Update on Influenza Vaccines

By Casey Kamps, Pharm.D., pharmacy resident, SpartanNash

Target Audience
This continuing education activity was designed specifically for pharmacists.

Disclosure Statement
The author has indicated that she does not have any conflicts of interest, nor does she have financial relationships with a commercial interest, related to this activity.

Learning Objectives
At the end of this activity, the participant should be able to:

• define the updated influenza vaccine recommendations for the 2013-2014 season.
• describe the antigen composition of the 2013-2014 influenza vaccines.
• compare and contrast the influenza vaccines available for the 2013-2014 season.
• identify the appropriate influenza vaccine(s) for an individual.
• outline a patient-specific immunization plan for the 2013-2014 influenza season.

The influenza virus is the cause of millions of cases of acute respiratory illness and half a million deaths worldwide annually. In the United States, 5 to 20 percent of the American population contracts the influenza virus each season and nearly 200,000 Americans are hospitalized due to influenza-related complications. In addition to illness and hospitalizations, it is estimated that an average of 6,309 influenza-associated deaths occur annually in the United States, though this number can vary widely from year to year. Of annual influenza-associated deaths in the United States, approximately 87.9 percent occur in those 65 years and older.

Influenza activity in the U.S. is monitored and tracked closely by the Centers for Disease Control and Prevention (CDC). Influenza surveillance data collected over 31 influenza seasons (1976 to 2007) and reported by the CDC estimates that annual influenza-associated deaths ranged from 3,349 during the 1986-1987 season to 48,614 during the 2003-2004 season. Overall, the annual rate of influenza-associated death in the United States during the 31 seasons studied ranged from 1.4 to 16.7 deaths per 100,000 persons.

In the United States and throughout the Northern Hemisphere, the influenza virus customarily circulates year-round but has a distinct seasonal prevalence. Typically, the annual influenza season occurs during the winter months, but timing and duration varies from year to year. Influenza surveillance data captured by the CDC for influenza seasons from 1982-1983 to 2012-2013 reveal that peak flu activity usually occurs in the United States in January or later. However, the CDC has reported influenza outbreaks occurring as early as October and as late in the season as March.

Influenza Viruses
The influenza virus is a single stranded, negative-sense, RNA virus. The viral structure renders it vulnerable to genetic mutation, contributing to antigenic drift and antigenic shift phenomena, which allow the viruses to evade our immune systems and necessitate a new vaccine each year. There are three antigenically distinct types of influenza viruses: A, B and C. Influenza A viruses are separated into subtypes based upon the two major surface antigens: hemagglutinin (H) and neuraminidase (N). Currently, there are 17 different recorded hemagglutinin subtypes and 10...
different neuraminidase subtypes. The variety and various combinations of surface antigens can contribute to the antigenic differences of the virus each year. The influenza B virus is separated into two categories based upon lineage: Yamagata and Victoria. The influenza C virus induces mild respiratory illness in humans and is not known to cause epidemics. The seasonal influenza vaccine does not contain influenza C antigens and does not protect persons from influenza C infections.

The influenza virus is transmitted by the respiratory route. The virus replicates within the columnar epithelial cells of the host’s respiratory tract and coalesces with the host’s respiratory secretions. The virus is then spread by way of small particle, respiratory droplets shed by the host during sneezing, coughing or talking. In addition, but less commonly, the virus may be spread by direct contact with respiratory secretions. These processes, in addition to a short incubation period, are responsible for the highly-contagious nature of the virus.

The virus incubates within the host for 1-4 days. Following the short incubation period, the infected individual typically presents with an abrupt onset of fever and chills, and may experience headache, sore throat, myalgia, malaise, anorexia and/or dry cough. Ordinarily, the characteristic fever peaks within 24 hours of symptom onset and may last 1-5 days. In otherwise healthy individuals, the disease is generally self-limiting. Persons with chronic health conditions, those who are immunocompromised and those at the extremes of age are at the highest risk for more severe disease and complications.

**Diagnosis and Treatment**

A definitive diagnosis of influenza requires laboratory confirmation. Laboratory confirmation is made by way of one of the following methods: virus isolation, detection of viral proteins, detection of viral nucleic acid or serological diagnosis. Rapid diagnostic tests are available to confirm a diagnosis of influenza within minutes.

Antiviral medications may be appropriate in select patients for prophylaxis or treatment of influenza. Two FDA-approved neuraminidase inhibitors, oseltamivir (Tamiflu®) and zanamivir (Relenza®), are recommended by the CDC for use during the 2013-2014 influenza season. Short-term prophylaxis is indicated for unvaccinated individuals who are household contacts of infected persons. Prophylaxis is also indicated for vaccinated individuals whose household contacts are diagnosed with influenza within 14 days post-vaccination. Prophylaxis would not be necessary for those who received LAIV4, as this vaccine provides nearly immediate protection and antiviral medications may prevent LAIV4 from being effective.

Treatment, with either oseltamivir or zanamivir, may reduce the severity of the illness, decrease the duration of illness (sometimes by 1-2 days), and reduce nasal shedding of the virus. Antiviral treatment, using either agent, must be initiated within 48 hours of symptom onset. Despite the treatment options available, prevention of the disease is key.

**Prevention**

*Introduction to Influenza Vaccines*

Influenza vaccines have been proven safe and effective for the prevention of influenza. Influenza vaccines contain viral antigens. When introduced to the immune system by way of immunization, the antigens are recognized as foreign and evoke an immune response. The immune response activates the host’s B cells and T cells, producing protective antibodies that will work to attack and destroy the antigens present in the vaccine. The memory B cells and T cells formed from the immunization provide long-term immunity from the influenza virus. If the antigen contained in the vaccine is encountered in the future, it will be recognized by the memory B cells and T cells. An
immediate immune response will occur; producing antibodies, which will eliminate the antigens encountered and prevent the disease.6,9,11

Influenza vaccines are formulated annually to antigenically match the influenza viruses anticipated to circulate that season. The CDC’s Advisory Committee on Immunization Practices (ACIP) develops recommendations for the utilization of influenza vaccines in an effort to prevent and control morbidity and mortality of the disease in the United States. The Committee’s expert opinion and recommendations are reviewed and approved by the director of the CDC as official vaccine guidance in the United States.

As it has since 2010, routine annual influenza vaccination remains recommended for all persons aged greater than or equal to six months for the 2013-2014 influenza season.6 The 2013-2014 ACIP/CDC influenza vaccine recommendations contain only minor changes from the previous season. The majority of changes included in the 2013-2014 ACIP recommendations are related to the novel formulations of influenza vaccines available for the first time this season.6 Newly-licensed vaccines include a quadrivalent live attenuated influenza vaccine, three quadrivalent inactivated influenza vaccines, a trivalent cell culture-based inactivated influenza vaccine and a trivalent recombinant hemagglutinin vaccine (see Table 1 for a list of accompanying abbreviations).6

### Table 1. 2013-2014 Influenza Vaccine Abbreviations

<table>
<thead>
<tr>
<th>Vaccine Formulation</th>
<th>Abbreviation</th>
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<tbody>
<tr>
<td>Quadrivalent inactivated influenza vaccine</td>
<td>IIV4</td>
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<tr>
<td>Quadrivalent live attenuated influenza vaccine</td>
<td>LAIV4</td>
</tr>
<tr>
<td>Recombinant hemagglutinin trivalent vaccine</td>
<td>RIV3</td>
</tr>
<tr>
<td>Trivalent cell culture-based inactivated influenza vaccine</td>
<td>ccIIV3</td>
</tr>
<tr>
<td>Trivalent inactivated influenza vaccine</td>
<td>IIV3</td>
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Historically, influenza vaccines have been trivalent (containing three viruses): two influenza A viruses and one influenza B virus. Previous season’s trivalent vaccines have contained only one B virus lineage, either Victoria or Yamagata. The B lineage included in each season’s vaccine is predicted annually by the CDC; however, prediction methods have resulted in many instances of disease occurrence. Over 12 influenza seasons, 2001-2002 to 2012-2013, the trivalent vaccine formulation mismatched the B lineage actually circulating during six of the seasons creating gaps in protection and disease.31,32 During the 2012-2013 influenza season, 34 percent of influenza cases were caused by the B lineage not included in the vaccine due to incorrect prediction.32 Quadrivalent vaccines were developed to prevent B lineage mismatch that occurred with trivalent vaccines in previous seasons. Quadrivalent vaccines contain both influenza B lineages and provide protection against both B lineages.

Both trivalent and quadrivalent influenza vaccines are available for the 2013-2014 influenza season. The 2013-2014 trivalent influenza vaccines contain an A/California/7/2009(H1N1)-like virus, an H3N2 virus antigenically like the cell-propagated prototype virus A/Victoria/361/2011 and a B/Massachusetts/2/2012-like virus (Yamagata lineage). The 2013-2014 quadrivalent influenza vaccines contain an additional B virus, a B/Brisbane/60/2008-like virus (Victoria lineage).26

### Trivalent Influenza Vaccines

Trivalent inactivated influenza vaccines (IIV3) are available from several manufacturers (see Table 2). The various IIV3 vaccines are similar, but not identical. IIV3 differ in inert ingredients, presence of preservative, route of administration and FDA-approved age indications. The standard-
dose intramuscular influenza vaccines each contain 45 mcg of antigen per 0.5 mL dose in the following composition: 15 mcg A/California/07/2009 (H1N1), 15 mcg A/Texas/50/2012 X-223A (H3N2) and 15 mcg B/Massachusetts/02/2012.2,6,14-21 The most common adverse effects associated with IIV3 include pain, localized injection site reactions, headache and myalgias.14-22

<table>
<thead>
<tr>
<th>Trade Name</th>
<th>Manufacturer</th>
<th>Age Indications</th>
<th>Route of Administration</th>
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<tbody>
<tr>
<td>Afluria®</td>
<td>CSL Limited</td>
<td>≥ 9 yrs*</td>
<td>IM</td>
</tr>
<tr>
<td>Fluarix®</td>
<td>GlaxoSmithKline</td>
<td>≥ 3 yrs</td>
<td>IM</td>
</tr>
<tr>
<td>FluLaval®</td>
<td>ID Biomedical Corporation of Quebec</td>
<td>≥ 3 yrs</td>
<td>IM</td>
</tr>
<tr>
<td>Fluvirin®</td>
<td>Novartis Vaccines and Diagnostics</td>
<td>≥ 4 yrs</td>
<td>IM</td>
</tr>
<tr>
<td>Fluzone®</td>
<td>Sanofi Pasteur</td>
<td>0.25 mL Single-dose prefilled syringe: 6-35 months</td>
<td>IM</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.5 mL Single-dose prefilled syringe: ≥ 36 months</td>
<td>IM</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.5 mL Single-dose vial: ≥ 36 months</td>
<td>IM</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5.0 mL Multi-dose vial: ≥ 6 months</td>
<td>IM</td>
</tr>
<tr>
<td>Fluzone® High Dose</td>
<td>Sanofi Pasteur</td>
<td>≥ 65 yrs</td>
<td>IM</td>
</tr>
<tr>
<td>Fluzone Intradermal®</td>
<td>Sanofi Pasteur</td>
<td>18-64 years</td>
<td>ID</td>
</tr>
<tr>
<td>Flucelvax®</td>
<td>Novartis Vaccines and Diagnostics</td>
<td>≥ 18 yrs</td>
<td>IM</td>
</tr>
<tr>
<td>FluBlok®</td>
<td>Protein Sciences</td>
<td>18-49 yrs</td>
<td>IM</td>
</tr>
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IM: intramuscular injection; ID: intradermal injection

*Afluria® is FDA approved for ages greater than or equal to five years; however, the ACIP recommends against use of Afluria® in children aged 5-8 years due to increased reports of febrile reactions in this age group.
High dose IIV3, Fluzone® HD, is approved for adults greater than or equal to 65 years of age. Like the standard dose IIV3, Fluzone® HD is a single, 0.5 mL intramuscular injection. The high dose IIV3 contains 180 mcg of antigen per 0.5 mL dose in the following composition: 60 mcg A/California/07/2009 (H1N1), 60 mcg A/Texas/50/2012 X-223A (H3N2) and 60 mcg B/Massachusetts/02/2012.

High dose IIV3 was designed specifically for the older adult population following publication of several studies consistently reporting decreased antibody response to standard dose IIV3 in this population. This phenomenon has been associated with the decrease of immune system function as people age. In clinical trials, the high-dose formulation provided older adults with improved antibody immune response versus the standard dose. Localized, injection site reactions are more frequent in patients receiving the high-dose formulation when compared to those receiving the standard dose formulation.

The intradermal IIV3 formulation, Fluzone® Intradermal, was first approved in 2011 for use in adults aged 18-64 years. Fluzone® Intradermal is supplied as a prefilled microinjection system and is administered into the skin covering the deltoid muscle. The intradermal IIV3 is formulated as a single 0.1 mL dose and contains 27 mcg of antigen per dose in the following composition: 9 mcg A/California/07/2009 (H1N1), 9 mcg A/Texas/50/2012 X-223A (H3N2) and 9 mcg B/Massachusetts/02/2012. The most common adverse reactions for the intradermal formulation include erythema, induration, swelling, pain and pruritus. In clinical trials, local adverse events occurred at a higher rate in those receiving the intradermal formulation as compared to the intramuscular formulation. To date, there are no studies demonstrating greater efficacy with this formulation as compared to traditional inactivated influenza vaccine formulations.

Two novel IIV3 preparations are available for the 2013-2014 influenza season: Flucelvax® (Novartis Vaccines and Diagnostics) and FluBlok® (Protein Sciences). Both new vaccines are produced by non-egg based technologies that allow more rapid vaccine production.

Flucelvax® is a culture-based influenza vaccine (ccIIV3) approved for use in persons greater than or equal to 18 years. The technology utilized for vaccine production propagates the vaccine virus within Madin Darby Canine Kidney cells. The vaccine virus is not propagated in eggs as with other IIV3 formulations; however, the original reference strains utilized in production are developed in eggs. Therefore, Flucelvax® is not considered-egg free, but is thought to contain less egg protein than other IIV3s. Flucelvax® is a single 0.5 mL dose administered intramuscularly.

FluBlok® is a recombinant hemagglutinin vaccine (RIV3) approved for use in persons 18-49 years of age. FluBlok® is the first egg-free influenza vaccine and can be safely administered to persons with egg allergy. The hemagglutinin protein component of each virus strain is produced by recombinant technology within an insect cell line and does not use egg or influenza viruses in production. FluBlok® is a single 0.5 mL dose administered intramuscularly.

Contraindications to inactivated influenza vaccine formulations are fairly universal; however, some contraindications are vaccine specific. In general, contraindications to inactivated influenza vaccines include anaphylaxis after a previous dose of any influenza vaccine and/or a severe allergic reaction to any vaccine component, including egg protein. Allergy to egg protein is not a contraindication to RIV3. Precautions for all inactivated formulations include moderate-to-severe illness (with or without fever) and prior history of Guillain-Barré Syndrome within six weeks of receipt of an influenza vaccine.

Quadrivalent Influenza Vaccines

Four new quadrivalent influenza vaccines are available for the 2013-2014 influenza season (see Table 3). Three inactivated quadrivalent influenza vaccines formulations are available: Fluarix® Quadrivalent, Flulaval® Quadrivalent and Fluzone® Quadrivalent. One live attenuated quadrivalent...
vaccine is available: FluMist® Quadrivalent. The safety and immunogenicity of IIV4 formulations are similar to the safety and immunogenicity of IIV3 formulations. To date, there is no data published to demonstrate greater efficacy of the quadrivalent vaccines in preventing disease, hospitalizations, or death as compared to trivalent vaccines.29,30,33

| Table 3. Quadrivalent Influenza Vaccines
| Quadrivalent inactivated influenza vaccines (IIV4) |
| --- | --- | --- | --- |
| **Trade Name** | **Manufacturer** | **Age Indication** | **Route of Administration** |
| Fluarix® Quadrivalent | GlaxoSmithKline | ≥ 3 yrs | IM |
| Flulaval® Quadrivalent | ID Biomedical Corporation of Quebec | ≥ 3 yrs | IM |
| Fluzone® Quadrivalent | Sanofi Pasteur | 0.25 mL single-dose prefilled syringe | IM |
| | | 0.5 mL single-dose prefilled syringe | |
| | | 0.5 mL single-dose vial | |

| Quadrivalent live attenuated influenza vaccine (LAIIV4) |
| --- | --- | --- |
| **Trade Name** | **Manufacturer** | **Age Indication** | **Route of Administration** |
| FluMist® Quadrivalent | MedImmune | 2-49 yrs* | Intranasal |

*FluMist® Quadrivalent is indicated for healthy, nonpregnant individuals who are aged 2-49 years only.

The quadrivalent formulation of the live attenuated influenza vaccine, FluMist® Quadrivalent, has replaced the trivalent formulation for the 2013-2014 influenza season. FluMist® Quadrivalent is the sole live attenuated intranasal influenza vaccine formulation available for the 2013-2014 influenza season. FluMist® Quadrivalent is indicated for healthy, nonpregnant persons age two through 49 years who do not have medical conditions that predispose them to medical complications from influenza.

FluMist® Quadrivalent contains four vaccine virus strains: A/H1N1, A/H3N2, B/Yamagata/16/88, and B/Victoria/2/87. Live attenuated viruses contained in the vaccine and administered to the recipient must infect and replicate within cells of the nasopharynx to induce immunity. The vaccine prevents influenza disease by prohibiting viral entry and infection.34-35

Children less than five years of age who experience recurrent wheezing and/or individuals of any age who have asthma may be at increased risk of wheezing following administration of FluMist® Quadrivalent. For this reason, it is important to consult the patient’s medical record (if available) and to ask the patient about a history of wheezing and/or asthma. Patients 2-4 years of age who have experienced episodes of wheezing in the past 12 months or have been diagnosed with asthma should not receive FluMist® Quadrivalent. Persons of any age who have asthma should not receive FluMist® Quadrivalent.34-35

Current expert consensus recommends against use of FluMist® Quadrivalent in those with chronic pulmonary, cardiovascular (exception: isolated hypertension), renal, hepatic, neurologic/neuromuscular, hematologic or metabolic disorders, and/or immunosuppression.6 In addition, it is recommended that FluMist® Quadrivalent not be administered to caregivers or other close contacts of severely immunosuppressed individuals who require a protective environment because of the low, but potential risk of transmission of the live attenuated vaccine virus.34,35
Contraindications to FluMist® Quadrivalent include prior anaphylaxis to any influenza vaccine or any component of FluMist® Quadrivalent, including egg protein, gentamicin, gelatin and arginine. An additional contraindication to FluMist® Quadrivalent is concomitant aspirin therapy in children and adolescents. The latter contraindication stands because Reye’s Syndrome in children and adolescents is a serious complication of pediatric viral infections, including wild-type influenza, and, additionally, because of the association of Reye’s Syndrome and aspirin in this population. Administration of FluMist® Quadrivalent is also contraindicated in pregnancy. Warnings and precautions to consider prior to administration of FluMist® Quadrivalent include moderate-to-severe illness with or without the presence of fever and a history of Guillain-Barré Syndrome within six weeks of receipt of any influenza vaccine.

In clinical trials, the most commonly reported side effects following administration of FluMist® Quadrivalent amongst patients of all ages (2-49 years) were rhinorrhea and nasal congestion. Thirty-two percent of children and adolescents (2-17 years) experienced rhinorrhea or nasal congestion and 7 percent of children and adolescents reported fever over 100°F following receipt of FluMist® Quadrivalent. Forty-four percent of adults (18-49 years) (n = 2,458) reported rhinorrhea or nasal congestion and 19 percent reported sore throat following FluMist® Quadrivalent administration. FluMist® Quadrivalent may be preferred in children, as multiple studies have demonstrated superior efficacy of LAIV4 as compared to IIV among children.

Changes for the 2013-2014 Season

While the universal influenza immunization recommendation remains the same, one significant difference between this season and previous seasons is the abundance of novel vaccines available for the 2013-2014 influenza season. The expanded selection of vaccines available allows immunizing providers several options for immunizing patients; however, the ACIP has not provided any preferential recommendation for one influenza vaccine over another when more than one product is otherwise appropriate. The immunizing provider must evaluate all patient-specific parameters, including age, past medical history and patient preference, to formulate a clinical decision regarding the best vaccine to administer.

Changes to the 2013-2014 influenza recommendations include items such as vaccine administration in the presence of egg allergy and modified 2-dose algorithms for certain children six months through eight years of age. The approval of RIV3 prompted changes in ACIP recommendations regarding influenza immunization in the presence of egg allergy. Individuals with egg allergy, who can consume lightly cooked eggs such as scrambled eggs without manifestation of an allergic reaction, may receive any influenza vaccine. Individuals who experience hives, without other signs and symptoms of anaphylaxis, after consuming egg or egg-containing foods, may receive RIV3 (if indicated) or IIV3/IIV4 if the individual can be observed for 30 minutes following immunization. If the patient experiences cardiovascular, respiratory or gastrointestinal symptoms, or has required emergency epinephrine or emergency medical attention after eating eggs or egg-

STOP AND REFLECT

An expectant mother comes to your pharmacy explaining that she is due in 16 weeks and would like to receive the influenza vaccine to protect her baby. Will you vaccinate this individual? If so, what vaccine is appropriate?
containing foods, the patient may receive RIV3 (if indicated) or the patient should be referred to an allergist or other physician with expertise in the management of allergic manifestation of egg allergy. In the 2013-2014 update, the ACIP added a recommendation relating to persons suspected of being allergic to egg based on allergy testing, but who have no history of exposure to egg. In this scenario, the ACIP recommends that immunizing providers either administer RIV3 (if indicated) or refer the patient to a physician with expertise in the management of allergic conditions prior to immunizing.6

STOP AND REFLECT
A 35-year-old male patient approaches your pharmacy requesting an annual influenza vaccine. While assessing the patient’s medical history, you learn he has an egg allergy. Further discussion with the patient reveals that he develops hives after eating eggs. What additional information is necessary for you to complete your assessment of the patient and determine if he is candidate for receiving the influenza vaccine today?

For the 2013-2014 influenza season, ACIP has modified recommendations and created two algorithms for immunizing children six months through eight years of age. The first algorithm recommends that children, who have not received or do not have record of previous influenza vaccine, receive two doses of influenza vaccine (administered at least four weeks apart). Children who have received a total of two or more doses of seasonal influenza vaccine since July 1, 2010, only require one dose of the 2013-2014 seasonal influenza vaccine. If the child has not received two doses of seasonal influenza vaccine since July 1, 2010, or if the vaccine history is uncertain, the child should receive two doses of influenza vaccine (administered at least four weeks apart).6

The second algorithm created by the ACIP requires knowledge of the child’s vaccine history prior to the 2010-2011 influenza season. If the child received greater than or equal to two doses of seasonal influenza vaccine during any previous season, in addition to greater than or equal to one dose of a H1N1-containing vaccine, the child should receive one dose of the 2013-2014 influenza vaccine. Children who do not meet both criteria (greater than or equal to two doses of seasonal influenza vaccine during any previous season and greater than or equal to one dose of a H1N1-containing vaccine) should receive two doses of the 2013-2014 seasonal influenza vaccine.

To sum up the two algorithms, a child less than nine years of age only requires one dose of the 2013-2014 influenza vaccine if any of the following are true:

- The child received greater than or equal to two doses of seasonal influenza vaccine since July 1, 2010.
- The child received greater than or equal to two doses of seasonal influenza vaccine before July 1, 2010, and greater than or equal to one dose of monovalent 2009 (H1N1) vaccine.
- The child received greater than or equal to one dose of seasonal influenza vaccine before July 1, 2010, and greater than or equal to one dose of seasonal influenza vaccine since July 1, 2010.6
The CDC recommends that health care providers begin offering influenza immunizations to the public as soon as the vaccine becomes available for any given season. Optimally, the CDC recommends that individuals are immunized for influenza by October each year. However, individuals may receive their annual influenza vaccination at any time throughout the year. Antibodies developed in response to influenza vaccine decline in the months following vaccination; however, there is evidence that antibody levels remain high enough to provide sufficient protection to the end of the influenza season. Protection from antigenically well-matched influenza vaccine extends to at least 6-8 months post-vaccination in most healthy individuals. Additional studies suggest that the duration of immunity can extend for multiple seasons.

Immunizing providers should avoid missed opportunities by using routine visits, acute care visits and hospitalizations to immunize patients. If a patient is eligible to receive multiple vaccines, keep in mind the CDC’s recommendations regarding simultaneous administration of vaccines:

- Inactivated influenza vaccines do not interfere with immune response to any other inactivated or live vaccines. Inactivated vaccines may be administered simultaneously with other inactivated vaccines or live vaccines.
- Live attenuated influenza vaccine may be administered simultaneously with other live and/or inactivated vaccines. However, if not administered simultaneously, two live vaccines should be administered at least four weeks apart.

**Documenting Vaccination**

Best practices for immunizing in Michigan include documenting the influenza vaccines you have administered within the Michigan Care Improvement Registry (MCIR) and providing your patient with a current Vaccine Information Statement (VIS). MCIR was originally founded in 1998 as the Michigan Childhood Immunization Registry. While the acronym MCIR remains the same, the name of the registry was changed to the Michigan Care Improvement Registry following the passage of Public Act 91 of 2006, which expanded MCIR to become a lifetime registry, including immunization records into adulthood.

Health care providers are required to report to MCIR all immunizations administered to individuals born after Dec. 31, 1993. Immunizations, including influenza, administered to individuals meeting the aforementioned criteria must be reported to MCIR within 72 hours of administration. Currently, providers are not required to report adult immunizations into MCIR; however, this practice is highly encouraged and is recommended. Online training and other MCIR training materials are available at [www.MCIR.org](http://www.MCIR.org). Accompanying MCIR documentation as part of best practices is the provision of VIS for all vaccines administered.

Under the National Childhood Vaccine Injury Act (NCVIA) of 1986, federal law requires that providers provide vaccine recipients and/or the parent/guardian of the vaccine recipient with the most current VIS for vaccines containing diphtheria, tetanus, pertussis, measles, mumps, rubella, polio, hepatitis A, hepatitis B, haemophilus influenza type B (Hib), influenza, pneumococcal conjugate, meningococcal, rotavirus, human papillomavirus (HPV) or varicella. In accordance with this provision, providers must document both the published date of the VIS and the date the VIS is
distributed to the patient/caregiver within the patient’s medical record.\textsuperscript{38,39} The CDC recommends that providers supply vaccine recipients with a VIS for all vaccines administered.

In addition to this federal regulation, Michigan state law requires that providers inform parents/guardians about MCIR.\textsuperscript{39} Due to this additional Michigan requirement, the Michigan Department of Community Health (MDCH) has Michigan-specific VIS forms available that indicate the required information on MCIR reporting. Vaccine information statements obtained from the CDC and/or Immunization Action Coalition (IAC) do not contain information regarding MCIR; however, these versions may be used if your practice has another mechanism in place to inform patients about MCIR. Current versions of Michigan VIS are available in several languages and may be obtained from the MDCH at [www.Michigan.gov/immunize](http://www.Michigan.gov/immunize).

**Adverse Event Reporting**

Best practices for immunizing continue even after the vaccine is administered to the patient. As an immunizing provider, it is imperative that you do your part in improving and ensuring patient safety by reporting vaccine adverse events that occur following administration. The Vaccine Adverse Event Reporting System (VAERS) was established in 1990 by the Food and Drug Administration (FDA) and the CDC. VAERS was constructed in response to the NCVIA, which requires that all health care providers report adverse events occurring post-vaccination.\textsuperscript{40} However, in the United States adverse event reporting to VAERS is not limited to health care providers. Vaccine recipients or their parents/guardians and even manufacturers are encouraged to report to VAERS any unexpected event or significant health problem occurring following vaccination. VAERS data are utilized by the FDA and the CDC to monitor vaccine safety and for additional research purposes such as identifying patient-specific risk factors for particular adverse events and to identify vaccine lots with unusually high volumes of adverse event reports.

Health care providers are required by law to report to VAERS any of the following:

1. Any adverse event defined by the vaccine manufacturer as a contraindication to further doses of the vaccine; or
2. Any adverse event listed in the VAERS Table of Reportable Events Following Vaccination that occurs within the specified time period after vaccination

In addition to the required reporting, health care providers are encouraged to report any adverse events that occur after vaccine administration, even if you are unsure if the vaccine caused the events.

Completed VAERS reports include detailed vaccine information, time of immunization, onset of the adverse event and the vaccine recipient’s demographic information, including concomitant illnesses and/or medications and past history of any previous adverse events following vaccination. VAERS forms can be completed online at [https://vaers.hhs.gov](https://vaers.hhs.gov), or paper forms may be completed and mailed or faxed directly to VAERS.\textsuperscript{40} The complete Reportable Events Table (RET) can also be found online.

**Additional Preventative Measures**

Annual receipt of the influenza vaccine remains the number one method of preventing influenza-related infections, but there are a variety of additional preventative measures and healthy habits we can discuss with our patients to help prevent influenza this season. When administering or recommending the influenza vaccine to patients, take the opportunity to discuss with your patient additional non-pharmacologic methods to prevent the transmission of the influenza virus. Educate and empower your patients! Inform them, using lay language, that the influenza virus may be spread by coughing, sneezing or touching contaminated objects and arm them with ways to protect
themselves.41 Urge patients to exercise caution this flu season. Recommend patients avoid going places where there is known flu activity and to avoid contact with infected individuals, whenever possible. Recommend that the patient wear a protective face mask or seek prophylactic drug therapy if they cannot avoid contact with infected individuals.

Counsel your patients regarding how to appropriately cover their coughs and sneezes. Inform your patients that aerosol spread is the primary method for transmission of the influenza virus. Instruct patients to cover both their mouth and nose when coughing or sneezing. Moreover, remind them to properly dispose of any used tissue. If tissue is not available or on-hand, suggest the patient sneeze or cough into their upper sleeve or elbow, rather than into their hands.41

Remind patients of the importance of clean hands in preventing the spread of bacterial and viruses such as the influenza. Properly washing ones hands with soap and water is recommended when hands are visibly soiled. Use of an alcohol-based hand rub may be appropriately recommended when ones hands are not visibly soiled.41,42

Advise patients to thoroughly wash their hands frequently throughout the day. Instruct patients to wash their hands for 20 seconds using soap and warm water. Counsel them to be conscious of washing all surfaces of their hands, including the back of hands, wrists, between fingers, finger tips and even their thumbs under fingernails. Suggest patients rinse hands well with fingers in a downward position and to dry hands with paper or a clean cloth towel. As an additional measure to prevent re-contamination, suggest the patient turn off the faucet and open the door with the towel rather than their bare, clean hands.42

Suggest an alcohol-based hand rub if access to soap and warm water is not available or inconvenient. Decontamination with alcohol-based hand rub includes using an amount sufficient to cover all surfaces of the hands. Proper technique requires applying the alcohol-based hand rub to the palm of one hand, rubbing hands together to cover all surfaces of hands and fingers and continuing to rub until all hand rub is absorbed.42 These measures in combination with recommended vaccination will provide patients with protection from influenza this and each flu season.

Conclusion

Every year, pharmacists, in coordination with other health care providers, have the opportunity to prevent hundreds of thousands of cases of influenza by offering and administering influenza vaccines. It is essential that pharmacists in all practice settings stay up-to-date with influenza-related information as the composition and formulation of influenza vaccine(s) is updated annually to match the influenza virus strains anticipated for the upcoming influenza season. Current influenza virus and vaccine information is relevant to pharmacists, even to those who are not immunizing, because this knowledge allows us to take advantage of opportunities to educate patients regarding prevention of this highly-contagious respiratory illness.
Continuing Education Self-assessment Questions

1. What is the expected minimum duration of protection from an antigenically well-matched influenza vaccine?
   a. 1-2 months
   b. 3-4 months
   c. 4-5 months
   d. 6-8 months

2. Which of the following is not included in the 2013-2014 trivalent influenza vaccine?
   a. A/California/7/2009(H1N1)-like virus
   b. A/Victoria/361/2011(H3N2)-like virus
   c. B/Massachusetts/2/2012-like virus (Yamagata lineage)
   d. B/Brisbane/60/2008-like virus (Victoria lineage)

3. ACIP recommends routine annual influenza vaccination for all persons aged ≥2 years who do not have contraindications.
   a. True
   b. False

4. FluMist® is available in two formulations this season, trivalent and quadrivalent.
   a. True
   b. False

5. Of the patients described, who is a candidate for receiving LAIV4?
   a. 6-year-old male with asthma
   b. 5-year-old healthy female
   c. 25-year-old pregnant female
   d. 60-year-old healthy female

6. Which vaccine formulation is the best to administer to an adult patient with a severe allergy to egg protein?
   a. IIV3
   b. IIV4
   c. LAIV4
   d. RIV3

7. Which vaccine should be administered to a hypertensive 75-year-old female who is otherwise healthy?
   a. FluBlok®
   b. Fluzone® Intradermal
   c. Fluzone® High Dose
   d. FluMist®

8. A patient can receive both Tdap and IIV3 at the same visit?
   a. True
   b. False
9. It is required by law for pharmacists to provide patients receiving IIV3 with a current VIS.
   a. True
   b. False

10. Non-pharmacologic recommendations to suggest to your patients to prevent the spread or contraction of the influenza virus include which of the following?
    a. Covering your cough
    b. Hand washing with soap and warm water
    c. Use of alcohol-based hand rub
    d. All of the above
References
15. FLUARIX [prescribing information], Research Triangle Park, N.C., GlaxoSmithKline, 2013.
16. FLUBLOK [prescribing information], Meriden, Conn., Protein Sciences Corporation, 2013.
17. FLUCELVAX [prescribing information], Manburg, Germany, Novartis Vaccines and Diagnostics, 2013.
19. FLUVIRIN [prescribing information], Liverpool, UK, Novartis Vaccines and Diagnostics, 2013.
22. FLUZONE HIGH-DOSE [prescribing information], Swiftwater, Penn., Sanofi Pasteur Inc., 2013.


29. FLUARIX QUADRIVALENT [prescribing information], Research Triangle Park, N.C., GlaxoSmithKline, 2013.

30. FLUZONE QUADRIVALENT [prescribing information], Swiftwater, Penn., Sanofi Pasteur Inc., 2013.


