By Patricia Kienle, RPh, MPA, FASHP,
and Kate Douglass MS, RN, CRNI

Perform an Assessment of Risk to Comply with USP <800>

On July 1, 2018, *USP <800> Hazardous Drugs – Handling in Healthcare Settings*[1] will become official, although some states, accreditation organizations, and facility policies may require earlier compliance. In the pursuit of USP <800> compliance, the first step is to identify all of the hazardous drugs (HDs) utilized by the entity, as well as their dosage forms and the specific handling practices for those products.

USP <800> is part of the USP Compounding Compendium, available for purchase at http://www.usp.org/store/products/usp-compounding-compendium.

Handling Options

USP <800> requires compliance with *all* containment strategies and work practices listed in the chapter (see **FIGURE 1**[1]) when entities handle:

- Any antineoplastic drug included in Table 1 of the NIOSH list[2] that requires manipulation
- Any active pharmaceutical ingredients (APIs) for any type of HD included in Tables 1, 2, and 3 of the NIOSH list[2] (See **SIDEBAR 1** for the definition of terms used in the NIOSH list.)

While there is no option for developing alternative handling strategies for these types of HDs, Chapter <800> does allow for some other HDs to be handled differently under specific circumstances. The only HDs that can be considered for alternative handling are antineoplastic drugs listed in Table 1 that will not be manipulated (ie, requiring only counting or packaging), non-antineoplastic drugs listed in Table 2 that are not APIs, and reproductive-only risk drugs listed in Table 3 that are not APIs.[2] These types of HDs may be treated in one of two ways:

1. Handle in the same manner as APIs and antineoplastic drugs that require manipulation, using all of the containment properties and work practices listed in <800>.
2. Perform an Assessment of Risk (AoR) to determine which specific dosage forms of these agents may be handled with alternative containment strategies and/or work practices. The alternative containment strategies and work practices must be sufficient to protect the health care workers from exposure to HDs (see **SIDEBAR 2**).

This article focuses on how to perform an AoR and provides a sample AoR reflecting actual work practice settings (see **FIGURE 2**), as well as an AoR template that may be downloaded and modified for your own use. AoRs are not limited to pharmacy practices only; rather, they are intended to detail organization-wide practice encompassing all areas in the facility that handle HDs. AoRs should include a list of all staff members who may handle HDs, including those who perform HD receiving, inventory storage, compounding, transport, administration, and disposal of items contaminated with HD residues. Designated personnel may include those from materials management, pharmacy, nursing, transport, environmental services, and other departments.

Compliance Steps

In the effort to comply with USP Chapter <800>, all organizations must undertake the following steps:

SIDEBAR 1

Definition of Terms

- **Entity** is the specific location where HDs are handled and is not limited to pharmacies. For example, a hospital is an entity, but the hospital's off-site locations, such as oncology clinics or ambulatory pharmacies, may develop a separate list of HDs, since the drugs used at those locations may differ from those used at the hospital campus.
- **HDs** are drugs that are hazardous to health care personnel, as defined by the National Institute for Occupational Safety and Health (NIOSH). See the NIOSH List of Antineoplastic and Other Hazardous Drugs in Healthcare Settings, 2016.[2] The NIOSH list sorts HDs into three tables: antineoplastics (Table 1), non-antineoplastics (Table 2), and reproductive-only hazards (Table 3). These drugs are different from hazardous materials as defined by the Environmental Protection Agency; those agents are hazardous to the environment. Note that there are some drugs that are on both the NIOSH list and the EPA list.
- **Cleanroom Suite** is an ISO 7 positive anteroom and an ISO 7 negative buffer room that meet the requirements of USP <797> and <800>.
- **Containment Segregated Compounding Area (C-SCA)** is a room that meets the requirements of USP <800>.

1. Download the NIOSH 2016 list[2]
2. Identify all of the HDs handled within the entity including each dosage form used. This review must encompass formulary items as well as any non-formulary items utilized. Be sure to consult work groups within the entity that may purchase or obtain drugs from sources other than the hospital pharmacy to ensure the creation of a complete master list
3. Divide the list into two categories:
   a. Drugs that are ineligible for an AoR (APIs and antineoplastics that require manipulation)
   b. Drugs that may be considered for an AoR (antineoplastics that will only be counted or packaged, non-antineoplastic and reproductive-risk-only drugs)
4. Evaluate each of the drugs and dosage forms eligible for an AoR, considering the following:
   a. Dosage form in which it is obtained
   b. Packaging (such as unit dose, unit-of-use, or bulk)
   c. Need for and type of manipulation (eg, crushing, opening capsules, compounding, etc)
5. Determine if practical alternative containment strategies and/or work practices could be developed and implemented to protect employees from ingesting, inhaling, or touching HD particulates or vapors
6. Create a written AoR for each drug dosage form for which alternate strategies will be used

FIGURE 1

Summary of Containment Strategies and Work Practices Required in USP Chapter <800>[1]

Description of Activity	Containment Strategy	Work Practice
Identification of drugs received as hazardous from inspection of the outside of the container	X	X
Protection of HDs received as they are unpacked and transferred to storage	X	X
Store HDs in a space that meets these four **minimum** requirements: ▸ Room with fixed walls and door that is separate from non-hazardous storage ▸ Negative pressure between 0.01" to 0.03" water column (w.c.) to adjacent space ▸ At least 12 air changes per hour (ACPH) ▸ Exhaust vented outside the building	X	
Decontamination of surfaces exposed to HDs or contaminated HD containers		X
Controls that result in protection from HD residue when HDs are transported	X	X
Controls during splitting, crushing, or otherwise manipulating a non-parenteral dosage form of an HD	X	X
Compounding non-sterile HDs in a room that meets these four **minimum** requirements: ▸ Room with fixed walls and door that is separate from non-hazardous storage ▸ Negative pressure between 0.01" to 0.03" w.c. to adjacent space ▸ At least 12 ACPH ▸ Exhaust vented outside the building	X	
Compounding *sterile* HDs in a cleanroom suite that meets these four **minimum** requirements: ▸ Room with fixed walls and door that is separate from non-hazardous storage ▸ Negative pressure between 0.01 to 0.03" w.c. to adjacent space ▸ Room supplied with HEPA-filtered air resulting in ISO Class 7 during dynamic operating conditions (*at least* 30 ACPH) ▸ Exhaust vented outside the building	X	
Compounding *sterile* HDs in a C-SCA that meets these four **minimum** requirements: ▸ Room with fixed walls and door that is separate from non-hazardous storage ▸ Negative pressure between 0.01" to 0.03" w.c. to adjacent space ▸ At least 12 ACPH ▸ Exhaust vented outside the building	X	
Use of PPE ▸ Gloves that meet ASTM standard D6978 ▸ Disposable gowns tested to resist HD permeation, back-closing, cuffed, no seams or sealed seams ▸ Head covers and surgical masks ▸ Double shoe covers ▸ Goggles and face shield if splash potential ▸ Respiratory protection per section 7.5		X
Compounding ▸ Use C-PEC and plastic-backed mat, which is changed daily and after spills ▸ Use of disposable/cleanable equipment such as mortar, pestles, and spatulas dedicated for use with HDs ▸ Consider use of CSTDs	X	X
Controls that result in protection from HD residue when HDs are transported or stored ▸ Labeled as an HD ▸ Labeled to require PPE precautions ▸ Warning message on ADC lidded bin to wear HD PPE ▸ Warning message on ADC lidded bin to wear chemo gloves	X	X
Decontamination of HDs ▸ Decontaminate reusable equipment where HDs are handled ▸ Decontaminate the work surface of the C-PEC at least daily and between different types of HDs ▸ Persons decontaminating are properly garbed ▸ Decontamination agents applied with wet applicator, never sprayed ▸ Decontamination occurs first followed by cleaning and disinfection in areas of sterile compounding ▸ Tray under C-PEC decontaminated at least monthly and consider additional respiratory protection		X
Use CSTDs during administration if the dosage form allows	X	X
Proper disposal of residual HDs and supplies according to local, state, and federal requirements	X	X
Comprehensive spill management and control		X

FIGURE 2

Sample Assessment of Risk

In this sample AoR for oxytocin injection, which is received in unit of use from an outsourced compounding pharmacy, the entity details the risk factor and the corresponding safety measures implemented to protect at-risk staff from exposure. As a result, the entity can utilize these handling procedures in lieu of the more extensive handling requirements detailed in <800>. CriticalPoint has provided an AoR template, which can be modified for your practice; it is available at **pppmag.com/assessmentofrisk**.

Drug Name: Oxytocin

Date Assessment of Risk (AOR) Initially Performed: January 17, 2017

Date AOR Reviewed: N//A; this is initial

HD Drug Category: ☐ Antineoplastic ☐ Non-antineoplastic ☒ Reproductive Risk Only

Dosage form (select one):

☐ Sterile dosage compounded by a vendor and not requiring additional manipulation

☐ Dosage form of conventionally manufactured product that require only packaging or counting

☐ Dosage form of conventionally manufactured non-antineoplastic or reproductive hazard product that requires only packaging and counting

☒ Other (explain): Obtained from FDA Registered 503B Outsourcing Facility

Describe Packaging: Oxytocin 30 units in 500 mL 0.9% sodium chloride injection

Rationale for not requiring all <800> containment strategies	Specific Alternative Administrative, Engineering and Work Practice Control Strategies
Document rationale here: Oxytocin is a human peptide hormone and neuropeptide that is used as a medication to facilitate childbirth. Oxytocin is normally produced in the hypothalamus and released by the pituitary. Oxytocin plays and important role in stimulating cervical dilation as well as stimulating uterine contractions in the 2nd and 3rd stages of labor. Exposure to oxytocin is believed to pose a risk to women in their third trimester of pregnancy relative to the risk of stimulating uterine contractions which may result in early labor.	• The following strategies are documented in administration of oxytocin in the nursing SOP 321.2 • Training in the SOP is scheduled for all nursing staff on January 23, 2017 Document specific alternative strategies below or ☐ N/A (see below) • Receive the compounded units from ABC 503B Outsourcing Facility • Nurses who are in their 3rd trimester and may also be exposed to oxytocin while caring for patients during their normal job duties will sign an Acknowledgement of Risk form after receiving training regarding the risks and proper use of PPE • Nurses and medical staff at risk of exposure to oxytocin during drug administration to patients will wear gloves tested to ASTM 6978 while administering, maintaining or discontinuing IV lines with oxytocin.

Based on Assessment of Risk will proceed as follow: ☒ Follow alternative strategies documented above ☐ Follow all USP <800> requirements

Assessment of Risk written by: Carl Smith, RPh Date: 1/17/2017

Reviewed by Pharmacy Manager: Jane Olsen, PharmD Date: 1/17/2017

F-700.g; Released 12/19/2016

Components of an AoR

USP Chapter <800> allows for certain HDs to be considered for alternative containment strategies or work practices, but only if a systematic AoR is completed and documented for each drug and dosage form. The required elements of an AoR include:

1. Type of HD (antineoplastic per List 1, non-antineoplastic per List 2, or reproductive-only risk per List 3[2])
2. Specific dosage form (for each AoR)
3. Risk of exposure
4. Packaging (ie, description of packaging in which the drug is received)
5. Type of manipulation performed by the organization to render the final dosage form (listed in **SIDEBAR 2**)
6. Specific alternative containment strategies and/or work practices that will be employed to reduce the risk of exposure

To create an AoR, a standard operating procedure (SOP) must first be created that determines how AoRs are performed, who performs them, how they are documented, and what staff training is required. It is important to note that implementing alternative containment strategies and/or work practices may necessitate the development of additional procedure-specific SOPs. Review the AoR annually, and document that this review occurred. As stated previously, any drug dosage forms for which an AoR has *not* been performed must be handled following all of the containment strategies and work practices required in Chapter <800>.

Some drugs present unique challenges due to the location in which they are administered. Review the containment strategies for HDs that are dispensed in vial form to procedural areas, as these are commonly handled improperly. Pay particular attention to drugs such as methotrexate injection (used in the treatment of ectopic pregnancies and rheumatoid arthritis), mitomycin for injection (used for ophthalmic or urology procedures), and Bacillus Calmette-Guerin, which is used during urology procedures. Work with staff in the departments administering these agents to ensure safe practices.

Conclusion

USP <800> is designed to protect patients, personnel, and the environment. The AoR component of the standard provides a systematic way for organizations to ensure safe practices. As the organization's primary drug steward, the sterile compounding pharmacist should lead this compliance effort and work collaboratively with other members of the health care team to assess and develop alterative containment strategies and work practices when possible. ■

Address any questions to Kate Douglass at kdouglass@criticalpointce.com.

References

1. USP Convention, Inc. <800> Hazardous Drugs-Handling in Health care Settings. *USP 40-National Formulary 35*. 1st supp. Rockville, MD: USP Convention, Inc , 2017.
2. Connor TH, MacKenzie BA, DeBord DG, et al. NIOSH list of antineoplastic and other hazardous drugs in healthcare settings, 2016. DHHS (NIOSH) Publication Number 2016-161 (Supersedes 2014-138). http://www.cdc.gov/niosh/docs/2016-161/pdfs/2016-161.pdf. Accessed February 17, 2017.

SIDEBAR 2

Alternative Containment Strategies

Alternative containment strategies and work practices might include:

- Use of CSTDs for HDs that are not antineoplastics
- Use of gloves tested to ASTM standard D6978 for HDs that are not antineoplastics
- Purchasing in unit dose or unit-of-use so that no manipulation or compounding is necessary
- Use of personal protective equipment (PPE) as detailed in the NIOSH list (Table 5),[2] which may differ based on the function performed (eg, compounding vs administration)
- Use of a dedicated, enclosed plastic tote that is decontaminated after use when needed to transport HDs from the pharmacy to other areas of the health system
- Labeling lidded automated dispensing cabinet bins so nurses and others who administer medications are reminded of the proper PPE

Patricia C. Kienle, RPh, MPA, FASHP, Director of Accreditation and Medication Safety for Cardinal Health, is a member of the USP Compounding Expert Committee and chair of the Hazardous Drug Subcommittee and Expert Panel, although her comments herein are her own and not official information from USP.

Kate Douglass, MS, RN, CRNI, is the vice president of CriticalPoint, LLC, and serves as the co-director of the annual USP Compliance Survey.