We Hear That!

- NPA member, Dave Randolph, PharmD, owner of Dave’s Pharmacy in Alliance and Hemingford was the 2019 Grand Marshal of the Heritage Days parade. He was officially crowned on July 16 at the Central Park Fountain in Alliance. Congratulations, Dave!

- NPA member, Densel Fankhauser, RP, Tecumseh, passed away June 5, 2019. After graduating from the University of Nebraska College of Pharmacy, he started a drug store in DuBois. In 1954, Densel worked at Colwell Drug in Pawnee City until 1957 when went to work for Nachtingall Drug Store in Tecumseh. In 1969, he purchased Chief Drug until he sold the store in 1991, but continued to work part-time until he retired in 2015. Condolences to the Fankhauser family.

- NPA members, Eric and Kim Hamik, PharmDs, reopened their U-Save Pharmacy in Kearney. The Hamiks had sold their pharmacy in 2014, but reopened it along with some of the same staff at the original location. The ribbon cutting ceremony was August 7, 2019. Congrats to owners, Eric and Kim!

- Two years after National Pharmacy, 33rd & A, Lincoln, closed, NPA member, Faheem Rashidi, PharmD, will be opening a new pharmacy in the same location in October. Besides serving area residents, he also plans to reach the Afghan population in Lincoln. Congratulations, Faheem!

Please send “We Hear That” news and photos to diane@npharm.org. You may think your news isn’t important, but M&P subscribers enjoy reading about their pharmacy friends from across the state.

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In Case You Missed It

Your NPA member benefits include a daily email with important drug and health information, as well as answers to member questions. Below is a partial list of some of the most recent Daily News Dose items and other important pharmacy news that you may have missed.

Welcome, Sarah Hunter!
On August 5, the NPA welcomed new employee, Sarah Hunter, Project Coordinator. Sarah is originally from Omaha and recently graduated from Nebraska Wesleyan University with degrees in Political Science, and Philosophy & Religion. Sarah will be the point of contact for the Nebraska MEDS Drug Disposal program and other NPA projects. Sarah can be reached at sarah@npharm.org.

Board of Pharmacy CBD Products Discussion
On July 22, the Nebraska Board of Pharmacy reviewed pending pharmacy practice and licensure regulations, and also discussed the legality of pharmacies and pharmacists selling hemp-based CBD products. The Board will send letters to the Nebraska Department of Agriculture and the Attorney General asking for guidance on licensees selling hemp-based CBD products, in light of the federal and state laws regulating hemp.

CBD Products
Can pharmacies sell THC or CBD products? It depends, among other things, on the intended use of the product and how it is labeled and marketed. Even if a CBD product meets the definition of "hemp" under the 2018 Farm Bill, it still must comply with all other applicable laws, including the FD&C Act.

Can THC or CBD products be sold as dietary supplements? No. Based on available evidence, the FDA has concluded that THC and CBD products are excluded from the dietary supplement definition under section 201(ff)(3)(B) of the FD&C Act [21 U.S.C. §321(ff)(3)(B)]. Visit www.fda.gov for more information.

State Patrol Cracks Down on Prescription Fraud
The Nebraska State Patrol has a direct phone number (402) 331-3335 for reporting of prescription fraud. Pharmacists have been reporting via the web-based tool (https://statepatrol.nebraska.gov/investigative-services-drug-diversion-reporting-form) with great success and response times. The voluntary reporting system provides healthcare professionals an avenue to contact law enforcement with questions and concerns surrounding drug diversion and pharmaceutical fraud.

USP Chapter <800> Becomes effective December 1
The purpose of USP Chapter <800> is to describe practice and quality standards for handling hazardous drugs in healthcare settings and help promote patient safety, worker safety, and environmental protection. The chapter defines processes intended to minimize the exposure to hazardous drugs in healthcare settings. All hospitals and pharmacies are expected to meet the requirements of USP Chapter <800> by December 1, 2019.

If your facility has not yet begun preparation, start by reviewing the Chapter information. One of the first steps is to evaluate the drugs in your inventory and perform an assessment of exposure risk. For more information about the Chapter and a list of hazardous drugs, visit www.usp.org.

Congressman Pharmacy Visit
Tim Kotschwar, PharmD, Owner, Alliance Community Pharmacy, Alliance, had a great visit with Congressman Adrian Smith. They discussed DIR fees and numerous other issues important to community pharmacies.
TOMORROW. IMAGINE THAT.
Gary Yee, Pharm.D., named associate vice chancellor for academic affairs

Gary Yee, Pharm.D., has been named the next associate vice chancellor for academic affairs effective July 1.

"Dr. Yee is ideally suited to take on the role of associate vice chancellor," Dr. Dele Davies, Senior Vice Chancellor for Academic Affairs, said. "He brings a variety of valuable leadership experiences in research, compliance-related matters and a strong understanding of academic-related matters and academic governance."

Dr. Yee is a professor of pharmacy practice and science and in the UNMC College of Pharmacy. He completed his B.S. in pharmacy at the University of Washington, his Pharm.D. at the Philadelphia College of Pharmacy and Science, and post-doctoral training at St. Jude Children's Research Hospital.

"The associate vice chancellor of academic affairs is a good fit for my strengths and experience, and I look forward to supporting Dr. Davies and joining his administrative team," Dr. Yee said.

"Dr. Yee's knowledge, expertise and many roles in research and education -- Including as an editor -- will have prepared him well for the associate vice chancellor position," Dr. Rowen Zetterman said. Dr. Zetterman retired from the position on June 30.

Dr. Bronich appointed Associate Dean for Research & Graduate Studies

Tatiana Bronich, Ph.D. has been named Associate Dean for Research & Graduate Studies. Dr. Bronich is currently a professor in the Department of Pharmaceutical Sciences, Parke-Davis Professor of Pharmaceutical Sciences, Director of COBRE Nebraska Center for Nanomedicine & Co-Director for the Center of Drug Delivery and Nanomedicine. Dr. Bronich has been part of the legacy that enhanced the College’s research portfolio over the past several decades.

Dr. Klepser named Associate Dean for Academic Affairs

Don Klepser, Ph.D., MBA has been appointed Associate Dean for Academic Affairs. Dr. Klepser is an Associate Professor in the Pharmacy Practice Department. Don has been instrumental in pioneering the use of Point of Care Testing (POCT) for infectious diseases in community pharmacy. Many pharmacies across the U.S. have been trained by a program developed by Dr. Klepser and colleagues and adopted into their respective pharmacies.

Kim Scarsi receives national research award

Kim Scarsi, Pharm.D., associate professor of pharmacy practice and science received the 2019 Constance B. Wofsy Women's Health Investigator Award at the annual AIDS Clinical Trials Group (ACTG) meeting in Washington, D.C.

The award was established to honor the memory of Wofsy, one of the pioneers in furthering the understanding of HIV in women and in establishing the ACTG's original Women's Health Committee, now morphed into the Women's Health Inter-Network Scientific Committee. Prior to her death in 1996, Wofsy was a tireless advocate for women with HIV. Like Wofsy, awardees must be active clinically in the care of HIV-positive women, active in researching questions important to women with HIV, active in the networks and dedicated to successfully mentoring junior investigators.
Influenza Vaccine in High-Risk Populations

Written by:
Stephanie Ung, PharmD; Karen O’Brien, BS Pharm, PharmD, RPh, Associate Professor of Pharmacy Science; *Jenny Tilleman, PharmD, RPh, Associate Professor of Pharmacy Practice; Kimberley Begley, PharmD, RPh, Associate Professor of Pharmacy Practice; and Eric Hoie, PharmD, RPh, Associate Professor of Pharmacy Practice at Creighton University School of Pharmacy & Health Professions. *Corresponding author

None of these authors have any relevant financial relationships that would be considered a conflict of interest for the purposes of this continuing pharmacy education activity.

Abstract
Pharmacists are accessible and trusted healthcare professionals. With the authority to administer immunizations throughout the United States, pharmacists assume a larger role in screening, recommending, and administering vaccines. Given the high rate of influenza illness, pharmacists should pay careful attention to populations with a higher risk of succumbing to the disease. Special populations include the young; elderly; patients with chronic illnesses; immunocompromised; and pregnant patients. Pharmacists must understand which influenza vaccine is appropriate for each patient population. With a proven track record of increasing immunizations nationwide, pharmacists can positively impact the influenza disease burden in high-risk populations.

Objectives
At the conclusion of this lesson, pharmacists and pharmacy technicians should be able to:

1. Identify patients at high risk for influenza complications.
2. List contraindications and precautions for the influenza vaccine.
3. Explain common misconceptions about the influenza vaccine.

Introduction
Influenza is a viral illness that commonly circulates in the United States from the fall through the spring months, although the onset, peak, and end of influenza activity can vary considerably and unpredictably from season to season.1 Symptom onset is typically rapid and may include fever or feeling feverish, chills, cough, sore throat, runny or stuffy nose, muscle or body aches, headaches, fatigue, nausea and vomiting. Most individuals fully recover from influenza in less than two weeks, but some develop complications requiring healthcare provider office visits or hospitalization, while other complications may be life-threatening and result in death.2

The Centers for Disease Control and Prevention (CDC) use a variety of modeling methods to estimate the influenza disease burden in the United States. The CDC estimates that influenza was responsible for 9.3 million – 49 million illnesses; 140,000 – 960,000 hospitalizations; and 12,000 – 79,000 deaths annually in the United States since 2010.3 See Figure 1.

Figure 1: Estimated Annual Influenza Disease Burden in the U.S. since 2010.2

![Figure 1: Estimated Annual Influenza Disease Burden in the U.S. since 2010.2](image-url)
Background

The pharmacist’s role in immunization administration has drastically evolved over the past few decades. In 1995, pharmacists were authorized to administer vaccines in only nine states. Today, pharmacists in all 50 states, Puerto Rico, and the District of Columbia have the authority to administer vaccines to varying degrees. Studies have shown that pharmacists play an active and integral role in boosting immunization rates. This is particularly important for influenza prevention as vaccination coverage is generally modest in the United States. The 2017-2018 influenza season was considered high severity with increased numbers of clinic visits and hospitalizations. Nevertheless, vaccine coverage for adults and children was low at 37% and 57.9%, respectively. Thus, it is imperative that pharmacists continue to actively screen and immunize patients against influenza as well as other vaccine preventable diseases. Patients at high-risk for developing severe influenza-related complications warrant special attention. These patients should be screened for vaccine needs at each pharmacy visit and should always be offered an annual influenza vaccination when indicated. Moreover, the CDC recommends the following high-risk patients be prioritized for vaccination in the event of an influenza vaccine shortage: children less than 2 years of age, adults ≥ 50 years of age, those with certain chronic health conditions, immunocompromised persons, and pregnant patients. This article reviews special considerations for and benefits of influenza vaccination in these high-risk populations.

Children 6-59 Months

Children younger than five years of age, but particularly those younger than two years of age, are considered a high-risk population due to the potential for severe influenza-related complications. These complications include pneumonia, dehydration, worsening of chronic conditions, brain dysfunction, and sinus and/or ear infections. The CDC reports that flu-related deaths in children have ranged from 37 to 187 deaths per season since formal reporting began in 2004. A population-based survey estimated the disease burden of outpatient visits associated with the 2003-2004 influenza season was 95 clinic visits and 27 emergency department visits per 1000 children. Additionally, the overall average annual rate of influenza-associated hospitalizations was 0.9 per 1000 children across the 2002-2003 and 2003-2004 seasons. A prospective evaluation of the 2017-2018 season found that influenza A (H3N2), the predominant strain of the season, affected nine percent of children aged six months to four years. This model estimated the 2017-2018 season’s influenza vaccine was effective in this cohort and prevented 41% of all expected hospitalizations in young children. These data speak to both the influenza disease burden and the efficacy of the influenza vaccine in this young, at-risk population. It is imperative that children younger than five years of age receive an age-appropriate influenza vaccine and dose each year. Of note, children aged six months through eight years who are being immunized for the first time should receive two doses of the vaccine, spaced at least four weeks apart, for optimal protection. One study showed that a single dose generally did not stimulate a protective antibody response in children who were seronegative (vaccine-naive) at baseline.

Older Adults

On the opposite end of the age spectrum, older patients are also at higher risk of developing influenza-related complications. The CDC’s Advisory Committee on Immunization Practices (ACIP) identifies this at-risk cohort as adults 65 years and older, but expands the group to include adults 50 years and older in the event of a vaccine shortage. Older patients who are residents of nursing homes or other chronic care facilities should be prioritized for immunization when vaccine is in short supply.

Immunosenescence, which refers to the age-related decline of the immune system, leaves older patients with weaker immune systems more vulnerable to infections, diseases, and influenza-related complications. These complications are similar to those experienced by the high-risk pediatric population, with pneumococcal pneumonia at the forefront of concern. This risk can be attenuated by assuring both influenza and full pneumococcal vaccine protection (PCV13 and PPSV23) when appropriate. Immunosenescence impedes both innate and adaptive immunity, limiting an older patient’s ability to mount a response to vaccines.

The CDC recommends that people aged 65 years and older receive any age-appropriate inactivated influenza vaccine (IIV) formulation or the recombinant influenza vaccine (RIV4), but not the live attenuated influenza vaccine (LAIV4). These formulations include SD-IIV3, aIIV3, HD-IIV3, IIV4, and RIV4. Table 1 lists the ACIP influenza vaccine abbreviations. Fluzone High-Dose (HD-IIV3) and Fludad (aIIV3) vaccines are only indicated for patients 65 years of age and older. Fluzone High-Dose is a trivalent IIV that contains four times the amount of antigen contained in standard-dose trivalent IIV. Flud is a standard-dose trivalent IIV that also contains an adjuvant to boost the immune response to the vaccine. Both vaccines were designed to induce a more robust immune response in older patients; however, ACIP does not express a preference for the high dose or adjuvanted vaccines over other influenza vaccines approved for use in patients 65 years of age and older. It should be noted that neither of these trivalent vaccines provides protection against the B strain that is included in quadrivalent influenza vaccines. As is the case with influenza A strains,
Table 1 | ACIP Influenza Vaccine Abbreviations

- IIV = Inactivated Influenza Vaccine
- RIV = Recombinant Influenza Vaccine
- LAIV = Live Attenuated Influenza Vaccine
- Numerals following letter abbreviations indicate the number of influenza strains present
  - 3 for trivalent vaccines (e.g., IIV3)
  - 4 for quadrivalent vaccines (e.g., IIV4; RIV4; LAIV4)
- Prefixes refer to some specific vaccine types
  - a for adjuvanted vaccine (e.g., aIIV3)
  - HD for high-dose vaccine (e.g., HD-IIV3)
  - SD for standard-dose vaccine (e.g., SD-IIV3)

Adapted from ACIP’s MMWR 2018-2019 Influenza Recommendations

There are reports of older age being associated with higher morbidity and mortality in patients with influenza B infection.17

A prospective evaluation of the 2017-2018 influenza season reported that 51% of vaccinated adults aged 65 years and older with known vaccine type received HD-IIV3, 47% received IIV4 or SD-IIV3, and 2% received all IV3. The same study reported that older patients accounted for only 15% of influenza-related illness, but a staggering 70% and 90% of influenza-related hospitalizations and deaths, respectively. Despite these high rates, it is estimated that influenza vaccine prevented approximately 715,000 influenza-related illnesses, 400,000 medical visits, 65,000 hospitalizations, and 6,800 deaths in persons ≥ 65 years of age. These statistics highlight the disease burden that can be prevented by annually vaccinating appropriate candidates in this high-risk elderly population.11

All Persons with Chronic Conditions

Patients of any age with chronic conditions are another group at high risk for developing serious influenza-related complications. ACIP generally identifies the following chronic conditions as high-risk: pulmonary disorders (including asthma), cardiovascular disorders (excluding hypertension alone), renal disorders, hepatic disorders, neurologic disorders, hematologic disorders, and metabolic disorders (including diabetes).18 See Table 2 for specific examples of high-risk chronic conditions. These chronic disorders put patients at high risk for various reasons. Asthma, for example, can be worsened by influenza and lead to increased pulmonary inflammation and, potentially, pneumonia.19 People younger than 19 years of age on extended aspirin therapy and extremely obese individuals (BMI >40) are also considered high-risk populations.18 Adolescents on long-term aspirin therapy are at increased risk of developing Reye’s Syndrome following viral illnesses such as the flu. Reye’s Syndrome precipitates metabolic encephalopathy and is associated with fatty degeneration of the liver.20 Obesity has been linked to an increased risk of hospitalizations and death associated with influenza. This is likely because many of the chronic conditions, including cardiovascular and metabolic diseases, that are correlated with these complications are also associated with obesity.21 A recent study found that obesity may increase the duration of influenza A virus shedding and, therefore, the duration of potential transmission of the flu in adults.22 As candidates for influenza vaccine, all of these patients are recommended to receive an IIV or RIV4 vaccine. There are no contraindications to IIV or RIV4 vaccines for the conditions listed above, other than history of a severe allergic reaction to any vaccine component or after a previous dose of any influenza vaccine. See Table 3 for contraindications and precautions for influenza vaccines. For the most part, LAIV has not been studied in high-risk groups. Therefore, ACIP recommends weighing the benefits of protection by LAIV against the unknown risks of adverse reaction in persons with

<table>
<thead>
<tr>
<th>High-Risk Chronic Conditions per the CDC</th>
<th>Examples</th>
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<tbody>
<tr>
<td>Pulmonary disorders</td>
<td>Asthma, COPD, cystic fibrosis</td>
</tr>
<tr>
<td>Cardiovascular disorders</td>
<td>Congenital heart disease, congestive heart failure, coronary artery disease, history of stroke</td>
</tr>
<tr>
<td>Renal disorders</td>
<td>Not specified by the CDC</td>
</tr>
<tr>
<td>Hepatic disorders</td>
<td>Not specified by the CDC</td>
</tr>
<tr>
<td>Neurologic disorders</td>
<td>Cerebral palsy, epilepsy, stroke, intellectual disability, moderate to severe developmental delay, muscular dystrophy, spinal cord injury</td>
</tr>
<tr>
<td>Hematologic disorders</td>
<td>Sickle cell disease</td>
</tr>
<tr>
<td>Metabolic disorders</td>
<td>Diabetes, inherited metabolic disorders, mitochondrial disorders</td>
</tr>
</tbody>
</table>
chronic conditions. The LAIV4 vaccine is contraindicated in children and adolescents on aspirin or salicylate-containing therapy, as well as children aged 2 through 4 years who have asthma.¹

Understanding the difference between a contraindication and precaution can help guide the decision about whether to withhold influenza vaccination. A contraindication means a condition exists which increases the likelihood that a patient will suffer a serious adverse reaction if she/he receives the vaccine. A precaution is “a condition in a recipient that might increase the chance or the severity of an adverse reaction or might compromise the ability of the vaccine to produce immunity.”²³ Precautions are generally either temporary situations or a matter of assessing benefit versus risk.

### Table 3 | Contraindications and Precautions for Influenza Vaccines¹

<table>
<thead>
<tr>
<th>Vaccine Type</th>
<th>Contraindications</th>
<th>Precautions</th>
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<tbody>
<tr>
<td>IIV (Inactivated Influenza Vaccine)</td>
<td>History of severe (life-threatening) allergic reaction to any component of the vaccine or after a previous dose of any influenza vaccine</td>
<td>Moderate or severe acute illness with or without fever</td>
</tr>
<tr>
<td></td>
<td></td>
<td>History of Guillain-Barré syndrome within 6 weeks of receipt of influenza vaccine</td>
</tr>
<tr>
<td>RIV (Recombinant Influenza Vaccine)</td>
<td>History of severe (life-threatening) allergic reaction to any component of the vaccine or after a previous dose of RIV</td>
<td>Moderate or severe acute illness with or without fever</td>
</tr>
<tr>
<td></td>
<td></td>
<td>History of Guillain-Barré syndrome within 6 weeks of receipt of influenza vaccine</td>
</tr>
<tr>
<td>LAIV (Live Attenuated Influenza Vaccine)</td>
<td>Children &lt; 2 years of age and adults ≥ 50 years of age</td>
<td>Moderate or severe acute illness with or without fever</td>
</tr>
<tr>
<td></td>
<td>History of severe allergic reaction to any component of the vaccine or after a previous dose of any influenza vaccine</td>
<td>History of Guillain-Barré syndrome within 6 weeks of receipt of influenza vaccine</td>
</tr>
<tr>
<td></td>
<td>Concomitant aspirin- or salicylate- containing therapy in children and adolescents</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Children 2-4 years of age who have an asthma diagnosis or whose parents/caregivers/medical records report a wheezing episode in the previous 12 months</td>
<td></td>
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<tr>
<td></td>
<td>Children or adults who are immunocompromised due to any cause (including immunosuppression caused by medications or HIV infection)</td>
<td></td>
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<tr>
<td></td>
<td>Close contacts and caregivers of severely immunosuppressed persons who require a protected environment.</td>
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<tr>
<td></td>
<td>Pregnancy</td>
<td>Auburn in children aged ≥ 5 years</td>
</tr>
<tr>
<td></td>
<td>Receipt of influenza antiviral medication within the previous 48 hours</td>
<td>Other underlying medication conditions that might predispose to complications after wild-type influenza infection, including</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Chronic disorders of the pulmonary or cardiovascular system (except hypertension)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Neurological/neuromuscular diseases</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Metabolic diseases, such as diabetes mellitus</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Renal or hepatic dysfunction</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Hematologic disorders, such as hemoglobinopathies</td>
</tr>
</tbody>
</table>

Adapted from ACIP’s MMWR 2018-2019 Influenza Recommendations

### Immunocompromised Persons

ACIP has identified immunocompromised persons as another population highly susceptible to influenza and its complications. Weakened immune systems put these vulnerable patients at risk of pneumonia and hospitalization and may blunt the immune responses to vaccines.¹ Despite the potential for decreased immune response, influenza vaccines are still considered...
beneficial for preventing influenza or reducing its severity or rate of complications in these patients. A meta-analysis published in 2012 found that populations of human immunodeficiency virus (HIV) positive, cancer, and transplant patients who received an influenza vaccine had significantly lower chances of developing influenza-like illness than patients who received a placebo.24 Both ACIP and the Infectious Diseases Society of America (IDSA) recommend annual influenza vaccinations for immunocompromised patients. ACIP recommends the use of IIVs or RIV4 in these populations but does not recommend LAIV due to the lack of safety data and the “uncertain but biologically plausible risk for disease attributable to the vaccine virus”.1 IDSA published guidelines in 2013 detailing the selection and timing of vaccines in various immunocompromising circumstances.25 Specific conditions are listed in Table 4. Like ACIP, IDSA recommends annual vaccination with IIVs, but not LAIV. RIV4 was not yet approved and is not explicitly discussed in the IDSA guidelines. IDSA does not specifically recommend IIV for cancer patients who have received intensive chemotherapy (such as induction or consolidation chemotherapy) within the last three months or cancer patients who have received anti-B-cell antibodies (such as Rituximab) within the last six months.25 This position is not due to concerns about vaccine safety, but rather lack of immune response. ACIP recommends that IIV be given to such patients without exempting this time window but cautions that providers should consider repeating doses given during these therapies.26 In this case, the rationale is that some immunity, even if sub-optimal, is better than none. Children receiving maintenance chemotherapy may be considered for IIVs, but administration of vaccines during this time should not be considered valid doses unless there is documentation of protective antibody levels. Additionally, IDSA recommends hematopoietic stem cell transplant (HSCT) patients wait six months after transplant to receive their annual IIV vaccine. If the local health department identifies an influenza outbreak, HSCT patients and solid organ transplant patients may receive an annual IIV vaccine four months and one month, respectively, after transplant.25 Again, the alternative of giving and then repeating the dose after the time window may be prudent if this window falls during influenza season. LAIV is not recommended and should not be used in any of these patient populations. Any of the IIVs, on the other hand, are considered safe for these high-risk groups.25

<table>
<thead>
<tr>
<th>High-risk Immunocompromising Conditions per IDSA</th>
<th>Examples</th>
</tr>
</thead>
</table>
| Primary immunodeficiency disorders | • Congenital complement deficiencies  
• Severe mannin-binding lectin deficiency  
• Phagocytic cell deficiencies (such as chronic granulomatous disease, leukocyte adhesion deficiency, and Chediak-Higashi Syndrome)  
• Innate immune defects that result in defects of cytokine generation/response or cellular activation (such as defects of the IFN-gamma/IL-12 axis)  
• Minor antibody deficiencies (such as IgA deficiency and specific polysaccharide antibody deficiency)  
• Major antibody deficiencies  
• Combined immunodeficiencies (such as DiGeorge syndrome and severe combined immunodeficiency disorder) |
| HIV infection | Not specified |
| Cancer | Not specified |
| Hematopoietic stem cell transplants | Not specified |
| Solid organ transplants | Not specified |
| Chronic inflammatory diseases on immunosuppressive medications | Not specified |
| Asplenia or sickle cell diseases | Not specified |
| Anatomic barrier defects | • Cochlear implants  
• Congenital dysplasias of the inner ear  
• Persistent cerebrospinal fluid communication with the oropharynx or nasopharynx |
Pregnant Patients

Pregnant patients are considered a high-risk population because of the potential for adverse outcomes in both the fetus and the mother if influenza is contracted during the gestational period. This risk for severe influenza-related complications is highest in the second and third trimester. Risks to the fetus include premature birth, reduced birth weight, and fetal death, while maternal risks include hospitalization, cardiopulmonary complications, and death. The American College of Obstetricians and Gynecologists (ACOG) considers the influenza vaccine a vital part of prepregnancy, prenatal, and postpartum care and recommends that all women who are pregnant or will be pregnant during influenza season receive an inactivated influenza vaccine.28 Both ACOG and ACIP recommend that any age-appropriate inactivated vaccine be administered during any trimester of the pregnancy; it should be given as soon as available for the upcoming influenza season. Additionally, vaccination should continue throughout the influenza season to protect pregnant women as long as influenza viruses are circulating. Of note, one small observational study conducted during the 2010-2011 and 2011-2012 flu seasons did observe a possible association between administration of IIV (which contained H1N1pdm09 antigen during these seasons) and spontaneous abortion (SAB) within 28 days following vaccine administration. The increased risk of SAB was only observed in women who had also received IIV containing H1N1pdm09 antigen the previous flu season.29 No other studies or reviews of previous influenza seasons have identified similar associations, but additional studies are ongoing. It should also be noted that other recent literature suggested that pregnant patients had decreasing immune response to influenza vaccination as their pregnancies progress.30 To reiterate, both ACOG and ACIP currently recommend that any age-appropriate IIV or RIV4 may be used during any trimester for pregnant women and should be given as soon as available. LAIV4 has not been studied, is contraindicated, and should not be used in pregnant women.28 Once a woman has given birth, however, LAIV4 is no longer contraindicated. Women who breastfeed can safely receive any of the influenza vaccines, inactivated or live.31

Indigenous Populations

A high-risk group that has not been previously discussed, but should also be prioritized, includes American Indians and Alaska Natives. These patient populations seem to have increased mortality rates from influenza and pneumonia compared to other racial groups, although the reason behind this association is unclear.21 It is important, therefore, to thoroughly screen and vaccinate these individuals each influenza season.

Live Attenuated Influenza Vaccine

Although LAIV4 is contraindicated in many of the high risk groups, it remains an excellent option for healthy children over two years of age. Pharmacists, as well as other healthcare providers, have been perplexed by ACIP’s frequently changing position on LAIV. Some background information may prove helpful. LAIV4 was first available during the 2013-2014 flu season, replacing the LAIV3 formulation.33 ACIP preferentially recommended LAIV4 for the 2014-2015 influenza season based on evidence that it worked better than inactivated vaccines, especially in the pediatric population.24 For the 2015-2016 season, ACIP did not express a preference for LAIV4 or IIV, and they recommended against the use of LAIV4 in the 2016-2017 and 2017-2018 seasons. The decision to not recommend the use of LAIV4 was based on poor vaccine effectiveness against influenza A(H1N1)pdm09 viruses during the 2013-2014 and 2014-2015 seasons.33 The manufacturer of LAIV4 has made changes to the A(H1N1)pdm09 strain which suggest improvements over the previous formulation, although the effectiveness of the updated LAIV4 against currently circulating A(H1N1)pdm09 strains is not yet known. In the 2018-2019 flu season, again ACIP reversed its position and expressed no preference for either IIV or LAIV.33 The American Academy of Family Physicians (AAFP) and the American Academy of Pediatrics (AAP) both cited a preference for IIV during the 2018-2019 flu season except when patients refused an injection and would not otherwise be immunized against influenza.35,36 AAP will recommend use of either LAIV4 or IIV without preference during the 2019-2020 season to protect children against influenza.36

Common Misconceptions

While it is particularly important to avoid missed opportunities to vaccinate high-risk populations against the flu, pharmacists should not forget to address missed opportunities in the general healthy population. Some concerns and points of confusion that may leave pharmacists hesitant to vaccinate are discussed below:

Precautions with Egg Allergies

Immunizing pharmacists are frequently hesitant about providing influenza vaccination for their patients with eggs allergies. However, current ACIP recommendations have simplified this dilemma considerably. All persons who report history of an egg allergy, but who have reactions that are not considered severe may still receive any otherwise appropriate influenza vaccine. When urticaria is the only symptom reported, any appropriate influenza vaccine may be administered. Even if additional symptoms are reported (such as angioedema, respiratory distress, lightheadedness, or recurrent emesis), patients may still receive an influenza vaccine. In these instances, however, the vaccine...
should be administered in an inpatient or outpatient medical setting (which does not include most community pharmacies) under the direct supervision of a healthcare provider who can recognize and manage severe allergic reactions. It is important that the immunizing pharmacist does not tell such a patient that the influenza vaccine is contraindicated for him/her. Rather, the patient should be referred to his/her healthcare provider practicing in an inpatient or outpatient medical setting to be vaccinated. If a provider or patient continues to have concerns about a potential egg allergy, RIV4 (Flubok Quadrivalent) may be a preferred option. Because embryonated eggs are not used to manufacture RIV4, it is considered egg-free. It is worth noting that patients who can tolerate scrambled eggs are unlikely to be allergic. Tolerance to egg-containing foods, however, does not exclude the possibility of a true allergy. In such cases, careful and thorough screening is warranted to determine the presence of a true egg allergy.1

**Trivalent vs Quadrivalent Formulations** As indicated by its name, trivalent IIVs contain three strains of the influenza virus – two A lineages and 1 B lineage. The quadrivalent IIVs contain an additional B lineage for a total of 4 influenza virus strains. Quadrivalent vaccines consequently provide more extensive coverage against circulating influenza B viruses. Theoretically, quadrivalent vaccines may provide more protection, but this is dependent on the prevalence of circulating influenza viruses for that specific season, with some variability at different points in the season. For example, during the 2017-2018 season, influenza A(H3N2) was the overall prevailing strain.37 Yet, influenza B viruses were more commonly reported than A viruses later in the season (early March to late May). Moreover, of the 2017-2018 seasonal viruses sub-typed by public health laboratories, > 85% were of B/Yamagata lineage. B/Yamagata was only available in the quadrivalent formulations. ACIP does not denote a preference for either trivalent or quadrivalent vaccine, apparently focusing on a primary objective of advocating for vaccination with whichever appropriate vaccine is available. It bears noting, however, those vaccinated with the trivalent vaccines (standard-dose, high-dose or adjuvanted standard-dose) would not have been protected against the dominant strain circulating from March through May 2018, as identified by the national surveillance data previously discussed.

**Too Late in the Season to Vaccinate** The influenza season typically begins in October and peaks around December or February. The season can extend as late as May depending on the year. It is a common misconception that patients do not need to be immunized near the end of the influenza season, or even after November or December. Community pharmacists are encouraged to continue vaccinating patients into the spring months. If patients receive the prior season’s vaccine in the early summer months (for example, receive the 2018-2019 vaccine in June 2019), they should wait at least four weeks before getting the new season’s influenza vaccine (2019-2020 formulation).40

**Quick Tips for Pharmacists**
- All influenza vaccines should be stored in the refrigerator with a temperature range of 36⁰F to 46⁰F. None of the available vaccines should ever be frozen.40
- Most influenza vaccines are suspensions and prefilled syringes, single-dose vials, or multidose vials should be shaken to re-suspend the vaccine. Check the composition of the flu vaccine you are planning to administer before you use it. Always determine whether the vaccine vial/syringe needs to be shaken before administering. See Table 5 for a list of vaccines available in the 2019-2020 season, their formulations and manufacturers’ recommendations pertinent to shaking/not shaking.
- Double check the “Rights of Medication Administration” when screening and administering vaccines. This means checking for the right patient, the right vaccine, the right time (including the correct age and interval, as well as prior to product expiration time/dose), the right dosage, the right route, the right site, and the right documentation.48
- The CDC does not express a preference for one influenza vaccine versus others also indicated for the target patient.1

**Conclusion**
The important take away message is that patients who fall into any of the previously discussed high-risk populations should receive an influenza vaccine annually unless a contraindication exists. Contraindications or precautions that might warrant withholding or delaying a specific influenza vaccine are dependent on patient-specific criteria and the type of influenza vaccine being considered for use. Barring the small percentage of patients who have a history of severe allergic reaction to any vaccine component or after a previous dose of any influenza vaccine, almost every other patient eligible for influenza vaccination can receive an annual IIV (if ≥6 months old) or RIV4 (if ≥18 years old). Consideration should be given to referral of these patients to an allergist for review and possible vaccination under close observation.

**Acknowledgments**
The authors would like to thank Linda Ohri, BS, PharmD, MPH, for her expert guidance in preparing this manuscript.
## Table 5 | Vaccine Formulations Available in 2019-2020 and Manufacturer Vaccine Preparation Instructions\textsuperscript{15,16,41-47}

<table>
<thead>
<tr>
<th>Trade Name (Manufacturer)</th>
<th>Formulation and How Supplied</th>
<th>Manufacturer Vaccine Preparation Instructions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Standard Dose Quadrivalent Inactivated Influenza Vaccines (IIV4s)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Afluria Quadrivalent (Seqirus)</td>
<td>0.25 mL PFS-Susp 0.5 mL PFS-Susp 5 mL MDV-Susp</td>
<td>Immediately before use, shake thoroughly.</td>
</tr>
<tr>
<td>Fluarix Quadrivalent (GlaxoSmithKline)</td>
<td>0.5 mL PFS-Susp</td>
<td>Shake well before administration.</td>
</tr>
<tr>
<td>Flulaval Quadrivalent (ID Biomedical Corp. of Quebec)</td>
<td>0.5 mL PFS-Susp 5 mL MDV-Susp</td>
<td>Shake well before administering.</td>
</tr>
<tr>
<td>Fluzone Quadrivalent (Sanofi Pasteur)</td>
<td>0.25 mL PFS-Susp 0.5 mL PFS-Susp 0.5 mL SDV-Susp 5 mL MDV-Susp</td>
<td>Shake PFS or vial before administering a dose.</td>
</tr>
<tr>
<td>Flucelvax Quadrivalent (Seqirus)</td>
<td>0.5 mL PFS 5 mL MDV</td>
<td>Shake PFS vigorously before use. Shake MDV each time before withdrawing a dose.</td>
</tr>
<tr>
<td><strong>High-Dose Trivalent Inactivated Influenza Vaccine (HD-IIV3)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluzone High-Dose (Sanofi Pasteur)</td>
<td>0.5 mL PFS-Susp</td>
<td>Shake PFS before administering dose.</td>
</tr>
<tr>
<td><strong>Adjuvanted Trivalent Inactivated Influenza Virus (aIIV3)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluad (Seqirus)</td>
<td>0.5 mL PFS-Susp</td>
<td>Gently shake PFS before administering.</td>
</tr>
<tr>
<td><strong>Quadrivalent Recombinant Influenza Vaccine (RIV4)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Flublok Quadrivalent (Sanofi Pasteur)</td>
<td>0.5 mL PFS-Sol</td>
<td>No shaking recommended. This formulation is a solution.</td>
</tr>
<tr>
<td><strong>Quadrivalent Live Attenuated Influenza Vaccine (LAIV4)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FluMist Quadrivalent (AstraZeneca)</td>
<td>0.2 mL prefilled single-use intranasal sprayer-Susp</td>
<td>Although FluMist Quadrivalent is a suspension, the manufacturer makes no mention of a need to shake prior to use. However, shaking is generally recommended for any suspension</td>
</tr>
</tbody>
</table>

\textsuperscript{PFS = prefilled syringe; SDV = single-dose vial; MDV = multidose vial; Susp = suspension; Sol = solution}
Influenza Vaccine in High-Risk Populations

Quiz #10, July/August 2019, ACPE 0128-0000-19-042-H06-P/T

1. Select the statement regarding immunizations that is true.
   a. Studies have shown that although pharmacists are authorized to administer vaccines, they have had no role in boosting immunization rates in the United States.
   b. The CDC recommends the influenza vaccine for high-risk patients such as immunocompromised persons and pregnant women.
   c. The influenza vaccination rate in the United States was close to 90% for the 2017-2018 influenza season.
   d. The rate of immunizations nationwide has improved because pharmacists currently have the authority to administer vaccines in 35 states.

2. One influenza-related complication in children is ________.
   a. Cardiomyopathy  c. Nephropathy
   b. Dehydration  d. Paresthesias

3. What is the recommended schedule for children aged six months to eight years being immunized against influenza for the first time?
   a. A single dose of the influenza vaccine.
   b. Three doses of the influenza vaccine spaced at least six weeks apart.
   c. Two doses of the influenza vaccine spaced at least eight weeks apart.
   d. Two doses of the influenza vaccine spaced at least four weeks apart.

4. Which influenza vaccine would NOT be recommended in persons aged 65 years and older?
   a. High-dose trivalent influenza vaccine.
   b. Inactivated influenza vaccine.
   c. Live attenuated influenza vaccine.
   d. Recombinant influenza vaccine.

5. Which chronic medical condition does NOT place patients at high risk for influenza-related complications?
   a. Asthma  c. Epilepsy
   b. Diabetes  d. Hypertension

6. In which patient would the live attenuated influenza vaccine be contraindicated?
   a. A female patient who is in the second trimester of pregnancy.
   b. A healthy child over 2 years old.
   c. A patient who is 35 years old with type II diabetes.
   d. A patient who is 45 years old with congestive heart failure.

7. Which of the following does the IDSA consider a high-risk immunocompromising condition warranting the influenza vaccine?
   a. A patient with asplenia.
   b. A patient with cancer.
   c. A patient with HIV infection.
   d. All of the above.

8. Which statement is true regarding patients with an egg allergy and the influenza vaccine?
   a. A history of respiratory distress, lightheadedness, or recurrent emesis in patients with an egg allergy is a contraindication to receiving the influenza vaccine.
   b. A patient who experienced angioedema after consuming eggs may receive the influenza vaccine in most community pharmacies, as long as a technician is observing them.
   c. If a provider or patient has concerns about a potential egg allergy, Afluria Trivalent (IIV3) may be a preferred option because it is considered egg-free.
   d. If urticaria is the only symptom reported with an egg allergy, any appropriate influenza vaccine may be administered.

9. What is the difference between the trivalent and quadrivalent influenza vaccine formulations?
   a. Quadrivalent vaccines provide more extensive coverage against circulating influenza A viruses.
   b. The CDC expresses a preference for the quadrivalent IIVs over trivalent IIVs.
   c. The trivalent IIVs contain three strains of the influenza virus, two A lineages and 1 B lineage, and the quadrivalent IIVs contain two A lineages and 2 B lineages.
   d. The trivalent IIV is preferred if the pharmacist is vaccinating patients into the spring months.

10. Select the statement that is true regarding the storage and administration of the influenza vaccine.
    a. All influenza vaccines should be stored in the refrigerator with a temperature range of 36°F to 46°F.
    b. Most influenza vaccines are solutions and do not require any agitation prior to administration.
    c. Prefilled syringes (PFSs) of influenza vaccine should never be shaken.
    d. The trivalent IIV is preferred if the pharmacist is vaccinating patients into the spring months.

---

Circle one (1) Answer:
1. a b c d  6. a b c d
2. a b c d  7. a b c d
3. a b c d  8. a b c d
4. a b c d  9. a b c d
5. a b c d  10. a b c d

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CPE Home Study Evaluation
1. Rate this lesson: (Excellent) 5  4  3  2  1 (Poor)
2. Did this lesson meet each of its objectives? ___ Yes ___ No
3. Was the content without commercial bias? ___ Yes ___ No
   If not, please explain
4. Did the lesson meet your educational/practice needs? ___ Yes ___ No
5. Comments/future topics are welcome.
2018 Recipients of the “Bowl of Hygeia” Award

The Bowl of Hygeia award program was originally developed by the A. H. Robins Company to recognize pharmacists across the nation for outstanding service to their communities. Selected through their respective professional pharmacy associations, each of these dedicated individuals has made uniquely personal contributions to a strong, healthy community. We offer our congratulations and thanks for their high example. The American Pharmacists Association Foundation, the National Alliance of State Pharmacy Associations and the state pharmacy associations have assumed responsibility for continuing this prestigious recognition program. All former recipients are encouraged to maintain their linkage to the Bowl of Hygeia by emailing current contact information to awards@naspa.us. The Bowl of Hygeia is on display in the APhA History Hall located in Washington, DC.

Boehringer Ingelheim is proud to be the Premier Supporter of the Bowl of Hygeia program.
Bowl of Hygeia

The Bowl of Hygeia award was presented to Charles Krobot, PharmD, Omaha, in recognition of his service to the profession through his work and actions.

Dr. Krobot has served on numerous committees and task forces, written many articles, taught classes and made presentations during his career, benefitting the profession, the state, and the Omaha community. From the Nebraska Patient Safety Coalition, to the Uniform Credentialing Rewrite Committee, the Nebraska Comprehensive Cancer Control Statewide Partnership, Omaha Metro Medical Response System, the NPA Legislative Committee, and many others. He also spent numerous years on the Nebraska Society of Health System Pharmacists Board, a few as President, and was instrumental in NSHP and NPA becoming a unified organization, for the betterment of Nebraska pharmacists. He is a Past President of the Nebraska Pharmacists Association, is currently on the NPA Finance Committee, and has served on many more committees and work groups.

Dr. Krobot practiced hospital pharmacy, loving the interprofessional clinical services, particularly in oncology where he spent many years before transitioning to teaching students. He received both the Hospital Pharmacist of the Year and Cora Mae Briggs awards, but the real community service he has provided is the countless number of law questions he has answered for the many pharmacists, student pharmacists, and pharmacy technicians over the years. He has always been a trusted and valued resource for law and pharmacy practice questions, going the extra mile to find the answer to assist pharmacists with questions. This service has impacted many pharmacists across the state and many the patients that have been served.

Dr. Krobot is a pillar of the pharmacy profession and has helped the practice in many ways. Congratulations to Dr. Charlie Krobot for this well deserved award.

The award was presented to Dr. Krobot by last year’s award recipient, Angie Svoboda, PharmD (left) and NPA CEO, Joni Cover (right).
**Distinguished Young Pharmacist**

The Distinguished Young Pharmacist award was presented to **Jolyn Merry, PharmD, Lincoln**. The award is presented to a pharmacist practicing 10 years or less, licensed in good standing, is a member of the NPA and actively engaged in state and national associations, and displays leadership in professional programs and community service.

Dr. Merry has done many outstanding things in pharmacy in her short career. She is an active member of the Nebraska Pharmacists Association and the UNMC Alumni Association. She has worked for CHI Health in Omaha and Bellevue and now works for Bryan Health in Lincoln.

During her time as a pharmacist she has worked with EPIC to improve the outpatient computer system for pharmacy - work she started at CHI Health and continues in specialty pharmacy at Bryan Health.

Dr. Merry was recently promoted to Pharmacist–in–Charge for Bryan Health East. The promotion was based on her work with EPIC, her improvements in specialty pharmacy billing and employee service, and her work with Lancaster County on the provision of rabies vaccines and rabies immunoglobulin for known or suspected rabies exposures in Lancaster County. Because of this work, when the NPA needed an extra CE article written, she stepped up and helped. Her efforts in pharmacy practice highlight the reasons she is this year’s Distinguished Young Pharmacist. Congratulations to Dr. Jolyn Merry.

The award was presented to her by last year’s recipient, Jeanie Shipman, PharmD (left) and Pharmacists Mutual Representative, Melissa McKean (right).
INTRODUCING NESP

The pharmacy industry has changed dramatically over the past five years. Many pharmacies are focused on just filling prescriptions. This might be ideal for patients who just want convenient access to medications. What about patients that require more care, more answers, and more time from their pharmacy? These patients need pharmacies that are members of NESP, a CPESN® Network.

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Visit the NESP website at: https://nebraskapharmacynetwork.com
New Dean Named for Creighton University School of Pharmacy and Health Professions

Evan T. Robinson, RPh, PhD, has been named dean of the School of Pharmacy and Health Professions, effective Aug. 19, 2019. He has served as the dean at the Western New England University College of Pharmacy and Health Sciences since 2008.

“The chance to lead such a talented and passionate group of faculty, staff, and administrators in the enactment of the College and University vision and mission is truly exciting to me and I look forward to getting started this August,” said Robinson.

Robinson facilitated the development of the pharmacy program at Western New England University, as the founding dean of the university’s College of Pharmacy. Beginning in 2017, he helped establish a new entry-level doctor of occupational therapy program within the college, and oversaw the transition of the college to the newly named College of Pharmacy and Health Sciences. In addition to serving as dean, Robinson served as the associate provost for academic affairs from September 2016 to July 2018.

Prior to Western New England University, Robinson participated in the development of two new schools of pharmacy at the University of Charleston, and served in senior roles at Shenandoah University.

Robinson received his Bachelor of Science in Pharmacy and Master of Science in Pharmacy Administration from St. Louis College of Pharmacy and his PhD in pharmacy administration from the Department of Pharmacy Care Systems at Auburn University.

Robinson was elected speaker of the house for the American Association of Colleges of Pharmacy (AACP) in 2015 and served in that role until 2017. He also served as the AACP chair of the Council of Deans for the 2018-2019 academic year.

Amy Friedman Wilson, PharmD’95, has served as interim dean following the retirement of J. Chris Bradberry, PharmD, in 2018.

Laham Receives an AACP Walmart Scholars Award

Delaney Laham was one of only 85 pharmacy students across the nation to receive a competitive American Association of Colleges of Pharmacy Walmart Scholars Award. Laham and her faculty mentor, Kevin Fuji, PharmD, associate professor of pharmacy practice, will attend the 2019 AACP Annual Meeting in Chicago. “Traditionally, the program has focused on students entering their P4 year or post-graduate training, so it is notable that Delaney received the award but is only entering her P3 year,” says Fuji. “I think this speaks to her clear passion and drive for a career in academic pharmacy, and the benefits of the structured mentoring relationship she and I have built together.”

Brown Receives a VALOR Internship

Mike Brown was the only pharmacy student accepted to the VALOR (VA Learning Opportunities Residency) internship at the Kansas City VA. VALOR is an honors program that provides opportunities for outstanding students in pharmacy to develop competency-based clinical practice skills while at an approved VA healthcare facility. Brown will be completing the internship at the Kansas City VA during the summer and upcoming academic year.
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EPA Ruling on the Handling of Hazardous Pharmaceuticals

Objectives
At the conclusion of this lesson, pharmacists and pharmacy technicians should be able to:
1. Explain the impact of EPA’s new ruling on handling hazardous pharmaceuticals in healthcare facilities.
2. Describe changes made in the classification of nicotine products as hazardous and non-hazardous waste.

Introduction
In February 2019 the Environmental Protection Agency (EPA) published updated information in the Federal Register on how all healthcare facilities should handle and dispose of hazardous pharmaceutical waste, which could drastically affect current practices in pharmacy. The final ruling, titled “Management Standards for Hazardous Waste Pharmaceuticals and Amendment to the P075 Listing for Nicotine,” contains distinctions between reverse distribution and reverse logistics centers, an amendment to the hazardous waste listing of nicotine products, and updates to the Resource Conservation and Recovery Act (RCRA) to better fit the healthcare sector while maintaining protection of human health and the environment. The nicotine listing amendment allows certain nicotine products to be treated as non-hazardous waste. Subpart P includes important information for healthcare facilities such as a ban on putting hazardous pharmaceuticals into the sewer system, determination of the point in which pharmaceuticals are considered solid waste, instructions on how to handle waste that is non-creditable or potentially creditable, and standards for containers to be considered “RCRA empty” and non-hazardous.
The reason for the EPA’s new ruling is to improve clarity, reduce the regulatory burden felt by healthcare facilities, and reduce concentrations of hazardous pharmaceuticals in surface and drinking water. The amount of pharmaceutical and other personal care products (PPCPs) contaminating aquatic environments is a growing concern. PPCP refers to “any product with healthcare or medical purposes for humans and/or animals.” Sewage treatment facilities are unable to remove all pharmaceutical products that enter the system; therefore, it is inevitable that some hazardous pharmaceutical products will still enter the environment. Pharmaceutical products enter the water system in many ways, but RCRA Part 266 Subpart P should reduce the amount of hazardous waste entering the environment by eliminating the practice of sewering hazardous pharmaceutical waste.

The ban on sewering hazardous waste went into effect for all healthcare facilities on August 21, 2019, with the adoption of Subpart P by certain healthcare facilities as early as 2020. Since the ban on sewering applies to all facilities, regardless of Subpart P adoption, pharmacies need to evaluate current methods of hazardous pharmaceutical waste disposal. Pharmacy professionals should understand the implications of the EPA’s final ruling and how to properly dispose of waste to lessen the impact of hazardous pharmaceutical waste on the environment.

RCRA and the Pharmaceuticals Final Rule
To better understand the new EPA ruling, it helps to explore the underlying Resource Conservation and Recovery Act of 1976. The Resource Conservation and Recovery Act, also known as RCRA, is contained within Title 40 of the Code of Federal Regulations (C.F.R.), specifically Parts 239-282. RCRA Subtitle D focuses on the management of non-hazardous solid waste, while Subtitle C is dedicated to hazardous solid waste. RCRA Subtitle C is a group of laws aimed at reducing the production of waste, determining which waste is considered hazardous, and tracking that hazardous material from production to destruction, or “cradle to grave.” For the purposes of this article, only hazardous waste will be discussed and RCRA Subtitle C will be referenced as RCRA.

The Nebraska Department of Environmental Quality (NDEQ), soon to be the Nebraska Department of Environment and Energy, was authorized by the EPA in 1985 to manage portions of RCRA in the state of Nebraska, and keep relevant chapters of Nebraska Administrative Code Title 128 updated as changes occur to the Federal RCRA regulations. The EPA began reviewing management of hazardous waste in 2008, and the Obama Administration tasked the EPA with reducing regulatory burden in 2011. The EPA collected input from various settings on the challenges faced in complying with regulations in the RCRA Retail Notice of Data Availability (Retail NODA) and used these comments to help shape Subpart P, which was first proposed in 2015. The final ruling containing the nicotine amendment, Subpart P, and reverse distribution and logistics distinction was signed by the EPA Administrator on December 11, 2018 and was published in the Federal Register on February 22, 2019.

Hazardous waste is addressed in C.F.R. Part 266 of RCRA, titled “Standards for the Management of Specific Hazardous Wastes and Specific Types of Hazardous Waste Management Facilities.” The EPA’s new ruling created a separate area to house regulations regarding hazardous pharmaceuticals in Part 266 Subpart P (referred to as Subpart P). Subpart P was designed to specifically address the management of hazardous waste pharmaceuticals within healthcare facilities and reverse distribution centers. Under previous regulations, healthcare facilities were tasked with managing hazardous waste in the same way as a manufacturer, even though the production and amount of waste differs significantly between settings. For example, a manufacturer may produce large amounts of one type of hazardous waste during a single point in the production line, while a healthcare facility will produce small amounts of many different types of waste at multiple points of operation. Pharmaceutical hazardous waste and the sector of healthcare have always been captured under RCRA, but the EPA’s new ruling has altered how they will be regulated moving forward. Although the new ruling and Subpart P has changed the practice of hazardous material handling in healthcare facilities, the EPA hopes it will provide clarity for hazardous waste management in healthcare facilities.
## Table 1 | Common Hazardous Pharmaceutical Products in Pharmacy Settings\(^{10,11,12}\)

<table>
<thead>
<tr>
<th>Hazardous Category</th>
<th>Example Pharmaceutical Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>P-listed</td>
<td>epinephrine, nicotine, nitroglycerin, phentermine, physostigmine, physostigmine salicylate, and warfarin &gt; 0.3%</td>
</tr>
<tr>
<td>U-listed</td>
<td>azaserine, chloral hydrate, chlorambucil, cyclophosphamide, daunomycin, hexachlorophene (pHisoHex Septisol), lindane, melphalan, methanol, methylthiouracil, mitomycin, paraldehyde, phenol, reserpine, resorcinol, selenium sulfide, streptozotocin, uracil mustard, and warfarin &lt; 0.3%</td>
</tr>
<tr>
<td>Ignitability</td>
<td>Methanol, silver nitrate, topical preparations such as erythromycin solution, Retin A gel, collodion-based preparations, Cleocin T solution, and rubbing alcohol if alcohol concentration &gt; 24%, including certain mouthwashes</td>
</tr>
<tr>
<td>Corrosivity</td>
<td>Concentrated solutions of acetic acid or sodium hydroxide</td>
</tr>
<tr>
<td>Reactivity</td>
<td>Lithium-sulfur batteries, nitroglycerin formulations</td>
</tr>
<tr>
<td>Toxicity</td>
<td>Mercury and mercury compounds, phenylmercuric acetate, m-cresol, lindane, and compounds with arsenic, barium, or other metals such as chromium, cadmium, selenium and silver</td>
</tr>
</tbody>
</table>

When discussing hazardous and non-hazardous waste, it is important to distinguish between waste that causes harm to the environment compared to waste that poses potential harm to personnel handling the products. The EPA has produced a list of products that are considered hazardous from the perspective of environmental protection, while the CDC’s National Institute for Occupational Safety and Health (NIOSH) has a list of hazardous products created to protect the individuals handling these items. Hazardous waste can be considered both hazardous by the CDC and the EPA such as arsenic trioxide and chemotherapy agents such as cyclophosphamide.\(^9\)

Although there is overlap between these lists, the products the EPA considers hazardous are described in Title 40 of the Code of Federal Regulations, Part 261. To be considered hazardous, a product must fall within one of the three EPA categories: P-listed, U-listed, or characteristically reactive. Characteristically reactive encompasses ignitability, toxicity, corrosivity and reactivity.\(^10\) Items that are P and U-listed differ in their degree of risk, with P-listed items considered acutely toxic, while U-listed are simply toxic.\(^11\) P-listed wastes are those that “can cause death or irreversible illness at low doses.”\(^12\) The EPA’s new ruling did not increase the number of pharmaceuticals that are considered hazardous, but rather how hazardous pharmaceuticals are handled and disposed. See Table 1 for a list of common P-listed, U-listed, and characteristically reactive products commonly found in pharmacy settings.\(^10,11,12\) For a complete listing of hazardous products, refer to RCRA Part 261.

### Nicotine Listing Amendment

Prior to the new EPA ruling, all products containing nicotine were P-listed and treated as acutely hazardous products. Under the EPA’s final pharmaceutical rule, an amendment was made to the nicotine listing in Part 261. Over-the-counter nicotine replacement products that are FDA approved...
will no longer be considered listed products, which will allow certain items to be discarded as non-hazardous pharmaceutical waste. Products that would fall under this distinction are nicotine lozenges, gum, and patches. Other nicotine replacement products will still be considered P-listed products and require hazardous waste management and disposal. Examples of products that will remain acutely hazardous are nicotine nasal sprays and inhalers, nicotine used in research and manufacturing, and e-liquid found in e-cigarettes, cartridges, and vials.

The nicotine amendment was created in part due to the large amount of nicotine waste produced by smaller facilities and retail settings such as pharmacies. The contribution of nicotine products to hazardous waste production was pushing facilities into larger generator classes, leading to increased regulation. After reviewing toxicity information, the EPA concluded that certain nicotine products do not meet the criteria for acutely hazardous waste under C.F.R. Title 40. Allowing FDA-approved OTC nicotine replacement products to be treated as non-hazardous waste could significantly reduce the burden on healthcare facilities and retail settings. Since this amendment is less restrictive than the prior requirements for nicotine disposal, healthcare facilities are not required to adopt this change and can treat all nicotine products as hazardous if desired. There is not a set date for when this amendment will go into effect in Nebraska, but it could occur as early as the second quarter of 2020. Healthcare facilities should continue to manage all nicotine products as P-listed waste until Nebraska’s adoption of the amendment.

Part 266 Subpart P
In theory, Subpart P will provide healthcare facilities and reverse distributors with a set of regulations that better reflect day-to-day operations and may reduce unnecessary regulatory burden. Complying with Subpart P may require healthcare facilities to make significant adjustments in current practices of hazardous waste pharmaceutical (HWP) disposal. One of the more notable changes Subpart P will bring to healthcare facilities will be that hazardous waste pharmaceuticals will be banned from being sewered. Subpart P also determines that hazardous waste pharmaceuticals that are sent to reverse distribution centers will be managed and regulated as hazardous waste while still at the healthcare facility, rather than waiting for this distinction to be made by the reverse distributor. Subpart P also changes the definition of when a container that once held a hazardous pharmaceutical can be considered empty and disposed of as non-hazardous waste.

According to the EPA, the new ruling will apply to all healthcare facilities and reverse distribution centers. A healthcare facility is defined as “any person that is lawfully authorized to: 1. Provide preventative, diagnostic, therapeutic, rehabilitative, maintenance or palliative care, and counseling, service, assessment or procedure with respect to the physical or mental condition, or functional status, of a human or animal or that affects the structure or function of the human or animal body; or 2. Distribute, sell or dispense pharmaceuticals, including over-the-counter pharmaceuticals, dietary supplements, homeopathic drugs, or prescription pharmaceuticals.”

This definition includes, but is not limited to, “wholesale distributors, third-party logistics providers that serve as forward distributors, military medical logistics facilities, hospitals, psychiatric hospitals, ambulatory surgical centers, health clinics, physicians’ offices, optical and dental providers, chiropractors, long-term care facilities, ambulance services, pharmacies, long-term care pharmacies, mail-order pharmacies, retailers of pharmaceuticals, veterinary clinics, and veterinary hospitals.” When referring to long-term care facilities, the EPA is including hospice facilities, nursing facilities, and skilled nursing facilities. Long-term care does not refer to group homes, independent living communities or assisted living facilities.

Although Subpart P is applicable to all healthcare facilities, there is an exemption for those that produce very little hazardous waste. Facilities that are considered very small quantity generators (VSQG) are not required to comply with Subpart P, but can choose to participate in the regulations. The term VSQG was introduced by the Hazardous Waste Generators Improvement Rule, which Nebraska has yet to adopt. Nebraska uses the older term Conditionally Exempt Small
Quantity Generator (CESQG). A VSQG, or CESQG in Nebraska, is one that produces 100 kilograms or less per month of hazardous waste or one kilogram or less per month of acutely hazardous waste. Since these terms refer to the same generator category, this article will use the term VSQG to match language in the EPA’s new ruling. If a facility is currently a small quantity generator (SQG) or large quantity generator (LQG), then they will be required to comply with Subpart P. For those facilities that follow Subpart P, hazardous waste pharmaceuticals are not required to be counted in determining a facility’s hazardous waste generator category. According to the EPA, “under Part 266 Subpart P, there are no generator categories, therefore, it is not necessary to know the quantity of hazardous waste pharmaceuticals being generated.” The EPA removed generator categories to encourage the treatment of more pharmaceutical waste as hazardous. The EPA hopes that this will decrease the amount of pharmaceutical waste entering the environment and remove the concern of moving up in generator category and acquiring additional regulations based on pharmaceutical hazardous waste production. Facilities can manage all pharmaceutical waste as hazardous, and only separate product by non-creditable and potentially creditable without concern for generator status.

See Table 2 for description of the EPA’s hazardous waste generator categories.

Subpart P also aims to clarify regulations that may fall on products that are both considered hazardous by the EPA and controlled by the DEA. Examples of products that are regulated by both entities are chloral hydrate, fentanyl sublingual spray, phenobarbital, testosterone gel and solutions, as well as diazepam gel and solutions. Chloral hydrate, U-listed for toxicity, is the only listed hazardous waste that is also DEA controlled. Although the active pharmaceutical ingredients of the other dually regulated substances are not hazardous, they are characteristically reactive due to their preparation in ignitable solutions. The new regulations state that hazardous waste pharmaceuticals that are also DEA controlled items are exempt from RCRA regulations as long as the items are not sewered, managed following DEA regulations, and destroyed in a way that the DEA has determined to be non-retrievable, or incinerated at an appropriate facility. Of note, the new rule maintains that hazardous waste pharmaceuticals produced in households and collected during pharmaceutical take-back programs and events are exempt from Subpart P if disposed of properly.

Once pharmaceutical waste is deemed hazardous, there are three different categorizations: non-creditable, potentially creditable, and evaluated. These categories are based on the ability for the waste to be returned to the manufacturer for credit. Non-creditable is described as having no reasonable expectation that the facility will receive manufacturer’s credit for returning a product. Examples the EPA has provided for non-creditable waste are floor swippings, items that are damaged or leaking, clean-up materials, investigational new drugs, waste not in the original manufacturer’s packaging, contaminated personal protective equipment, items that are over one year past their expiration date, and items that have been dispensed. A potentially creditable item is one that there is a reasonable expectation that a healthcare facility would receive credit from the manufacturer for the return of the product. Examples for this category would be items that have not been dispensed, unexpired or less than one year past the expiration date, and items in the original manufacturer’s
packaging unless it has been recalled. Products are only considered evaluated once their creditability has been determined by a reverse distributor or logistics center; therefore, this category has limited use for a healthcare facility. These categories determine the storage and shipping requirements to which healthcare facilities must adhere. See Table 3 for creditability of hazardous pharmaceutical waste.

The new ruling also provided clarification on when containers that once held hazardous materials need to be treated as hazardous waste and when they may be considered “RCRA Empty.” The new empty container standards apply to anyone with containers of hazardous waste pharmaceuticals, healthcare facilities, and reverse distributors following Subpart P. The standards include all containers with both acute and non-acute hazardous waste pharmaceuticals. If requirements are met, “RCRA empty” containers are not required to be treated as hazardous waste. The empty container standards include rules for four different container categories: stock bottles and unit dose containers, syringes, IV bags, and other. For stock bottles and unit dose containers to be considered empty, the contents of the container must be removed. Stock/dispensing bottles are those containing less than 1 liter or 10,000 tablets/capsules. Syringes, containing either acutely or non-acutely hazardous materials, must have the plunger fully depressed to be considered empty. IV bags need to have the contents fully administered to the patient for both acute and non-acute products. New RCRA regulations no longer recommend triple rinsing containers which held acutely hazardous materials, meaning IV bags with remaining acutely hazardous material “must be placed with its remaining hazardous waste pharmaceuticals into a container that is managed and disposed of as non-creditable.” If the IV bag contains non-acute HWP it can be treated as empty under C.F.R Title 40 § 261.7(b)(1). Containers that have held non-acutely hazardous waste are considered empty when all the product has been removed using common practices such as pouring, pumping and aspirating. In addition, no more than one inch of residue can remain at the bottom of the container, or no more than 3% by weight of the total container capacity if the container is less than or equal to 119 gallons or 0.3% by weight if the container is greater than 119 gallons in size. Containers that do not fit into one of the previous three categories (inhalers, tubes of creams/gels, nebulizers, etc.) fall into the “other containers” category. Within this category, if the container held acutely hazardous material then it cannot be considered RCRA empty. If it contained non-acutely hazardous material it should be treated following C.F.R Title 40 § 261.7(b)(1) or (2) depending on the container type. C.F.R Title 40 § 261.7(b)(2) states that “a container that has held a hazardous waste that is a compressed gas is empty when the pressure in the container approaches atmospheric.” These distinctions will allow facilities to better distinguish between which containers can be disposed of as non-hazardous waste.

Specifics of the new regulations are dependent on the type of facility and the type of hazardous waste pharmaceutical, with different rules for healthcare facilities compared to reverse distributors and logistics centers. Prescription hazardous pharmaceutical waste requires separate procedures than non-prescription or retail items, and non-creditable waste is handled differently than material that is potentially creditable. To appropriately handle pharmaceutical waste, healthcare facilities need to separate hazardous waste materials into items that are potentially creditable vs. non-creditable, and

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Creditability of Hazardous Pharmaceutical Waste</th>
</tr>
</thead>
<tbody>
<tr>
<td>Potentially Creditable</td>
<td>Reasonable expectation that credit would be received from the manufacturer for the return of the product. Ex: undispensed, unexpired or less than &lt; 1 year past expiration, original manufacturer packaging</td>
</tr>
<tr>
<td>Non-Creditable</td>
<td>No reasonable expectation that credit will be received from the manufacturer for the return of the product. Ex: dispensed, damaged, leaking, clean-up materials, floor sweepings, investigational new drugs, &gt; 1 year past expiration, not in original manufacturer packaging, contaminated personal protective equipment</td>
</tr>
<tr>
<td>Evaluated</td>
<td>Creditability has been determined by a reverse distributor or logistics center</td>
</tr>
</tbody>
</table>
the potentially creditable items into those that are prescription vs. non-prescription.\textsuperscript{1} Items that are non-creditable, prescription and non-prescription, need to be sent to a Treatment, Storage and Disposal Facility (TSDF).\textsuperscript{29} Prescription HWP should be sent to a reverse distribution center if there is the potential for manufacturer’s credit, and a non-prescription product or retail item should be sent to a reverse logistics center if there is a reasonable assumption it could be reused or reclaimed.\textsuperscript{1,30} If the hazardous pharmaceutical waste is a prescription pharmaceutical product, it will now be considered solid waste regardless of creditability at the healthcare facility, rather than the reverse distributor.\textsuperscript{1} According to the EPA’s new ruling, over-the-counter and other non-prescription pharmaceuticals “are not considered solid or hazardous wastes when they are sent through reverse logistics for the purpose of determining whether they can be redistributed for their intended purpose or legitimately reused or reclaimed.”\textsuperscript{1} If the waste is a non-prescription product, or a retail item, then the distinction of hazardous solid waste is dependent on the creditability. Items that are determined to be non-creditable are considered solid waste at the healthcare facility, but those that are potentially creditable will not be considered solid waste until the determination is made by the reverse logistics center and therefore are not subject to Subpart P at the healthcare facility.\textsuperscript{1,31}

Storage and shipment requirements are also based on the product’s creditability and whether the waste is prescription or non-prescription. Items that are determined by the healthcare facility to be non-creditable need to be kept in a container that is structurally sound, will not react with the contents, and can be kept closed and secured to prevent unauthorized access.\textsuperscript{32} Non-creditable products can be accumulated at the healthcare facility for one year without needing a RCRA permit, and the container must be labeled with “Hazardous Waste Pharmaceuticals.”\textsuperscript{33} Non-creditable products must be sent to a TSDF through an appropriate hazardous waste transporter and with the appropriate manifest code, “PHARMS.”\textsuperscript{29} For items that are potentially creditable, there are no labeling requirements, limits on accumulation time, or container requirements or storage standards set by the EPA.\textsuperscript{1} Potentially creditable prescription pharmaceutical hazardous waste should be sent to a reverse distributor, and these items do not require a hazardous waste transporter or manifest to be shipped to their appropriate location. Common carriers such as UPS or FedEx, are allowed for shipment of these potentially creditable products, but the facility shipping the products must receive confirmation of delivery to the reverse distribution or logistics center within 35 days of the shipment date.\textsuperscript{30,34} Electronic confirmation usually supplied by common carriers should meet these requirements, and records of receipt should be kept for three years.\textsuperscript{35} The EPA has put these requirements in place to ensure the whereabouts of hazardous waste can be tracked from cradle to grave. See Table 4 for storage, labeling, and accumulation requirements, and Figure 1 for shipment information.

<table>
<thead>
<tr>
<th>Waste Categories</th>
<th>Potentially Creditable Prescription HWP</th>
<th>Potentially Creditable Non-Prescription HWP</th>
<th>Non-Creditable HWP (Prescription &amp; Non-Prescription)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solid Waste Status</td>
<td>Considered solid waste at the healthcare facility</td>
<td>Not considered solid waste at the healthcare facility</td>
<td>Considered waste at the healthcare facility</td>
</tr>
<tr>
<td>Storage Requirements</td>
<td>No storage requirements by EPA</td>
<td>No storage requirements by EPA</td>
<td>Container that is structurally sound, will not react with contents, and prevents unauthorized access.</td>
</tr>
<tr>
<td>Labeling Requirements</td>
<td>No labeling requirements by EPA</td>
<td>No labeling requirements by EPA</td>
<td>Container must state “Hazardous Pharmaceutical Waste”</td>
</tr>
<tr>
<td>Accumulation Limits</td>
<td>No accumulation limit</td>
<td>No accumulation limit</td>
<td>1 year accumulation limit</td>
</tr>
</tbody>
</table>
Prohibition of Sewering

Although many sections of Subpart P will affect current practices for disposal of hazardous pharmaceuticals in healthcare facilities, the section that may have the greatest impact is the sewer ban. Pharmaceutical products can enter the groundwater through sewering of products from both households and healthcare facilities, discarded products leaching into groundwater from landfills, and elimination of pharmaceuticals in urine and feces. Although the EPA acknowledges that the sewer ban will not remove contributions from human elimination of consumed medications or sewering and discarded items from households, it does estimate that adopting Subpart P could reduce the amount of pharmaceutical waste in the water by 1,644-2,300 tons annually.\(^2\)

The prohibition of sewering is contained within Subpart P, but the ban applies to all healthcare facilities and reverse distributors, regardless of whether Subpart P is adopted.\(^5\) The ban is universal regardless of adoption since the rule was promulgated under the authority of Hazardous and Solid Waste Amendments (HSWA).\(^1\) The sewer ban only applies to hazardous waste pharmaceuticals or items that are dually regulated by the EPA and DEA, but the EPA strongly discourages sewering of any pharmaceuticals by any entity.\(^{1,5}\) Since the practice of putting hazardous pharmaceutical material down a sink or flushing is fairly common practice in healthcare facilities to make a product irretrievable, alternative disposal methods should be considered.

Preparation for Subpart P Adoption

Although Subpart P may not be adopted in Nebraska until 2020, pharmacies and other healthcare facilities should evaluate their current practices and the steps that need to be taken to comply with the new regulations. First, the EPA Regional Administrator will need to be notified of Subpart P compliance through form 8700-12.\(^{1,37}\) This notification requirement is only applicable to facilities that are currently a SQG or larger, those that are required to follow Subpart P, and will be due 60 days prior to the effective date of Subpart P in Nebraska. There are no notification time requirements for VSQG who choose to operate under Subpart P, but the facility must be in compliance at the time of their form submission. If a facility currently files biennial reports, then they may submit form 8700-12 in accordance with their biennial reporting schedule.\(^{1,37}\) EPA notification is dependent on a facility’s current generator status and indicates to the EPA that the entity is operating under Subpart P.

One of the most important steps in preparing for implementing Subpart P is to determine which inventory items are considered hazardous by the EPA and to create a system to properly sort hazardous by the EPA and to create a system to properly sort:
facilities are encouraged to treat all pharmaceutical waste as hazardous, and therefore, are not required to separate items by acute and non-acutely hazardous.\textsuperscript{17,18} Hazardous pharmaceutical waste should, at a minimum, be separated into items that are non-creditable and those that are potentially creditable, with the potentially creditable items further broken down into those that are prescription and non-prescription. Refer to C.F.R. Title 40 § 261.2 for a list of hazardous pharmaceutical waste products.

Facilities that produce non-creditable hazardous waste pharmaceuticals need to ensure that employees are properly trained to manage hazardous material. Employees should be familiar with the proper handling and the emergency procedures related to the hazardous pharmaceutical waste relative to their job description. Documentation of this training is not required, but it is beneficial to keep records of any training completed.\textsuperscript{38} See Table 5 for a checklist to aid in preparation for Subpart P.

### Important Dates and Resources

With all the changes required by the final pharmaceutical ruling, pharmacies and healthcare facilities should know when each part goes into effect and what resources are available to make the transition easier. Regardless of whether Subpart P applies to or is adopted, the ban on sewering for all healthcare facilities and reverse distributors began on August 21, 2019.\textsuperscript{15} The timeline for Subpart P adoption will vary from state to state, and will not be applicable to all healthcare facilities depending on their current generator status. Subpart P is considered more stringent than previous regulations and is not optional for states to adopt.\textsuperscript{4,40} Subpart P adoption could happen as early as 2020 in the state of Nebraska.

The nicotine amendment will not go into effect until adopted by individual states and is not required to be adopted since the amendment is less restrictive than previous treatment of nicotine products. Since there is no deadline for states to adopt the amendment to the nicotine listing, healthcare facilities should continue to treat nicotine products as hazardous waste at this time. For more information on the EPA’s new ruling and how it will affect healthcare facilities, visit the EPA website, where you can find quick summaries of the changes, a free webinar on the topic, and a link to the final rule in the Federal Register.

### Conclusion

Although some components of the EPA’s final ruling may not go into effect in Nebraska until 2020, it is important to evaluate how hazardous pharmaceutical waste is currently managed, and what will need to change in the coming years. Pharmacy professionals must always be mindful of how the pharmaceutical waste produced can impact the environment, and what measures can be taken to reduce harm. These changes will provide healthcare entities with regulations that better reflect their day-to-day operations and can provide more clarity on how to best handle pharmaceutical hazardous waste.

### Table 5 | Checklist for Subpart P Preparation\textsuperscript{39}

- [ ] Determine your generator status – LQG & SQG are subject to Subpart P
- [ ] If you are a VSQG, or CESQG, determine whether it makes sense to opt-in to Subpart P
- [ ] Determine which products in inventory are considered hazardous by the EPA. Mark these products physically or electronically
- [ ] Restrict sewering of any hazardous waste pharmaceutical material by August 21, 2019
- [ ] Know which HWP should be sent to reverse distribution, reverse logistics center, or a Treatment, Storage and Disposal Facility
- [ ] Select a Reverse Distributor if the facility creates potentially creditable prescription HWP
- [ ] Select a Reverse Logistics center if the facility creates potentially creditable non-prescription HWP
- [ ] Select a Hazardous Waste Vendor if the facility creates non-creditable HWP
- [ ] Ensure supplies for proper disposal are available: waste containers, personal protective equipment, etc.
- [ ] If subject to Subpart P, ensure employees have proper training on the handling of non-creditable HWP and document completed training
- [ ] If compliant with Subpart P, inform EPA Regional Administrator of compliance through form 8700-12. If required to comply with Subpart P, reporting is required 60 days prior to the effective Subpart P date.
References

17. Amendment to 40 C.F.R. § 266.502(c) as published February 22, 2019, in 84 FR 5939. Effective date August 21, 2019.
18. Amendment to 40 C.F.R. § 266.503(a) as published February 22, 2019, in 84 FR 5939. Effective date August 21, 2019.
19. Amendment to 40 C.F.R. § 266.506(a) (t) & (b) as published February 22, 2019, in 84 FR 5939. Effective date August 21, 2019.
25. Amendment to 40 C.F.R. § 266.507(c) as published February 22, 2019, in 84 FR 5939. Effective date August 21, 2019.
27. Amendment to 40 C.F.R. § 266.507(d) as published February 22, 2019, in 84 FR 5939. Effective date August 21, 2019.
30. Amendment to 40 C.F.R. § 266.509(a) as published February 22, 2019, in 84 FR 5939. Effective date August 21, 2019.
32. Amendment to 40 C.F.R. § 266.502(d) as published February 22, 2019, in 84 FR 5939. Effective date August 21, 2019.
33. Amendment to 40 C.F.R. § 266.502(e) & (f) as published February 22, 2019, in 84 FR 5939. Effective date August 21, 2019.
34. Amendment to 40 C.F.R. § 266.509(b) as published February 22, 2019, in 84 FR 5939. Effective date August 21, 2019.
35. Amendment to 40 C.F.R. § 266.503(e) as published February 22, 2019, in 84 FR 5939. Effective date August 21, 2019.
37. Amendment to 40 C.F.R. § 266.502(a) as published February 22, 2019, in 84 FR 5939. Effective date August 21, 2019.
38. Amendment to 40 C.F.R. § 266.502(b) as published February 22, 2019, in 84 FR 5939. Effective date August 21, 2019.

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2. If more than three questions are missed, the quiz will be returned. The quiz can be resubmitted.
3. CPE transcripts can be printed from NABP e-Profiles at www.nabp.net.
4. CPE credits are submitted to NABP by the 15th of each month. For example, M&P CPE quizzes completed in the month of August 2019 will be sent to NABP e-Profiles before September 15, 2019.

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Quiz Answers may be submitted:

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Mail: Nebraska Mortar & Pestle
6221 S 58th St, Ste A
Lincoln, NE 68516
EPA Ruling on the Handling of Hazardous Pharmaceutical Waste

Quiz #11, July/August 2019, ACPE 0128-0000-19-044-H03-P/T

1. When does the ban on sewering hazardous pharmaceuticals go into effect?
   a. After each individual state chooses to adopt the ban.
   b. August 21, 2019
   c. January 1, 2020
   d. July 1, 2020

2. Which of the following is included in the EPA's new ruling?
   a. Additional items classified as hazardous pharmaceutical products.
   b. Amendment to the listing of certain nicotine products.
   c. Ban on sewering of all waste regardless of hazardous classification.
   d. Encouraging sewering of products that are not considered hazardous.

3. What is the appropriate method to handle hazardous pharmaceutical waste when the product is dually regulated by RCRA and the DEA?
   a. There are no pharmaceutical products dually regulated by the EPA and DEA.
   b. Treat dually regulated products as if they were non-controlled.
   c. Waste must be sewered to be considered non-retrievable by the DEA.
   d. Waste should not be sewered, but should be destroyed in a way that the DEA has determined to be non-retrievable or incinerated at an appropriate facility.

4. The EPA describes hazardous waste pharmaceuticals as non-creditable when:
   a. The common courier determines that credit will not be received.
   b. The facility has no reasonable expectation that the manufacturer will provide credit for the product’s return.
   c. The pharmaceutical product is < 6 months past expiration.
   d. The product is no longer being produced by the manufacturer.

5. Potentially creditable items require:
   a. Original manufacturer packaging
   b. Undispensed
   c. Unexpired or < 1 year past date of expiration
   d. All of the above

6. When reviewing hazardous waste, healthcare facilities should first separate items into potentially creditable and non-creditable waste. Items that are potentially creditable waste should then be separated into:
   a. Expired and non-expired
   b. Items do not need to be further separated
   c. Prescription and non-prescription
   d. Solid dosage forms and liquid dosage forms

7. Which of the following scenarios represents the proper method of hazardous pharmaceutical waste shipment?
   a. All potentially creditable waste should be sent to a TSDF through a common carrier.
   b. If a common courier is used to transport potentially credible waste, the shipping facility must receive receipt of delivery within 35 days.
   c. Waste deemed non-creditable should be sent to a TSDF through common courier.
   d. Waste is only sent to a reverse logistics center if considered non-creditable.

8. The EPA predicts that adopting Subpart P could reduce the amount of pharmaceutical waste in the water by:
   a. 500 tons total
   b. 1,644-2,300 pounds
   c. 1,644-2,300 tons annually
   d. 2,000 tons in the first 5 years

9. The type of pharmaceutical products regulated under the new sewer ban include:
   a. All hazardous waste pharmaceuticals, but the EPA discourages sewering any pharmaceutical products.
   b. All waste produced outpatient settings.
   c. Any excipients used in the manufacturing process.
   d. Any intravenous solutions.

10. Healthcare facilities should notify EPA Regional Administrators through form 8700-12 when:
    a. Choosing to opt-out of Subpart P.
    b. Compliance with Subpart P has been met.
    c. Compliance with the sewer ban has been met.
    d. Form 8700-12 is not required if complying with Subpart P.

Keep the TOP portion for your records. Return the BOTTOM portion to the NPA office. Or, take this quiz online at www.npharm.org.

Name ___________________________________________
Mailing Address ____________________________________
City/State/Zip ______________________________________

2019 Quiz #11 - EPA Ruling on the Handling of Hazardous Pharmaceutical Waste
ACPE #0128-0000-19-044-H03-P for Pharmacists
ACPE #0128-0000-19-044-H03-T for Technicians
1.5 Contact Hours - Knowledge Based CPE Activity

The deadline for this quiz is December 12, 2019.

Circle one (1) Answer:
1. a b c d
2. a b c d
3. a b c d
4. a b c d
5. a b c d
6. a b c d
7. a b c d
8. a b c d
9. a b c d
10. a b c d

CPE Home Study Evaluation
1. Rate this lesson: (Excellent) 5 4 3 2 1 (Poor)
2. Did this lesson meet each of its objectives? ___ Yes ___ No
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   If not, please explain ____________________________________________
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**Member Spotlight**

**SHANNON SHORT, DIRECTOR OF PHARMACY**

**Where do you practice?** Cardinal Health Innovative Delivery Solutions, Brodstone Memorial Hospital, Superior, Nebraska

**What inspired you to pursue a career in pharmacy?** Shannon grew up around health care in Salina, Kansas. He liked science and helping others making pharmacy a great fit. Initially, he was interested in compounding pharmacy until he was an intern at Lawrence Memorial Hospital working with clinical pharmacists providing direct patient care. His rotations during pharmacy school at the Kansas University School of Pharmacy strengthened this passion. Shannon completed a PGY-1 residency at Wesley Medical Center in Wichita, Kansas.

**Who is your role model/mentor?** Shannon values helping others and learning from others. He considers the CEO of Brodstone Memorial Hospital, Treg Vyzourek, an important mentor who has helped him grow and gain a better understanding of pharmacy operations, budgeting, and the big picture of patient care in the hospital. Shannon has also learned a great deal regarding pharmacy management and best practices from his manager with Cardinal Health, Dave Olson.

**What do you enjoy most about your job?** Shannon enjoys interacting with patients and members of the health care team. Shannon looks for opportunities to take information that might be confusing to a patient and make it more practical and useable. He likes the working environment at Brodstone Memorial.

**What is the hardest part of your job?** Shannon identifies time and project management as the greatest challenges of his position, especially as he has many roles in the hospital. He does a lot of reading to find successful ideas on management to implement at Brodstone Memorial.

**What have you done to improve pharmacy services at Brodstone?** Shannon has worked to strengthen the pharmacy’s protocols and best practices. He has implemented clinical pharmacy rounding services and attends patient rounds with select providers every day. Shannon has set up a clinical rotation site for pharmacy students from the University of Kansas School of Pharmacy as well as the University of Nebraska Medical Center. He also works with pharmacy technician students from Central Community College in Hastings to provide clinical experience. He has worked closely with Austin Farnstrom, a clinical staff pharmacist, to enhance the antibiotic stewardship program at Brodstone. Shannon advocated for upgrading all infusion pumps at the hospital with smart pumps which have additional safety features. He is on a Steering Committee to oversee implementation of Substance Misuse strategies in partnership with South Heartland District Health Department. Shannon has worked to expand outpatient infusion services, including designing a USP Chapter <800> compliant chemotherapy infusion suite. He also founded a national user group with his EHR vendor, CPSI Health, for pharmacists. This platform has served as a role model for other user groups within the company. Shannon is currently working on a team to design a pharmacy EHR to improve pharmacy order management with CPSI.

**How has being a member of NPA helped you professionally?** Shannon finds the NPA to be vital to networking and finding important resources. As he was not originally from Nebraska, he was able to develop a grass roots network with other pharmacists in Critical Access Hospitals (CAHs).
A GUIDE TO THE UPDATES IN USP <795> NONSTERILE COMPOUNDING AND USP <797> STERILE COMPOUNDING

Written by
Ku'ulei Stuhr

This continuing pharmacy education lesson was written by Ku'ulei Stuhr, PharmD Candidate, University of Nebraska Medical Center College of Pharmacy who does not have any conflicts of interest, nor does she have any financial relationships with a commercial interest related to this continuing pharmacy education activity.

Objectives
At the conclusion of this lesson, pharmacists and pharmacy technicians should be able to:
1. Identify important changes between the current and updated USP Chapter <795>.
2. Describe new sections in the updated USP Chapter <795> and Chapter <797> including, but not limited to: labeling requirements, record keeping requirements, and how to handle complaints and adverse drug effect reports.
3. Identify important changes between the current and updated USP Chapter <797>.

Introduction
On December 1, 2019, the updates released by the United States Pharmacopeia (USP) on nonsterile and sterile compounding standards (USP Chapter <795> and USP Chapter <797>) will go into effect. These new standards will impact all facilities and personnel who compound. In addition, USP Chapter <800> will go into effect at the same time and outlines the handling of drugs in a healthcare facility that are considered hazardous by the National Institute for Occupational Safety and Health (NIOSH). The proposed updates were posted on March 30, 2018 (USP <795>) and July 27, 2018 (USP <797>) with the intention to better align these chapters with the new USP <800>. All three chapters are now formatted to present related sections aligned in a similar order.

The two chapters were officially published on June 1, 2019 and had significant changes from the current chapters and from that which the expert committee had proposed in March and July of 2018. Although changes in this article are not all-inclusive, the goal is to summarize the changes that will affect pharmacy professionals who compound. These new chapters must be reviewed before they go into effect so that any necessary changes to a facility’s standard operating procedures and related compounding activities can be addressed in order to meet them.

USP Chapter <795>
New Definition
In the USP Chapter <795> update, minimum standards for compounded nonsterile products (CNSPs) are described. Nonsterile compounding is defined as “combining, admixing,
diluting, pooling, reconstituting other than as provided in the manufacturer package insert, or otherwise altering a drug or bulk drug substance to create a nonsterile medication."² Based on this definition and the practices that are not subject to chapter requirements, activities such as reconstituting antibiotic suspensions with water or preparation of erythromycin/benzoyl peroxide with ethyl alcohol, is not considered compounding. Reconstitution per the manufacturer's guidelines is not considered compounding as long as the product is for an individual patient and is not stored for future use. Activities such as splitting tablets, repackaging, and administration of single doses are also not subject to the requirements of this chapter.²

Personnel Training and Evaluation
Per the current standards, all members who perform compounding are responsible for ensuring that proper training is in place and is reinforced.³ In the updated <795>, a designated person (or persons) is now responsible for all procedures and operations that involve the preparation of CNSPs. This requirement for a designated individual is uniform with the revised USP Chapters <797> and <800> requirements. These responsibilities are enumerated as follows:²⁴
- Establishing, monitoring and documenting procedures for handling and storing CNSPs and components.
- Establishing, monitoring and documenting procedures for handling and storing CNSPs and components.
- Overseeing a training program.
- Selecting components.
- Monitoring and observing compounding activities and taking immediate corrective action if deficient practices are observed.
- Deciding if staff will be allowed to compound while experiencing certain conditions (i.e. rashes or the common cold).
- Ensuring that standard operating procedures (SOPs) are fully implemented and follow-up is carried out if problems, deviations or errors are identified.

The new training requirements for personnel involved in the preparation and handling of CNSPs differs from the current standards in many ways. Personnel involved in preparation of CNSPs must be initially trained, must demonstrate competency, and must undergo refresher training every 12 months. When the designated person develops this training, he or she must ensure that proficiency can be demonstrated in a set of basic core competencies as described in the new standards. These core competencies include hand hygiene, garbing, cleaning and sanitizing, component selection, handling and transport, performing calculations, measuring and mixing, use of equipment, and documentation.²

Personal Hygiene and Garbing
Although the current chapter requires "good hand hygiene and clean clothing appropriate for type of compounding," it fails to go into detail about how to define this requirement.³ In the updated chapter, there is more detail about hand hygiene procedures as well as garb and glove requirements for preparation of CNSPs. Personnel must remove personal outer garments (such as hats and scarves), remove all exposed jewelry, remove headphones/earphones, and keep nails clean and neatly trimmed. Hand hygiene is required when initially entering the compounding area, when re-entering after a break, and before initiating any activity in relation to a new CNSP. There is also a specific hand hygiene procedure that is to be followed for all compounding activities:²
1. Wash hands and forearms to the elbows with soap and water for at least 30 seconds.
2. Dry completely with disposable towels or wipes.
3. Hands and forearms should be allowed to thoroughly dry before putting on gloves.

Gloves are now required for all compounding activities regardless of the hazard risk or whether or not the final product needs to be sterile. Other garb is used when appropriate depending on the type of compounding being performed.

Building and Facilities
This heading is now divided into compounding space, storage area and water sources. Facilities that prepare CNSPs are now required to designate a space, as described in the SOP, that is specifically for compounding and separated from areas not directly related to compounding activities. They also must be set in a way that minimizes cross-contamination from non-compounding areas. There is no requirement for there to be walls or doors that partition this area, but it must be separate, clearly distinct, and only used for compounding activities. Carpet is not allowed in the compounding area and all surfaces must be easily cleanable and not easily damaged by cleaning products. Surfaces must be cleaned at a minimum of every three months (walls, ceilings, and storage shelving) or daily (floors) in addition to cleaning after spills or when the surface is contaminated.² Work surfaces must be cleaned at the beginning and end of each shift, when contamination is suspected, and between the preparation of compounds with different ingredients.

There is a new requirement for the continuous temperature monitoring of the area where CNSPs components are stored. Continuous recording devices or a once daily manual recording (when facility is open) of temperatures is permitted. Discarding
of components is also required if it is determined that temperature excursions exceed established limits causing loss of component integrity or quality.2

In addition to the requirement of an easily accessible sink with a source of hot and cold water, the sink must also be empty and cleaned before being used to clean equipment. There cannot be any defects in the plumbing system linked to the sink. It is also recommended, but not required, that purified, reverse osmosis, or distilled water be used to rinse equipment.2

Equipment and Components
A most notable change in required equipment is the addition of a closed system processing device. All compounding activities that may create airborne contamination from drug particles must be performed in a closed system processing device such as a containment ventilated enclosure (CVE), a biological safety cabinet, or a single use disposable glove bag.2 This requirement is only specific to drugs being used that are manufactured and acquired in a powder formulation. Note that tablet splitting of manufactured drugs is exempted from this chapter but crushing a dosage form could generate airborne chemical particles and that may have to be conducted in a closed system processing device.

Master Formulation and Compounding Records
A master formulation is a “detailed record of procedures that describes how the CNSP is to be prepared” and is required for each unique formulation of a CNSP.2 Any changes made to a master formulation must be approved and documented according to the facility’s SOPs. A compounding record documents each time a CNSP is made and is required for every instance that a CNSP is prepared. The requirements for both the master formulation and the compounding records per the new standards are in Table 1. This section was also added to the updates in USP <797> and applies to the preparation of sterile compounds. All compounding records require review for completeness and the person completing the review must sign or initial the record. The chapter, however, does not specify that this person has to be a pharmacist or the designated person.2

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Requirements for Master Formulation and Compounding Records²</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Master Formulation Record Requirements</strong></td>
<td><strong>Compounding Record Requirements</strong></td>
</tr>
<tr>
<td>Name, strength, and dosage form</td>
<td>Name, strength, and dosage form</td>
</tr>
<tr>
<td>Identities and amounts of all components</td>
<td>Date and time of preparation</td>
</tr>
<tr>
<td>Any relevant characteristics of components (if applicable)</td>
<td>Assigned internal identification number such as a prescription number</td>
</tr>
<tr>
<td>Physical description of final product</td>
<td>Name, vendor or manufacturer, lot number, and expiration date of each component</td>
</tr>
<tr>
<td>Type and size of container-closure systems</td>
<td>Weight or measurement of each component</td>
</tr>
<tr>
<td>Complete instructions including equipment and supplies necessary</td>
<td>Total quantity compounded</td>
</tr>
<tr>
<td>Beyond-use date assignment and storage requirements</td>
<td>Beyond-use date assignment and storage requirements</td>
</tr>
<tr>
<td>Reference source of the beyond-use date assignment and storage requirements</td>
<td>Identity of all individuals involved in each step</td>
</tr>
<tr>
<td>Calculations to determine and verify quantities/concentrations of components and strengths/activity of API (if applicable)</td>
<td>Calculations to determine and verify quantities/concentrations of components and strengths/activity of API (if applicable)</td>
</tr>
<tr>
<td>Labeling requirements (e.g. shake well)</td>
<td>Physical Description of final product</td>
</tr>
<tr>
<td>Quality control procedures (if applicable)</td>
<td>Results of quality control procedures (if applicable)</td>
</tr>
<tr>
<td>Other information needed to ensure repeatability (if applicable)</td>
<td>Master formulation record reference (if applicable)</td>
</tr>
</tbody>
</table>

Release Inspections
A release inspection is required for preparations at the completion of compounding and before dispensing. The CNSP must be visually inspected to ensure that its physical appearance is as expected. The inspection must also include:²
- Labeling to match the Compounding Record and prescription/chart order.
- Certain characteristic of the compounded formulation.
- Other tests required by the Master Formulation Record for the CNSP (e.g., sampling test results for capsule uniformity).
- Visual inspection of the container-closure integrity.

Labeling
“Labeling” is defined as all labels and written, printed, or graphic matter on a product’s immediate container or on/in any package or wrapper that contains the product. A “label” is the part of labeling that is on the immediate container.² Although labeling specifications are a part of normal practice in compounding, the requirements were not specified in the currently accepted standards. See Table 2 for a summary of label and labeling requirements for CNSPs products.
Establishing Beyond-Use Dates

As a review, the definitions of an expiration date and a beyond-use date (BUD) are:

- **Expiration Date** - Time during which a conventionally manufactured drug product is expected to maintain its labeled identity, strength, purity, and quality in its specific container if it is kept at provided storage conditions.
- **BUD** - Time period after which a CNSP must not be used and must be discarded.

If a compounded preparation monograph is available for a specific CNSP via USP or National Formulary (NF), then the BUD described in that monograph must be used. If one is not available, all physical and chemical aspects of the compound should be considered when determining a BUD. The updated standards, however, do provide a maximum BUD recommendation for cases where specific stability information is not available. For this guideline to apply, the CNSP must be packaged in a tight, light-resistant container. See Table 3 for summary of the maximum BUD allowed for nonsterile compounds based on the preparation.

The updates also provide circumstances in which shorter BUDs may be necessary. These are:

- Active pharmaceutical ingredient (API) or any other ingredients/components have an expiration date that is earlier than the assigned BUD.
- If other compounded preparations are utilized in compounding another CNSP, then the BUD of the final product shall not exceed the shortest remaining BUD on any of the used preparations.
- APIs or other ingredients that are known to be susceptible to decomposition.

Regardless of chemical and physical characteristics and any available antimicrobial activity information, assigned BUDs cannot exceed 180 days.

### Standard Operating Procedures

A significant change in the revised <795> occurs in the SOP section. It requires that SOPs must be developed for all aspects of the compounding operations. The current chapter only recommends their development. The new revision requires that all personnel who conduct or oversee these activities must be trained in the SOPs and ensure that they are followed. The responsibility for ensuring that all SOPs are fully implemented, and any problems, deviations or errors are addressed falls to an individual or individuals designated by the facility.

### CNSP Packaging and Transporting

This new section requires the SOPs to describe the packaging materials needed to protect both the CNSPs and personnel. It also addresses the transporting of CNSPs and requires that SOPS describe mode of transportation, special handling instructions and the necessity of temperature monitoring devices.

### Complaints and Adverse Events

The handling of complaints and adverse drug events reporting is a new section and provides a guidance on how these situations should be handled.

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**Table 2 | Label/Labeling Requirements for Compounded Nonsterile Products**

<table>
<thead>
<tr>
<th>Label Requirements</th>
<th>Labeling Requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assigned internal identification number (such as a prescription number)</td>
<td>Route of administration</td>
</tr>
<tr>
<td>Active component or API and its amounts, activities or concentrations</td>
<td>Indication that the preparation is a compound</td>
</tr>
<tr>
<td>Dosage form</td>
<td>Any special handling directions</td>
</tr>
<tr>
<td>Total amount or volume in each container</td>
<td>Any applicable warning statements</td>
</tr>
<tr>
<td>Storage conditions if other than controlled room temperature</td>
<td>Name, address, and contact information of compounding facility if CNSP is to be sent outside of facility in which it was originally compounded</td>
</tr>
<tr>
<td>Beyond-use date</td>
<td></td>
</tr>
</tbody>
</table>

**Table 3 | Recommended Maximum BUDs for CNSP**

<table>
<thead>
<tr>
<th>Type of Preparation</th>
<th>Maximum BUD in days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-preserved aqueous dosage form</td>
<td>14 days in refrigerator</td>
</tr>
<tr>
<td>Preserved aqueous dosage form</td>
<td>30 days at controlled room temperature/reefrigerator</td>
</tr>
<tr>
<td>Non-aqueous dosage form</td>
<td>90 days at controlled room temperature/reefrigerator</td>
</tr>
<tr>
<td>Solid dosage form</td>
<td>180 days at controlled room temperature/reefrigerator</td>
</tr>
</tbody>
</table>
handled for CNSPs. The designated person must review all complaints to determine if there is a potential quality problem with the CNSP. Investigation must be initiated and completed if a quality problem is indicated. All complaints must be kept as a written or electronic record and must contain the name of the complainant, date received, nature of complaint, and the response. If an investigation was completed, its findings and any follow-up must be included.2,4

The designated person (or persons) must also review all reports of potential ADEs. If other patients may be harmed, then those potential patients and their prescribers must be informed. All ADEs must be reported according to state regulations and to the FDA via the MedWatch program for human drugs and via form FDA 1932a for animal drugs.2,4

**USP Chapter <797>**

**Scope**

The standards described in USP <797> are intended to prevent harm to patients that could result from microbial contamination, excessive bacterial endotoxins, variability from intended strength, chemical/physical contaminants, and ingredients of unacceptable quality in compounded sterile products (CSPs). USP <797> is applicable to all persons and places involved in CSP preparation. This chapter, however, does not apply to the administration of sterile products, proprietary bag and vial systems, repackaging, and reconstitution/dilution of a commercially manufactured product in accordance to labeling.5

Immediate use of CSP is not subject to the requirements of the new categories of CSPs.4 There are conditions placed on this designation:

- Aseptic processes are followed, and written procedures are in place to minimize possible contamination.
- The preparation is performed in accordance with appropriate information for physical and chemical compatibility of the drugs.
- Not more than three different sterile products are used in the preparation.
- Any unused starting component from a single-dose container must be discarded after preparation for the individual patient is complete.
- Single-dose containers are used for one patient only.
- Administration must begin within 4 hours following the start of preparation.
- If administration has not begun within 4 hours following the start of preparation, it must be discarded according to requirements.
- CSPs must be labeled with the names and amounts of all active ingredients, the name or initials of the person who prepared it when the preparer is not present at its administration.

**Category Update**

There are several risk factors associated with the compounding of sterile products including batch size, the complexity of the process, the inherent nature of the drug, and the length of time between the beginning of the compounding preparation and product administration. In the current chapter, CSPs are divided into three levels based on their potential risk for contamination (low, moderate, and high).6 Examples of types of compounds that would be included in each of the current risk levels is summarized in Table 4.

There will now only be two risk categories which are defined by their BUD and the environment in which they are prepared in. Category 1 CSPs are those assigned to a maximum BUD of 12 hours or less at controlled room temperature or 24 hours or less if refrigerated. Category 2 CSPs may be assigned a BUD of up to 24 hours if refrigerated or up to 12 hours at room temperature. There are exceptions for longer BUD dates for products that are terminally sterilized as allowed in the chapter.4

This condensation of risk categories places more products in Category 1, requiring more stringent care of products in order to remain compliant. If a CSP does not meet all minimum requirements to be considered a Category 2 CSP, then it must be considered Category 1.4 The remaining minimum requirements are the same for both categories except:

- Sterility testing may be required for Category 2 CSPs based on the assigned BUD date, but is not required for Category 1 CSPs.
- Endotoxin testing is required for Category 2 CSPs prepared from

<table>
<thead>
<tr>
<th>Current Risk Levels</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low-Risk Level</td>
<td>Single-volume transfers of sterile dosage forms using sterile syringes with sterile needles</td>
</tr>
<tr>
<td>Medium-Risk Level</td>
<td>TPN preparation that involves multiple injections, detachments, and attachments of products</td>
</tr>
<tr>
<td>High-Risk Level</td>
<td>Dissolution of nonsterile bulk drug and nutrient powders before terminal sterilization</td>
</tr>
</tbody>
</table>
nonsterile ingredients, but is not required for Category 1 CSPs.  
• Category 2 CSPs are required to be prepared in a PEC (primary engineering control such as a laminar flow hood) that is located in a classified area (See Facilities and Equipment).4

Personnel Training and Evaluation
Personnel training in the updated USP Chapter <797> has become significantly more detailed in order to ensure proper training of everyone involved in CSP preparation. A written training program is required at all compounding facilities, and a designated person (or persons) must oversee the training of personnel.6 This unifies <797> with <795> and <800> requirements for a designated individual. All personnel that are involved in the preparation of CSPs must complete written or electronic testing every 12 months.5 They are required to have documented training of sterile compounding core competencies and skills. These include calculations, measuring, and mixing as well as use of equipment and primary engineering controls. An annual requalification of compounding personnel is required. In addition, competency testing must be performed immediately post-training and then regularly as long as he or she continues to perform sterile compounding.4 Competency testing includes visual observations, gloved fingertip testing, media fill testing, and retraining in disinfection protocols. The new chapter provides significantly more detail about competency testing such as directions on how gloved fingertip testing and media fill testing should be done. Table 5 describes the minimum frequency of reevaluation for each type of test. The minimum skills that are to be assessed include:*6

<table>
<thead>
<tr>
<th>Competency Test</th>
<th>Initial Testing and Minimum Reevaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visual observation</td>
<td>Initially and then every 6 months</td>
</tr>
<tr>
<td>Gloved fingertip sampling</td>
<td>Three times initially and then every 6 months</td>
</tr>
<tr>
<td>Media-fill testing</td>
<td>Initially and every 6 months thereafter</td>
</tr>
<tr>
<td>Cleaning and disinfecting</td>
<td>After a change in cleaning and disinfecting procedures</td>
</tr>
</tbody>
</table>

• Hand hygiene  
• Gloving and Garbing  
• Cleaning and disinfection  
• Calculations, measuring and mixing  
• Aseptic technique  
• Achieving, maintaining sterility and apyrogenicity  
• Use of equipment  
• Documentation of compounding process  
• Principles of HEPA filtered unidirectional airflow pertaining to ISO class 5 areas  
• Proper use of primary engineering controls (PECs)  
• Placement and movement of materials and personnel within the compounding area

All facilities where CSPs are prepared must have and maintain written or electronic documentation to demonstrate compliance with the requirements in this chapter. Personnel training, competency assessments, and qualification records including corrective actions for any failures.6 The retention time of those related training documents, however, is not specifically defined in the chapter.

Facility and Engineering Controls
The revised <797> reemphasizes that facilities must be designed, outfitted, and properly maintained to minimize the risk of contamination during the compounding processes. It consolidates and expands on areas provided in the current chapter, establishing this section and subsections that include such things as the types of PECs and their placement, air changes requirements, and maintenance of easily cleanable conditions. The revised chapter also provides definitions on the different types of PECs such as restricted-access barrier system (RABS), laminar airflow system (LAS), and a pharmaceutical isolator. The specific definitions can be found in the new chapter.

Currently, the only requirement for separation of the anteroom and the buffer room is a demarcation (e.g. some sort of marker or line) that segregates the two areas.6 In the updated chapter, the areas must be separated by walls and doors and must have controlled air flow.4,5 This change in demarcation is significant as it will require facilities to undergo major construction in order to be compliant. Although various pharmacies have a taped off area in the anteroom where personnel can place their foot once they put on a shoe cover, this is not a requirement.6 This was mentioned in an appendix of the current standards but was simply an example guideline of how to assess personnel and was not a requirement.6 The updated chapter does not mention this as a requirement, but the facility must have SOPs for appropriate garbing sequences and entry into the restricted areas.
Depending on the type of compounding and PEC used, the placement and air quality requirements should be reviewed in order to remain compliant. Most PECs must be placed in an area with ISO Class 7 air quality or better if used to prepare CSPs. There are instances where a PEC can be located in an unclassified area. The area is designated as a segregated compounding area (SCA). There are general requirements for selecting the location of an SCA and it is to be used only for the preparation of Category 1 CSPs. The new chapter provides a table summarizing the minimum requirements for placement of a PEC for compounding Non-Hazardous Drug CSPs.

**Establishing Beyond-Use Date**

Due to the new categorization of CSPs, new guidelines for establishing a BUD were also created. Using the defined temperatures in the USP, Category 1 CSPs have a BUD of ≤ 12 hours at controlled room temperature and ≤ 24 hours when refrigerated. Category 2 CSPs, prepared from only sterile starting components and that are not terminally sterilized are given these BUDs: controlled room temperature 4 days, refrigerator 10 days and freezer 45 days. There are exceptions for longer BUD dates for products which are terminally sterilized as allowed in the chapter.5,6

**Conclusion**

This review summarizes many of the most important changes in the USP <795> and <797> chapter updates. It does not provide a review of all the changes. The official publications go into effect on December 1, 2019 and can be found on USP’s official website. All pharmacists and staff who perform both sterile and nonsterile compounding should review these standards in order to ensure appropriate practice activities. In addition to these two updates, USP has added a new chapter: USP <800>. USP <800> is specific for the handling of hazardous drugs and is the preferred reference if using materials considered hazardous by NIOSH. For questions about these chapters, contact USP at https://www.usp.org/contact-us.

**References**


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**Policies for the Nebraska Mortar & Pestle (M&P) continuing pharmacy education lessons and quizzes:**

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2. If more than three questions are missed, the quiz will be retired. The quiz can be resubmitted.
3. CPE transcripts can be printed from NABP e-Profiles at www.nabp.net.
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**Quiz Answers may be submitted:**

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6221 S 58th St, Ste A
Lincoln, NE 68516
A Guide to the Updates in USP <795> NonSterile Compounding and USP <797> Sterile Compounding

Quiz #12, July/August 2019, ACPE 0128-0000-19-043-H03-P/T

1. When do the changes to USP chapters <795> and <797> go into effect?
   a. June 1, 2019
   b. December 1, 2019
   c. December 31, 2019
   d. January 1, 2020

2. Which of the following is considered nonsterile compounding?
   a. Diluting erythromycin in ethyl alcohol and then mixing with benzoyl peroxide as directed by manufacturer.
   b. Opening omeprazole capsules and adding them to sodium bicarbonate.
   c. Reconstitution of an antibiotic powder with distilled water.
   d. All of the above

3. Which of the following is required when compounding regardless of hazard risk or sterility?
   a. Gloves
   b. Gown
   c. Protective eyewear
   d. Shoe covers

4. At a minimum, how often must the walls and storage shelving in a designated non-sterile compounding area be cleaned according to chapter <795>?
   a. Every 3 hours
   b. Every 3 days
   c. Every 3 weeks
   d. Every 3 months

5. What is the recommended maximum beyond-use date (BUD) for compounded nonsterile products that are non-preserved aqueous dosage forms?
   a. 180 days in a freezer
   b. 30 days at room temperature
   c. 14 days in a refrigerator
   d. There is no recommended maximum BUD for this product.

6. Which of the following appropriately defines Category 1 compounded sterile products (CSPs) as defined in the proposed chapter <797>?
   a. Category 1 CSPs are those assigned to a maximum BUD of 12 hours or less at controlled room temperature or 24 hours or less if refrigerated.
   b. Category 1 CSPs are those assigned to a maximum BUD of 24 hours or less at controlled room temperature or 48 hours or less if refrigerated.
   c. Category 1 CSPs are those assigned to a maximum BUD of 24 hours or less at controlled room temperature or 12 hours or less if refrigerated.
   d. Category 1 CSPs are those assigned to a maximum BUD of 48 hours or less at controlled room temperature or 24 hours or less if refrigerated.

7. Visual observation and gloved fingertip sampling reevaluations must be done at a minimum of every __________.
   a. Quarter
   b. 6 months
   c. Year
   d. 2 years

8. Which of the following is an appropriate way of separating the anteroom and buffer room according to the proposed chapter <797>?
   a. Tape on the floor
   b. Walls and doors
   c. All of the above are appropriate
   d. None of the above are appropriate

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Keep the TOP portion for your records. Return the BOTTOM portion to the NPA office. Or, take this quiz online at www.npharm.org

Name __________________________________________ Mailing Address ____________________________________
City/State/Zip ______________________________________

Circle one (1) Answer:
1. a b c d 5. a b c d
2. a b c d 6. a b c d
3. a b c d 7. a b c d
4. a b c d 8. a b c d

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2. Did this lesson meet each of its objectives? ___ Yes ___ No
3. Was the content without commercial bias? ___ Yes ___ No
   If not, please explain_______________________________________
4. Did the lesson meet your educational/practice needs? ___ Yes ___ No
5. Comments/future topics are welcome. ________________________

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