USP General Chapter <800> and EPA
Implications for LTC and Community Pharmacies

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USP Chapter <800>

Hazardous Drugs

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Speaker Disclosure

Dana Saffel is the President/CEO of PharmaCare Strategies, Inc. The conflict of interest was resolved by review of the slide content.
Learning Objectives

1. Discuss important updates to USP standards and the impact on pharmacies and LTC facilities.
2. List common medications most likely impacted by USP <800> standards.
3. Discuss implications of the EPA final rule on pharmacies and LTC facilities.
The United States Pharmacopeia (USP)

- The mission of the USP is to:
  - Improve global health through public standards and related programs that help ensure the quality, safety, and benefit of medicines and foods.

- The USP compendium contains thousands of chapters that set standards for
  - Identity, strength, quality, and purity of
  - Medicines, food ingredients, and dietary supplements, that are
  - Manufactured, distributed, and consumed worldwide.

- USP Chapter <800> requires healthcare entities that handle Hazardous Drugs to incorporate USP <800> standards into their occupational safety plan

**Becomes effective December 1, 2019**

Purpose of USP Chapter <800> – Hazardous Drugs

• Expands upon information contained in USP chapter <795> (non-sterile compounding) and chapter <797> (sterile compounding)
• Makes OSHA standards a priority
• Adds the element of CONTAINMENT of Hazardous Drugs
  • Exposure should be limited to the lowest possible level by using engineering controls and personal protective equipment

Purpose
• Describe practice and quality standards for handling hazardous drugs in health care settings
• Promote patient safety, worker safety, and environmental protection

Philosophy
There is No Acceptable Level of Exposure to Hazardous Drugs

OSHA – Occupational Safety and Health Administration
Hazardous Drugs (HD)

- Any drug or active pharmaceutical ingredient (API) identified on the NIOSH list
- HD designation is based on six criteria:
  - Carcinogenicity
  - Teratogenicity or developmental toxicity
  - Reproductive toxicity in humans
  - Organ toxicity at low doses in humans or animals
  - Genotoxicity
  - New drugs that mimic existing hazardous drugs in structure or toxicity
- NIOSH groups HDs into three groups.

Group 1
Antineoplastics

Group 2
Non-Antineoplastics

Group 3
Reproductive Risk

NIOSH HD Drugs

Drugs on the NIOSH list that must follow all Chapter <800> requirements:
- Any HD active pharmaceutical ingredient
- Any antineoplastic HD requiring manipulation

Drugs on the NIOSH list that do not have to follow all the containment requirements of Chapter <800> if an assessment of risk is performed and implemented include:
- Final dosage forms of compounded HD preparations and conventionally manufactured HD products that do not require any further manipulation other than counting or repackaging (unless required by the manufacturer)

For dosage forms of other HDs on the NIOSH list, the entity may perform an assessment of risk to determine alternative containment strategies and work practices.
Current NIOSH HDs Often Encountered in LTC

Group 1: Antineoplastic Drugs
1. Methotrexate
2. Tamoxifen
3. Anastrozole
4. Megestrol
5. Hydroxyurea
6. Letrozole

Group 2: Non-Antineoplastic Drugs
1. Carbamazepine
2. Rasagiline
3. Spironolactone
4. Ocarbazepine
5. Azathioprine
6. Cyclosporine
7. Methimazole
8. Propylthiouracil
9. Estradiol / Estrogens
10. Estrogen / progesterone combinations
11.Raloxifene
12. Progesterone / progestins
13. Leflunomide
14. Sirolimus
15. Tacrolimus
16. Valganciclovir
17. Zidovudine

Group 3: Reproductive Risk Drugs
1. Paroxetine
2. Warfarin
3. Clonazepam
4. Topiramate
5. Ziprasidone
6. Zonisamide
7. Colchicine
8. Fluconazole
9. Dutasteride
10. Finasteride
11. Vigabatrin
12. Temazepam
13. Testosterone
14. Misoprostil
15. Ribavirin

Drugs are listed in order of general importance to LTC. Orange font indicates a high-use LTC drug.
USP Chapter <800> General Requirements

- Entities that handle HDs must incorporate USP <800> standards into their occupational safety plan

- Occupational safety plan must include:
  - List of HDs used in the facility
    - Based on NIOSH list but can include additional agents
    - Reviewed annually
    - Updated whenever a new agent or dosage form is used
  - Determination of hazardous status based on pharmacology/toxicology
    - Is the drug designated as Therapeutic Category 10:00 (Antineoplastic Agent) in the American Hospital Formulary Service Drug Information?
    - Does the manufacturer suggest the use of special isolation or other techniques in its handling, administration, or disposal?
    - Is the drug known to be a human mutagen, carcinogen, teratogen or reproductive toxicant?
    - Is the drug known to be carcinogenic or teratogenic in animals or mutagenic in multiple bacterial systems or animals?
    - Is the drug known to be acutely toxic to an organ system?
USP Chapter <800> General Requirements (con’t)

• Competent staff who demonstrate safe work practices
  • Designated person formally in charge of HD program
  • Oversees development of and compliance with policies and procedures
  • Ensures competency of personnel
  • Oversees monitoring of facility (surveillance program)

• Designated areas for HD receipt, storage, compounding, packaging
• Facility and engineering controls (primary and secondary)
• Availability and proper use of appropriate personal protective equipment (PPE)
• Policies for HD waste segregation and disposal
Enforcement of USP Standards

- USP standards are only legally enforceable when an entity with authority over the medical professional, clinic, hospital or nursing home chooses to make elements of those chapters enforceable.

**Federal Enforcement**

- Drug Quality and Security Act (DGSA)
  - Requires compounding pharmacies to comply with USP chapters <795> and <797> in order to avoid having to file a NDA

**State Enforcement**

- Boards of Pharmacy
  - 87% of states BoP enforce chapters <795> & <797>
  - *Approx. 10% of states BoP have decided to enforce chapter <800> to date*
- Boards of Medicine
- Occupational Safety department

- Federal Law also requires
  - Hazard communication program
  - Occupational safety program (OSHA)
    - Safety Data Sheets (SDS)
      - Formerly Material Safety Data Sheets (MSDS)
Key Enforcement Points for Pharmacies

• State Board of Pharmacy (BoP) rules and regulations will be necessary for enforcement of USP standards at most pharmacies.
  • At least one state BoP (Texas) has already decided not to enforce USP chapter <800>, and some states may decide to enforce only portions or create their own standards.

• Even if state BoP do not require the Pharmacy to adopt USP <800> standards, in the LTC setting, the consultant pharmacist has a duty to advise the nursing facility on safe handling of HDs.
  • F755: The facility must employ or obtain the services of a licensed pharmacist who provides consultation on all aspects of the provision of pharmacy services in the facility.¹
    • Pharmaceutical Services” refers to the:
      • Process (including documentation, as applicable) of receiving and interpreting prescriber’s orders; acquiring, receiving, storing, controlling, reconciling, compounding (e.g., intravenous antibiotics), dispensing, packaging, labeling, distributing, administering, monitoring responses to, using and/or disposing of all medications, biologicals, chemicals (e.g., povidone iodine, hydrogen peroxide);
        • Provision of medication-related information to health care professionals and residents;
        • Process of identifying, evaluating and addressing medication-related issues including the prevention and reporting of medication errors; and
        • Provision, monitoring and/or the use of medication-related devices.
Key Enforcement Points for Nursing Facilities

• **Nursing Facilities**: Current CMS rules and regulations regarding medication administration (F759 & F760) require medications to be administered according to1:
  • Accepted professional standards and principles which apply to professionals providing services.
  • Accepted professional standards and principles include the various practice regulations in each State, and current commonly accepted health standards established by national organizations, boards, and councils.

• **Liability Insurance Carriers**
  • Are focusing more intently on management of prescription drugs

• **Accrediting Organizations**
  • JCAHO

Crushing medications that should not be crushed is usually a medication error and may be a significant medication error if it causes discomfort or places the resident in jeopardy, such as with an HD drug.

### Types of HD Exposure Often Encountered in LTC

<table>
<thead>
<tr>
<th>Activity</th>
<th>Potential Opportunity of Exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Receipt</td>
<td>• Contacting HD residents present on drug containers, individual dosage units, other containers, work surfaces or floors</td>
</tr>
<tr>
<td>Dispensing</td>
<td>• Counting or repacking tablets or capsules</td>
</tr>
</tbody>
</table>
| Compounding and other manipulations | • Crushing or splitting tablets  
• Pouring oral or topical liquids from one container to another  
• Weighing or mixing components  
• Constituting or reconstituting powdered or lyophilized HDs  
• Withdrawing or diluting injectable HDs from parenteral container  
• Expelling air or HDs from syringes  
• Contacting HD residue present on PPE or other garments  
• Deactivating, decontaminating, cleaning and disinfecting areas contaminated with or suspected to be contaminated with an HD  
• Maintenance activities for potentially contaminated equipment and devices |
| Administration                   | • Generating aerosols during administration or HDs by various routes  
• Performing certain specialized procedures  
• Priming an IV administration set |
| Patient-care activities           | • Handling body fluids                                                                               |
| Spills                           | • Spill generation, management and disposal                                                          |
| Transport                        | • Moving HDs within a healthcare setting                                                            |
| Waste                            | • Collection and disposal of hazardous waste and trace contaminated waste  |
Personnel Potentially Exposed to HDs

• USP Chapter <800> applies to all healthcare facilities where hazardous drugs are handled.

• Personnel at risk of exposure include:
  • Pharmacists
  • Pharmacy technicians
  • Nurses
  • Physicians
  • Physician assistants
  • Home health care workers
  • Veterinarians
  • Veterinary assistants

Includes LTC Pharmacies and Nursing Facilities
Personal Protective Equipment (PPE) Recommendations of Importance to LTC

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Activity</th>
<th>Double Chemo-therapy Gloves</th>
<th>Protective Gown</th>
<th>Eye/Face Protection</th>
<th>Respiratory Protection</th>
<th>Ventilated Engineering Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Types of HDs</td>
<td>Receiving, unpacking &amp; placing in storage</td>
<td>No (single glove can be used unless spills occur)</td>
<td>No – unless spills or leaks occur</td>
<td>No</td>
<td>No – unless spills or leaks occur</td>
<td>No</td>
</tr>
<tr>
<td>Intact Tablet or Capsule</td>
<td>Administration from unit-dose package</td>
<td>No (single glove can be used)</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>Cutting, crushing, or manipulating tablets or capsules; handling uncoated tablets</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes, if not done in a control device</td>
<td>Yes</td>
</tr>
<tr>
<td>Tablets or Capsules</td>
<td>Administration</td>
<td>No (single glove can be used)</td>
<td>No</td>
<td>Yes, if vomit or potential to split up</td>
<td>No</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>Drug-contaminated waste Disposal and cleaning</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes, if liquid could splash</td>
<td>Yes, if inhalation potential</td>
<td>N/A</td>
</tr>
</tbody>
</table>

HD Handling Requirements

• Entity must maintain a list of HDs in use
  • Based on NIOSH list
  • Reviewed at least every 12 months
  • Updated whenever a new agent or dosage form is used

• Components of HD handling include, but not limited to:
  • Receipt
  • Storage
  • Mixing
  • Preparing
  • Compounding
  • Dispensing
  • Transporting
  • Administering
  • Disposing, and
  • *Otherwise altering, counting, crushing, or pouring HDs*

• Includes both non-sterile and sterile products and preparations

Select HD Handling Procedures

**Dispensing**
- Counting & repackaging equipment dedicated for HD use
- Decontaminated after every use
- Antineoplastic HDs must not be placed in automated counting or packaging machines
- Package is labeled HD & other info as appropriate

**Transport**
- Appropriate containers must be used
- Labels must include HD category, storage instructions and disposal instructions
- Adherence to SOPs to reduce exposure risk
- SOP address waste handling

Select HD Handling Procedures (con’t)

**Administration**
- Must use protective medical devices & techniques
- Avoid manipulating HDs (crushing tablets, opening capsules).
  - If not possible, don appropriate PPE and use plastic pouch to contain dust or particles generated.
  - PPE available and worn

**Disposal**
- Consider all PPE worn handling HDs to be contaminated
- Place waste in appropriate waste container
- Dispose per jurisdictional regulations

**Spill Management**
- Spill kit required
- SOPs address location of spill kit, cleanup materials, PPE requirements, who is responsible for spill management
- Spill training and drills required
- Spill reporting required

HD Risk Assessment

- Some dosage forms of HDs may not pose a significant risk of direct occupational exposure
  - Tablets or capsules (solid, intact dosage formulations) administered to patients without modifying the formulation may post low risk
    - Single pair of gloves may be all that is required
  - Dust from tablets or capsules may still present a risk due to skin exposure or inhalation
  - Cutting, crushing or otherwise manipulating tablets and capsules will increase the risk of exposure to workers
    - Refer to manufacturer’s safe-handling guidance (MSHG) usually found in Section 16 of the Package Insert

- An assessment of risk may be performed for solid, intact dosage formulations to determine alternate containment strategies or work practices
  - If a risk assessment is not performed, all HDs must be handled with all defined containment strategies
HD Risk Assessment

• Assessment of risk must consider:
  • Type of HD
    • Is HD a antineoplastic, non-antineoplastic, reproductive-risk?
  • Dosage form
    • How can HD potentially enter the body: skin, inhalation, ingestion?
  • Risk of exposure
    • Personal Protective Equipment (PPE) available?
    • Engineering controls available?
  • Manipulation required
    • How is HD handled?
    • How often is HD handled?
  • Packaging

• Entity must document:
  • Alternative containment strategies and/or work practices being employed for specific dosage forms to maintain occupational exposure
  • Annual review (at least every 12 months) of each risk assessment
Repeated Counting, Cutting, or Crushing Tablet Formulations of HDs

• Should take place in a containment device such as a Class II biological safety cabinet or a compounding aseptic containment isolator

• If a containment device is not available, then should use:
  • Double gloves, a protective gown,
  • Respiratory protection, and a
  • Disposable pad to protect the work surface
If an Assessment of Risk is not performed, all HDs must be handled with all containment strategies defined in Chapter <800>
Alternative Oral Dosage Formulations are a Way to Avoid Crushing Medications\textsuperscript{1,2}

- Tablets are often crushed to facilitate easier medication administration.
- Inappropriate tablet crushing can alter the pharmacokinetic properties, therapeutic efficacy and safety of the medication.
- Drug loss may occur with powder being spilled or left behind in the vessel.
- Cutting, crushing or otherwise manipulating tablets and capsules will increase the risk of exposure to workers

\textsuperscript{1} Steadman K, et al. Drug loss while crushing tablets: Comparison of 24 tablet crushing devices. PLOSONE https://doi.org/10.1371/journal.pone.0193683 March 1, 2018
\textsuperscript{2} The United States Pharmacopeial Convention. USP Chapter <800>. December 1, 2017.
Steps for LTC Pharmacies and Nursing Facilities to Consider in Assessing HD Risk

1. Create a list of HD dosage forms and where they are located.
2. Check each HD (PI and SDS) for risk of exposure, PPE, deactivation agent, spill cleanup, storage, handling, transport, administration and disposal.
3. Identify HDs that qualify for an Assessment of Risk (e.g., solid, intact dosage formulations).
4. Develop a plan of action for managing the risks of each drug.
5. Perform Assessment of Risk using PI, SDS, NIOSH and other resources.
Environmental Protection Agency
Management of Hazardous Waste Pharmaceuticals

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Speaker Disclosure

Paul Baldwin declares no conflicts of interest or financial interest in any product or service mentioned in this program, including grants, employment, gifts, stock holdings, and honoraria.
Short History

- Effort began in 2008
- EPA’s Objectives
  - Clarify management of OTC nicotine replacement products
  - Simplify compliance for healthcare facilities
  - Reduce the amount of pharmaceuticals disposed of in the drains
  - Reduce overlap between EPA RCRA regulation and DEA controlled substance regulation
  - Clarify regulatory status of drugs disposed of through reverse distributors
- Effective Date: August 19, 2019
Key Definitions

- **Pharmaceutical**: any drug or dietary supplement for use by humans or other animals

- **Hazardous Waste Pharmaceutical**: A solid waste, as defined in 21CFR §261.2 and exhibits characteristics from 261 Subpart C or is listed in part 261 Subpart D.
  - Ignitable
  - Corrosive
  - Reactive
  - Toxic

- **Potentially Creditable**: A prescription pharmaceutical that has reasonable expectation to receive manufacturer credit
  - In original manufacturer’s package
  - Undispensed
  - Unexpired, or less than one year past expiration

- **Non-Creditable**: A prescription drug that does not have a reasonable expectation to receive manufacturer credit.

- **Reverse Distributor**: person that receives and accumulates potentially-creditable pharmaceuticals for facilitating credit.
Facilities Subject to this Rule

- Pharmacies
- LTC Pharmacies
- Hospice
- SNFs and NFs
  - Not Assisted Living
  - Not Independent Living

Participation Voluntary if:

- Facility is a very small quantity generator (VSQG)
  - Not more than 100 Kg of hazardous waste per month
  - Not more than 1 Kg of acute hazardous waste per month

Sewering prohibition applies to all healthcare facilities, as does conditional exemption for hazardous waste that are also controlled substances.
Operating under Part 266 Subpart P

Make a one-time notification to EPA Regional Administrator by filing EPA Site Identification Form 8700-12

- One-time notification
- Must be retained as long as the facility is operating under Subpart P
- Separate notification required for each facility
Managing Non-Creditable Hazardous Pharmaceutical Waste

• Determining Hazardous Status
  • Make individual determination
  • Treat all non-creditable drugs as hazardous

• Container Standards
  • Structurally sound, compatible with the contents, and that would prevent any leaks or spills under reasonably foreseeable conditions

• Non-hazardous, non-creditable waste may be co-mingled
• Containers must be labeled: “Hazardous Waste Pharmaceuticals” during accumulation
• One-year accumulation time limit
Managing Non-Creditable Hazardous Pharmaceutical Waste

Compliance with Land Disposal Restrictions (LDRs)

Most HWPs are organic and can be incinerated. Some must be treated before being disposed of in landfills.

These compounds are primarily metallic and are identified under EPA Hazardous Waste Codes D004-D043, U151 (mercury), U205 (selenium sulfide), and P012 (arsenic trioxide)

These compounds must be segregated in a separate container from other non-creditable waste.
Managing Non-Creditable Hazardous Pharmaceutical Waste

Recordkeeping Requirements

• Waste must be accompanied by a signed hazardous waste manifest and maintained for 3 years.

• Exception report required when facility does not receive signed copy of manifest from transporter within 60 days of date when waste was accepted by transporter. Maintain for 3 years.

• Any records of test results of hazardous waste must be maintained for 3 years. Not required when facility manages all non-creditable waste as hazardous.

• Retention periods are extended during ongoing enforcement actions.
Healthcare Facilities that Accept Hazardous Waste Pharmaceuticals from Off-site VSQG Healthcare Facilities

Healthcare Facilities may accept under these conditions

• The “sending” facility and receiving facility are under same ownership, or the sending facility has agreement with receiving facility to supply Rx Drugs.

• Sending facility is operating under Subpart P

• Receiving facility manages the hazardous waste pharmaceuticals it receives under Subpart P

• Receiving facility keeps records of all shipments of waste it receives from sending facility for three years.
Managing Potentially-Creditable Hazardous Pharmaceutical Waste

• Determining Hazardous Status
  • Make individual determination, or
  • Treat all potentially-creditable drugs as hazardous
  • Co-mingled waste will be subject to all of Subpart P

• Container Standards
  • EPA has not implemented specific standards
  • EPA has not implemented specific labeling standards

• No Accumulation Time Limit
• Recordkeeping
  • Must maintain delivery confirmation for 3 years
  • Must maintain shipping papers for 3 years
LTCF VSQGs May Dispose of Hazardous Waste Pharmaceuticals in Drug Enforcement Administration Collection Receptacles

• LTCFs that are VSQGs may dispose of hazardous waste pharmaceuticals in DEA authorized collection receptacles
• Receptacle must be on site
• Contaminated personal protective equipment or clean-up residues may not be disposed of in these receptacles
Sewering Prohibited

• The prohibition on sewering hazardous waste pharmaceuticals applies to all reverse distributors and all healthcare facilities, including healthcare facilities that are VSQGs.

• EPA is not providing any exceptions to the prohibition on sewering.
Hazardous Pharmaceutical Wastes That are Also DEA Controlled Substances: LTC Facilities

• Most LTCFs are VSQGs and are exempt from RCRA Regulation, except for prohibition on sewering
• LTCFs have option of returning hazardous waste, controlled drugs, to LTC pharmacy under provisions of DEA regulations.
• LTCFs may place resident controlled drugs in DEA receptacles, but not facility inventory.
Management of Residue in Containers

• Stock, dispensing and unit-dose containers
  • Stock bottle or dispensing bottle (up to one liter or 10,000 tablets), and unit-dose container considered empty when contents have been removed (no longer hazardous)

• Syringes
  • Syringe is considered empty and the residues are not regulated as hazardous waste provided the contents have been removed by fully depressing the plunger of the syringe.
  • Non-empty syringes containing hazardous waste pharmaceuticals must be managed as non-creditable hazardous waste.
Management of Residue in Containers

• Other Containers, Including Delivery Devices-IV Bags
  • IV bag is considered empty and the residues are not regulated as hazardous waste provided the pharmaceuticals in the IV bag have been fully administered to a patient.
  • In cases where the IV bag has not been fully administered and the IV bag held non-acute hazardous waste pharmaceuticals, then IV bag can be shown to be empty and the remaining residues not regulated as hazardous waste.
  • If an IV bag is not empty through either of these means the IV bag must be placed with its remaining hazardous waste pharmaceuticals into a container that managed and disposed of as a non-creditable hazardous waste pharmaceutical.
Management of Residue in Containers

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  • If an IV bag is not empty through either of these means the IV bag must be placed with its remaining hazardous waste pharmaceuticals into a container that managed and disposed of as a non-creditable hazardous waste pharmaceutical.
Management of Residue in Containers

• This includes, but is not limited to, residues in inhalers, aerosol cans, nebulizers, tubes of ointments, gels, or creams.
  • Hazardous waste pharmaceuticals remaining in all other types of unused, partially administered, or fully administered containers must be managed as non-creditable hazardous waste pharmaceuticals under this subpart, unless the container held non-acute hazardous waste pharmaceuticals and is empty.
Key Elements

- Rule effective August 19, 2019
- For most of us, participation in Subpart P is optional, except for the “no sewering’ provision
- Register with EPA
- Two Management Classes
  - Non-creditable
  - Potentially Creditable
- LTC Pharmacy may manage waste for LTCF
- Recordkeeping requirements
- Hazardous Controlled Substances
- Container Residues
Questions?

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