Understanding USP 800: A Resource for Long-Term Care Providers

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Introduction

When many long-term care providers first hear about USP General Chapter <800> Hazardous Drugs–Handling in Healthcare Settings ("USP 800"), they naturally confuse it with the final EPA hazardous pharmaceuticals rule ("EPA Rule"), which became effective in August, 2019. While there certainly are areas in which the two overlap, the provisions of the EPA Rule concern hazardous pharmaceuticals once they are no longer used for their intended purpose and thus become waste. USP 800, however, concerns hazardous drugs ("HDs") throughout their entire post-manufacturing lifecycle—from receiving and storage through disposal. As such, USP 800 is likely to have a profound effect on pharmacy and health care facility operations.

USP 800 is not a rule, but rather a series of practice and quality standards for handling HDs developed in 2016 by The United States Pharmacopeial Convention ("USP"). It is part of USP's compendium of standards related to compounding of drugs.[1] USP will become official on December 1, 2019; however, revisions to other chapters in the compendium of compounding standards are being appealed and USP has stated that until such time as those appeals are resolved, USP 800 will be "informational and not compendially applicable."[2]

USP 800 will be enforced at the federal level primarily by the Occupational Safety and Health Administration ("OSHA")[3], and at the state level by state boards of pharmacy. The U.S. Food and Drug Administration ("FDA") also may ultimately have some degree of regulatory authority as well.

Compliance

USP calls for the provider to designate a "qualified and trained" person responsible for the following:

- Developing and implementing appropriate policies and procedures;
- Overseeing compliance;
- Ensuring the competency of personnel; and
- Ensuring environmental control of storage and compounding areas (as applicable).

USP stresses that the designated person must "thoroughly understand" the risks associated with HDs, both from a safety and compliance standpoint. Additionally, the designated person must oversee testing and sampling at the facility. While USP 800 does not specify the exact qualifications that the designated person must possess, such person should have an understanding of the risks presented by HDs and the engineering controls and work practices designed to mitigate those risks. If the facility has an in-house pharmacy, then the pharmacist would be the logical choice for this

1 In addition to USP 800, there are three other chapters related to pharmaceutical compounding—795 (nonsterile preparations), 797 (sterile preparations), and 825 (preparation, compounding, dispensing and repackaging of radiopharmaceuticals).

2 *See* https://www.usp.org/compounding.

3 It is also possible that the Food and Drug Administration ("FDA"), which regulates drug compounding, will exercise some degree of regulatory control over relevant provisions of USP 800.

position. In the absence of an in-house pharmacy, a nurse is likely to be tasked with responsibility for compliance, though additional training may be necessary.

Facility staff that handle HDs are responsible for understanding the fundamental practices and precautions involved with handling HDs, and for continually evaluating them, to prevent harm to residents, minimize exposure to other staff, and minimize contamination. Accordingly, USP 800 calls for extensive staff training prior to employees independently handling HDs. Additionally, staff competency must be demonstrated, documented and reassessed at least every 12 months. These training requirements are discussed in greater detail below, under TRAINING.

Risk Assessment

Because USP 800 applies in a variety of health care settings and thus is very comprehensive, not all of the standards will be applicable in all settings. As a result, it will be critical for long-term care providers to become familiar with USP 800, then undertake a risk assessment that considers the following:

- Identifying HDs present in the facility.
  - Type of HD – Antineoplastic, non-antineoplastic, or reproductive risk only (see IDENTIFYING HAZARDOUS DRUGS below for descriptions).
  - Dosage form – Different forms (e.g., tablets, capsules, or liquids) pose different degrees of risk depending on the degree of manipulation prior to administration.
  - Packaging – Different packaging methods (e.g., single-dose packs, vials, bottles) present greater risks of exposure to the contents than others.
- Analyzing how HDs move through a facility.
  - Receipt
  - Storage
  - Preparation – Compounding activities or other manipulations necessary for administration, i.e., crushing, splitting, etc.
  - Disposal
- Identifying staff members who may come into contact with HDs as part of their job duties.
  - Pharmacists
  - Nursing staff
  - Aides
  - Therapists
  - Housekeeping and janitorial staff
  - Others
- Identifying and quantifying the risk for exposure from HDs at each stage of their progression through the facility.

Once the risk assessment has been completed, an analysis of the effectiveness of existing controls and containment methods, as well as policies and procedures, for preventing or minimizing exposure to HDs in light of the USP 800 requirements should be undertaken to determine if additional measures will need to be implemented. Depending on the nature of the activities being undertaken in a facility, special engineering controls for compounding and other manipulations of HDs may be required.

Identifying Hazardous Drugs

For purposes of USP 800, HDs are those listed in National Institute for Occupational Safety and Health (NIOSH) Publication No. 2016-161.[4] NIOSH utilizes the following criteria to determine whether a drug is hazardous:

- Carcinogenicity – drugs that tend to produce a cancer.
- Teratogenicity – drugs that disturb the development of an embryo or fetus.

4 Please note that the current NIOSH list of HDs is dated 2016. On Feb. 14, 2018, NIOSH published a Federal Register notice regarding drugs that the agency proposes to add to the list.

- Reproductive toxicity – drugs that interfere with sexual function and fertility.
- Genotoxicity – drugs that have a destructive effect on a cell's genetic material.
- Drugs that have organ toxicity at low doses.
- Drugs that mimic existing HDs in structure or toxicity.

Accordingly, there are three (3) groups of drugs that NIOSH has categorized as hazardous:

- Group 1 – Antineoplastic drugs – These are drugs that act to prevent, inhibit or halt the development of tumors, i.e., chemotherapy drugs such as tamoxifen and others.
- Group 2 – Non-antineoplastic drugs that meet one or more of the NIOSH criteria for a hazardous drugs. Examples include certain estrogen and progesterone drugs, cyclosporine and other drugs.
- Group 3 – Drugs that primarily pose a reproductive risk to men and women who are actively trying to conceive and women who are pregnant or breast feeding. Examples include clonazepam, fluconazole, testosterone, and warfarin, among others.

As part of their compliance efforts with respect to the OSHA Hazard Communication Standard[5], nursing homes and other long-term care facilities in which HDs are administered or encountered by other means, must use the NIOSH lists and criteria to generate their own facility-specific list of HDs. USP 800 requires that such list be reviewed and updated at least every 12 months. To facilitate the identification of HDs, USP has developed the <800> HazRx™ Mobile App. In addition to identifying HDs, the app also provides information regarding safe handling practices for the HDs in its database.

Types of Exposure

USP 800 provides examples of unintentional occupational exposure to HDs through dermal and mucosal absorption, inhalation, injection, or ingestion during various activities. Not all of the potential opportunities for exposure will be present in long-term care facilities, particularly if there is not an in-house pharmacy. Nevertheless, there are substantial risks even for long-term care facilities that utilize an outside pharmacy.

- Receipt of Drugs – HD residues are often found on drug containers, individual dosage units, outer containers, work surfaces, and floors.
- Dispensing (in long-term care facilities having an in-house pharmacy) – Counting or repackaging tablets and capsules.
- Compounding and Other Manipulations – There are significant opportunities for exposure to HDs through compounding, which is the process of combining, mixing, or altering ingredients to create a medication tailored to the needs of an individual patient and includes the combining of two or more drugs. However unlikely it is that drugs will be compounded in a long-term care facility, particularly if the facility utilizes an external long-term care pharmacy, there are other manipulations of HDs that may result in occupational exposure. Examples include:
  - Crushing or splitting tablets or opening capsules.
  - Constituting or reconstituting powdered HDs.
  - Expelling air or HDs from syringes.
- Administration
  - Generating aerosols during administration of HDs by various routes, such as injection, irrigation, oral, inhalation, or topical application.
  - Priming an IV administration set.
- Patient Care Activities – Handling bodily fluids or clothing, dressings, linens, or other materials contaminated with such fluids.
- Spills – Spill generation, management, and disposal activities.
- Transport – Moving HDs within the facility.
- Waste – Collection and disposal of hazardous waste and trace-contaminated waste.

5 29 C.F.R. § 1910.1200(g). See generally https://www.osha.gov/dsg/hazcom/index.html.

Facilities and Engineering Controls

USP states that HDs must be handled in such a manner so as to "promote patient safety, worker safety, and environmental protection." Toward that end, certain facilities and engineering controls, ranging from hazard signs and restricted access areas, to extensive and costly containment rooms for compounding activities are required to be implemented under USP 800. Designated areas for receipt and unpacking, storage and compounding of HDs must be situated away from staff break rooms and refreshment areas for staff, residents or visitors. While most of the requirements below are more appropriate to the pharmacy environment than the typical long-term care facility that receives medications from a long-term care pharmacy, they nevertheless are instructive in terms of the nature and extent of the precautions needed to minimize exposure to HDs.

- Receipt – Antineoplastic HDs and HD Active Pharmaceutical Ingredients ("APIs") must be removed from external shipping containers in an area that is neutral/normal or negative pressure relative to surrounding areas.
- Storage – HDs must be stored in such a manner as to prevent spillage or breakage, but should not be stored on the floor. HDs generally may be stored with non-hazardous drugs. Antineoplastic HDs that require manipulation other than counting or repackaging of final dosage forms, however, must be stored separately in an externally vented, negative pressure room. Refrigerated antineoplastic HDs must be stored in a dedicated refrigerator within a negative pressure room.
- Compounding – Both nonsterile and sterile compounding activities require very specific, costly engineering controls. These consist of the containment primary engineering control ("C-PEC"), which is an externally-vented device designed to minimize worker and environmental exposure to HDs; the containment secondary engineering control ("C-SEC"), which is the room in which the C-PEC is situated; and supplemental engineering controls.

Environmental Quality and Control

USP 800 calls for routine wipe sampling for HD surface residue at least every six (6) months to verify containment. In long-term care facilities without a pharmacy, this sampling should be conducted in patient administration areas. Although not addressed in USP 800, wipe-sampling other possible avenues for contamination, such as medication carts used to transport HDs for administration to residents, would add another layer of confidence that HD residue is not coming into contact with staff handling the carts.

USP notes that there presently are no standards for acceptable limits for HD surface contamination. Thus, if any measurable contamination is detected, the facility's designated compliance individual must identify, document, and contain the cause of the contamination. The area must then be cleaned according to the deactivation, decontamination, and cleaning procedures of USP 800 (see DEACTIVATION, DECONTAMINATION, AND CLEANING below) and measures implemented to address the root cause of the contamination.

Personal Protective Equipment

Use of Personal Protective Equipment ("PPE") is critical to reduce exposure to HD residues and aerosols. USP 800 notes that providers must establish policies and procedures for the use of PPE appropriate to the activity and the risk of exposure. Once worn, PPE should be treated as if it is contaminated with at least trace quantities of HDs. Disposable PPE should be placed in an appropriate waste container and disposed of in accordance with applicable law. Reusable PPE must be decontaminated and cleaned.

- Gloves – Two pairs of so-called "chemotherapy gloves," which are special medical gloves made from nitrile or natural rubber latex and are used for handling chemotherapy drugs, must be worn to administer injectable anti-neoplastic HDs. USP notes, however, that chemotherapy gloves should be worn for handling all HDs. Chemo-therapy gloves must be powder-free to prevent the powder from absorbing HDs and contaminating the work area.
- Gowns – Gowns must be worn to administer injectable antineoplastic HDs. They must be selected based on the type of HDs handled, and must (a) be disposable, (b) be shown to resist permeability by HDs, (c) be long-sleeved, (d) have closed, elasticized or knit cuffs, and (d) close in the back. Gowns must be changed according to manu-facturers' information regarding permeability. If no such information is available, they should be changed every

2-3 hours or immediately after a spill or splash of HDs. They must not be worn outside the immediate area in which they are being used to prevent contamination of other areas of the facility.

- Head, Hair, Shoe, and Sleeve Covers – Depending on the activity and the risk of HD contamination for staff, these types of PPE may be indicated. As with gowns, shoe covers in particular should not be worn outside the immediate area in which they are being used to prevent contamination of other areas of the facility.
- Eye and Face Protection – Eye and face protection must be worn when HDs present a risk for spills or splashes. Goggles, together with full face shields, provide adequate protection, as do full-facepiece respirators. Eye glasses or safety glasses are not sufficient to prevent against contamination from splashes.
- Respiratory Protection – USP notes that for most activities requiring respiratory protection, a fit-tested NIOSH-certified N95 respirator is sufficient for protecting against inhalation of airborne particles but do not offer adequate protection against gases and vapors. Once again, the level of protection required will be dependent on the risk presented by the activities being undertaken, the HDs involved, and their form. For administration of HDs in tablet or capsule form, for example, the risk of inhalation is low. If those tablets need to be crushed or the capsules opened, then the risk of inhalation of airborne particles increases. In situations where there is a risk of respiratory exposure, an appropriate full-facepiece chemical cartridge-type respirator or powered air-purifying respirator should be worn.

Hazard Communication Program

OSHA's Hazard Communication Standard[6] seeks to ensure chemical safety in the workplace by requiring that employers develop a written hazard communication program for making information about the identities and hazards presented by chemicals available and understandable to workers through labeling and the use of Safety Data Sheets ("SDSs"), and training. HDs in long-term care and other health care workplaces implicate the Hazard Communication Standard.

Insofar as USP 800 is concerned, USP states that the hazard communication program must include the following elements:

- Written plan that describes how the standard will be implemented;
- Containers of hazardous chemicals must be labeled, tagged, or marked with the identity of the material and appropriate hazard warnings;
- SDSs for all hazardous chemicals used in the workplace;
- SDSs are readily accessible to personnel during each shift and when they are in their work areas;
- Information to and training of personnel before initial assignment to work with a hazardous chemical; and
- Written confirmation by personnel of reproductive capability that they understand the risks of handling HDs.

Training

Staff that handle HDs must be trained based on their job functions before they independently handle HDs. The effectiveness of training for HD handling competencies must be demonstrated and must be reassessed at least every 12 months. If a new HD or new equipment is to be introduced that requires new or significant changes in the provider's HD policies and procedures, staff must be trained prior to the change. The training program must include the following topics:

- Overview of the provider's list of HDs and their associated risks;
- Review of the provider's policies and procedures related to handling HDs;
- Proper use of PPE;
- Proper use of engineering controls;
- Response to known or suspected HD exposure;
- Spill management; and
- Proper disposal of HDs and trace-contaminated materials.

6 29 C.F.R. § 1910.1200. General information about the Hazard Communication Standard can be found at: https://www.osha.gov/dsg/hazcom/.

Receiving

Though geared to the pharmacy environment, USP 800 addresses receiving practices and requires that the provider establish policies and procedures for safe handling and response to damaged shipping containers. All HDs received at a facility must be inspected visually for signs of damage or breakage. Any damaged packages must be considered spills and managed accordingly.

Labeling, Packaging, Transport and Disposal

The provider must develop policies and procedures for labeling, packaging, transport and disposal of HDs that address prevention of accidental exposures or spills, training of staff regarding response to exposure, and use of a spill kit. To the extent that the HDs constitute hazardous waste under the EPA Rule, then that regulation comes into play as well.

- Labeling – To the extent that the provider identifies HDs that require special handling precautions, such HDs must be clearly labeled at all times during their transport within the facility.
- Packaging – The packaging requirement is more applicable in the context of pharmacy operations. It states that packaging containers and materials must be selected that will maintain physical integrity, stability, and sterility (if needed).
- Transport – HDs must be transported in containers that minimize the risk of breakage or leakage. They must be labeled, stored, and handled in accordance with applicable law, including the EPA Rule if they are no longer being used for their intended purpose and are to be discarded, and thus constitute waste.
- Disposal – USP 800 requires that all personnel who perform routine custodial waste removal and cleaning activities must be trained in appropriate procedures to prevent HD contamination. Further, HD waste (including trace-contaminated PPE), must comply with all applicable laws and regulations, including the EPA Rule.

Dispensing and Administering HDs

In the case of facilities having an on-site pharmacy, the pharmacist should visually inspect all HD containers prior to dispensing to check for indications of possible HD exposure, such as leakage or dust. HDs that do not require manipulation may be dispensed without any further requirements, other than those required by the manufacturer. Dedicated equipment should be used for dispensing HDs and it must be properly cleaned and stored after each use.

USP 800 requires that HDs be administered safely using “protective medical devices and techniques,” such as needleless systems, spiking or priming of IV tubing with a non-HD solution in a C-PEC, and of particular importance to long-term care providers, crushing tablets in a plastic pouch to contain dust or particles. However, USP warns that health care personnel should avoid manipulating HDs by crushing tablets or opening capsules if possible and states that liquid formulations are preferred if solid oral dosage forms are not appropriate. If such manipulation is required, then PPE must be worn. Also, USP notes that a closed-system drug transfer device (“CSTD”) must be used for administration of antineoplastic HDs. CSTDs are a form of supplemental engineering control.

Deactivating, Decontaminating, and Cleaning

Areas in which HDs are handled and all non-disposable equipment and devices, such as respirators, must be deactivated, decontaminated, and cleaned. Deactivation refers to the process of rendering a compound inert or inactive. Decontamination involves removing any HD residue, and cleaning removes organic and inorganic material.

Providers must establish written policies and procedures for these practices. Procedures for cleaning must specify the cleaning agents to be used, the dilution levels (if any) of those agents, the frequency of cleaning, and documentation requirements.

Personnel who undertake deactivation, decontamination and cleaning must wear PPE resistant to the cleaning agents used (as well as the HD residues), including two pairs of chemotherapy gloves and impermeable disposable gowns. If splashing is likely, eye protection and face shields are also required as is respiratory protection depending on the

situation.

The agents used for deactivation, decontamination and cleaning must be appropriate for the type of HD contaminant(s), location, and surface materials. The agents should be applied with wetted wipes rather than a spray bottle. The wipes must be discarded in compliance with EPA regulations.

Spill Control and Clean Up

Spills must be contained and cleaned up immediately by personnel trained in spill management and the use of PPE. Such personnel must be available at all times while HDs are being handled. Spill kits, which are a collection of items to be used in the event of a spill, must be readily available in all areas where HDs are routinely handled. Such kits typically contain PPE, sorbents (i.e., absorbent pads or towels) to quickly absorb and hold in a variety of liquids, a handbook, a disposal bag, and other materials. Any clean up materials must be treated as hazardous waste in compliance with EPA regulations.

Staff that have had direct skin or eye contact with HDs or are potentially exposed as a result of the spill or cleanup, must be evaluated immediately. Residents, guests and other non-employees should be evaluated by emergency personnel.

Providers must have policies and procedures designed to prevent spills as well as to document and govern their clean up. Such policies and procedures must address the following:

- Size and scope of the spill;
- Who is responsible for spill management;
- Type of PPE required and use of same; and
- Location, contents and capacity of spill kits.

Policies, Procedures and Documentation

As noted throughout this resource, USP requires that providers develop and implement policies and procedures for the safe handling of HDs. These policies and procedures must be reviewed at least every 12 months by the designated compliance person. Such review must be documented. USP 800 recommends the following policies and procedures:

- Hazard communication program;
- Occupational safety program;
- Designation of HD areas;
- Receipt;
- Storage;
- Compounding (if applicable);
- Use and maintenance of engineering controls;
- Hand hygiene and use of PPE according to activity being undertaken;
- Deactivation, decontamination, and cleaning;
- Dispensing (if applicable);
- Transport;
- Administration;
- Environmental monitoring;
- Spill control;
- Disposal; and
- Medical surveillance.

Medical Surveillance

USP notes that medical surveillance of employees who handle HDs as a regular part of their job responsibilities is a vital

component of any exposure control program. Medical surveillance involves assessment and documentation of symptom complaints, physical findings, and laboratory values to detect any adverse health effects attributable to HD exposure. As such, it is a means of early detection, generates trends data, and provides a means to evaluate the effectiveness of engineering controls, PPE, work practices, and training.

Elements of a medical surveillance program should include:

- An organized approach for identifying staff who are potentially exposed to HDs as a result of their job duties;
- Use of a health service to perform the medical surveillance;
- Establishment of a baseline assessment of each individual's health status and medical history, including:
  - Medical history (including reproductive history)
  - Work history to assess previous exposure to HDs
  - Physical examination
  - Laboratory testing
- Medical records of surveillance should be maintained according to OSHA regulations;[7]
- Monitoring workers' health prospectively through periodic assessments;
- Monitoring of the data to identify prevention failure that leads to health effects;
- Development of a follow up plan for individuals who have shown health changes indicative of toxicity or who have experienced an acute exposure to HDs (see below);
- Completion of an exit examination when an enrolled individual leaves employment with the provider.

The following steps are advisable as part of any follow up plan in the event that a staff member experiences exposure-related health changes or an acute exposure event:

- Perform a post-exposure physical examination tailored to the type of exposure. This examination should focus on both the involved area and other organ systems commonly affected. Treatment and laboratory studies will follow based on the physical examination;
- Ensure that an exposed individual receives confidential notification of any adverse health effect;
- Ensure confidential, two-way communication between the affected individual and health care providers;
- Offer alternative duty or temporary reassignment;
- Compare performance of controls with recommended standards;
- Verify and document that all engineering controls are functioning properly;
- Verify and document that the staff member complied with existing policies and procedures.
- Develop and document a plan of action to prevent additional exposure; and
- Provide and document a follow-up medical survey to demonstrate that the follow up plan is effective.

Conclusion

For long-term care providers, the presence (or absence) of an in-house pharmacy will be the determining factor regarding the nature and extent of their compliance obligations under USP 800. Facilities with an in-house pharmacy will have enhanced responsibilities with respect to receipt, storage, transport and disposal of HDs because of the increased quantities of drugs coming in to the facility. Extensive and costly engineering controls, as well as more sophisticated PPE, also could be required if an in-house pharmacy is engaged in compounding activities. But even for facilities that do not have an in-house pharmacy, the compliance challenge could prove daunting for the simple reason that facilities without an in-house pharmacy do not have a pharmacist on staff that understands and likely has experience dealing with HDs. As a result, facilities will need to secure advanced training for a member of the clinical staff before that staff member will be able to undertake oversight duties for compliance with USP 800.

But while the requirements of USP 800 may seem daunting, a robust and fully implemented compliance program focused on risk assessment, tailored engineering controls and work practices, exposure prevention, environmental monitoring, training, and medical surveillance may ultimately pay dividends to providers as a risk mitigation tool by better protecting both residents and staff from potential adverse health effects posed by exposure to HDs. Key to the success of any

7 *See* generally https://www.osha.gov/SLTC/medicalsurveillance/.

compliance program, however, is the effectiveness of the policies, procedures and training protocols established as part of the program, as well as the provider's commitment to continuous evaluation and improvement of the program. A program that is not conceived of organizational commitment and implemented fully with buy-in from staff is doomed to failure. In this case, failure of the interventions and systems required by USP 800, would expose residents and staff to potential adverse health effects from HDs, and thus increase the potential for the provider to be held liable for any such adverse health effects.

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