Need-to-know information for the 2016-2017 flu season

ACIP now advises against using the LAIV nasal spray. In addition, 2 new vaccines are available and 2 more may soon be approved.

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The Advisory Committee on Immunization Practices (ACIP) took the unusual step at its June 2016 meeting of recommending against using a currently licensed vaccine, live attenuated influenza vaccine (LAIV), in the 2016-2017 influenza season.[1] ACIP based its recommendation on surveillance data collected by the US Influenza Vaccine Effectiveness Network of the Centers for Disease Control and Prevention (CDC), which showed poor effectiveness by the LAIV vaccine among children and adolescents during the past 3 years.

The US Food and Drug Administration (FDA), however, has chosen not to take any action on this matter, saying on its Web site it "has determined that specific regulatory action is not warranted at this time. This determination is based on FDA's review of manufacturing and clinical data supporting licensure … the totality of the evidence presented at the ACIP meeting, taking into account the inherent limitations of observational studies conducted to evaluate influenza vaccine effectiveness, as well as the well-known variability of influenza vaccine effectiveness across influenza seasons."[2]

CDC data for the 2015-2016 flu season showed the effectiveness of LAIV to be just 3% among children 2 years through 17 years of age.[3] The reason for this apparent lack of effectiveness is unknown. Other LAIV-effectiveness studies conducted in the 2015-2016 season—one each, in the United States, United Kingdom, and Finland—had results that differed from the CDC surveillance data, with effectiveness ranging from 46% to 58% against all strains combined.[2] These results are comparable to vaccine effectiveness found in observational studies in children for both LAIV and inactivated influenza vaccines (IIV) in prior seasons.[2]

Vaccine manufacturers had projected that 171 to 176 million doses of flu vaccine, in all forms, would be available in the United States during the 2016-2017 season.[3] LAIV accounts for about 8% of the total supply of influenza vaccine in the United States,[3] and ACIP's recommendation is not expected to create shortages of other options for the upcoming season. However, the LAIV accounts for one-third of flu vaccines administered to children, and clinicians who provide vaccinations to children have already ordered their vaccine supplies for the upcoming season. Also, it is not clear if children who have previously received the LAIV product will now accept other options for influenza vaccination—all of which involve an injection.

Whether the recommendation against LAIV will continue after this season is also unknown.

What happened during the 2015-2016 influenza season?

The 2015-2016 influenza season was relatively mild with the peak activity occurring in March, somewhat later than in previous years. The circulating influenza strains matched closely to those in the vaccine, making it more

The Advisory Committee on Immunization Practices recommends against using the nasal aerosol LAIV vaccine this flu season.

TABLE 1

Groups who shouldn't forego influenza vaccination[9]

• Children ages 6 to 59 months
• Adults ≥50 years
• Individuals with chronic pulmonary (including asthma) or cardiovascular disease (except hypertension alone), or renal, hepatic, neurologic, hematologic, or metabolic disorders (including diabetes mellitus)
• Individuals with immunosuppression, including that caused by medications or by HIV infection
• Women who are pregnant, or will be, during the flu season
• Individuals ages 6 months through 18 years who are receiving long-term aspirin therapy and who might be at risk for Reye's syndrome following influenza virus infection
• Residents of nursing homes
• American Indians/Alaska natives
• Morbidly obese individuals (BMI ≥40 kg/m^2)
• Health care personnel
• Household contacts and caregivers of children ≤59 months and adults ≥50 years
• Household contacts and caregivers of individuals with medical conditions putting them at high risk for severe complications from the flu

BMI, body mass index; HIV, human immunodeficiency virus.

effective than the previous year's vaccine. The predominant circulating strain was A (H1N1), accounting for 58% of illness; A (H3N2) caused 6% of cases and all B types together accounted for 34%.[4] The hospitalization rate for all ages was 31.3/100,000 compared with 64.1 the year before.[5] There were 85 pediatric deaths compared with 148 in 2014-2015.[6]

Vaccine effectiveness among all age groups and against all circulating strains was 47%.[4] No major vaccine safety concerns were detected. Among those who received IIV3, there was a slight increase in the incidence of Guillain-Barré syndrome of 2.6 cases per one million vaccines.[7]

Other recommendations for 2016-2017

Once again, ACIP recommends influenza vaccine for all individuals 6 months and older.[8] The CDC additionally specifies particular groups that should not skip vaccination given that they are at high risk of complications from influenza infection or because they could expose high-risk individuals to infection (**TABLE 1**).[9]

There will continue to be a selection of trivalent and quadrivalent influenza vaccine products in 2016-2017. Trivalent products will contain 3 viral strains: A/California/7/2009 (H1N1), A/Hong Kong/4801/2014 (H3N2) and B/Brisbane/60/2008.[10] The quadrivalent products will contain those 3 antigens plus B/Phuket/3073/2013.[10] The H3N2 strain is different from the one in last year's vaccine. Each year, influenza experts analyze surveillance data to predict which circulating strains will predominate in North America, and these antigens constitute the vaccine formulation. The accuracy of this prediction in large part determines how effective the vaccine will be that season.

Two new vaccines have been approved for use in the United States. A quadrivalent cell culture inactivated vaccine (CCIV4), Flucelvax, was licensed in May 2016. It is prepared from virus propagated in canine kidney cells, not with an egg-based production process. It is approved for use in individuals 4 years of age and older.[8] Fluad, an adjuvanted trivalent inactivated influenza vaccine, was licensed in late 2015 for individuals 65 years of age and older.[8] This is the first adjuvanted influenza vaccine licensed in the United States and will compete with high-dose quadrivalent vaccine for use in older adults. ACIP does not express a preference for any vaccine in this age group.

Two other vaccines should also be available by this fall: Flublok, a quadrivalent recombinant influenza vaccine for individuals 18 years and older, and Flulaval, a quadrivalent inactivated influenza vaccine, for individuals 6 months of age and older. **TABLE 2**[11] lists approved influenza vaccines.

Issues specific to children

Deciding how many vaccine doses children need has been further simplified. Children younger than 9 years need 2 doses if they have received fewer than 2 doses of trivalent or quadrivalent influenza vaccine before July 1, 2016. The interval between the 2 doses

TABLE 2

Influenza vaccines available for the 2016-2017 season[11]

Vaccine/manufacturer	How supplied	Age group
Trivalent inactivated influenza vaccine (IIV3)		
Afluria/Seqirus	0.5 mL (single-dose syringe) 5 mL (multi-dose vial)	≥9 years
Fluad/Seqirus	0.5 mL (single-dose syringe)	≥65 years
Fluvirin/Seqirus	0.5 mL (single-dose syringe) 5 mL (multi-dose vial)	≥4 years
Fluzone High-Dose/Sanofi Pasteur	0.5 mL (single-dose syringe)	≥65 years
Quadrivalent inactivated influenza vaccine (IIV4)		
Fluarix/GlaxoSmithKline	0.5 mL (single-dose syringe)	≥3 years
FluLaval/ID Biomedical Corp. of Quebec	0.5 mL (single-dose syringe) 5 mL (multi-dose vial)	≥3 years
Fluzone/Sanofi Pasteur	0.25 mL (single-dose syringe) 5 mL (multi-dose vial)	6–35 months
	0.5 mL (single-dose syringe) 0.5 mL (single-dose vial) 5 mL (multi-dose vial)	≥3 years
Fluzone Intradermal/Sanofi Pasteur	0.1 mL (single-dose microinjection system)	18–64 years
Flucelvax (cc)/Seqirus	0.5 mL (single-dose syringe)	≥4 years
Live attenuated influenza vaccine (LAIV4)*		
FluMist/AstraZeneca	0.2 mL (single-use nasal spray)	2–49 years
Trivalent recombinant hemagglutinin influenza vaccine (RIV3)		
Flublok/Protein Sciences Corp.	0.5 mL (single-dose vial)	≥18 years

cc, cell cultivated.

*The Centers for Disease Control and Prevention recommend against using the LAIV4 product in the 2016-2017 influenza season.

Adapted from: Immunization Action Coalition. Influenza vaccine products for the 2016-2017 influenza season.[11]

should be at least 4 weeks. The 2 doses do not have to be the same product; importantly, do not delay a second dose just to obtain the same product used for the first dose. Also, one dose can be trivalent and the other one quadrivalent, although this offers less-than-optimal protection against the B-virus that is only in the quadrivalent product.

Children younger than 9 years require only one dose if they have received 2 or more total doses of trivalent or quadrivalent influenza vaccine before July 1, 2016. The 2 previous doses need not have been received during the same influenza season or consecutive influenza seasons.

In children ages 6 through 23 months there is a slight increased risk of febrile seizure if the influenza vaccine is co-administered with other vaccines, specifically pneumococcal conjugate vaccine (PCV 13) and diphtheria-tetanus-acellular-pertussis (DTaP). The 3 vaccines administered at the same time result in 30 febrile seizures per 100,000 children;[12] the rate is lower when influenza vaccine is co-administered with only one of the others. ACIP believes that the risk of a febrile seizure, which does no long-term harm, does not warrant delaying vaccines that could be co-administered.[13]

Egg allergy requires no special precautions

Evidence continues to grow that influenza vaccine products do not contain enough egg protein to cause significant problems in those

TABLE 3

Antiviral treatment is indicated when patients with the flu are at high risk of complications[14]

• Children <2 years
• Adults ≥65 years
• Individuals with chronic pulmonary (including asthma) or cardiovascular disease (except hypertension alone); renal, hepatic, hematologic (including sickle cell disease), or metabolic disorders (including diabetes mellitus); or neurologic and neurodevelopmental conditions. The last group includes disorders of the brain, spinal cord, peripheral nerve, and muscle, such as cerebral palsy, epilepsy [seizure disorders], stroke, intellectual disability, moderate to severe developmental delay, muscular dystrophy, or spinal cord injury
• Individuals with immunosuppression, including that caused by medications or by HIV infection
• Women who are pregnant or postpartum (within 2 weeks of delivery)
• Individuals <19 years who are receiving long-term aspirin therapy
• American Indians/Alaska natives
• Morbidly obese individuals (BMI ≥40 kg/m^2)
• Residents of nursing homes and other chronic-care facilities

BMI, body mass index; HIV, human immunodeficiency virus.

TABLE 4

Consider antiviral chemoprophylaxis for these individuals[15,16]

The following examples are commonly encountered in practice, but other individuals not listed here may also benefit from preventive medication. Consult your state or local health department, if needed, with questions regarding specific cases.

• Those at high risk of complications from influenza who, during a community outbreak or following exposure to an infected individual, are still unvaccinated (eg, due to a medical contraindication)
• Those at high risk of influenza complications who have been exposed to an infectious individual during the 2 weeks following influenza immunization
• Unimmunized family members or health care workers who have been exposed to an infected individual and care for unimmunized high-risk individuals, including infants and toddlers <24 months
• Unimmunized staff and all residents in a closed institutional setting (eg, extended-care facility) during an outbreak at that institution
• Those at high risk who require a supplement to immunization—eg, those who are immunocompromised and may not develop immunity with vaccination—following exposure to an infectious individual

CDC, Centers for Disease Control and Prevention.

Two new vaccines are available: A quadrivalent cell-culture inactivated vaccine for those ≥4 years and an adjuvanted trivalent inactivated influenza vaccine for those ≥65 years.

with a history of egg allergies. This year's recommendations state that no special precautions are needed regarding the anatomic site of immunization or the length of observation after administering influenza vaccine in those with a history of allergies to eggs, no matter how severe. All vaccine-administration facilities should be able to respond to any hypersensitivity reaction, and the standard waiting time for observation after all vaccinations is 15 minutes.

Antiviral medications for treatment or prevention

Most influenza strains circulating in 2016-2017 are expected to remain sensitive to oseltamivir and zanamivir, which can be used for treatment or disease prevention. A third neuraminidase inhibitor, peramivir, is available for intravenous use in adults 18 and older. Treatment is recommended for those who have confirmed or suspected influenza and are at high risk for complications

(**TABLE 3**).[14] Consideration of antiviral chemoprevention is recommended under certain circumstances (**TABLE 4**).[15,16] The CDC influenza Web site lists recommended doses and duration for each antiviral for treatment and chemoprevention.[15] JFP

References

1. Grohskopf LA, Sokolow LZ, Broder KR, et al. Prevention and control of seasonal influenza with vaccines: Recommendations of the Advisory Committee on Immunization Practices—United States, 2016-17 influenza season. *MMWR Recomm Rep*. 2016;65:1-54.
2. U.S. Food and Drug Administration. FDA information regarding FluMist quadrivalent vaccine. Available at: http://www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm508761.htm. Accessed July 13, 2016.
3. Centers for Disease Control and Prevention. ACIP votes down use of LAIV for 2016-2017 flu season. Available at: http://www.cdc.gov/media/releases/2016/s0622-laiv-flu.html. Accessed July 13, 2016.
4. Flannery B, Chung J. Influenza vaccine effectiveness, including LAIV vs IIV in children and adolescents, US Flu VE Network, 2015-2016. Presented at: meeting of the Advisory Committee on Immunization Practices; June 22, 2016; Atlanta, GA. Centers for Disease Control and Prevention Web site. Available at: http://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2016-06/influenza-05-flannery.pdf. Accessed July 22, 2016.
5. Centers for Disease Control and Prevention. FluView. Laboratory-confirmed influenza hospitalizations. Available at: http://gis.cdc.gov/GRASP/Fluview/FluHospRates.html. Accessed July 25, 2016.
6. Centers for Disease Control and Prevention. FluView. Number of influenza-associated pediatric deaths by week of death. Available at: http://gis.cdc.gov/GRASP/Fluview/PedFluDeath.html. Accessed July 25, 2016.
7. Shimabukuro T. End-of-season update: 2015-2016 influenza vaccine safety monitoring. Presented at: meeting of the Advisory Committee on Immunization Practices; June 22, 2016; Atlanta, GA. Centers for Disease Control and Prevention Web site. Available at: http://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2016-06/influenza-04-shimabukuro.pdf. Accessed July 22, 2016.
8. Grohskopf L. Proposed recommendations 2016-2017 influenza season. Presented at: meeting of the Advisory Committee on Immunization Practices; June 22, 2016; Atlanta, GA. Centers for Disease Control and Prevention Web site. Available at: http://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2016-06/influenza-08-grohskopf.pdf. Accessed July 22, 2016.
9. Centers for Disease Control and Prevention. Influenza vaccination: a summary for clinicians. Available at: http://www.cdc.gov/flu/professionals/vaccination/vax-summary.htm. Accessed July 13, 2016.
10. Centers for Disease Control and Prevention. What you should know for the 2016-2017 influenza season. Available at: http://www.cdc.gov/flu/about/season/flu-season-2016-2017.htm. Accessed July 13, 2016.
11. Immunization Action Coalition. Influenza vaccine products for the 2016-2017 influenza season. Available at: http://www.immunize.org/catg.d/p4072.pdf. Accessed July 13, 2016.
12. Duffy J, Weintraub E, Hambidge SJ, et al. Febrile seizure risk after vaccination in children 6 to 23 months. *Pediatrics*. 2016;138.
13. Centers for Disease Control and Prevention. Childhood vaccines and febrile seizures. Available at: http://www.cdc.gov/vaccinesafety/concerns/febrile-seizures.html. Accessed August 11, 2016.
14. Centers for Disease Control and Prevention. Use of antivirals. Background and guidance on the use of influenza antiviral agents. Available at: http://www.cdc.gov/flu/professionals/antivirals/antiviral-use-influenza.htm. Accessed July 13, 2016.
15. Centers for Disease Control and Prevention. Influenza antiviral medications: summary for clinicians. Available at: http://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm. Accessed July 13, 2016.
16. American Academy of Pediatrics. Recommendations for prevention and control of influenza in children, 2015-2016. *Pediatrics*. 2015;136:792-808.