Clinical Update

Priyanka Saxena, D.O., CDPH

Updated Boosters Now Recommended

- August 31, 2022
  - FDA Emergency Use Authorization provided for Pfizer Bivalent, Covid-19 Vaccine for use as a booster in individuals 12 and older and Moderna Bivalent, Covid-19 Vaccine for use as a booster in 18 and older
- September 1, 2022
  - ACIP meeting, CDC issued recommendation
- September 3, 2022
  - Western States Scientific Safety Review Workgroup Recommendation

FDA Press Announcement 8/31/22 | CDC Press Release 9/1/22
Western States Scientific Safety Review Workgroup Recommendation 9/3/22

Updated Booster Recommendations

- People ages 12 years and older are recommended to receive **1 age-appropriate bivalent mRNA booster dose** after completion of any FDA-approved or FDA-authorized monovalent primary series or previously received monovalent booster dose(s).
  - Can be administered at least 2 months after either completion of the primary series or last monovalent booster dose
  - This new booster recommendation **replaces all prior booster recommendations for this age group.**
  - Monovalent mRNA vaccines are no longer authorized as a booster dose for people ages 12 years and older.
- Children ages 5–11 years are recommended to continue receiving 1 monovalent mRNA booster dose if eligible
- J&J vaccine remains available as first booster for certain people

Fall Booster "Reset"

- Recommendations are simplified
- Change from dose counting to 1 bivalent booster for everyone eligible
- If eligible, a bivalent should not be denied based on total number of doses

Vaccination history	→	Next dose
Primary series	At least 2 months →	1 bivalent booster dose
Primary series + 1 booster	At least 2 months →	1 bivalent booster dose
Primary series + 2 booster	At least 2 months →	1 bivalent booster dose

Interim Clinical Considerations for COVID-19 Vaccines: Bivalent Boosters, ACIP Presentation, 9/1/22

15-Minutes Observation Period Now Optional

- 15-minutes post-vaccination observation period previously recommended by CDC
- Vaccination providers ***should consider*** an observation period:
  - Consider 15 min observation: Adolescents (risk of syncope)
  - Consider 30 min observation:
    - Allergy-related contraindication to a different type of COVID-19 vaccine
    - Non-severe, immediate (onset within 4 hours) allergic reaction after a previous dose of COVID-19 vaccine.
    - Anaphylaxis after non-COVID-19 vaccines or injectable therapies

Bivalent Booster Schedule, 6 months-11 years

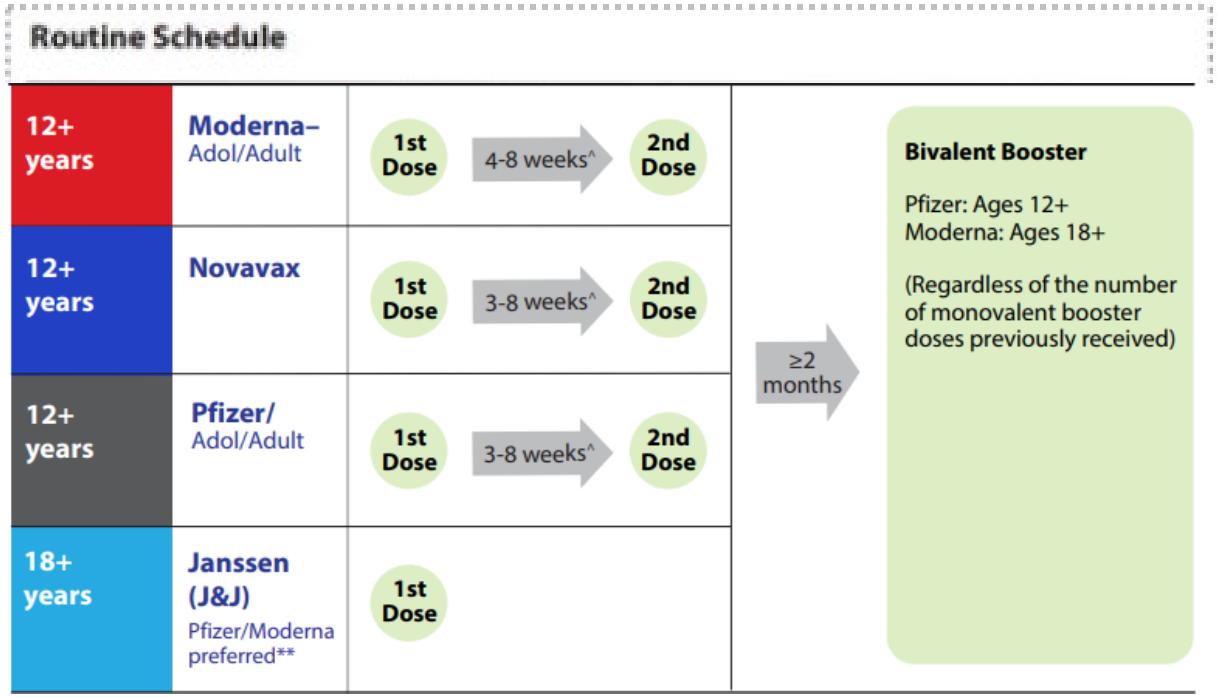
Routine Schedule

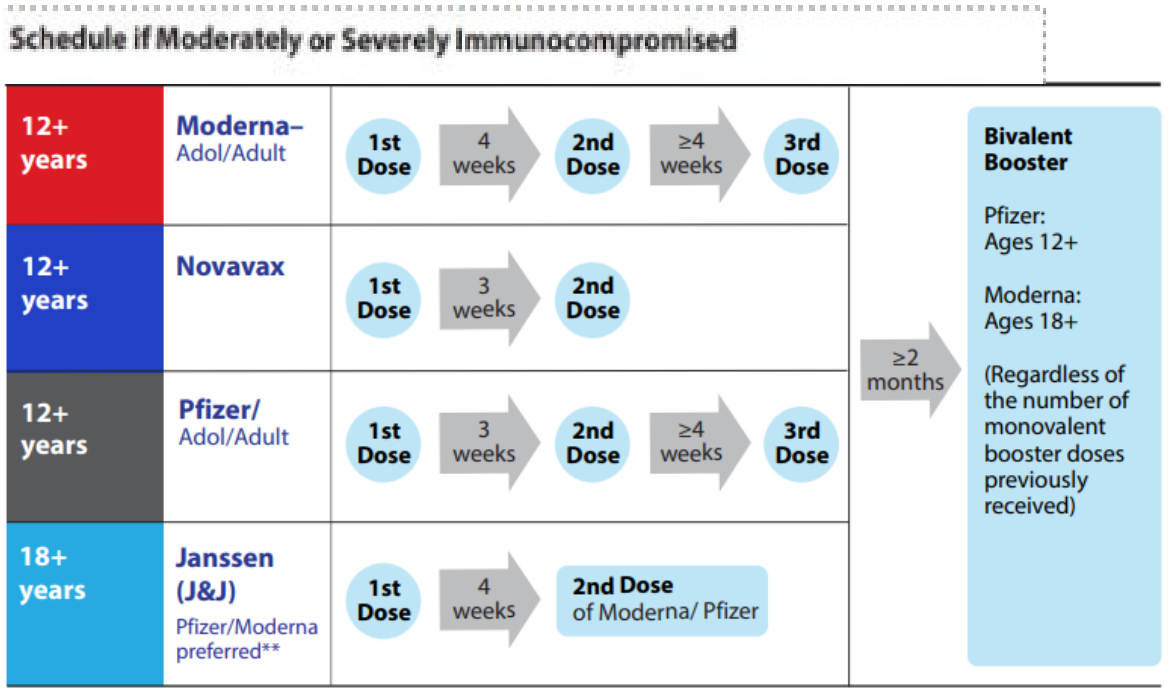
Age*	Vaccine	Primary Doses	Booster Dose
6 months–4 years	Pfizer–Infant/Toddler	1st Dose → 3-8 weeks^ → 2nd Dose → ≥8 weeks → 3rd Dose	
6 months–5 years	Moderna–Infant/Toddler	1st Dose → 4-8 weeks^ → 2nd Dose	
5–11 years	Pfizer–Pediatric	1st Dose → 3-8 weeks^ → 2nd Dose → ≥5 months	Monovalent Booster Pfizer 5-11 years
6–11 years	Moderna–Pediatric	1st Dose → 4-8 weeks^ → 2nd Dose	

Schedule if Moderately or Severely Immunocompromised

Age*	Vaccine	Primary Doses	Booster Dose
6 months–4 years	Pfizer–Infant/Toddler	1st Dose → 3 weeks → 2nd Dose → ≥8 weeks → 3rd Dose	
6 months–5 years	Moderna–Infant/Toddler	1st Dose → 4 weeks → 2nd Dose → ≥4 weeks → 3rd Dose	
5–11 years	Pfizer–Pediatric	1st Dose → 3 weeks → 2nd Dose → ≥4 weeks → 3rd Dose → ≥3 months	Monovalent Booster Pfizer 5-11 years
6–11 years	Moderna–Pediatric	1st Dose → 4 weeks → 2nd Dose → ≥4 weeks → 3rd Dose	

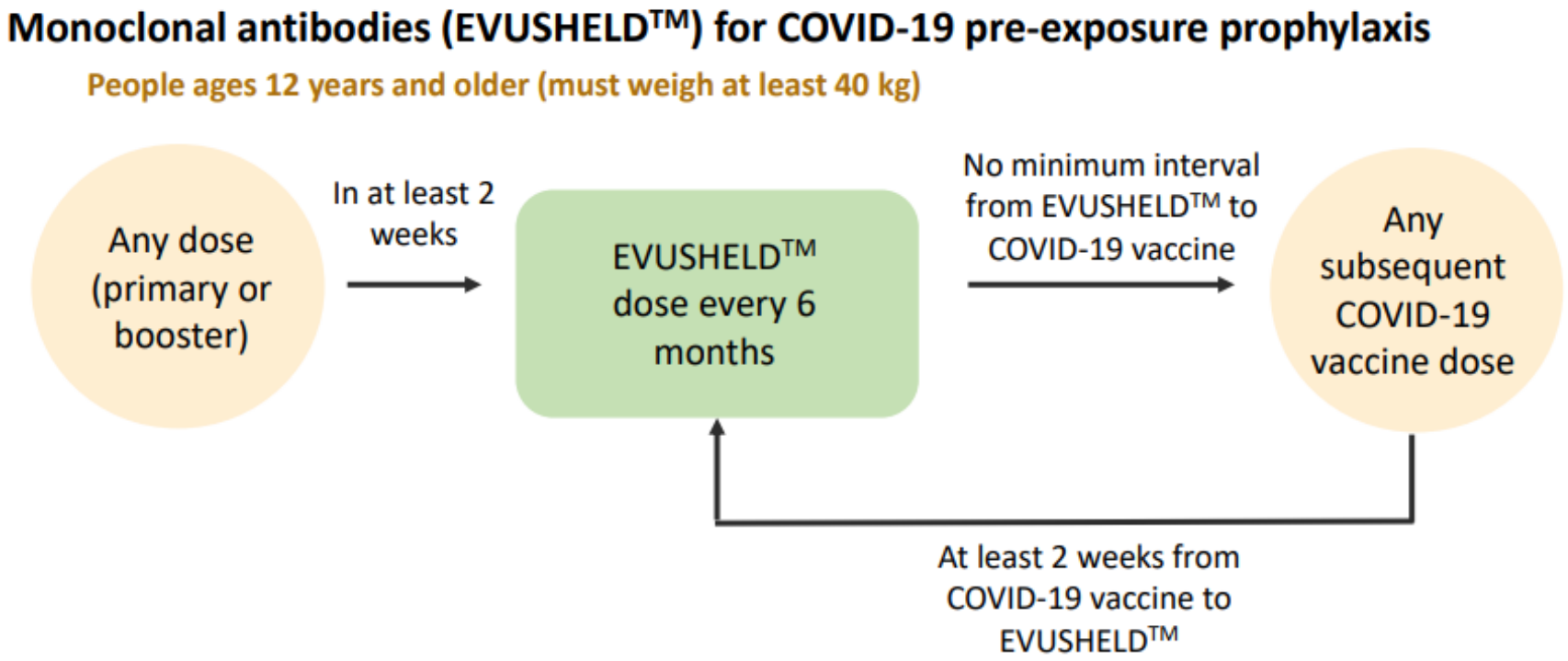
Bivalent Booster Schedule, 12 and older





Evusheld

People ages ≥12 years with moderate to severe immune compromise may benefit from Evusheld

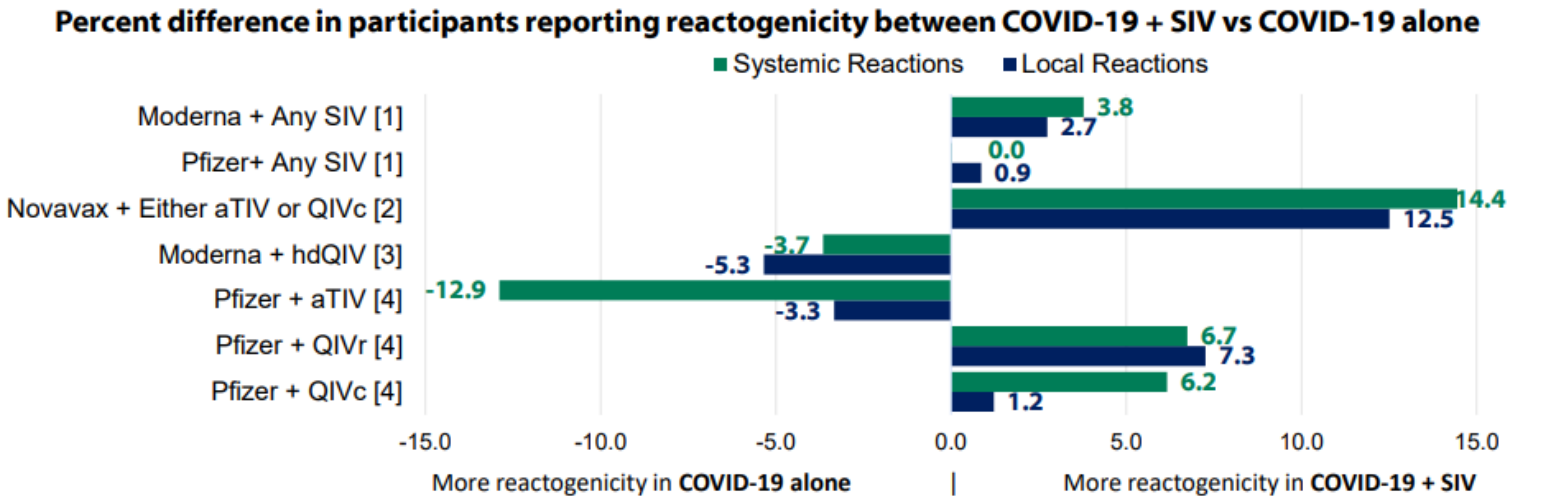


Coadministration of Flu and COVID-19 Vaccines

- Extensive experience with non-COVID 19 vaccines has demonstrated that immunogenicity and adverse event profiles are generally similar when vaccines are administered simultaneously as when they are administered alone.
- Providers should offer influenza and COVID-19 vaccines at the same visit, if eligible.
- With both influenza and SARS-CoV-2 circulating, getting both vaccines is important for prevention of severe disease, hospitalization, and death.
- Getting both vaccines at the same visit increases the chance that a person will be up to date with their vaccinations.

Flu + COVID Vaccine Coadministration is Safe

- Generally, COVID-19 vaccines administered with seasonal influenza vaccine (SIV) showed similar or slightly higher reactogenicity, however no specific safety concerns were identified.



SIV: seasonal influenza vaccine; aTIV: adjuvanted trivalent influenza vaccine; QIVc: quadrivalent influenza cell-based vaccine; hdQIVc: high-dose quadrivalent influenza vaccine; QIVr recombinant quadrivalent vaccine

1. Hause AM, Zhang B, Yue X, et al. Reactogenicity of Simultaneous COVID-19 mRNA Booster and Influenza Vaccination in the US. JAMA Netw Open. 2022;5(7):e2222241.
2. Toback S, Galiza E, Cosgrove C, et al. Safety, immunogenicity, and efficacy of a COVID-19 vaccine (NVX-CoV2373) co-administered with seasonal influenza vaccines: An exploratory substudy of a randomised, observer-blinded, placebo-controlled, phase 3 trial. Lancet Respir. Med. 2021,10, 167–179.
3. Izikson R, Brune D, Bolduc JS, et al. Safety and immunogenicity of a high-dose quadrivalent influenza vaccine administered concomitantly with a third dose of the mRNA-1273 SARS-CoV-2 vaccine in adults aged ≥65 years: A phase 2, randomised, open-label study. Lancet Respir. Med. 2022.
4. Lazarus R, Baos S, Cappel-Porter H, et al. Safety and immunogenicity of concomitant administration of COVID-19 vaccines (ChAdOx1 or BNT162b2) with seasonal influenza vaccines in adults in the UK (ComFluCOV): A multicentre, randomised, controlled, phase 4 trial. Lancet 2021, 398, 2277–2287.

Error and Deviation Guidance Updated

- Please see Appendix D in CDC guidance
- All vaccine administration errors should be reported to VAERS

• Bivalent vaccine incorrectly administered for the primary series	• Bivalent Pfizer-BioNTech vaccine: Do not repeat dose. • Bivalent Moderna vaccine: Repeat dose immediately (no minimum interval)[§] because administration of the booster dose will result in a lower-than-authorized dose.
• Monovalent vaccine incorrectly administered for a booster dose (if bivalent booster indicated)	• In general, do not repeat dose. • However, providers may administer 1 bivalent booster dose as a repeat dose based on clinical judgement and patient preference. In this case, space the repeat dose after the dose given in error by at least 2 months.

Summary

Clinical trial data

- Bivalent booster doses of both Moderna & Pfizer-BioNTech COVID-19 vaccines **increase immune response** in those who have completed a primary series and a previous booster
  - Compared with ancestral booster dose
    - Demonstrated superior response to Omicron
    - Demonstrated non-inferior response to ancestral strain
- Similar reactogenicity profile to primary series (and ancestral booster dose)
- Data from clinical trial limited in size, age, and bivalent booster type

ACIP 9/1/22, S. Oliver presentation

Bivalent COVID-19 vaccines:

Data to inform recommendations

- Experience from using COVID-19 vaccine mRNA platform for nearly 2 years and over 600 million doses in the United States alone
  - Extensive vaccine effectiveness studies as well as robust post-authorization safety data across multiple platforms
- Clinical (human) data from bivalent COVID-19 vaccines in >1700 persons
  - Includes bivalent vaccines with Beta and Omicron variants, both from manufacturers and NIH studies
  - Over 1400 individuals received bivalent vaccine with **Omicron** component specifically
  - While there are subtle differences in mutations between BA.1 and BA.4/BA.5 spike protein sequences, do not anticipate differences in safety or reactogenicity of vaccines based on these limited mutations
  - Overall composition of the vaccine as well as total antigenic load are the same as current booster doses
- Antigenic cartography and antibody studies
- Modeling data

Flu Recommendations

ACIP approved the following recommendations by majority vote at its June 22-23, 2022 meeting:

- Adults aged ≥65 years should preferentially receive one of the following influenza vaccines:
  - ✓ Quadrivalent high-dose inactivated influenza vaccine (HD-IIV4),
  - ✓ Quadrivalent recombinant influenza vaccine (RIV4), or
  - ✓ Quadrivalent adjuvanted inactivated influenza vaccine (aIIV4).

- If none of these three vaccines is available at an opportunity for vaccine administration, then any other age-appropriate influenza vaccine should be used.

Prevention and Control of Seasonal Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices — United States, 2022–23 Influenza Season | MMWR (cdc.gov)

New ≥65-year Preferential Recommendation

What are the higher dose and adjuvanted influenza vaccines?

- Fluzone High-Dose Quadrivalent (HD-IIV4): contains 4x the hemagluttinin (HA) dose/virus than standard dose vaccines (SD-IIV's)
- Flublok Quadrivalent (RIV4): recombinant vaccine which contains 3x the HA dose/virus than SD-IIV's
- Fluad Quadrivalent (aIIV4): contains the adjuvant MF59

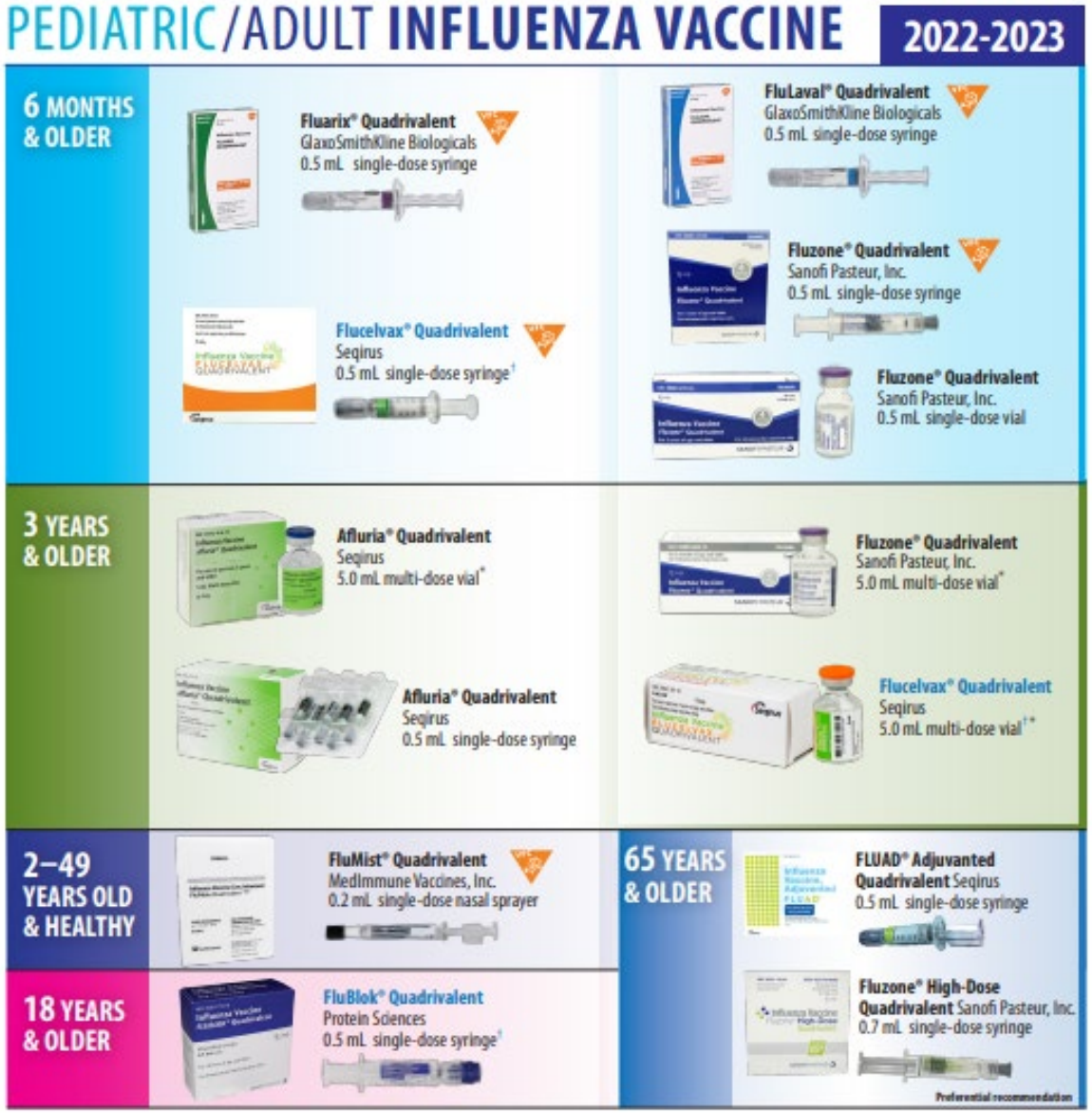
Prevention and Control of Seasonal Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices — United States, 2022–23 Influenza Season | MMWR (cdc.gov)

New ≥65-year Preferential Recommendation

What is the evidence for the preferential recommendation?

- Effectiveness
  - Evidence favors HD-IIV in preventing influenza illness, outpatient visits, hospitalization, and death.
  - For influenza hospitalizations, evidence favors HD-IIV, RIV, and aIIV, though extent of evidence varies.
- Safety
  - Each vaccine has demonstrated safety in prelicensure trials.
  - Increased frequency of some reactogenicity events in some studies of HD-IIV and aIIV, but most were mild or moderate.

GRADE: Higher Dose and Adjuvanted Influenza Vaccines for Adults Aged ≥65 Years | CDC; ACIP June 22-23, 2022 Presentation Slides; ACIP February 23-24, 2022 Presentation Slides


PEDIATRIC/ADULT INFLUENZA VACCINE
2022-2023
6 MONTHS & OLDER
Fluarix® Quadrivalent
GlaxoSmithKline Biologicals
0.5 mL single-dose syringe
FluLaval® Quadrivalent
GlaxoSmithKline Biologicals
0.5 mL single-dose syringe
Flucelvax® Quadrivalent
Seqirus
0.5 mL single-dose syringe†
Fluzone® Quadrivalent
Sanofi Pasteur, Inc.
0.5 mL single-dose syringe
Fluzone® Quadrivalent
Sanofi Pasteur, Inc.
0.5 mL single-dose vial
3 YEARS & OLDER
Afluria® Quadrivalent
Seqirus
5.0 mL multi-dose vial*
Fluzone® Quadrivalent
Sanofi Pasteur, Inc.
5.0 mL multi-dose vial*
Afluria® Quadrivalent
Seqirus
0.5 mL single-dose syringe
Flucelvax® Quadrivalent
Seqirus
5.0 mL multi-dose vial†*
2–49 YEARS OLD & HEALTHY
FluMist® Quadrivalent
MedImmune Vaccines, Inc.
0.2 mL single-dose nasal sprayer
18 YEARS & OLDER
FluBlok® Quadrivalent
Protein Sciences
0.5 mL single-dose syringe†
65 YEARS & OLDER
FLUAD® Adjuvanted Quadrivalent Seqirus
0.5 mL single-dose syringe
Fluzone® High-Dose Quadrivalent Sanofi Pasteur, Inc.
0.7 mL single-dose syringe
Preferential recommendation