Pharmacist Immunization Update: Advances in Vaccine Recommendations and Regulations

by Nicole Van Hoey, PharmD

Upon successful completion of this article, the pharmacist should be able to:

1. Describe flu vaccine products available for the 2013-2014 season, with a particular emphasis on new formulations and special populations, such as egg-allergic and elderly patients.
2. Discuss the newly updated ACIP recommendations for pertussis immunization, incorporating age restrictions, high-risk populations, and repeated doses.
3. Explain the importance of adult Measles, Mumps, and Rubella vaccination for international travelers and at-risk populations.
4. List the two required, not just recommended, vaccines for international travel and their latest public health regulations.
5. Identify the best practices for vaccine storage in a community setting, especially regarding refrigeration and documentation procedures.

The pharmacist role as community vaccinator is growing but still highly variable across the country. Each state has separate regulations covering legality of community vaccinations as well as regulations for business and professional licensure requirements. Any community pharmacist providing immunizations should be aware of vaccine information and guidance provided by government agencies such as the Centers for Disease Control and Prevention (CDC) Advisory Committee on Immunization Practices (ACIP), the Food and Drug Administration (FDA), Vaccine Adverse Event Reporting System (VAERS), and the CDC Yellow and Pink Books on Vaccine-Preventable and Travel Diseases.

The importance of annual flu vaccination in particular has driven the growing rate of community-based vaccination. In 2009, in response to the H1N1 pandemic, accessible community pharmacists were charged to meet increased vaccination demand and stave the public health crisis. Pharmacists responded, and the public did too, and those roles have remained or expanded since.

Standards for vaccination schedules, formulations, and research are determined for all vaccine providers whether office- or community-based providers by ACIP, which works in conjunction with the CDC, FDA, and nonprofit Immunization Action Coalition (IAC) to get
Pharmacists are poised to meet and exceed standards for administration of vaccines for flu, pneumonia, shingles, and more. The ability to provide vaccinations in the pharmacy introduces challenges for providers and patients, though. For example, vaccination without appointments shifts medical record accountability. Although the number of people getting vaccinated is growing, communication of preventive measures with primary care physicians (PCPs) is not systematic. Advances in electronic record sharing, in addition to legal requirements for physician involvement in clinic vaccination protocols and statewide vaccination registries, can streamline documentation. However, on a practical level, patient proof of vaccination for personal medical records and direct communication to the physician remain the responsibility of the pharmacist vaccinator whenever possible. Initiating this link to PCPs can in turn build a provider network to boost pharmacy clinic referrals and improve PCP medical recordkeeping.

Pharmacists also need to establish their own recordkeeping systems for vaccine stock and administration history; observe and document procedures for cold chain storage and efficient product disposal; and implement up-to-date and ongoing training and VAERS reporting. Storage and documentation in particular are guided by CDC-recommended procedures that have been updated online in 2013. Current vaccine recommendations, too, are accessible online; updates for commonly administered adult vaccines, including influenza, pertussis, and select travel immunizations, are new in 2013.

**INFLUENZA VACCINE UPDATE**

Since the first vaccine-preventable flu season in the 1940s, viral strains in annual U.S. products have been determined by evaluating disease trends across the globe and selecting the three most likely strains to protect against. Although the flu season of October to March peaks in January and February and wanes by May, the CDC evaluates strains and vaccine effects year-round. Effectiveness is measured by reductions in flu occurrences, symptoms, symptom severity, hospitalizations, and mortality. Even with reliable products and research advances, prevention rates typically reach only 50–60 percent each season, and vaccination reduces the need for medical care by 60 percent on average. Influenza is not always considered a serious preventable disease, but there is room for improvement in disease control, particularly for high-risk populations.

The 2009 H1N1 pandemic awakened the public to the severe risk potential of this commonplace disease. The numbers of vaccinated individuals of all ages increased dramatically in 2009, and 2010 CDC guidelines recommended vaccination in all individuals 6 months of age or older for the first time—a recommendation that remains in place today.

Ensuring adequate vaccine quantities became extremely relevant during and after the initial H1N1 outbreak, and product innovations moved quickly into research. Interest in bulk-quantity, cell-based technologies grew,
because the technique avoided tenuous egg culture methods. In 2010, the FDA provided guidance on developing vaccines in both mammalian and insect-based cell lines.

**Cell Culturing Advances**

In traditional flu vaccine development, strains selected in February are injected into available eggs and incubated, harvested, and purified—taking at least six months. Then, the growths are tested, combined into three-strain products, retested, and assigned lots. Finally, the quantities and quality control checks are enacted before distribution. Because of the time to development, flu vaccine production is truly a year-round, not just seasonal, event.

Cell cultures offer numerous benefits over egg mediums. Along with the obvious benefit of use in egg-allergic individuals, cell-culture products are not as limited in producible quantity or incubation timing. For emergency preparedness, cell cultures offer a fast start-up time and the potential to freeze incubated cells for later use in cases of egg-growth incubation failure or epidemic vaccine shortages. Such rapid production and stockpiling ability could revolutionize flu vaccine shortage risks across the United States.

In 2012 and 2013, the first flu vaccines developed without eggs were approved by the FDA. Both new products will supplement the traditional, egg-grown vaccines for the 2013-2014 season. Flucelvax (Novartis), approved in November 2012 for people ages 18 years and older, uses a process similar to egg growth that is based in mammalian cells. In clinical trials during 2007 and 2008, Flucelvax offered similar protection rates against the flu and similar adverse effects as traditional injections. Flublok, approved Jan. 16, 2013, relies on insect-growth recombinant technology. Like some vaccines for cervical cancer, Flublok uses viral proteins from modified insect mediums to trigger protection through antibody development. Flublok is approved for people ages 18 to 49 years who cannot receive egg-grown injection because of severe allergy. Flublok’s only downside so far is its short shelf life: The product is only viable for disease protection for 16 weeks after production. Therefore, pharmacists must check the product expiration date before administration in case its acceptable date has passed.

**Seasonal Vaccine Development**

Each year, ACIP closes a flu season in March; collects available disease, inoculation, and population data; and releases guidance for the coming season. For 2012–2013, vaccines coupled the 2009 H1N1-like A/California strain with two new strains: the 2011 H3N2-like A/Victoria strain and the 2010 Wisconsin-like (Yamagata lineage) B strain. Vaccine efficacy was as expected, at approximately 47 percent versus A strains and 67 percent against B, leading to 56 percent overall efficacy at reducing illness and doctor visits.

In February 2013, ACIP released their interim recommendations for 2013–2014 on vaccine schedules, strains, populations, and timing. In conjunction, the FDA released its list of approved influenza vaccine products, which includes live, attenuated influenza virus (LAIV) and inactivated influenza virus (IIV, previously trivalent inactivated virus or TIV) products. The new products available in 2013 incorporate research advances in the following ways.

- Inactivated influenza vaccines for injection include egg-based trivalent (IIV3s) and quadrivalent formulations (IIV4s), which are both acceptable for ages 6 months and older.
- LAIV nasal spray is now only available with quadrivalent coverage; it remains acceptable for patients age 2 to 49 years with no contraindications.
- Intradermal versions return for a second season to provide a low-volume, smaller-needle option for secondary, niche use in 18 to 64 year olds.
- A high-dose IIV injection is also available for a second season for patients ages 65 years and older. This year’s product will provide quadrivalent coverage in an extended attempt at protection.
- Two egg-free injected products that resulted from research momentum are approved for adults who have egg contraindications.

All approved products include the recommended strains selected Feb. 27, 2013. The 2009 H1N1-like A/
California; 2011 H3N2-like A/Victoria; and 2012 B/Massachusetts-like offer trivalent protection. Quadrivalent coverage, which will likely become increasingly common in future seasons, includes these strains and adds coverage for B/Brisbane-like (B/Victoria).

ACIP interim recommendations highlight the egg-grown, live product, cell-grown, and recombinant formulations but state no preference among them (Table 1).

### Age-Related Restrictions

Though the CDC recommendation of flu vaccinations for everyone 6 months or older seems all encompassing, implementation is challenging. Acute illness, allergy, respiratory disease, and more factors compromise product selection and administration.

#### YOUTH

Not all children have an optimal immune response to a single flu vaccination. Any children receiving their first flu vaccine, or a child with unknown vaccination history, should receive two doses, four weeks apart if they are 6 months to 8 years of age. Similarly, any child who has not received a vaccination with H1N1 protection (between 2009 and 2012) requires two doses that include H1N1 coverage. In all of these children, the first dose is an immune primer; only the second dose develops viral protection for the season. As of 2012, though, the American Academy of Pediatrics recommends that any child ages 6 months to 8 years who has received two doses of trivalent, H1N1-containing vaccine since July 2010 only requires one dose per season moving forward.

A CDC flow chart for providers is available at www.cdc.gov/vaccines/ed/imzupdate/downloads/doses-algorithm.pdf; the CDC also provides pediatric flu vaccine fact sheets about thimerosal and Guillain-Barre syndrome (GBS) on its free resources website (http://www.cdc.gov/flu/freeresources/indexhtm).

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**Table 1. Available Flu Vaccine Products for 2013–2014**

<table>
<thead>
<tr>
<th>Brand</th>
<th>Formulation</th>
<th>Administration</th>
<th>Contents</th>
<th>Restrictions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Afluria (CSL)</td>
<td>0.5-mL prefill</td>
<td>IM</td>
<td>0 Hg; trivalent</td>
<td>≥9 years old (yo)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>5-mL MDV</td>
<td>IM 0.5 mL</td>
<td>24.5 μg Hg/dose</td>
<td></td>
</tr>
<tr>
<td>Flumist (MedImmune)</td>
<td>0.2-mL prefill</td>
<td>Nasal syringe</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Intranasal</td>
<td>Quadrivalent LAIV, 0 Hg</td>
<td>Store 2–8 C; avoid in pregnancy, asthma, &lt;2 yo, &gt;49 yo</td>
</tr>
<tr>
<td>Fluarix (GSK)</td>
<td>0.5-mL prefill</td>
<td>IM</td>
<td>0 Hg; tri- or quadrivalent IV</td>
<td>≥3 yo</td>
</tr>
<tr>
<td>Fluvirin (Novartis)</td>
<td>0.5-mL prefill</td>
<td>IM</td>
<td>&lt;1 g Hg trivalent IV</td>
<td>≥4 yo</td>
</tr>
<tr>
<td></td>
<td>5-mL MDV</td>
<td>IM 0.5 mL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Flublock (PSCorp)</td>
<td>0.4-mL SDV</td>
<td>IM</td>
<td>Recombinant inactivated trivalent (RIV3)</td>
<td>18–49 yo</td>
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<tr>
<td>Flucelax (Novartis)</td>
<td>0.5-mL prefill</td>
<td>IM</td>
<td>IIIV trivalent</td>
<td>≥18 yo</td>
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<tr>
<td>Fluzone (sanofi-pasteur)</td>
<td>0.5-mL prefill SDV</td>
<td>IM</td>
<td>0 μg Hg</td>
<td>≥36 months</td>
</tr>
<tr>
<td></td>
<td>5-mL MDV</td>
<td>IM</td>
<td>IIIV trivalent; 25 μg Hg</td>
<td>≥6 months</td>
</tr>
<tr>
<td>Fluzone ID</td>
<td>0.1-mL ID</td>
<td>0 Hg; IIIV trivalent</td>
<td>Smaller need, concentrated antigen, 18–64 yo only</td>
<td></td>
</tr>
<tr>
<td>Fluzone HD</td>
<td>0.5-mL prefill</td>
<td>IM</td>
<td>0 Hg; 60 μg each antigen (180 mg total); IIIV trivalent</td>
<td>≥65 yo</td>
</tr>
</tbody>
</table>
ELDERLY

Elderly patients, defined as age 65 years or older, are at higher risk of hospitalization from flu symptoms, so they represent a particularly significant focus group for vaccination. Vaccine efficacy depends on multiple factors, including selection of the most appropriate strains, length, and voracity of the season, and strength of the patient’s own immune response. In the elderly, immune response is poor, so efforts to better protect them from disease development are essential.

Fluzone High-Dose (HD) IV was introduced for this population in 2012. Fluzone contains four times the amount of each antigen strain to build greater immune protection. In ongoing studies that compare Fluzone HD with traditional IVs, Fluzone led to higher antibody levels. Evaluation of whether higher antibody titers translate into lower hospitalization and mortality rates in this population is unclear. Full explanations of high-dose benefits will be available at 2015, when trials are complete.

In 2012–2013, trivalent IV and high-dose IV were significantly less effective for elderly patients, preventing only about 50 percent of flu-related physician visits overall. For unknown reasons, these patients responded particularly poorly to H3N2 A strain, with only 9 percent efficacy. The quadrivalent IV and high-dose IV injections available in 2013–2014 could minimize disease complications in elderly by expanding coverage.

PREGNANCY

Influenza protection is recommended for all pregnant women. The highest risks of hospitalization occur in the second and third trimesters. Because the flu season could span multiple trimesters of any pregnancy, an inactivated injection is encouraged as early as possible for protection throughout gestation. The LAIV nasal spray is contraindicated in pregnancy, but the inactivated injection is recommended and acceptable for pregnant or nursing women.

Adverse Events and Contraindications

Flu vaccines are generally mild and well tolerated. Injections are most often associated with one or two days of soreness, redness, or swelling at the administration site along with headache, fever, and nausea/vomiting. Nasal administration shares the latter risks and also may cause one to two days of wheezing, congestion, nasal drainage or myalgias, especially in children ages 5–6 years. In VAERS and trial data collections, no differences in adverse effects have been noted from unvaccinated populations at two weeks after injections. Gastric complaints with any product appear more common in children.

Serious adverse events are rare and include palpitations, high fever, and allergic reactions. Anaphylaxis occurs most often in patients with severe egg allergies. FluMist does cause high rates of wheezing in 6- to 35-month olds with asthma diagnoses, which are particularly significant in children ages 6 to 23 months (a contraindicated population).

Patient-centered concerns include flu development with LAIV, GBS, and febrile seizure risks. Knowledgeable pharmacist vaccinators can reassure patients and parents with simple vaccination facts: LAIV products cannot cause infection, because the virus is incapable of surviving in the heat of the body’s respiratory passageways, and no increased rates of GBS or febrile seizures are documented in general populations. GBS, a neurologic condition linked to immune response, has not been causally connected to any flu vaccination in more than 30 years; however, GBS appears to develop in susceptible individuals in response to immune system changes. In people with no history of or reason to suspect GBS risk, vaccination is considered safe and acceptable.

The association of flu vaccination with febrile seizures is cloudier. Australian studies in children younger than 3 years of age who received a particular formulation, Afluria, in 2010 identified greater seizure risks in children ages 6 to 8 months of age. Though not enough data are available to definitively state a connection, prudence suggests avoiding this product in the youngest ages.

General contraindications to any flu vaccine include acute moderate fevers, which can temper the protective immune response; severe egg allergy; history of GBS; and history of severe adverse events with flu vaccina-
tion. LAIV-specific contraindications include pregnancy, age over 50 years, HIV-positive status, chronic respiratory diseases, age 2 to 4 years with asthma symptoms or diagnosis within the past year; and age younger than 2 years because of increased wheezing rates. Patients with nasal congestion should avoid LAIV until congestion clears, or should receive an injectable form instead, because congestion impairs product absorption. Certain prefilled injectable formulations, notably the Fluzone products, should be used with caution in people with latex allergy, because the products contain natural latex in the syringe tips.

Despite the myriad formulations, restrictions, and covered strains, flu vaccination remains consistently effective, and implementation improves each season with active public health efforts. Inactivated products remain the standard, with application in a broad patient population, and advances like LAIV and high-dose or egg-free formulations continue to meet specialty needs.

PERTUSSIS AND MMR: STABILIZING PROTECTION AGAINST RE-EMERGING DISEASE

Although routine childhood vaccination schedules are typically the domain of pediatricians, pharmacists do have an opportunity to address some of the vaccine-preventable diseases in teens and adults both with information and with vaccine boosters. Preventable diseases currently experiencing especially high re-emergence rates are pertussis, measles, and mumps.

PERTUSSIS

Also known as whooping cough, pertussis is an insidious disease resulting from the gram-negative bacteria Bordetella pertussis. Infection starts with cold-like symptoms, which can be minimized with antibiotic treatment. Its identifying trait is a piercing whistle cough (heard interactively at http://www.cdc.gov/pertussis/pubs-tools/audio-video.html) that can last approximately six weeks and can be strong enough to fracture ribs. This distinctive symptom gives pertussis infection its common name, whooping cough.

The disease is highly contagious and quickly turns serious in young infants, who are at the greatest risk of hospitalization. Half of infected children younger than 12 months become hospitalized from the disease; of these, 20 percent develop subsequent pneumonia, and 1 percent of all hospitalized children die as a result. Mortality is most likely in children younger than 6 months and is usually secondary to pneumonia. Therefore, starting the routine vaccination series is recommended at the earliest possible age of 2 months.

Incidence

In the 1930s, more than 250,000 cases of whooping cough occurred in the United States each year. Thanks to standard use of childhood immunization schedules that included DTP, pertussis occurrences dropped to nearly zero across the country from the 1970 through the 1990s. Though the disease was not seen for at least a full generation, its presence is now growing again.

In 2012, twice as many cases of whooping cough were reported as in 2011, reaching epidemic numbers in pockets of 21 states across the country. The nearly 42,000 cases in 2012 comprised the largest outbreak of whooping cough since 1955, according to the CDC. Of the 18 deaths that resulted, most of them were children younger than 3 months of age. Newborns are best protected from outbreaks when their mothers and any adults in close contact become vaccinated.

Products Available for Prevention

Two products currently protect against pertussis: DTaP for childhood immunizations and Tdap for boosters. The DTaP vaccine combines a full dose of acellular pertussis (aP; capitalization indicates full strength) with full doses of diphtheria and tetanus toxoid (DT) vaccines. Tdap boosters for teenaged, adult, and elderly patients contain a full dose of tetanus toxoid (T) and half doses of diphtheria and acellular pertussis (dap).

As part of the routine vaccination schedule, children receive five DTaP injections by age 7 years, sequenced at 2, 4, 6, and 15–18 months, and 4–6 years. Tdap boosters, manufactured as Adacel by sanofi-pasteur and Boostrix by GlaxoSmithKline, are recommended at 11–12 years and for any older age.
as a single dose. The Tdap booster can be used even with a recent administration of Td (tetanus toxoid/diphtheria) or can replace a routine Td booster. Immunity develops within two weeks after Tdap injection and is recommended at least four weeks before international travel for full protection.

The most common adverse effects associated with Tdap boosters at age 11 years and in adults include fever, achiness, and diarrhea as well as injection-site reactions such as pain, redness, and swelling. Like flu vaccinations, patients with a history of febrile seizures or GBS should not receive Tdap boosters without physician evaluation and approval. Patients with severe latex allergy should also consult their PCP or allergist before receiving Tdap, because the vial lids contain dry rubber latex that could trigger an allergic reaction.

**Contributions to Re-Emergence**

Three factors have contributed to new whooping cough outbreaks: first, lower rates of immunization schedule opt-ins by parents that have reduced “herd immunity,” or group protection within communities; second, an updated, acellular vaccine formulation that conveys less protective longevity; and third, resistance of bacterial strains to the standard acellular vaccine.

As parents refuse vaccinations because of religious beliefs or adverse effect concerns, unprotected children experience avoidable and serious diseases. An unfortunate risk exists for neighboring children, especially those too young to receive the vaccine itself or whose medical conditions preclude their own vaccinations. This loss of herd immunity has led to pockets of whooping cough outbreaks that in the past were contained to fewer individuals.

Less well-known but equally challenging causes of increased pertussis infections in the United States relate to a change in the vaccine formulation and a change in the bacterial response. The originally developed pertussis vaccine, DTP, contained live, whole-cell pertussis bacteria. Although the vaccine eradicated whooping cough, its high risks and mortality rate led parents to refuse vaccinations. As a result, the acellular formulation was developed in 1981 to trigger immune protection through specific antigen, not whole-organism, recognition.

The downside to the acellular version has been clearly documented: the new DTaP protection is lower and less durable than the original immunization. The full DTaP series might only offer full protection to children for a few years after completion. Even more striking—immunity starts waning rapidly, within a year after administration, in teens and adults who receive single-dose boosters of Tdap.

A final threat to protection is bacterial resistance. The acellular organism in every formulation contains a particular antigen, pertactin, which is key to triggering a protective response. The mutated infectious strain lacks pertactin, so the immune system response is not clearly directed against it. In 2011 and 2012, for the first time in the United States, 12 cases of whooping cough in Philadelphia, from this mutated developed despite pertussis vaccination.

**ACIP Guidelines for 2013: Focus on Pregnancy**

The ACIP has been searching for optimal methods to address the rising pertussis rates in newborns since 2011, when it recommended that all unvaccinated pregnant women receive one Tdap booster to protect infants from pertussis at birth. However, this recommendation was poorly implemented, and vaccination rates remained low; only approximately 2.6 percent of needed women received the vaccine. Therefore, in October 2012, the ACIP Pertussis Vaccine Working Group released its expert opinion that all pregnant women, regardless of prior Tdap or DTaP vaccine history, should receive a booster during each pregnancy.

The rationale centers on the longevity of pertussis vaccine protection. Because Tdap-developed antibodies are short lived, every pregnancy presents a new pertussis risk. The maximum time to antibody response in the mother is two weeks, and passive immunoglobulin antibody transfer confers protection to the fetus only after 30 weeks’ gestation. Therefore, optimal vaccine timing is near the due date during the third trimester, between weeks 27 and 36 of gestation.
Postpartum maternal administration is still protective for the newborn, and the vaccine is safe in nursing individuals. Administration after birth, though, is decidedly less protective than fetal exposure. To document compliance with ACIP recommendations and to obtain real-world data about Tdap vaccinations during pregnancy, providers can report pregnancy Tdap administrations to the manufacturer of either product (sanofi-pasteur or GlaxoSmithKline Biologics).

Concerns about adverse effects from over-vaccination can be addressed by knowledgeable clinicians. In ACIP-reported data on vaccinations of closely timed pregnancies, low-grade fever was the most frequent side effect. In women who received multiple Tdap vaccines, the fever rate of 2.4 percent to 6.5 percent was no higher than in one-time receivers. The risk of adverse events overall did not appear higher than the risk of single vaccinations, even in the 2.5 percent of women who had fewer than 12 months between pregnancies. Because of its established safety record, Tdap, along with the inactivated flu vaccine, is one of the only two vaccines clearly recommended for pregnant women.

Cocooning
According to 2012 ACIP recommendations, all other adults surrounding the newborn in its first 12 months should “cocoon,” or provide herd immunity protection to the infant by receiving a Tdap booster. Pharmacists can encourage vaccination in this little-known but important protection group, especially if the adult has not previously received a Tdap booster.

Related Populations
Whooping cough can strike a person more than once and at any age. Recent pertussis outbreaks affected teenage populations who received acellular formulations and who contracted resistant strains of the bacteria. Children who receive their last series injection at age 6 years, for example, could develop a pertussis infection at age 10 years, because of waning immunity.

Likewise, people age 65 years or older have limited remaining vaccine protection against pertussis. Because they are at higher risk of respiratory complications from infections, and because they frequently inhabit group homes with greater rates of infectious disease transmission, ACIP recommends in 2013 that all people in this age bracket receive a Tdap booster.

Tdap protection is relevant to travelers of all ages, too, because pertussis exposure is more likely in developing countries with low immunization rates. A one-shot booster within two to four weeks before travel is valid to avoid contracting the disease during travel or re-entering the United States as a carrier.

MEASLES AND MUMPS
Rates of measles and mumps, also, are on the rise, with outbreaks documented in Virginia, Maryland, and Tennessee. Both diseases are still common internationally, with outbreaks in 2012 and 2013 in the United Kingdom, for example. Here and abroad, the option to avoid vaccination because of autism scares or other adverse effect concerns, particularly for parents who have not seen the effects of these diseases first hand, has led to re-emergence of these dangerous diseases.

High-risk populations remain those with chronic illnesses, those living in close quarters, and those traveling to countries with higher rates of endemic disease or unvaccinated populations. In particular, re-emergence concerns have resulted in changing recommendations for travel even to first-world countries. CDC and ACIP strongly recommend a two-dose MMR booster before travel to avoid contracting the disease or bringing it into the United States in all travelers older than 6 months of age.

MMR Vaccine Options and Administration Requirements
The MMR vaccine was first used in 1967. Current formulations, both containing live attenuated virus, include MMR against measles, mumps, and rubella, and MMRV against these and varicella. Both formulations are highly effective against measles and mumps threats: By 2005, vaccinations had reduced outbreaks by 99 percent in the United States. The standard 2-dose childhood MMR regimen prevents 78 percent of infections after on the first dose at age 12–15 months, and up to
95 percent of cases by ages 4–6 years at the second dose. Contraindications and adverse effects are well known. More than 80 percent of children experience no side effects, and the most common adverse effects are related to administration. Small numbers of children can develop fever greater than 103 degrees Fahrenheit approximately one week after vaccination, especially with MMRV; vaccinated adults may experience mild and brief joint swelling or pain. Because both formulations contain live virus, they are contraindicated in pregnant or nursing women and in immunocompromised individuals (such as HIV-positive patients with symptoms or low T cell counts). Patients with gelatin allergy also should not receive either vaccine without consulting a PCP or allergist.

After claims of MMR links to autism developed in the late 1990s, research to examine a causal relationship grew dramatically. Multiple studies have debunked the original research claims and identified no connections between live measles or mumps vaccinations and this genetic disease. The public now deserves fact-based reassurance to re-establish disease eradication in the United States and abroad. Pharmacists can routinely screen outpatients for measles and mumps risk and inform patients of vaccine safety for best care. Patient handouts, available from the IAC (http://www.immunize.org/handouts/measles-mmr-vaccines.asp) are successful at explaining the safety of formulations and the importance of the vaccine’s lifelong protection from serious measles and mumps consequences.

TRAVEL VACCINATIONS
An estimated 1.6 billion people will travel internationally by 2020. Pre-travel preparation balances a traveler’s schedule, age, health status, and destination country requirements. Vaccine selection, timing, and counseling add complexity. Unfortunately, travel immunization rates are surprisingly low because of poor patient awareness about the need for protection, even to countries with traditionally strict health regulations.

This opens the door to community and specialty clinic sites for travel vaccinations. Overall, health care providers have low knowledge and training experiences. Pharmacist-run travel clinics (PTCs) serve to fill an important need for knowledge and action in patients. Though infrequently described in the literature, one 2011 comparison of PTC pharmacists with general physician care. Durham et al’s “A Comparison of Pharmacist Travel-Health Specialists’ versus Primary Care Providers’ Recommendations for Travel-Related Medications, Vaccinations, and Patient Compliance in a College Health Setting” demonstrates the useful role of pharmacists in travel protection. Although no statistical differences were present, the trained pharmacists provided evidence-based care more consistently than primary care physicians, and pharmacists took more opportunities to discuss travel settings with the patients to avoid missed vaccination opportunities. Pharmacists were more likely to vaccinate against typhoid for Southeast Asian travel and to prescribe antibiotics or antimalarial agents for post-exposure use, in accordance with evidence-based guidelines.

PTCs are popular resources for the public because they are more accessible and timely than physician office visits. Travel vaccinations within the PTC can become an entirely separate specialty for pharmacists, just as they are for some physicians. The subfield extends beyond just re-emerging diseases like measles into location-specific diseases rarely found as primary infections in the United States.

Pharmacists who want to start a travel clinic have some new options for training purposes. Along with post-doctoral residencies, several organizations offer training videos, continuing education activities, and certificate programs. The CDC travel vaccination CE program, newly developed in 2011, is free and complements existing immunization courses.

Vaccine Recommendations Introduced
The CDC Yellow Book on Travel Health is the ultimate preventive care guidebook for professionals. Available online as a comprehensive, searchable textbook, it describes up-to-date details about diseases prevalent in specific countries and about the selection, timing, and administration methods for thorough travel vaccination.
For frequent travelers, WHO and CDC suggest that U.S. travelers stay up to date on Tdap and MMR boosters for any foreign travel and protect against polio, malaria, meningitis, and hepatitis diseases for select locales. Vaccination four to six weeks before travel is usually sufficient to develop full immunity, but any time before travel is better than not at all. The CDC provides a travel checklist of vaccination choices by timing, location, and patient ages at http://cdc.gov/travel/destinations/list.

Only two travel vaccines are required by international regulatory agencies for country entry. Yellow fever vaccination is required for travelers to tropical countries with endemic disease, and meningococcal vaccination is required for travel within the African meningitis belt and to Saudi Arabia for Hajj pilgrimages.

**YELLOW FEVER**

**Description and Incidence**

Yellow fever is caused by flavivirus, which is endemic to tropical locations in Africa and South America. The virus transmits through multiple vectors, including the *Aedes aegypti* mosquito in urban areas; monkey and multiple mosquito carriers are common in jungle transmission, which occurs most often in South America.

The disease results in hemorrhagic fever and can be difficult to distinguish from other African diseases; in its early stages, though, yellow fever is deceptive and initially asymptomatic. The virus enters the blood immediately and spreads rapidly to lymph nodes and viscera, with a three- to six-day incubation period. After the disease takes hold, flu-like symptoms of acute fever, chill, headache, myalgias, and nausea/vomiting are common. Symptoms then improve over hours to days, but the virus and the risk of visceral complications remain. Approximately 15 percent of infected individuals develop a secondary toxic presentation of jaundice, hemorrhagic shock, and multi-organ system failure. Fatality rates are as high as 50 percent in people who experience renal or hepatic dysfunction.

As of 2003 data, approximately 200,000 cases have been documented annually, with 30,000 deaths. Approximately 90 percent of cases occurred in African cities or jungle areas. There is no antiviral medication to counter infection, so treatment involves only symptom management.

**Endemic Areas**

Countries in South America with frequent yellow fever outbreaks include tropical regions such as Ecuador, Panama, or Trinidad and Tobago, as well as Bolivia, Argentina, Peru, Colombia, Venezuela, and more. Costa Rica and Malaysia report high endemic disease rates as well. South American outbreaks are most common during the rainy season from January to May, and urban epidemics are especially common in February and March.

Yellow fever occurs seasonally in Africa, too, and is especially prevalent at the end of the rainy season and start of the dry season, which runs from July to October. Even during the dry season, urban epidemics can develop in especially crowded locations. The sub-Saharan yellow fever risk zone in Africa ranges from 15 degrees north to 15 degrees south of the equator.

Yellow fever, because it is borne primarily by mosquitoes concentrated in equatorial areas and because of its latent period, is transmitted quite easily from infected individuals. Disease containment relies on mosquito netting as a primary means of preventing infectious spread. Lowered indigenous rates, from previous highs in the 1980s, have resulted from local vaccination program efforts. Rates are instead rising in travelers, who must do their part to reduce transmission across countries by receiving primary and booster yellow fever vaccinations when necessary and by maintaining mosquito bite precautions.

**Regulations**

International health regulation agencies oversee the stringent proof of vaccination requirements for travel among countries with endemic yellow fever. Such travel requires an International Certificate of Vaccination or Prophylaxis (ICVP); consequences of traveling without one include quarantine/isolation or total bans from entry. Prohibitions vary by country. For example, Costa Rica, Malaysia, and other high-risk countries require a completed ICVP even to
disembark within an airport for layover flights. Saudi Arabia requires anyone entering from a country with known yellow fever infections to show proof of vaccination with an ICVP, also.

Only certified clinics in private or community practice may order and administer the yellow fever vaccine and provide travelers with an ICVP. U.S. yellow fever vaccine providers are approved by state health departments to meet WHO standards. Once evaluated, these clinics are listed on an interactive CDC registry of official providers at http://cdc.gov/travel/yellow-fever-vaccination-clinics/search.

After vaccination, the completed ICVP is signed and stamped. It is valid 10 days after injection for up to 10 years. ICVP blanks can be ordered by providers from the WHO online bookstore or from 866-512-1800. The most recently updated form was released Dec. 15, 2007.

The ICVP has a section for waivers of medical necessity, which may completed by a certified provider or PCP. Medical necessity arises from contraindications to yellow fever vaccine and are discussed below. Waivers should be accompanied by provider communication on official letterhead, though neither document guarantees entry. Upon arrival to a high-risk country, travelers with waivers may be refused entry or may undergo a six-day quarantine upon country entry or departure.

**Dynamic Country Travel Requirements**
The list of countries requiring proof of vaccination is dynamic and is based primarily on outbreaks and secondarily on a country’s mosquito concentrations. Select countries, including French Guiana, Sierra Leone, and Cote d’Ivoire have an ongoing disease threat and always require an ICVP from travelers for entry. Epidemics are monitored by International Health Regulation authorities, and WHO provides the most current list of protected countries for providers and travelers through its international travel and health book. Countries in Latin America with the greatest risks are Bolivia, Brazil, Colombia, Ecuador, and Peru. The 2012 Yellow Book provides a printable map of yellow fever risk in the American countries at http://wwwnc.cdc.gov/travel/pdf/yellowbook-2012-map3-19-yellow-fever-vaccine-recommendations-americas-2010.pdf.

To optimize yellow fever protection and supplement its list, WHO and the CDC developed detailed, real-time categories of risk and vaccination needs for travelers in Chapter 3 of the updated Yellow Book. Countries are specified as endemic (always requiring a shot for entry), transitional (currently requiring a shot), low exposure potential (vaccine considered reasonable especially for high-risk travelers), and no-risk countries or areas (shot not required and only recommended in highest risk patients). True evaluation of disease risk involves the traveler’s perspective, too. High-risk travelers include those who have lengthy travel plans, multiple countries, or heavy mosquito presence/exposure likelihood.

**Product**
The only formulation made is yellow fever 17D, which refers to the product’s viral strain; it has a 60-year history of use. It is a live attenuated virus and is the primary vaccination method for 9- to 12-month-old children in endemic-risk countries. The vaccine comes as a 0.5-mL subcutaneous (SQ) injection (although intramuscular use does not invalidate its effect) that must first be reconstituted. Lyophylized powder in single-dose vials must be kept refrigerated at 2–8 degrees (Celsius), and the non-medicated diluent may be kept with the powder or at room temperature. Multi-dose powder vials should be kept at 2–8 degrees C as well. Both products should be used within one hour of reconstitution.

Yellow fever vaccine is approved for all equatorial travelers aged 9 months and older unless they have an explicit contraindication. Vaccination causes antibody development in 90 percent of people within 10 days after injection, and in 99 percent of people by 30 days. The vaccine is so effective that it confers up to 35 years of protection against the disease. However, the 10-year ICVP requirement provides extra safety measures, and booster requirements as of May 2013 remain stringent despite the product’s confirmed longevity of effect.

**Pregnancy**
YFV is a live-virus vaccine, which is traditionally contraindicated in pregnant women. However, it may be
administered to women who are pregnant, because risks of the disease generally outweigh the risks of vaccination. Little data support concerns during any stage of pregnancy or nursing, but avoiding conception for four weeks after injection is recommended. The vaccine has a strong history of success and safety in multiple populations since the 1960s.

Adverse Effects and Contraindications
Mild adverse effects occur in approximately 10–30 percent of people, most often within five to 10 days after injection. These include headache, myalgias, weakness, and low fever as well as local reactions such as rash, redness, and pain, which are especially common with the initial injection rather than with repeated boosters. Fever risk is greatest in young infants.

Serious adverse events are rare but include immediate anaphylaxis, neurotropic disease (YEL-AND), and viscerotropic disease (YEL-VAS). Anaphylaxis is mostly isolated to people allergic to egg or gelatin. Neurotropic disease is reversible, with one documented fatality in an HIV-positive patient. Viscerotropic disease is an atypical host response to the live attenuated virus.

Neurotropic adverse effects from the vaccine appear most common in extremely young children, guiding approved age ranges for injections. Patients up to 6 months old have potentially higher rates of neurologic disease. Patients between 6 to 8 months old and over 60 also appear at a slight increased risk of serious but rare adverse effects, according to VAERS reporting data. Thus, children ages 6-8 months or adults over 60 are discouraged from receiving the vaccine (caution recommended) unless an epidemic is ongoing, and the vaccination requirement for infants 6 months and younger is always waived.

Egg and chicken protein allergies, as well as gelatin allergies, are strict contraindications to vaccination, and an allergy risk for latex also is present because the vial stoppers contain dry latex. All patients, especially those with unknown allergies, should be observed for 15 minutes after injection of the vaccine to screen for anaphylaxis, and epinephrine for intramuscular injection must be kept on hand. Anaphylaxis rates are low, approximately two per 100,000 injections.

Patients with immunodeficiencies such as thymus dysfunction, neoplasms, transplantations, or use of immunosuppressive agents cannot receive the yellow fever vaccine. However, patients with HIV who are asymptomatic or whose T cell counts remain high (approximately 200–499) can receive the vaccine with caution. Patients with contraindications in this paragraph and previously mentioned should obtain an ICVP waiver in lieu of the yellow fever vaccination.

Extra Considerations
Because the product has live virus, vaccinated individuals should not donate blood for two weeks after injection to avoid risk of disease transmission. Vaccine administration should be simultaneous with other live travel vaccines or should be separated by at least 30 days to avoid immune inhibition of the second live-vaccine response. Administration of yellow fever vaccine with inactivated products, such as flu, measles, hepatitis, or meningococcal vaccines, is considered safe.

MENINGOCOCCAL VACCINE
The second required, not just recommended, travel vaccine covers meningococcal diseases. Like yellow fever, meningococcal disease is easily transmitted; however, anyone can stock and provide meningococcal vaccines. Disease rates are low across the United States, and the goal of vaccination is containment.

Disease overview
Bacterial disease stems from Neisseria meningitidis and can develop viscerally or neurologically. The invasive infection presents in the lungs as pneumonia, in the blood as sepsis, or in the brain as meningitis. Regardless of presentation, it is carried in the nasal mucosa and transmitted by respiratory passage secretions.

Bacteria are differentiated into six serotypes—A, B, C, X, W135, and Y—which can be location or epidemic specific. In the United States, serotypes C, Y, and W account for 73 percent of all infections in patients 11 years or older, though B serotype is also common. Serotype A is most common in the African
meningitis belt, but emerging serotype W135 is becoming a larger threat.

The disease is fatal if untreated. Even with proper antibiotic care, mortality is 10 percent (even as recently as 2003). Greater numbers experience permanent damage from the infectious process, because pretreatment symptoms may be irreversible.

**Risk populations**

Risk is higher in crowded living accommodations, in the presence of viral infections, in people with chronic illnesses, and in people exposed first or second hand to smoke. Rapid outbreaks are most likely to occur in concentrated groups of children or teenagers. Vaccinations in youth, college freshmen, and elderly in group homes minimize morbidity and mortality.

Two additional risk settings require protection internationally: countries with endemic disease, or high annual rates of 2–10 (moderate risk) or greater than 10 (high risk) per 100,000 people; and countries with low endemic rates but frequent epidemics both require protection within the country and for international travelers.

In the Sub-Saharan African meningitis belt that spans Ethiopia to Senegal, the highest risk is during the dry season of December to June. Active outbreaks there are documented in real time by the CDC, and travelers can be notified online or at 877-FYI-TRIP. Meningococcal vaccines are recommended but not required for meningitis belt travel. Conversely, the vaccine is required for travelers who visit Saudi Arabia for Hajj pilgrimages. The vaccine must have been administered within three years of travel date.

**Products**

Formulations of meningococcal vaccine include variations of coverage against serotypes A, C, W, and Y; serotype B is not covered by products available in the United States. Of the four vaccines available in the United States, three are conjugated to proteins for improved immune system recognition and memory. Conjugation maintains long-term protection after childhood series and after boosters for older populations. Each formulation has its own unique dosages, age groups, and administration concerns.

The oldest product, Menomune (sanofi-pasteur), is an unconjugated polysaccharide quadrivalent (MPSV4) product for patients two years and older. It is administered as a 0.5-mL SQ injection. MPSV4 is the preferred vaccine in patients age 56 years or older, and it can be repeated every five years in this population for continued disease risk. No adverse effects are noted in pregnant women who received MPSV4 and it is pregnancy category C, but CDC lists it in guidelines for pregnant women when meningococcal vaccination for travel is indicated; the product can be used safely in adults who are immunocompromised as a single-dose booster.

Menactra (MenACWY, by sanofi-pasteur) was approved in 2005 and was a big advance in prevention options. The meningococcal conjugate vaccine quadrivalent (MCV4) product contains 4 mg of each serotype conjugated to 48 mg of diphtheria toxoid. One 0.5-mL intramuscular dose is recommended in most 2 to 55 year olds, but a two-dose series two months apart provides the best protection for 9 to 23 month olds as part of routine childhood immunizations. There are no clear data on pregnancy risk with MenACWY so far, but CDC lists it in guidelines for pregnant women when routine meningococcal vaccination is indicated. Menactra is pregnancy category C. Patients with a history of GBS or with latex allergy should not receive Menactra.

In 2010, Menveo (MenACWY-cRM, by Novartis) was approved as a quadrivalent conjugate with Corynebacterium diphtheria (33–64 mg). The product contains 10 mg of live serotype A and 5 mg of the other serotypes in a 0.5-mL intramuscular dose for 2 to 55 year olds. Although it provides quadrivalent coverage, Menveo has the highest administration error rate because of its unusual admixture requirements. The liquid diluent contains CWY protection that is combined with the powdered A serotype. Administration of only the liquid product accounts for a 15.5 percent error rate. Menveo is pregnancy category B.

MenHibrix (Hib-MenCY/TT, by GlaxoSmithKline), which covers N. meningitidis serotypes C and Y and...
Haemophilus influenzae was approved in 2012. The product is available as a powder with saline non-medicated diluents. In a single 0.5-mL intramuscular dose, there are 5 mg C and Y each, 5 to 6.25 mg tetanus toxoid, and 2.5 mg Hib. The recommended dosage is a four-injection series for ages 6 weeks to 18 months; and it could become incorporated into future childhood immunization schedules, with MCV4 products providing extended-serotype booster coverage. MenHibrix is pregnancy category C.

**Vaccine Administration**

ACIP recommendations of 2005 were updated in 2013 to incorporate the latest vaccine formulations and serotypes and to recommend booster updates on the basis of age, health history, and travel.

In addition to the childhood series, anyone who has not received meningococcal protection within the past five years should receive an MCV4 booster product (such as Menactra or Menveo) before traveling; children age 9 months or older on routine schedules that use MenHibrix who have not received A/W protection need a booster eight weeks after their routine shot to be cleared for travel.

Either quadrivalent conjugated vaccine (MCV4) is recommended for ongoing protection in children older than 10 years, especially during the highest-risk age range of 16 to 21 years, and in traveling adults up to age 55 years. Similarly, adults with an immunocompromised condition such as asplenia require regular MCV4 boosters, and any immunocompromised individual (such as with asplenia, thymus disorder, or HIV infection) should receive two booster doses spaced two months apart for best efficacy. Individuals 56 or older who require regular boosters (such as for group living) should receive quadrivalent polysaccharide vaccine (MPSV4). Expert suggestions for multiple meningococcal vaccination scenarios are provided by the IAC at http://www.immunize.org/askexperts/experts_men.asp.

**Adverse Effects and Contraindications**

Adverse effects vary with the products but primarily comprise fever, headache, redness at the injection site, dizziness, and nausea/vomiting. People with allergy to components and with severe acute illnesses should not receive a meningococcal vaccine. Some precaution is warranted for individuals with a history of GBS; although no statistical association of the syndrome with meningococcal vaccines in healthy patients is documented, GBS risk might be higher in patients with prior symptoms, especially with Menactra.

**STORAGE AND DOCUMENTATION CONSIDERATIONS**

Vaccines are unlike traditional classes of drugs. Not only do they have specialized administration techniques, but they also have especially high costs and storage standards. U.S. federal regulations and oversight have resulted in the safety and most effective vaccination outreach in our history, but there is still room to improve in the management of these fragile therapeutic agents.

Providers contribute to best standards and practices with their expertise on screening, administration, and education. These actions comprise proper storage, admixture procedures, vaccination timing, screening patients for contraindications before and adverse events after administration, documentation of lot numbers, provider communications, and

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**Resources for Best Immunization Practices**

- Call the shots: CDC vaccination, regularly updated and expanding annually at http://www.cdc.gov/vaccines/ed/youcalltheshots.htm
- CDC travel training specifically for yellow fever vaccine providers at http://www.cdc.gov/travel-training/
- Immunization Action Coalition: VIS printables for patients at http://www.immunize.org/vis/ and printable clinic resources at http://www.immunize.org/handouts/ (including administration posters for professionals, clinic needs checklists, adult vaccination summaries, and more)
- CDC Vaccine Storage and Handling Toolkit 2012: Thorough action procedures for community sites at http://www.cdc.gov/vaccines/recs/storage/toolkit/storage-handling-toolkit.pdf
patient education. The CDC supports these efforts with multiple tools, such as their vaccine scheduler, VACScheduler.org for organizing staggered or simultaneous administrations.

Importance of the Cold Chain
Vaccine storage is one of the most crucial behind-the-scene aspects of effective preventive care. The cold chain, in which vaccines are maintained at refrigerated states from manufacturer to administrator, is essential to prevent product loss and maintain effectiveness. Most vaccines, whether inactivated or live, require continual storage. Temperature drift, or temperature excursion, occurs when storage conditions stray outside of the recommended range (often 2–8 degrees C) and the cold chain is broken. This drift is costly in time, money, and health, because it results in ineffective and unusable vaccine. Product loss has consequences to providers and patients: revaccination, the typical recommendation after ineffective administration, concerns patients, and cost of the lost product and of the replacements impacts distributors and providers.

Maintaining the cold chain involves avoiding excessive heating or freezing, which depends on trained staff, standard transportation and storage measures, and efficient management procedures. Temperature maintenance within the 2–8 degrees C “normal” range is required constantly for potency and efficacy of vaccine products; 14 percent to 35 percent of vaccines worldwide are accidentally frozen, and therefore lost to use. Every link is vital: manufacturer, distributor, provider facility, transport, facility storage, and administrator.

Vaccine Safety Gaps
The cold chain is compromised by power outages, national disasters, staff error, and poor training. Like other aspects of vaccination care, cold chain procedures should be implemented according to CDC principles. The CDC Pink Book Appendix C instructs vaccinators on the how, when, and what of immunization storage protocols. The twelfth edition was released online in May 2012.

In October 2012, the CDC went further and revised the Storage Recommendations for all immunizing practices with interim guidance recommendations (not requirements) that took effect in January 2013. With data gathered from its Vaccines for Children grant program, the CDC commissioned the National Institute of Standards and Technology (NIST) to evaluate real-world vaccine storage and administration practices. NIST found that temperature maintenance was inadequate in practice, despite knowledge of refrigeration needs. Storage difficulties and improper temperature practices led to lower potency, increased revaccination rates, and waste at multiple sites.

Similarly, separate Institute for Safe Medication Practice reports described errors associated with poor vaccine storage, incorrect vaccine formulation selection and inadequate stock (such as Tdap only instead of Tdap and DTap availability). However, the errors occurred most often with diluent-powder products. Diluents are infrequently stored with their powders in the original combination packaging, so awareness of the need for both items before administration is low. These concerns were the impetus to improve storage and documentation standards across the board.

Guided Improvements: Five Main Points
The goals of the CDC interim guidance are to reduce the identified storage-related errors for best clinical care. Visual changes to the vaccine product might not occur to reflect a break in the cold chain, so following guidance for storage and documentation are the best ways to ensure temperature maintenance. The following five practices are supported by NIST as improving cold chain retention and reducing waste.

1. Biosafe glycol digital thermometer probes: Temperature-buffered units like these avoid recording ambient temperatures and instead accurately reflect the state of liquids stored inside a cooling system. In ideal settings, thermometers should be visible without opening the doors of the system, too, to avoid temperature drifts.

2. Calibrated digital data loggers to record temperatures constantly. Digital memory units that hold 4,000
readings are sufficient to monitor cooling units for temperature breaches regardless of personnel on hand. Optimal recorders are visible on the outside of units, can be detachable to download data, and have an alarm to signal temperature drift outside of present ranges. Recordkeeping goals include manually logging the temperature data at least once daily at a consistent time to maintain staff awareness, downloading the data once weekly for computerized tracking, and retaining computer files for three years.

3. Cooling units reserved only for temperature-sensitive biologics. Eliminating multipurpose refrigeration isolates vaccines for more spacious storage and labeling, and it helps maintain temperature consistency by avoiding overcrowded conditions. Full-size refrigerator units with 24-hour digital temperature recording are suggested as optimal, and the CDC offers a buying guide with varying size and cost levels for vaccinators able to fully comply.

4. No combination storage unit: Combination units maintain refrigerated temperatures with freezer water coolants, which do not provide consistent temperatures. In 2009, NIST documented potency changes that occurred primarily from inadvertent freezing by combination unit cooling processes, including dorm-or bar-style combination refrigerator units. Stand-alone refrigerators are essential for proper cold chain vaccine care. This recommendation becomes more of a directive for grant participants, who are required to have stand-alone, non-combination, full-size cooling systems.

5. Weekly expiration date evaluations and stock rotation. In addition to daily visual temperature checks, weekly review of actual products minimizes waste from expired forgotten stock. Weekly visual review and rotation also ensure appropriate labeling and storage space for refrigerated or frozen vaccines.

A vaccine coordinator can maintain consistency in these and all vaccine-handling procedures, designate staff to record daily temperatures, and take charge of stock rotation and expired/wasted vaccine storage. The coordinator also implements protocols for vaccine safety and admixture, and he or she develops and reviews an emergency plan to save vaccines when storage is unavailable.

**Emergency Procedure Action Plans**

Emergency vaccine retrieval and storage plans are essential preparation for a breakdown of the cold chain. Emergency planning answers the question: How do you avoid product loss when temperature-regulating systems fail?

Recommendations from manufacturers and state health departments to preserve vaccines in the event of power outages include storing bottles of water in strategic locations within the refrigerator that prevent rapid warming inside unit. If fewer than two hours will pass without cold storage, it is okay to use a cooler and "conditioned" ice packs (partially thawed to prevent freezing refrigerated product). For longer durations, contacts and off-site storage locales must be in place, and managers should verify these accesses quarterly. The CDC, in its November 2012 online storage toolkit, details these measures but also encourages reliance on manufacturer prescribing information (PI) data for the most current storage safety data. Current PIs are available from manufacturers, through the FDA Web site, or courtesy of the IAC at http://www.immunize.org/packageinserts/.

Multiple responsible parties are needed to get vaccines to the community in any scenario. Training must include all personnel at every step of vaccine care, from ordering to stocking, and from mixing to administration and counseling. Vaccine protocols to cover stock ordering, placement, disposals, and emergencies should be reviewed at least once annually by the entire vaccination team.

**Addressing Practical Concerns**

The CDC acknowledges that its guidance is not required, in part because the costs to implement changes are admittedly steep, and community-based locations have limited space and staff available for storage and management concerns. Instead, guidance encourages vaccine providers to aim for as many of these optimal goals as possible to maintain the cold chain. Community vaccination sites
are considered the weakest link in the cold chain by some distributors. Implementing even low-cost efforts can better optimize storage and boost distributor confidence.

Storage labels are an easy way to enhance safety and avoid errors, even in less-than-ideal storage settings. Bin labels and locations should be clear for any staff who prepare, label, mix, or administer vaccines. Compromised products should be isolated in a bin labeled “DO NOT USE.” Another important and easy label technique uses posted reminders on diluent bins so the liquids are not given without their lyophilized powder. Similar recommendations include color codes that differentiate formulations and tags that clearly list approved age ranges or contraindications. Downloadable examples recommended by the ACIP (http://www.cdc.gov/vaccines/recs/storage/guide/vaccine-storage-labels.pdf) include “LAIV: DO NOT INJECT” and MCV4 brand-name indicated populations.

Additional vaccine-specific information is available at http://immunize.org. Vaccine information sheets (ViSs) required with each immunization are printable to share with consumers. For health professional use, IAC provides printable tables on storage requirements and how-to- posters for adult vaccination techniques, which are especially useful for occasional vaccinators in a community setting.

EXPANDING THE PHARMACIST’S ROLE
Community vaccination is a public health service that expands the pharmacist role as caregiver. In many settings, flu vaccines have become ubiquitously associated with the local pharmacy. Like other specialty provisions, though, challenges of optimal health professional interactions and reimbursements remain for pharmacy vaccination clinics. Providing adult vaccinations in the community requires the pharmacist to shoulder a burden for patient care, proper storage, legal and ethical documentation, provider communications, adverse event follow-up and reporting, and more.

The installation of a pharmacy vaccine manager can streamline the ordering, storage, and administration procedures; ensure preparation for emergency occurrences; and ease the vaccination clinic’s burdens. The established CDC and ISTM education programs for vaccinators are expanding rapidly to cover immunization topics relevant to community pharmacists. Vaccine formulations and availabilities change frequently. Pharmacists who administer and counsel on immunizations can improve patient safety and effectively prevent disease by keeping current on the marketed products and guidelines for vaccine use.

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Editor’s Note: For the list of references used in this article, please contact America’s Pharmacist Managing Editor Chris Linville at 703-838-2680, or at chris.linville@ncpanet.org.
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A score of 70 percent is required to successfully complete the CE quiz. If a passing score is not achieved, one free reexamination is permitted.

Answer sheet for your use below

1. a b c d e
2. a b c d e
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15. a b c d e
16. a b c d e
17. a b c d e
18. a b c d e
19. a b c d e
20. a b c d e

CONTINUING EDUCATION QUIZ
Select the correct answer.

1. As a highly regulated industry, vaccines
   a. Are approved by the ACIP each year after formulations are manufactured.
   b. Are carefully regulated by the CDC with respect to target patient populations and provider resources.
   c. Require monitoring of all administration logs by the Immunization Action Coalition.
   d. Can be recalled by the CDC if formulations do not meet quality standards.

2. In the most successful years at disease prevention, flu vaccinations
   a. Reach average prevention rates of 85 percent
   b. Achieve better rates at reducing need for medical care than at full disease prevention
   c. Only prevent just over half of expected flu occurrences.
   d. Have attacked at least four different viral strains.

3. Your pharmacy is stocking Flucelvax for its first season of use. Which of the following patients in your clinic should receive it?
   a. 18-year-old with history of GBS
   b. Healthy 19-year-old with unknown history of flu vaccination
   c. 24-year-old with mild egg allergy and history of successful injectable influenza vaccination
   d. 60-year-old with history of egg allergy with undocumented allergic response

4. If your pharmacy runs out of Flucelvax stock, can this patient receive Flublok instead?
   a. Yes, because recombinant Flublok is safe for patients with egg allergy.
   b. No, because Flublok is associated with higher rates of GBS.
   c. Yes, because Flublok remains stable longer than Flucelvax.
   d. No, because Flublok is only indicated in patients up to age 49 years.
5. Fluzone ID (intradermal) is indicated especially for which population?
a. Smaller-needle ID administration is not indicated as a primary vaccine for any population
b. ID is recommended for elderly patients as a post—high-dose booster
c. Infants with low muscle mass should receive Fluzone ID instead of traditional IM administration
d. ID is specifically for patients ages 18 to 64 years who have a history of myalgias with traditional inactivated (such as IIv) injectable flu vaccines

6. In your seasonal flu clinic, a mother brings in her 7-year-old for a flu vaccine and requests the nasal spray if possible. The child has a history of wheezing with colds (most recently two months ago), and the parent does not remember when her child’s last flu vaccination was. Which product and regimen is most appropriate?
a. Live attenuated FluMist nasal spray is best, because the parent requested it for her age-appropriate child and it will avoid unnecessary pain
b. A single quadrivalent injection with H1N1 coverage is sufficient, because the child has likely received H1N1 protection at some time in her vaccination history.
c. Two trivalent traditional intramuscular injections are required four weeks apart—the first as a primer and the second to develop immunity—because her protection against H1N1 strains since 2010 is unknown.
d. Two quadrivalent intramuscular injections are required two weeks apart to prime and protect the child, because quadrivalents offer the best protection in children for the 2013-2014 season.

7. FluMist use in children is guided by which of the following?
a. Egg allergy, because people with mild egg reactions can receive an LAIV product
b. Predisposition to fever, because live virus can be potentially infectious in the respiratory passages
c. Seasonal allergies, because nasal congestion permanently reduces nasally administered vaccine efficacy
d. Asthma diagnosis or recent wheezing history, especially in risk-group ages under 2 years and under 35 months

8. Pertussis vaccination options for children include
a. One Tdap booster in anyone older than 11 years, given 4 weeks before travel
b. Tdap as a two-dose booster at 11 years
c. Tdap directly after DTaP for immediate protection before travel
d. DTaP as a single booster at 11 years

9. Educated arguments against parent concerns about DTaP and Tdap product safety should focus on what facts?
a. A Tdap booster at 11 years is sufficient protection into adulthood, just like the discontinued DTP vaccine.
b. Acellular pertussis cannot trigger disease and mortality like that associated with DTP use.
c. Vaccinations are highly effective against resistant bacteria.
d. Fewer outbreaks occur when herd immunity is ignored.

10. As a counseling measure, best newborn protection against pertussis can be rated, best to worst, as follows:
a. 1st trimester > 2nd trimester > 3rd trimester > postpartum maternal administration
b. 3rd trimester > nursing maternal administration > infant series within first year
c. 3rd trimester > postpartum maternal vaccination > maternal vaccination within infant’s first year > after nursing is complete (but before childhood series begins)
d. Any trimester during the first pregnancy only
11. In your travel vaccination clinic, MMR products
   a. Are stored with MMRV in combination bins so that the
      products are used interchangeably in adults.
   b. Are stored in the refrigerator because it contains live virus
   c. Commonly require epinephrine and VAERS forms for
      anaphylactic reactions.
   d. Are contraindicated with latex allergies.

12. Yellow fever mosquito transmission
   b. Affects Africa throughout the rainy season.
   c. Occurs only in jungle travel expeditions.
   d. Impacts South American travelers in a dynamic way.

13. A pregnant traveler should receive
   a. MPSV4 and a yellow fever vaccine
   b. MPSV4 and a yellow fever prophylaxis waiver
   c. MenHibrix vaccine and yellow fever vaccine
   d. MenHibrix vaccine and yellow fever prophylaxis waiver

14. Which allergies, when severe, require ICVP waivers in
    lieu of yellow fever vaccination?
   a. Gelatin
   b. Latex
   c. Egg
   d. All of the above

15. A teenager is referred to your pharmacy from her PCP
    for MCV4 booster protection before the start of her freshman
    college year. What questions should be included in
    your screening session?
   a. History of childhood vaccination for pneumococcal
      diseases
   b. History of seizure disorders to eliminate GBS risk
   c. Living arrangements and course load to evaluate
      crowd exposure
   d. None of the above

16. Which of the following is the preferred booster product
    for meningococcal protection in teenagers and
    healthy adults up to age 55 years?
   a. MPSV4
   b. MenHibrix
   c. Either MCV4 product
   d. Menveo only

17. The immunization action coalition (IAC) provides the following resources for vaccination
    professionals:
   a. Manufacturer-marketed patient information
   b. CDC-approved drug information package inserts
   c. Federally required storage temperature charts
   d. Federally required vaccine information sheets (VISs)

18. In your pharmacy, vaccines are stored in a
    combination refrigerator/freezer with insulin and
    other temperature-sensitive agents. Which risks
    are associated with this storage method?
   a. Temperature drift resulting from freezer coolant system
   b. Inadvertent administration error among similar products, such as MCV4 and MPSV4
   c. Neither of the above
   d. Both A and B

19. What best storage practices could avoid
    these risks?
   a. Diluents stored separately from the lyophilized powder to avoid overcrowding
   b. Well-labeled, separate bins for similar products within the refrigerator
   c. A defroster to avoid product freezing, one of the most frequent causes of vaccine waste
   d. Both A and B

20. Emergency storage plans implemented by a vaccine manager include the following
    regular checks:
   a. Weekly downloads of temperature data for computer backup
   b. Hourly visual temperature logs from digital thermometer displays
   c. Monthly review of emergency procedures with entire pharmacy staff
   d. Purchase of new buffered temperature gauges with five years of digital storage available