
Egg-based IIV4s	History of severe allergic reaction to any component of the vaccine, or to a previous dose of any influenza vaccine (i.e., any IIV, RIV, or LAIV) ^{†§}	<p>Moderate or severe acute illness with or without fever</p> <p>History of Guillain-Barré syndrome within 6 weeks of receipt of influenza vaccine</p>
cIIV4	History of severe allergic reaction to cIIV4, cIIV3 or to any component of cIIV4 [§]	<p>Moderate or severe acute illness with or without fever</p> <p>History of Guillain-Barré syndrome within 6 weeks of receipt of influenza vaccine</p> <p>History of severe allergic reaction to a previous dose of any other influenza vaccine (i.e., egg-based IIV, RIV, or LAIV)[†]</p>
RIV4	History of severe allergic reaction to RIV4, RIV3 or to any component of RIV4 [§]	<p>Moderate or severe acute illness with or without fever</p> <p>History of Guillain-Barré syndrome within 6 weeks of receipt of influenza vaccine</p> <p>History of severe allergic reaction to a previous dose of any other influenza vaccine (i.e., any IIV or LAIV)[†]</p>

Proposed Contraindications and Precautions

Additional footnotes concerning precautions:

- If cclIV4 or RIV4 is administered to an individual with a history of severe allergic reaction (e.g., anaphylaxis) to any other influenza vaccine, vaccination should occur in an inpatient or outpatient medical setting and should be supervised by a health care provider who is able to recognize and manage severe allergic reactions.
 - Providers can also consider consultation with an allergist to help determine the vaccine component responsible for the allergic reaction.

Thank you!

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