

Update—Influenza Vaccination and Antiviral Recommendations

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Overview

- ❑ Update on 2015-16 ACIP influenza vaccination recommendations
- ❑ Very brief overview of indications for antiviral treatment for influenza

2015-16 ACIP Influenza Vaccination Statement

- ❑ 2015-16 ACIP statement published in MMWR August 7, 2015

- ❑ Annual influenza vaccination is recommended for all persons aged 6 months and older

- ❑ Topics discussed:
 - Influenza vaccine virus composition for 2015-16
 - New FDA-approvals since the 2014-15 statement
 - Update in dosing algorithm for children aged 6 mos. through 8 yrs.
 - Updated recommendations regarding use of LAIV and IIV for healthy 2 through 8 year olds, including removal of LAIV preference

- ❑ For topics not addressed, refer to 2013-14 statement

Vaccine Composition for 2015-16

Two strain changes compared with the 2014-15:

- ❑ For trivalent vaccines,
 - an A/California/7/2009 (H1N1)pdm09-like virus (same as 2014-15);
 - An A/Switzerland/9715293/2013 (H3N2)-like virus (replaces A/Texas/50/2012 (H3N2)-like)
 - A B/Phuket/3073/2013-like virus (Yamagata lineage; replaces previous B/Massachusetts/2/2012-like Yamagata lineage virus)

- ❑ For quadrivalent vaccines,
 - The above three viruses and a B/Brisbane/60/2008-like virus (Victoria lineage; same as 2014-15)

TABLE. Influenza vaccines — United States, 2015–16 influenza season*

Trade name	Manufacturer	Presentation	Mercury (from thimerosal) µg/0.5 mL	Ovalbumin µg/0.5 mL	Age Indications	Latex	Route
Inactivated influenza vaccine, quadrivalent (IIV4), standard dose							
<i>Contraindications*: Severe allergic reaction to any vaccine component, including egg protein, or after previous dose of any influenza vaccine.</i>							
<i>Precautions*: Moderate to severe acute illness with or without fever; history of Guillain-Barré syndrome within 6 weeks of receipt of influenza vaccine.</i>							
Fluarix Quadrivalent	GlaxoSmithKline	0.5 mL single-dose prefilled syringe	—	≤0.05	≥3 yrs	No	IM†
FluLaval Quadrivalent	ID Biomedical Corp. of Quebec (distributed by GlaxoSmithKline)	5.0 mL multi-dose vial	<25	≤0.3	≥3 yrs	No	IM†
Fluzone Quadrivalent	Sanofi Pasteur	0.25 mL single-dose prefilled syringe	—	§	6 through 35 mos	No	IM†
		0.5 mL single-dose prefilled syringe	—	§	≥36 mos	No	IM†
		0.5 mL single-dose vial	—	§	≥36 mos	No	IM†
		5.0 mL multi-dose vial	25	§	≥6 mos	No	IM†
Fluzone Intradermal® Quadrivalent	Sanofi Pasteur	0.1 mL single-dose prefilled microinjection system	—	§	18 through 64 yrs	No	ID**
Inactivated influenza vaccine, trivalent (IIV3), standard dose							
<i>Contraindications*: Severe allergic reaction to any vaccine component, including egg protein, or after previous dose of any influenza vaccine.</i>							
<i>Precautions*: Moderate to severe acute illness with or without fever; history of Guillain-Barré syndrome within 6 weeks of receipt of influenza vaccine.</i>							
Afluria	bioCSL	0.5 mL single-dose prefilled syringe	—	<1	≥9 yrs††	No	IM†
		5.0 mL multi-dose vial	24.5	<1	≥9 yrs†† via needle; 18 through 64 yrs via jet injector	No	IM†
Fluvirin	Novartis Vaccines and Diagnostics	0.5 mL single-dose prefilled syringe	≤1	≤1	≥4 yrs	Yes§§	IM†
		5.0 mL multi-dose vial	25	≤1	≥4 yrs	No	IM†
Fluzone	Sanofi Pasteur	5.0 mL multi-dose vial	25	§	≥6 mos	No	IM†
Inactivated influenza vaccine, cell-culture-based (ccIIV3), standard dose							
<i>Contraindications*: Severe allergic reaction to any vaccine component, including egg protein, or after previous dose of any influenza vaccine.</i>							
<i>Precautions*: Moderate to severe acute illness with or without fever; history of Guillain-Barré syndrome within 6 weeks of receipt of influenza vaccine.</i>							
Flucelvax	Novartis Vaccines and Diagnostics	0.5 mL single-dose prefilled syringe	—	**	≥18 yrs	Yes§§	IM†
Inactivated influenza vaccine, trivalent (IIV3), high dose							
<i>Contraindications*: Severe allergic reaction to any vaccine component, including egg protein, or after previous dose of any influenza vaccine.</i>							
<i>Precautions*: Moderate to severe acute illness with or without fever; history of Guillain-Barré syndrome within 6 weeks of receipt of influenza vaccine.</i>							
Fluzone High-Dose***	Sanofi Pasteur	0.5 mL single-dose prefilled syringe	—	§	≥65 yrs	No	IM†
Recombinant influenza vaccine, trivalent (RIV3), standard dose							
<i>Contraindications*: Severe allergic reaction to any vaccine component.</i>							
<i>Precautions*: Moderate to severe acute illness with or without fever; history of Guillain-Barré syndrome within 6 weeks of receipt of influenza vaccine.</i>							
Flublok	Protein Sciences	0.5 mL single-dose vial	—	0	≥18 yrs	No	IM†
Live attenuated influenza vaccine, quadrivalent (LAIV4)							
<i>Contraindications*: Severe allergic reaction to any vaccine component, including egg protein, or after previous dose of any influenza vaccine. Concomitant use of aspirin or aspirin-containing medications in children and adolescents.</i>							
<i>In addition, ACIP recommends LAIV4 not be used for pregnant women, immunosuppressed persons, persons with egg allergy, and children aged 2 through 4 years who have asthma or who have had a wheezing episode noted in the medical record within the past 12 months, or for whom parents report that a health care provider stated that they had wheezing or asthma within the last 12 months.</i>							
<i>LAIV4 should not be administered to persons who have taken influenza antiviral medications within the previous 48 hours.</i>							
<i>Persons who care for severely immunosuppressed persons who require a protective environment should not receive LAIV4, or should avoid contact with such persons for 7 days after receipt.</i>							
<i>Precautions*: Moderate to severe acute illness with or without fever; history of Guillain-Barré syndrome within 6 weeks of receipt of influenza vaccine; asthma in persons aged 5 years and older; medical conditions which might predispose to higher risk for complications attributable to influenza.</i>							
FluMist Quadrivalent†††	MedImmune	0.2 mL single-dose prefilled intranasal sprayer	—	<0.24 (per 0.2 mL)	2 through 49 yrs	No	IN

Licensed Seasonal Influenza Vaccines, United States, 2015-16 Season

MMWR (2015) 64;30: 818-825

See table footnotes on page next page.

Influenza Vaccine Product Updates for 2015-16

New licensures, labeling information, and other changes:

- ❑ Fluzone® Intradermal Quadrivalent IIV
 - Replaces previous trivalent formulation of Fluzone Intradermal
 - Non-inferior immunogenicity, similar adverse event profile to trivalent
- ❑ Expanded age indication for Flublok® (now 18 and older)
 - Previously licensed for 18 through 49 years
 - Similar immunogenicity and safety among persons 50 years and over
- ❑ Approval of administration of Afluria® by Stratis® jet injector for persons 18 through 64 years of age
 - Ages 9 through 17 years, 65 years and over—needle/syringe only
 - ACIP does not recommend Afluria under 9 years
 - No other influenza vaccines currently licensed for use with a jet injector
- ❑ Some presentation changes
 - Flulaval and Fluarix trivalents no longer available (quadrivalents only)
 - Fluzone standard dose trivalent still available, but only multidose vial (quadrivalent available in all four presentations)

Available Influenza Vaccine Products, 2015-16

General Characteristics

- Live virus vs. not
- Trivalent vs. quadrivalent
- Standard-dose vs. high-dose
- Egg-based vs. non-egg based
- Intramuscular vs. intradermal vs. intranasal

Currently Available Influenza Vaccines (N=11)

Common Features

- Contain hemagglutinin (HA) derived from
 - an Influenza A(H1N1) virus,
 - an Influenza A(H3N2) virus, and
 - One (if trivalent) or two (if quadrivalent) Influenza B viruses

Available Influenza Vaccine Products, 2015-16 (11 Branded Products)

- **9 inactivated vaccine products (IIVs)**
 - 4 quadrivalent
 - All standard dose, all egg-based
 - 3 intramuscular, 1 intradermal
 - 3 trivalent, standard dose, egg-based (IIV3)—intramuscular
 - 1 trivalent, standard dose, cell culture-based (cIIV3)—intramuscular
 - 1 trivalent, high dose, egg based (high dose IIV3)—intramuscular

- **1 live attenuated vaccine product (LAIV)**
 - Quadrivalent only (LAIV4)—intranasal

- **1 recombinant vaccine product (RIV)**
 - Trivalent only (RIV3)—intramuscular

Trivalent Inactivated Influenza Vaccines (IIV3s)

- **Have different age indications; need to check package insert**
 - An age-appropriate product should be used
 - Products available for persons as young as 6 months
- **All are egg-based EXCEPT Flucelvax[®] (Novartis)—MDCK cells**
- **All contain 15µg of HA per virus EXCEPT Fluzone[®] High-Dose**
 - Contains 60µg HA per virus
 - Approved for persons aged 65 years and older
 - 24.2% more effective than standard dose IIV3 in preventing lab confirmed influenza among persons 65 and older in one RCT
- **All are administered intramuscularly (needle/syringe)**
- **One (Afluria[®], bioCSL) approved for administration via jet injector**
 - *May be administered by sterile needle and syringe (ages 9 and older),*
 - *OR by Stratis[®] (PharmaJet) jet injector (ages 18 through 64 years ONLY)*

Quadrivalent Inactivated Influenza Vaccines (IIV4s)

- **Provide broader protection against Influenza B viruses**
 - There are two Influenza B lineages: Victoria and Yamagata
 - Immunization against virus from one lineage provides only limited cross-protection against viruses in the other
 - Predominant lineage difficult to predict ahead of each season
 - *Trivalent vaccines contain only one B vaccine virus*
 - *Quadrivalents contain two B viruses (one from each lineage)*
- **All contain 15µg of HA per virus EXCEPT Fluzone® Intradermal Quadrivalent**
- **All are administered intramuscularly EXCEPT Fluzone Intradermal Quadrivalent (intradermal)**
 - *Administered with device included in packaging*
 - *9 mcg per HA virus*
- **Three different products; one approved for as young as 6 mos**

Vaccines Produced via Non-Egg-Based Technologies

- **May permit more rapid scale up of vaccine production (e.g., as might be needed during a pandemic)**

- **Two vaccines this season, both only trivalents currently:**
 - Cell culture-based
 - Recombinant HA

Cell Culture-Based Inactivated Influenza Vaccine (ccIIV3)

- **Flucelvax[®] (Novartis)**
- **Approved for persons aged 18 and older**
- **Licensed in the U.S. in 2012; in the EU since 2007**
- **Currently available only in a trivalent formulation**
- **Vaccine viruses propagated in Madin-Darby Canine Kidney cells rather than in eggs**
- **However, initial reference strains are passaged in eggs**
 - Cannot be considered egg-free in the U.S.
 - Per mfr, estimated to be <50 femtograms (5×10^{-8} μg) per 0.5mL dose)
- **For egg allergic persons, ACIP recs treat ccIIV same as egg-based IIVs**

Recombinant Influenza Vaccine (RIV3)

- **FluBlok® (Protein Sciences)**
- **Approved for persons aged 18 years and over**
- **Currently available only in trivalent formulation**
- **Considered egg-free**
- **Vaccine contains recombinant influenza virus HA**
 - HA produced via introduction of the gene sequence into an insect cell line (Fall Armyworm) using a baculovirus vector
 - Contains 45 mcg HA derived from each vaccine virus (135 mcg total)
- **Per ACIP recs, is an option for persons with egg allergy of any severity (for those within the indicated age range)**

Live Attenuated Influenza Vaccine (LAIV4)

- **FluMist® (MedImmune)**
- **Administered intranasally**
- **Quadrivalent only since 2013-14**
- **Approved for persons aged 2 through 49 years**
 - ACIP recommends only for certain populations

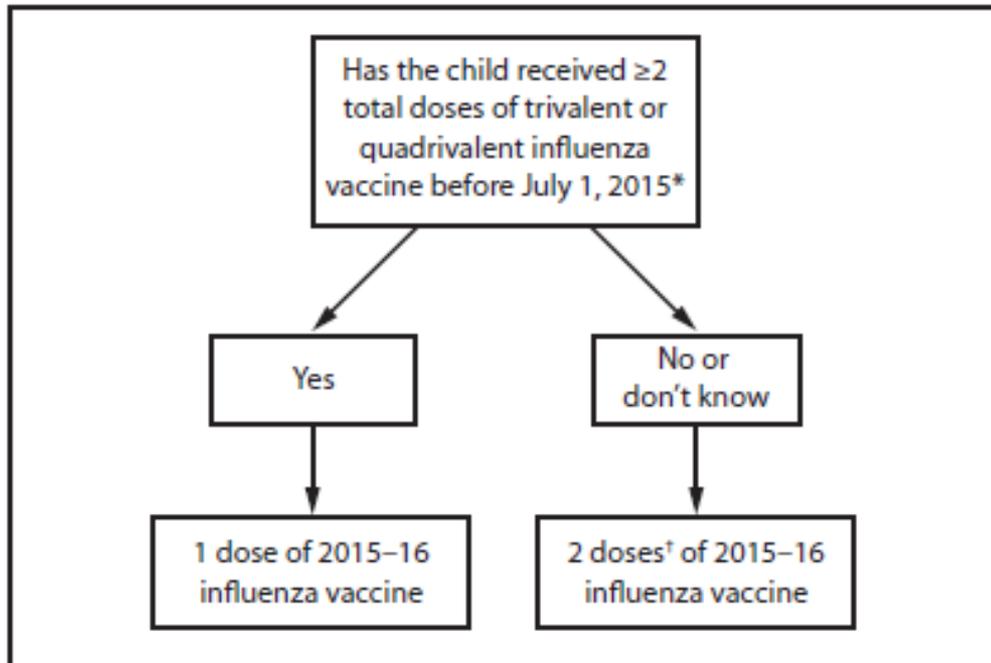
Currently Available Influenza Vaccines (N=11)

- **For many people, more than one option—examples:**
 - Healthy 2 through 49 year olds—LAIV or IIV?
 - 65 years and older—standard dose or high dose IIV?
 - Pretty much anyone—quadrivalent or trivalent?

- **ACIP makes no preferential recommendations for one product over another in situations where more than one is appropriate for a given individual**

Determining Doses Needed for Children 6 months through 8 Years of Age

FIGURE 1. Influenza vaccine dosing algorithm for children aged 6 months through 8 years — Advisory Committee on Immunization Practices, United States, 2015–16 influenza season



* The two doses need not have been received during the same season or consecutive seasons.

† Doses should be administered ≥4 weeks apart.

- Since 2010, counted doses of A(H1N1)pdm09 (2009 pandemic virus) separately
- For 2015-16, not counting separately doses of vaccine containing A(H1N1)pdm09
- If child in this age group has received ≥2 doses trivalent or quadrivalent influenza vaccine before July 2015, needs only one dose of 2015-16 vaccine
 - The 2 doses do not need to be from same or consecutive seasons)

Persons for Whom LAIV Should Not Be Used (1)

LAIV should not be used in the following populations:

- ❑ Persons aged <2 years or >49 years;
- ❑ Those with contraindications listed in the package insert:
 - Children and adolescents receiving aspirin or aspirin-containing products;
 - Persons who have experienced severe allergic reactions to the vaccine or any of its components, or to a previous dose of any influenza vaccine;
- ❑ Pregnant women;
- ❑ Immunosuppressed persons;
- ❑ Persons with a history of egg allergy;
- ❑ Children aged 2 through 4 years who have asthma or who have had a wheezing episode noted in the medical record within the past 12 months, or for whom parents report that a health care provider stated that they had wheezing or asthma within the last 12 months;

Persons for Whom LAIV Should Not Be Used (2)

In addition to those on the previous slide, LAIV should not be used in the following populations (continued):

- ❑ Persons who have taken influenza antiviral medications within the previous 48 hours.
- ❑ Persons who care for severely immunosuppressed persons who require a protective environment should not receive LAIV, or should avoid contact with such persons for 7 days after receipt.

Precautions for the Use of LAIV

In addition to groups for whom LAIV is not recommended, the following are precautions for use of LAIV:

- ❑ Medical conditions that predispose to high risk of complications due to influenza (labeled precaution per the package insert);
- ❑ Asthma in persons aged ≥ 5 years (package insert notes potential increased risk of wheezing).
- ❑ Guillain-Barré Syndrome within 6 weeks of a prior dose of influenza vaccine (a precaution for all influenza vaccines)
- ❑ Moderate to severe illness with or without fever (a precaution for all influenza vaccines)

Influenza Antiviral Drugs: 2015-16

- ❑ **Neuraminidase inhibitors (NAIs): oseltamivir (Tamiflu), zanamivir (Relenza), peramivir (Rapivab)**
 - For treatment and prevention of influenza A and B
 - >99% of all circulating viruses were susceptible to NAIs during 2014-15
 - *Are recommended* for use during this season

- ❑ **Investigational drug available: IV zanamivir**

- ❑ **Adamantanes: rimantadine and amantadine**
 - High levels of resistance
 - *Not recommended* for use during this season

CDC Antiviral Recommendations

- ❑ **All patients in the following categories with suspected or confirmed influenza should be treated as soon as possible, without waiting for confirmatory influenza testing**
 - Hospitalized patients
 - Patients with severe, complicated, or progressive illness
 - Patients at high risk for complications from influenza (either outpatient or hospitalized)

CDC Antiviral Recommendations

- ❑ **Antiviral treatment may be prescribed on the basis of clinical judgment for any previously healthy (non-high risk) outpatient with suspected or confirmed influenza**

Persons at High Risk for Influenza Complications

❑ Children <2 years

❑ Adults ≥ 65 years



❑ Pregnant and postpartum (2 weeks after delivery)

❑ American Indians and Alaska Natives

❑ Persons who are morbidly obese (BMI ≥ 40)

❑ Residents of long-term care facilities

Persons at High Risk for Influenza Complications (continued)

- ❑ Persons with immunosuppression**
- ❑ Persons <19 years who are receiving long-term aspirin therapy**
- ❑ Persons with underlying medical conditions: chronic pulmonary, cardiovascular (except hypertension alone), renal, hepatic, hematologic, and metabolic disorders (incl. diabetes), or neurologic and neurodevelopment conditions**

Influenza Antiviral Medications: The Data Behind the Recommendations

Clinical trials and observational data show that early antiviral treatment can:

- ❑ Shorten the duration of fever and illness symptoms**
- ❑ Reduce the risk of complications (such as otitis media in children and pneumonia requiring antibiotics in adults)**
- ❑ Reduce the risk of death among hospitalized patients**

Efficacy of Neuraminidase Inhibitors: Uncomplicated influenza

Uncomplicated influenza (ambulatory patients)

- Reduces duration of influenza symptoms by average of 1-1.5 days when administered within 2 days of illness onset based on randomized placebo-controlled clinical trials (RCTs)
- Reduces shedding by 20-30% each day, compared to placebo
- Persons treated develop immunity

Thank You!

For more information please contact Centers for Disease Control and Prevention

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