USP Chapters <797> and USP <800>
FROM A MANAGER’S PERSPECTIVE
NANCY MYERS PHARMD, MBA, BCPS, CDE

Objectives
• Discuss how to prioritize compliance with USP <797> and USP <800>
• Discuss how to develop a system to handle hazardous drugs and who should be on the multidisciplinary team
• Develop a plan to hardwire systems for compliance

USP Chapter <797>
United States Pharmacopeia
• “The intent of <797> is to prevent harm and fatality to patients that could result from microbial contamination (non-sterility), excessive bacterial endotoxins, large content errors in the strength of correct ingredients, and incorrect ingredients in compounded sterile products (CSPs).”
• Applies to pre-administration manipulations of compounded sterile preparations including compounding, transportation, and storage.
• Applies to all compounding personnel without distinction as to site or profession – all patients deserve to be protected from errors and contamination.
• The Compounding Expert Committee continues to review and revise the chapter based on the public comments submitted by January 31, 2016.
• USP does not have an anticipated date for the chapter’s republication for comments.
Steps to Getting Prepared

- USP <797>
  - Compliance should already exist
  - Consistent education and quality assurance should be ongoing
  - Possible struggles
    - Design of the IV Room
    - In-process checking
    - Consistency of staff
    - Maintaining quality assurance – annual media fill, glove testing, surface testing, humidity
  - Updating Policies and Procedures

Steps to Getting Prepared

- What can you do now before revisions are finalized:
  - Beyond Use Dating Evaluation
    - Restricted access barrier system (RABS)
  - Proprietary Bag And Vial Systems
  - Allergen Extracts
  - Master Formulation Record
  - Compounding Record
  - CMS Conditions of Participation

USP Chapter <800>

- Published February 2016, as Hazardous Drugs – Handling in the Healthcare Settings
- Compliance: July 1, 2018
- Written to promote patient, staff and environmental safety — not just safe ordering and administration
- Defines a process on how to handle hazardous drugs (HD) from procurement to disposal
  - Various disciplines: Pharmacists, pharmacy techs, nurses, environmental services, veterinarians, etc
  - Involves areas that receive, store, compound, dispense, administer and dispose
- Works in conjunction with USP <795> or USP <797>
Steps to Getting Prepared

- Gap analysis with USP <800>
- Create a Hazardous Drug (HD) list (refer to NIOSH 2016)
- Establish an interdisciplinary team:
  - Examples include: employee health, nursing, risk/safety/quality, human resources, materials management, environmental services, engineering, leadership
- Assess if capital is needed for facility design

USP <800> Gap Analysis Tool

- Develop or use a tool that has the categories in sections
- May want to delineate difficult in achieving compliance (low, medium, high)

Hazardous Drug (HD) List

- An entity must maintain a list of HDs that must include any items from the current NIOSH list that the entity handles.
- Review every 12 months and when a new agent or dosage form is used
- Groups
  - Group 1: Antineoplastic drugs
  - Group 2: Non-antineoplastic drugs
  - Group 3: Drugs that pose a reproductive risk. May not be a risk for some workers due to age or infertility
What Does Hazardous Drugs Mean

• Drugs considered hazardous include those that exhibit one or more of the following 6 characteristics:
  – Carcinogenicity
  – Teratogenicity
  – Reproductive toxicity
  – Organ toxicity at low doses
  – Genotoxicity
  – Structure of new drugs that mimic old drugs that are hazardous

NIOSH: Groups 1-3 Examples

<table>
<thead>
<tr>
<th>Group 1: Antineoplastic</th>
<th>Group 2: Non-antineoplastic</th>
<th>Group 3: Reproductive effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cisplatin</td>
<td>Abacavir</td>
<td>Chinomycin</td>
</tr>
<tr>
<td>Epirubicin</td>
<td>Asparagin</td>
<td>Colchicine</td>
</tr>
<tr>
<td>Hydroxyurea</td>
<td>Carbamazepine</td>
<td>Finasteride</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>Divalproex</td>
<td>Fluoxamol</td>
</tr>
<tr>
<td>Oxaliplatin</td>
<td>Etretinate</td>
<td>Misoprostil</td>
</tr>
<tr>
<td>Paclitaxel</td>
<td>Fluphenazine</td>
<td>Oxytocin</td>
</tr>
<tr>
<td>Pentostatin</td>
<td>Methotrexiprogesterone</td>
<td>Paroxetine</td>
</tr>
<tr>
<td>Tamoxifen</td>
<td>Progestosterone</td>
<td>Voriconazole</td>
</tr>
<tr>
<td>Vinorelbine</td>
<td>Spironolactone</td>
<td>Warfarin</td>
</tr>
</tbody>
</table>

Development of Your Organizations Hazardous List

• OSHA requires organizations to develop a hazardous communication program. Steps include:
  – Identify all hazardous drugs encountered
  – Does not mean evaluate every marketed drug
  – Know this is a continual process
  – Evaluate new drugs
  – Reassessment of drugs on the hazardous list (re-categorize)
  – Investigational drugs: Assess the mechanism of action to see if there is a concern (hazard list data typically incomplete)
Development of Your Organizations Hazardous List

- Label all hazardous drugs
  - Prevention of mishandling
  - Do not place in an automatic counting machine
  - Do not use a Packager machine
  - Care with crushing, dissolving, counting, pouring
- Overall: AVOID stressing dosage forms thus causing powdered contamination
  - Use liquids when possible

Assessment of Risk

- Assessment
  - Type of Hazardous Drug (HD) (antineoplastic, non-antineoplastic, reproductive risk only)
  - Dosage form
  - Risk of exposure
  - Packaging
  - Manipulation
- Alternative Strategy
  - The organization must document the alternative work practice for the specific dosage form to minimize exposure
  - Review every 12 months and document

Containment Requirements for your Organization

All Containment <800>
- API (Active Pharmaceutical Ingredient) of any an HD
- Antineoplastic requiring manipulation

Alternative Strategy
- Counting or packaged antineoplastic
- Non-antineoplastics
- Reproductive hazards
Precautions for Handling Hazardous Drugs

- Receipt
- Storage
- Appropriate labeling
- Proper preparation
  - Ventilated engineering controls
  - Closed System Transfer Devices (CSTDs)
- Cleaning
- Protective Equipment and Engineering Controls
  - Gloves
  - Gown
  - Eye protection
  - Respiratory protection

Receipt

- Antineoplastic HDs and all HD APIs must be unpacked in an area that is neutral/normal or negative pressure relative to the surrounding areas.
- HDs must not be unpacked from their external shipping containers in sterile compounding areas or in positive pressure areas.
- PPE, including chemotherapy gloves, must be worn when unpacking HDs.
  - Personnel who are unpacking HDs that are not contained in plastic should wear an elastomeric half-mask with a multi-gas cartridge and P100 filter. A spill kit must be accessible in the receiving area.
- The entity must enforce policies that include a tiered approach, starting with visual examination of the shipping container for signs of damage or breakage.

Storage

- Storage of antineoplastic HDs shall be separate from storage of non-HDs
  - Refrigerator in negative pressure room
- Storage of non-antineoplastic HDs shall be separate from storage of non-HDs, unless only coated, final-manufactured dosage forms are clearly labeled as HDs and safety strategies are included in the entity’s policies and procedures.
- Storage of sterile and non-sterile HDs may be intermingled
- HD storage in a sterile compounding buffer area shall be limited to those used for sterile compounding
Pressure and PEC

- HDs shall not be stored, unpacked, compounded or otherwise manipulated in an area that is positive pressure relative to the surrounding areas
  - Externally vented
  - At least 12 ACPH
  - Negative pressure between 0.01 and 0.03 inches of water column
- A laminar air flow workbench (LAFW) or compounding aseptic isolator (CAI) shall not be used for the compounding of a HD
- Class II BSCs or Compounding Aseptic Containment Isolators (CACIs) may be used for sterile compounding
- CVEs, Class I or II BSCs, or CACIs may be used for non-sterile compounding

Cleaning

- Deactivation
  - Render compound inert or inactive
  - Multi-component system
    - Sodium hypochlorite and sodium thiosulfate
- Decontamination
  - Remove HD residue
  - Between compounding of different HDs, at least daily, any time a spill occurs, below and after ventilation, any time voluntary interruption occurs, and if the ventilation tool is stored
- Cleaning
  - Remove organic and inorganic material
  - Germicidal detergent
- Disinfecting
  - Sterile Alcohol
- Train pharmacy staff and/or environmental services staff

Personal Protective Equipment (PPE)

- Appropriate PPE must be worn when handling HDs during:
  - Receipt
  - Storage
  - Transport
  - Compounding (sterile and nonsterile)
  - Administration
  - Deactivation/decontamination, cleaning, and disinfecting
  - Spill control
  - Waste disposal
Personal Protective Equipment (PPE)

- Chemotherapy gloves must meet American Society for Testing and Materials (ASTM) standard D6978 or its successor.
  - When used for sterile compounding, the outer chemotherapy gloves must be sterile.
- Gowns must be disposable and shown to resist permeability by HDs.
- Head and hair covers (including beard and moustache, if applicable), shoe covers, and sleeve covers provide protection from contact with HD residue.
  - Two pairs of shoe covers when compounding HDs.
- Goggles must be used when eye protection is needed.
- Fit-tested NIOSH-certified N95 or more protective respirator is sufficient to protect against airborne particles.
  - However, N95 respirators offer no protection against gases and vapors and limited protection against direct liquid splashes.

Table 9: Personal protective equipment and engineering controls for working with Hazardous Drugs in Healthcare settings

| Condition | Activity | Eye Protection | Respiratory Protection | Personal Protective Equipment | Engineering Control
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Compounding</td>
<td>no</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>2. Dispensing</td>
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<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
</tr>
<tr>
<td>3. Administration</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
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<tr>
<td>4. Non-patient care</td>
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<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
</tr>
<tr>
<td>5. Household</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
</tr>
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Table 9 (Continued): Personal protective equipment and engineering controls for working with Hazardous Drugs in Healthcare settings

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<td>yes</td>
<td>yes</td>
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<td>no</td>
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</table>
Policies and Procedures

- Hazard communication program
- Occupational safety program
- Designation of HD areas
- Receipt
- Storage
- Compounding
- Use and maintenance of proper engineering controls
- Hand hygiene and use of PPE based on activity
- Deactivation, decontamination, cleaning and disinfection
- Dispensing
- Transport
- Administering
- Environmental monitoring (e.g., wipe sampling)
- Disposal
- Spill control
- Medical surveillance

Policies and Procedures

- P&P should encompass the following:
  - Interdisciplinary team and Pharmacy and Therapeutics (P&T) annual review classification of drugs on the hazardous list; new drugs added to formulary should automatically be reviewed
  - Signage designated HDs
  - Who can access; where is HD handling; designated areas
  - Who can prepare HD: licensed, trained individuals
  - Detailed process, garbing, washing hands
  - Spill containment and clean up (who to call; action to be taken; exposure)
  - Location of HD storage and preparation guidance: no food, gum, drinking, eating in the designated area
  - Cleaning of the areas: not performed during prep; use a dust containment method (do not dry sweep/mop)

Policies and Procedures

- Closed System Transfer Devices (CSTD)
  - USP <800> only required for administration of hazardous drugs
  - USP <800> recommends you use a CSTD for preparation. In some cases you have to prepare with a CSTD in order for administration to take place with a CSTD

- Transportation of product
  - Wiping end product
  - Knowledgeable about spill kits

- Administration
  - CSTD
  - PPE

- Environmental Services
  - Trained to wear PPE
  - Trained with spill kits
Policies and Procedures

• P&P should encompass the following:
  – Patient Signage
  – Patient transportation
  – Waste Management
  – Laundry
    • All laundry treated as if contaminated
    • Gloves worn
    • Prewash prior to washing
  – Investigational Drugs
  – Non-formulary Drugs
  – Home Health Care

Quality Assurance

• Annual HD Competency
  – Upon hire and annual: demonstrate
• USP <800> recommends environmental monitoring for unintended contamination by HDs
  – Environmental wipe sampling for HD surface residue should be performed routinely
  – Initially as a benchmark and at least every six months, or more often as needed, to verify containment

• Medical surveillance

Medical Surveillance and Exposure Reporting

• Include workers who are directly exposed nurses, pharmacists, pharmacy technicians, nurse aides, laundry workers, veterinarians, workers who ship, transport or receive HD, etc.
• Goal: minimize adverse health effects in workers exposed to hazardous substances
• Employees of reproductive capability must in writing accept understanding of the risks of handling HDs before working in the area
  – Baseline assessment (lab at regular intervals) and exit interview
• Medical Surveillance is the 2nd line of defensive
  – 1st line is engineering controls, work place controls, PPE, education/training
Medical Surveillance Data

- The following is evaluated:
  - Medical (reproductive) and Occupational history
  - Physical examination
  - Lab
  - Biological monitoring

Barriers to Compliance

- Studies document HD contamination and worker exposure but few document why safety efforts have not been successful.
- Improved compliance by knowledgeable nurses were with:
  - Fewer patients
  - Few barriers (availability/convenience of PPE)
  - Better safety environment (training, P&P)

Challenges to Compliance

- Percentage of respondents

0 5 10 15 20 25 30

- Lack of knowledge among leadership
- Lack of leadership support
- Training/competency resources
- Physical limitations
- Financial/budgetary restrictions
- Time required
- Staff resistance to change
- Leadership resistance
- Lack of information among leadership
### The TEAM

<table>
<thead>
<tr>
<th>Responsible Person</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Director of Pharmacy and/or Manager</td>
<td>Hazardous drug officer. Oversight to the program</td>
</tr>
<tr>
<td>Department (Leadership)</td>
<td>Education and training (orientation and annual)</td>
</tr>
<tr>
<td></td>
<td>Provide PPE</td>
</tr>
<tr>
<td></td>
<td>Periodically QA</td>
</tr>
<tr>
<td></td>
<td>Access to information of this plan is available to all employees</td>
</tr>
<tr>
<td>Employee</td>
<td>Demonstrate competency in safe handling</td>
</tr>
<tr>
<td></td>
<td>Administers, stores, transports, cleans spills and disposes of waste</td>
</tr>
<tr>
<td></td>
<td>appropriately</td>
</tr>
<tr>
<td>Local Employee Health Services</td>
<td>Manage Medical Surveillance Program</td>
</tr>
</tbody>
</table>

### Now, let's get started?

- Ensure appropriate facility design and engineering controls
  - Secure major capital expenditures
- Hazardous Drug Identification
  - Organize drugs and start using CSTD
- Develop Policies and Procedures
- Hazardous Communication Program
  - Train staff: start training during orientation; annual training (prep, transportation, administration)
  - Medical Surveillance and Exposure Reporting
- Appropriate Waste System (i.e., Clean Harbors, Stericycle)

### GET READY FOR JULY 1, 2018

USP <800> IS COMING
Questions?