Protocol for Inactivated Influenza Vaccines and Recombinant Influenza Vaccines
Inactivated Influenza Vaccine (Afluria®, Fluarix®, FluLaval®, Fluzone®), Recombinant Influenza Vaccine (Flublok®), Cell Cultured Influenza Vaccine (Flucelvax®), Adjuvanted Inactivated Influenza Vaccine (Fluad®)

1. What's New

A. ACIP Recommended that all egg-based inactivated influenza vaccines for use in the 2023-2024 influenza season Northern Hemisphere[9] contain the following:
   a. A/Victoria/4897/2022 (H1N1) pdm09-like virus
   b. A/Darwin/9/2021 (H3N2)-like virus
   c. B/Austria/1359417/2021-like virus (B/Victoria lineage)
   d. B/Phuket/3073/2013-like virus (B/Yamagata lineage)

B. ACIP Recommended that all cell-culture-based inactivated or recombinant-based influenza vaccines for the 2023-2024 influenza season Northern Hemisphere[9] contain the following:
   a. A/Wisconsin/67/2022 (H1N1) pdm09-like virus
   b. A/Darwin/6/2021 (H3N2)-like virus
   c. B/Austria/1359417/2021-like virus (B/Victoria lineage)
   d. B/Phuket/3073/2013-like virus (B/Yamagata lineage)

C. ACIP recommends that adults aged ≥65 years preferentially receive any one of the following higher dose or adjuvanted influenza vaccines: quadrivalent high-dose inactivated influenza vaccine (HD-IIV4), quadrivalent recombinant influenza vaccine (RIV4), or quadrivalent adjuvanted inactivated influenza vaccine (aIIV4).[10]

D. All persons ages ≥6 months with egg allergy should receive influenza vaccine. Any influenza vaccine (egg based or non-egg based) that is otherwise appropriate for the recipient's age and health status can be used.[11]

2. Immunization Protocol

A. Administer a 0.25-mL, 0.5-mL, or 0.7-mL dose, IM, of an appropriate influenza vaccine, to persons ≥ 6 months of age based on the patient's age and the formulation being used.

B. May be given with all ACIP-recommended child and adult vaccinations, including COVID-19 vaccines.

C. When co-administering COVID-19 vaccines and adjuvanted or high-dose influenza vaccines that might be more likely to cause a local reaction, different limbs should be used, if possible.[10]

3. Vaccine Schedule

Inactivated Influenza Vaccine (IIV) and Recombinant Influenza Vaccine (RIV) Schedule for the 2023–2024 Flu Season[1-8] Dose and Route – 0.25-mL or 0.5-mL (dose based on age and formulation), IM		
Dose	**Acceptable Age Range**	**Minimum Acceptable Spacing**
1	≥ 6 months	
2*	≥ 6 months through <9 years of age	28 days, *see flowchart in recommendations for use for determining 1 or 2 doses

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4. Licensed Vaccines

Product Name	Presentation	Hemagglutinin (IIV and RIV) for each vaccine virus (mcg/per dose)	FDA Age Range	Thimerosal (mcg Hg)
Afluria® Quadrivalent[1]	0.5 mL prefilled syringes	15 mcg/0.5 mL	≥ 3 years	None
	5-mL multi-dose vial†	7.5 mcg/0.25 mL 15 mcg/0.5 mL	≥ 6 through 35 months ≥ 3 years	24.5
Fluad® Quadrivalent[8]	0.5 mL prefilled syringes	15 mcg/0.5 mL	≥ 65 years	None
Fluarix® Quadrivalent[2]	0.5 mL prefilled syringes	15 mcg/0.5 mL	≥ 6 months	None
Flublok® Quadrivalent[6]	0.5 mL prefilled syringes	45 mcg/0.5 mL	≥ 18 years	None
Flucelvax® Quadrivalent[7]	0.5 mL prefilled syringes	15 mcg/0.5 mL	≥ 6 months	None
	5-mL multi-dose vial	15 mcg/0.5 mL		25
FluLaval® Quadrivalent[3]	0.5 mL prefilled syringes	15 mcg/0.5 mL	≥ 6 months	None
Fluzone High Dose® Quadrivalent[4]	0.7 mL prefilled syringes	60 mcg/0.7 mL	≥ 65 years	None
Fluzone® Quadrivalent[5]	0.5 mL prefilled syringes‡	15 mcg/0.5 mL	≥ 6 months	None
	0.5 mL single dose vial‡	15 mcg/0.5 mL		None
	5 mL multi-dose vial‡	7.5 mcg/0.25 mL 15 mcg/0.5 mL		25

IIV4= inactivated influenza vaccine, RIV4= recombinant influenza vaccine

† The approved dose volume for Afluria® Quadrivalent is 0.25 mL for ages 6 through 35 months and 0.5 mL for ages ≥3 years. However, 0.25-mL prefilled syringes are no longer available. For ages 6 through 35 months, a 0.25-mL dose must be obtained from a multidose vial.

‡Fluzone® Quadrivalent is approved for children aged 6 through 35 months at either 0.25 mL or 0.5 mL per dose; however, 0.25-mL prefilled syringes are no longer available. If a prefilled syringe of Fluzone® Quadrivalent is used for a child in this age group, the dose volume will be 0.5 mL per dose.

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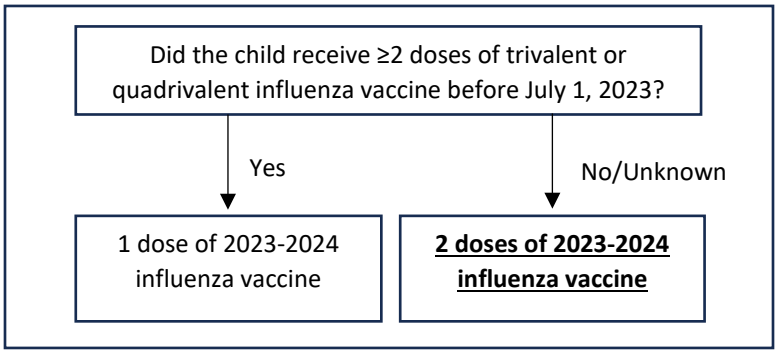
5. Recommendations for Use

A. All persons ≥ 6 months of age that do not have contraindications. Children < 9 years of age receiving flu vaccine for the first time need 2 doses, separated by at least 28 days. Children who receive the first dose at age 8 years and turn 9 during flu season should receive the 2nd dose in the same season.[10]



B. Persons who are pregnant may be vaccinated with inactivated influenza vaccine during any trimester.[10]

C. Persons with history of egg allergy may receive any vaccine (egg-based or non-egg-based) that is otherwise appropriate for their age and health status. Beginning with the 2023-2024 season, additional safety measures are no longer recommended for flu vaccination of people who are allergic to eggs beyond those recommended for receipt of any vaccine, regardless of the severity of previous reaction to egg. All vaccines should be administered in settings in which personnel and equipment needed for rapid recognition and treatment of allergic reactions are available, such as a pharmacy.[11]

D. For non-pregnant adults, vaccination in July or August should be avoided, even if vaccine is available, unless there is serious concern that later vaccination might not be possible.[10]

E. Providers should offer flu vaccination to unvaccinated persons by the end of October, if possible. Vaccination should continue to be offered as long as unexpired vaccine is available.[10]

6. Contraindications

A. Severe allergic reaction (e.g., anaphylaxis) to a previous dose or to any vaccine component. However, ACIP makes an exception for allergy to egg (see Persons with a History of Egg Allergy above).

   a. Most flu shots and the nasal spray flu vaccine are manufactured using egg-based technology. Because of this, they contain a small amount of egg proteins, such as ovalbumin. However, studies that have examined the use of both the nasal spray vaccine and flu shots in egg-allergic and non-egg-allergic patients indicate that severe allergic reactions in people with egg allergies are unlikely.[11]

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Vaccine	Contains[14]
Afluria® Quadrivalent	Sodium chloride, monobasic sodium phosphate, dibasic sodium phosphate, monobasic potassium phosphate, potassium chloride, calcium chloride, sodium taurodeoxycholate, ovalbumin, sucrose, neomycin sulfate, polymyxin B, beta-propiolactone, thimerosal (multidose vials)
Fluad® Quadrivalent	Squalene, polysorbate 80, sorbitan trioleate, sodium citrate dihydrate, citric acid monohydrate, neomycin, kanamycin, barium, hydrocortisone, egg proteins, cetyltrimethylammonium bromide (CTAB), formaldehyde
Fluarix® Quadrivalent	Octoxynol-10 (TRITON X-100), α-tocopheryl hydrogen succinate, polysorbate 80 (Tween 80), hydrocortisone, gentamicin sulfate, ovalbumin, formaldehyde, sodium deoxycholate, sodium phosphate-buffered isotonic sodium chloride
Flublok® Quadrivalent	Sodium chloride, monobasic sodium phosphate, dibasic sodium phosphate, polysorbate 20 (Tween 20), baculovirus and Spodoptera frugiperda cell proteins, baculovirus and cellular DNA, Triton X-100
Flucelvax® Quadrivalent	Madin-Darby Canine Kidney (MDCK) cell protein, phosphate buffered saline, protein other than HA, MDCK cell DNA, polysorbate 80, cetyltrimethylammonium bromide, and βpropiolactone, Thimerosal (multi-dose vials)
FluLaval® Quadrivalent	Ovalbumin, formaldehyde, sodium deoxycholate, α-tocopheryl hydrogen succinate, polysorbate 80, thimerosal (multi-dose vials), phosphate-buffered saline solution.
Fluzone High Dose® and Fluzone® Quadrivalent	formaldehyde, egg protein, octylphenol ethoxylate (Triton X100), sodium phosphate-buffered isotonic sodium chloride solution, thimerosal (multi-dose vials)

7. Warnings and Precautions

A. **Persons with a history of Guillain-Barré Syndrome (GBS)** within 6 weeks following influenza vaccination have a substantially greater likelihood of subsequently developing GBS than persons without such a history. Whether influenza vaccination might be causally associated with this risk for recurrence is not known. Consult with an individual's health care provider and consider avoiding a subsequent influenza vaccination in persons known to have developed GBS within **6 weeks** of a previous influenza vaccination. Experts believe that the benefits of influenza vaccination justify yearly vaccination for most persons who have a history of GBS and who are at risk for severe complications from influenza.[10]

B. **History of severe allergic reaction to a previous dose of an egg-based influenza vaccine** is a precaution to both Flublok® and Flucelvax. ®[10]

8. Other Considerations

A. **Foreign travelers:** Travelers who want to reduce the risk for influenza infection should consider influenza vaccination, preferably at least 2 weeks before departure. In particular, persons who live in the United States and are at higher risk for complications of influenza and who were not vaccinated with influenza vaccine during the previous Northern Hemisphere fall or winter should consider receiving influenza vaccine before departure if they plan to travel to the tropics, with organized tourist groups or on cruise ships, or to the Southern Hemisphere during the Southern Hemisphere influenza season (April–September).[10]

B. **Lactation:** Inactivated and recombinant influenza vaccines are safe for breastfeeding mothers and their infants.[12]

C. **Immunocompromised:** Persons with immunocompromising conditions should receive an age appropriate IIV or RIV4. Immune response to influenza vaccines might be blunted in persons with some conditions, such as persons with congenital immune deficiencies, persons receiving cancer chemotherapy, and persons receiving immunosuppressive medications.[13]

D. **Novel adjuvants:** Because of the limited data on the safety of simultaneous administration of two or more vaccines containing novel adjuvants and the availability of nonadjuvanted influenza vaccine options, selection of a nonadjuvanted influenza vaccine may be considered in situations in which influenza vaccine and another vaccine containing a novel adjuvant are to be administered concomitantly. However, vaccination should not be delayed if a specific product is not available.

E. **Antiviral agents for influenza:** consult CDC's most recent recommendations for guidance on clinical management of influenza using antiviral agents. Available at: www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm

F. **Hematopoietic Stem Cell Transplant (HSCT) recipients:** Influenza vaccine should be administered beginning at least 6 months after HSCT and annually thereafter for the life of the patient. A dose of vaccine can be given as soon as 4 months after the transplant, but a second dose should be considered in this situation. Do not use live influenza vaccine in this population.[13]

G. **Ocular and Respiratory Symptoms after Vaccination: Oculo-respiratory syndrome** (ORS) The cause of ORS has not been established; however, studies suggest that the reaction is not IgE-mediated. When assessing whether a patient who experienced ocular and respiratory symptoms should be revaccinated, providers should determine whether signs and symptoms concerning for IgE-mediated immediate hypersensitivity are present. Health care providers who are unsure whether symptoms reported represent an IgE-mediated hypersensitivity immune response should seek advice from an allergist/immunologist. See https://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/flu.html

9. Side Effects and Adverse Reactions [1-8]

Adverse Event	Frequency
Local reactions: soreness, erythema, induration at injection site	Up to 60%
Fever, malaise, chills	10% -15%
Severe allergic reactions	1 per 3 million doses

10. Storage and Handling

A. Store medications according to OAR 855-041-1036.
B. All clinics and pharmacies enrolled with the Vaccines for Children (VFC) Program must immediately report any storage and handling deviations to the Oregon Immunization Program at 971-673-4VFC (4823).

Vaccine	Temp	Latex	Storage Issues	Notes
Afluria® Quadrivalent [1]	Store at 2° to 8°C (36° to 46°F)	No	Store in original package to protect from light. Store multi-dose vials in recommended conditions.	Discard opened multi-dose vials 28 days after opening.
Fluad® Quadrivalent[8]				Use opened multi-dose vials through the expiration date
Fluarix® Quadrivalent[2]				
Flublok® Quadrivalent[6]				
Flucelvax® Quadrivalent[7]				
FluLaval® Quadrivalent[3]				
Fluzone High Dose® and Fluzone® Quadrivalent[4,5]				

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12. Appendix

A. N/A