USP <797> & USP <800> Standards: Compliance Challenges in Pharmaceutical Compounding, Design and Disposal

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Disclaimer

• The opinions and views expressed are those of the presenter and do not necessarily represent those from the Department of Veterans Affairs.
Objectives

• Describe current challenges and expectations in United States Pharmacopoeia (USP) Pharmaceutical Compounding Chapters (USP <797> and USP <800>)

• Outline key observations from regulatory oversight around environmental cleanliness, facility design and personnel competency at health-system pharmacies

• Outline strategies for managing the environmental control requirements for compliance with USP compounded sterile preparations standards
Basis of Pharmaceutical Compounding

• Maximize use of commercially approved and prepared medicines
• Outsourcing the preparation of compounded sterile preparations (CSPs) as an alternative to in-house compounding when:
  • Frequency of use for certain CSPs is very low and minimize need for staff competency
  • The volume of use for certain CSPs is high and staff resources are limited
  • The organization does not possess the technological resources to ensure sterility of CSPs to follow United States Pharmacopoeia (USP) Chapter 797
• A commercially manufactured product is not available including medicine shortages (ISMP Guidelines)
The Need for Oversight to Ensure Uniform Compliance in Pharmaceutical Compounding Standards in the U.S.

- Medicine shortages and need for extended expiration dating for CSPs led community and hospital pharmacists to rely on outsourced compounding pharmacies for complex patient needs, e.g.
  - Especially large volume sterile injectable medications
  - Specialized pain medications (e.g. Patient Controlled Analgesia)
- CSPs direct impact on patient care makes their quality and safety essential
- To ensure safe use of CSP pharmaceuticals, regulatory oversight/enforcement must assure non sterile compounded products and sterile compounded products (CSPs) meet standards of quality, purity and sterility in accordance with USP <795>, USP <797> and USP <800> compendial standards.
Impact of Medicine Shortages (Table 1)

• Medicine shortages are challenging to both patients and healthcare practitioners

• Shortages of pharmaceutical ingredients for critical therapy e.g. parenteral nutrition directly affect patient outcomes in healthcare settings (e.g. amino acids, electrolytes, trace elements, intravenous (IV) multivitamins, IV fat emulsions)

• In the first quarter of 2017, there were 176 drugs reported in shortage in the U.S.

• Of concern is the shortage of medically necessary medications which can comprise a significant number of shortages
First Quarter 2017: 176 drug shortages

Table 1

<table>
<thead>
<tr>
<th>Year</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
</tr>
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<tbody>
<tr>
<td>2016</td>
<td></td>
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</table>

Short Supply
Number of active drug shortages in the U.S., quarterly
Impact of Medicine Shortages (Table 2)

• Increase in drug expenditures (87 %)
• Increase in pharmacy workload (75 %)
• Increase in on-hand-inventory (65 %)
• Decreased staff productivity and satisfaction (40 %)
• **In-house pharmaceutical compounding of replacement shortage products (36 %)** *
• Compromised patient care and patient safety (31 %)
• **Outsourced pharmaceutical compounding of replacement shortage products (27 %)** *
• Delayed or cancelled procedures (20 %)
• Loss of credibility with medical staff (14 %)
• Increase in adverse drug events (4 %)
• Increase in sentinel drug events (1 %)
Table 2: Impact of Medicine Shortages and Resultant Effects
Current Outsourced Pharmaceutical Compounded Replacement of Products

- Patient controlled analgesia 70%
- Operating room medication filled syringes 64%
- Pitocin/oxytocin 60%
- Epidural 57%
- Total parenteral nutrition 43%
- Narcotics and controlled drug substances 37%
- Cardioplegia 24%
- Critical care infusions 23%
- Antibiotics 22%
- Radiopharmaceuticals 20%

- **Products on shortage (19%)**
  - Nerve block products 13%
  - Electrolyte solutions 12%
  - Emergency cart medications 8%
  - Dialysis fluids and drugs 5%
  - Oncology drugs 3%
  - Research/study drugs 2%
  - Other 3%
The Need for Oversight for Uniform Compliance

• In the United States, the USP <795>, USP <797> and USP <800> are the established standards for compounding pharmacists to prepare non-sterile, sterile non-hazardous and sterile hazardous pharmaceutical preparations respectively. Less rigorous than current Good Manufacturing Practice Standards (cGMPs).

• USP <795>, <797> and <800> standards appropriate for traditional pharmacies providing patient-specific or for individualized patient prescriptions but may not always be effectively applied in large-scale compounding for pharmaceutical batch quantities.

• Drug Quality & Security Act of 2013
  • Differentiates between 503A and 503B facilities
Pharmaceutical Compounding - Scope

• An integral part of Pharmacy Practice that meets customized patient needs based on a physician-patient-pharmacist relationship

• Important to distinguish between manufactured drug product and compounded product given to patients.
# Pharmaceutical Compounding (Practice) vs Manufacturing

<table>
<thead>
<tr>
<th>Good manufacturing Practices:</th>
<th>Pharmaceutical Compounding (Practice) under the Drug Quality Security Act (503A Pharmacies):</th>
</tr>
</thead>
<tbody>
<tr>
<td>Product focus</td>
<td>Patient-specific</td>
</tr>
<tr>
<td>Production (not in real time)</td>
<td>Real-time provision of service</td>
</tr>
<tr>
<td>cGMP (21 CFR 210/2110)</td>
<td>Local or state regulatory oversight</td>
</tr>
</tbody>
</table>
**Example of a Patient Specific CSP**

1 Prescription for 1 Patient = Compounding Pharmacy Prepares one syringe/one dose

<table>
<thead>
<tr>
<th>Patient Name: JD</th>
<th>11-01-13</th>
</tr>
</thead>
<tbody>
<tr>
<td>Address:</td>
<td></td>
</tr>
<tr>
<td>Preservative Free Morphine Sulfate 0.25mg in 5 mL Normal Saline for intra-thecal administration</td>
<td></td>
</tr>
<tr>
<td>Amount:</td>
<td>5 mL</td>
</tr>
<tr>
<td>Provider: Dr. PA</td>
<td>No refills</td>
</tr>
<tr>
<td></td>
<td>Security Prescription Form</td>
</tr>
</tbody>
</table>
Example of Batched and/or Shortage Compounded Sterile Product: Patient Controlled Analgesia (PCA) Syringes for Smart Pumps

• Some PCA devices (Smart Pumps) do not have commercially-available pharmaceutical syringe suitable to fit into the device.
Examples of Patient Specific High Risk Compounded Sterile Products with Reported Shortages

• Morphine 18mg/mL, Bupivacaine 9mg/ml preservative free intra-thecal syringe 20 mL Syringe
• Morphine 30 mg, Baclofen 150 mcg, Bupivacaine PF 15mg/mL preservative free x 40mL
• Sodium phosphate monobasic monohydrate 27.8 g/Sodium phosphate dibasic anhydrous 14.2 g
• Sterile water for injection qs 100 mL
• Sodium Bicarbonate (per 100 mL) 8.4 % 8.4 g Sterile water for injection qs 100 mL
• Magnesium sulfate heptahydrate 10 g/Sulfuric acid and/or sodium hydroxide qs pH 5.5 to 7.0/Sterile water for injection qs 100 mL
Challenges for Pharmacists in Pharmaceutical Sterile Compounding

- Regulatory Gaps
- USP <797> compliance is
Challenges in Pharmaceutical Sterile Compounding

• Healthcare Delivery
• Difficulty to trace CSPs through healthcare system; CSPs are repackaged,
Compounded Sterile Product Quality and Safety Assurance Established by:

• Focusing on systems to comply with USP <797> Standards for sterile compounding.
• Improving awareness of Compounded Sterile Products (CSPs) that are preservative-free (PF) have a high risk of microbial contamination if sterile compounding standards are not strictly followed.
• Ensuring appropriate use of single-dose-vials (SDVs) which the Center for Disease Control has determined only to be used for one patient at a time.
Compounded Sterile Product Quality and Safety Assurance Established by:

- Improving clinicians’ awareness of product quality problems or contamination originating from compounded drug products.

- Ensuring robust surveillance systems to detect and report adverse reactions from a public health perspective.

- Facilitating root cause analyses of sterile compounding quality/contamination outbreaks (regulatory gaps, compounding processes, clinician awareness).
Examples of Shortage and/or Batched Compounded Sterile Products

• ELECTROLYTES:
  • Magnesium Sulfate
  • Sodium Bicarbonate
  • Calcium Gluconate
• Sodium Citrate
• Hydromorphone 0.75 mg/ml preservative free IT Syringe
Examples of Batched and/or Shortage Compounded Sterile Products: Crash Cart Drugs

Crash Carts require single dose syringes with extended BUDs.

Atropine Syringe
Calcium Chloride Syringe
Dextrose 50% Syringe
Ephedrine Syringe
Phenylephrine Syringe
Sodium Bicarbonate Syringe
Verapamil
Drivers for Outsourced Pharmaceutical Compounding for Replacement of Products

• Streamline pharmacy workflow
• Reduce workload
• Simplify record keeping
• Reduce pharmaceutical waste
• Meet regulatory requirements
• Eliminate difficult to prepare pharmaceutical compounded products

• **Product shortage**

• In the US, approximately 6 out of 10 hospital pharmacies use a FDA-registered outsourcing facility (i.e. a 503B company under FDA oversight as defined under the US Drug Quality and Security Act of 2013 (DQSA))
To Whom Does Sterile Compounding (USP <797>; USP <800>) Standards Apply?

• To all persons who performing compounding sterile preparations (CSPs) and all places where CSPs are prepared (e.g., facilities in which CSPs are prepared, stored, and transported).
How Do I Comply With Sterile Compounding (USP <797>; USP <800>) Standards And Requirements?
Basis of the US Drug Quality Security Act – DQSA- 2013

• The DQSA became law in 2013 as a result of public health outbreaks from compounded sterile products related to:
  • The New England Compounding Center (NECC) of Framingham, MA that was responsible for the manufacturing of preservative-free methylprednisolone acetate that was delivered intra-thecally (directly into the spinal column)
  • Raised concerns about the quality of compounded drugs.
  • Three lots of this product exposed over 20,000 individuals to risk of fungal meningitis.

• Source: www.cdc.gov/hai/outbreaks/meningitis.html
Drug Quality and Security Act - DQSA (2013; US)

• In the United States of America, the 2013 DQSA permits registered outsourced pharmaceutical compounding facilities supervised by a pharmacist to compound from APIs to meet needs from medicine shortages or patients’ clinical needs.

• Pharmaceutical compounding must comply with United States Pharmacopoeia (USP) monograph standards and the USP chapters in pharmacy compounding in assurance of quality of pharmaceutical compounded products and conform to USP <795> for non-sterile drugs; USP <797> for sterile drugs; and USP <800> for sterile hazardous drugs.
FDA 483 Observation in Sterile Pharmaceutical Compounding

- As a result the FDA embarked on an aggressive inspection schedule that resulted in multiple “Form 483” list of findings:
  - Lack of procedures to prevent microbial contamination
  - Problems with the Environmental Monitoring program
  - Problems with batch release
  - Lack of validation of the sterilization method
  - Inadequate control/cleaning/qualification of critical equipment used in manufacture
  - Issues with personnel gowning
  - Expiry dating of manufactured medicines not supported by a stability study
  - Issues with laboratory procedures or control of contract lab
  - Issues with investigations
  - Control of incoming raw materials and components
    (www.fda.gov/enforcement actions)
Example of Observations from FDA 483 Warning Letters Issued to 503A Compounding Pharmacies

1. Your firm failed to establish and follow appropriate written procedures that are designed to prevent microbiological contamination of drug products purporting to be sterile, and that include validation of all aseptic and sterilization processes (21 CFR 211.113(b)).
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• Policies and procedures: complete?
• Addresses all aspects of USP <797> standards?
  • Training and competencies
  • Personnel oversight
  • Product Quality Control
  • Facilities performance/environmental sampling
  • Contingency operations during suspension of services
How many of these do we fail?

2. Your firm failed to adequately design the facility with adequate separation or defined areas or such other control systems necessary to prevent contamination or mix-ups (21 CFR 211.42(b)).

• Design for success: Design to best practices rather than minimum compliance.
• Dedicate the space: Do NOT try to fit USP compliance into closets
• Get professional design help!!!!!
• Participate in overseeing construction: Engineering does not have the expertise.
How many of these do we fail?

3. Your firm failed to ensure that manufacturing personnel wear clothing appropriate to protect drug product from contamination (21 CFR 211.28(a)).

• Provide proper personal protective equipment (PPE) – Work with facility Logistics Service for them to buy PPEs for the pharmacy
• Train personnel and document training and competency annually
• Supervisory observation of compounding personnel daily
• Remediate personnel failures with corrective actions based on appropriate administrative process.
How many of these do we fail?

4. Your firm failed to establish a system for cleaning and disinfecting the room and equipment to produce aseptic conditions (21 CFR 211.42(c)(10)(v)).

• Document and evaluate Environmental Management Services (EMS) cleaning training and competencies
• EMS memorandum identifying personnel allowed to clean Pharmacy ISO classified areas to comply with USP <797> and USP <800> standards
• Record all cleaning activities
• Repeat Cleaning and over-clean. USP standards are MINIMUMS.
How many of these do we fail?

4. Your firm failed to establish a system for cleaning and disinfecting the room and equipment to produce aseptic conditions (21 CFR 211.42(c)(10)(v)).

- Minimize clutter in the cleanrooms to maximize cleaning efficiency and efficacy.
- Design cleanable facilities with smooth, impervious surfaces (e.g. Plexiglas, stainless steel and epoxy paint)
- Review cleaning solutions and establish bacteriocidal and sporocidal requirements for the cleaning solutions to be used.
How many of these do we fail?

5. Your firm failed to establish an adequate system for monitoring environmental conditions in aseptic processing areas (21 CFR 211.42(c)(10)(iv)).

• Establish reliable environmental sampling contract to ensure compliance with USP <797> and USP <800>.
• Record and trend results
• Document corrective actions
Engineering Controls and Personal Protective Equipment

- Recommendations harmonized across all organizations
- Focus is on facilities, engineering controls and work practices for containment of HDs
Primary Engineering Control (PEC) Devices in Sterile Pharmaceutical Compounding Cleanrooms To Assure Product Quality and Sterility

- Laminar Air Flow Workbench (LAFW) – for non hazardous drug sterile compounding of products
- Biological Safety Cabinet (BSC) for hazardous drug sterile compounding of products
USP 800 COMPLIANCE

• Compounding Aseptic Isolator  vs.  
• Compounding Aseptic Containment Isolator
Verification of Pharmaceutical Compounding

Quality and Sterility

- Refer to USP Chapters <797>, <800>, and guidance on cleanroom methods and sterilization and compounding validation.
Pharmaceutical Compounding - Applications

- Necessary when
- Commercially manufactured products are unavailable due to shortage
- Preparation of sterile drug products (as distinct from non-sterile compounding) using pharmaceutical ingredients to prepare:
  - Sterile manufactured drug dosage forms to make a final drug formulation
  - Intravenous admixtures
  - Total parenteral nutrition solutions
  - Small or large volume parenteral solutions
Cleanroom Suite: Is an ISO Class 7 positive anteroom and ISO Class 7 positive anteroom and room that meets requirements of USP <800> and USP <797> and USP <800>.

Containment Segregated Compounding Area (C-SCA): Is a room that meets requirements of USP <800>.
Initial Steps to Cleanroom Compliance

- Maintain appropriate room air pressure
  - USP <797>: -0.01” wc to adjacent areas
  - USP <800>: -0.01 to 0.03” wc
  - Use a pressure monitor gauge to target air pressure

- Ensure adequate air changes per hour (ACPH)

- Containment Secondary Engineering Control (C-SEC) or Containment Segregated Compounding Area (C-SCA) should have independent duct work with HEPA filtration with required external venting
Biological Safety Cabinet (BSC)

• ISO Class 5 BSC
  • Requires alarm to be certified as direct connected type Class II, Type A2 or canopy-connected A2 cabinet to USP <797> standards, to detect possible failures in air handling system

*Note:* Laminar airflow workbenches (LAFW) or compounding aseptic isolators (CAI) must not be used for the compounding of an antineoplastic HD.
USP <800> Compliance

• Engineering controls that are used in HD sterile compounding:
  • ISO Class 5
    • Direct compounding area inside of a Containment Primary Engineering Control (C-PEC) such as a BSC or CACI
  • ISO Class 7 buffer room
    • A negative pressure ISO Class 7 hazardous buffer room (Containment Secondary Engineering Control; C-SEC).
    • 30 ACPH; -0.01 to 0.03” wc; HEPA filter at ceiling level and near door
  • Anteroom
    • ISO Class 8 anteroom if adjacent to non hazardous buffer area
    • ISO Class 7 positive anteroom if adjacent to hazardous buffer area
    • 30 ACPH; +0.02 to 0.05” wc; HEPA filter at ceiling level and near door
Example of Cleanroom Design- HD buffer, non-HD buffer and Anteroom

• Left: HD buffer room; ISO Class 7; -0.01 to 0.03” wc
• Center: Anteroom; ISO Class 7; +0.02 to 0.05” wc
• Right: Non-HD buffer room: ISO Class 7; +0.02 to 0.05” wc
Example of Cleanroom Design- HD buffer, non-HD buffer and Anteroom

• Left: HD Cleanroom + Anteroom
• Right: Non-HD Cleanroom + Anteroom
Containment Segregated Compounding Area (C-SCA)

• Separate negative pressure room, with fixed walls, externally vented with 12 ACPH with an externally vented Containment Primary Engineering Control (C-PEC)

• Does not need to be an ISO classified area

• Between 0.01 to 0.03” water column negative pressure

• Does not need a high-efficiency particulate air (HEPA) filters in the ceiling

• CSPs of HDs limited to 12 hours BUD
Example of design - Containment Segregated Compounding Area (C-SCA)

- Left: C-SCA; Non-ISO Room; -0.01 to 0.03” wc; 12 ACPH
- Right: BSC or CACI; Sink; Storage; Pass-through chamber
USP <800>

• **Storage of HDs**
  
  • HDs must be stored in a manner that prevents spillage or breakage if the container falls. Do not store HDs on floor

  • In areas prone to natural disasters the manner of storage must meet applicable safety precautions, such as secure shelves with raised front lips

  • Antineoplastic HDs requiring manipulation *other than counting or repackaging of final dosage forms* and any HD API must be stored separately from non-HDs in a manner that prevents contamination and personnel exposure
USP <800>

• **Storage of HDs**
  
  • Antineoplastic HDs requiring manipulation other than counting or repackaging of final dosage forms and any HD API must be stored in a separate *externally ventilated, negative-pressure room with at least 12 ACPH*
  
  • Refrigerated antineoplastic HDs must be stored in a *dedicated refrigerator* in a negative pressure area with at least 12 ACPH
    
    • If a refrigerator is placed in a negative pressure buffer room, an exhaust located adjacent to the refrigerator's compressor and behind the refrigerator should be considered
USP <800>

• **Storage of HDs**
  - Non-antineoplastic, reproductive-risk only, and final dosage forms of antineoplastic HDs may be stored with other inventory
  - Other HDs may be stored together, but HDs used for nonsterile compounding should *not be stored in areas* designated for sterile compounding to minimize traffic into the sterile compounding area
Example of design - HD Storage Room

- 12 ACPH; -0.01 – 0.03” wc; dedicated pharmacy exhaust.
USP <797> and USP <800> Compliance

Key Points:

• USP <800> eliminates the low volume exemption
What Makes a Hazardous Drug?
NIOSH Definition of a Hazardous Drug

• All drugs are hazardous to some degree
• NIOSH defines a hazardous drug as:
• Any drug identified by at least one of the following six characteristics:
  • Carcinogenicity
  • Teratogenicity or developmental toxicity
  • Reproductive toxicity in humans
  • Organ toxicity at low doses in humans (<10 mg/day) or animals (<1 mg/kg/day)
  • Genotoxicity
  • New drugs that mimic existing hazardous drugs in structure or toxicity

(2004 NIOSH Alert on Preventing Occupational Exposure to Antineoplastic and Other Drugs in Health Care Settings)
NIOSH Alert on Antineoplastic and Other Hazardous Drugs

- Preventing Occupational Exposure to Antineoplastic and Other Hazardous Drugs in Health Care Settings
  www.cdc.gov/niosh/docs/2004-165/

- Adopted by three states; proposed by others

- Currently being updated (2017)

- Reviewing ~400 new publications
Developing the HD List

Comply with all requirements of USP <800>

• Active Pharmaceutical Ingredient of any HD in list
• Antineoplastic HDs requiring manipulation
• Dosage forms not part of Assessment of Risk

Alternative strategies for implementation (Can be used in Assessment of Risk)

• Antineoplastic HDs requiring only counting or packaging (NIOSH Table 1)
• Non-antineoplastic HDs (NIOSH Table 2)
• Reproductive hazards (NIOSH Table 3)
<table>
<thead>
<tr>
<th>USP &lt;800&gt; primary focus is on...</th>
</tr>
</thead>
<tbody>
<tr>
<td>NIOSH Hazardous Drug (HD) list</td>
</tr>
<tr>
<td>Facility design and storage of HDs</td>
</tr>
<tr>
<td>Workplace practices</td>
</tr>
<tr>
<td>Monitoring of Personnel</td>
</tr>
<tr>
<td>Monitoring of Facilities</td>
</tr>
<tr>
<td>Assessment of Risk (AoR)</td>
</tr>
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</table>

- Review NIOSH list of HDs
- Determine the drugs and dosage forms handled
- Perform Assessment of Risk
- Review and document list annually
Consideration of Personnel

• Receiving
• Transport
• Pharmacy Technicians
• Pharmacists
• Nursing
• EMS – Cleaning and Disposal
• Other personnel (surgical, occupational health, safety)
Receiving and Storage of HDs for Assessment of Risk steps

• **Receiving:**
  • Antineoplastics to negative pressure room
  • Otherwise if done an AoR, identify and document strategy
  • Identify as HD and wipe off outside of container

• **Storage:**
  • If identified as HDs, store in proper bins
  • Identify procedure if manipulation is required
Examples of Alternative Containment Strategies

• Closed System Transfer Devices (CSTDs)
• ASTM tested gloves
• Purchase of unit-dose or unit of use HDs
• Use of PPEs per NIOSH 2016 Drug List
• Use of dedicated enclosed container or plastic tote to transport HDs
• Labeling of bins with HDs to alert for use of PPEs at point of care
Disposal of Hazardous Drugs CSPs

• Disposal of HDs is under the EPA Resource Conservation and Recovery Act (RCRA)
• Regulations differ by state
• USP <800> requires compliance with applicable federal, state and local regulations
• Distinguish between NIOSH HDs and EPA hazardous materials
USP 800 COMPLIANCE

• Closed-system transfer devices for HD administration "when the dosage form allows”
• Two pairs of powder-free, ASTM–tested gloves, when administering hazardous drugs
• Double gloving is also required when disposing of hazardous drugs and PPE used during the handling of the drugs
• Sink available for hand washing. Eyewash station readily available.
  • Locate water sources and drains in areas where their presence will not interfere with required ISO classifications.
  • Water sources and drains must be located at least 1 meter away from the C-PEC.
USP 800 COMPLIANCE

• Personnel unpacking HDs that are not contained in plastic should wear an elastomeric half-mask with a multi-gas cartridge and P100-filter until assessment of the packaging integrity can be made to ensure no breakage or spillage occurred.

• Full-facepiece, chemical cartridge-type respirator or powered air-purifying respirator (PAPR) should be worn when there is a risk of respiratory exposure to HDs, including when:
  • Attending to HD spills larger than what can be contained with a spill kit
  • Deactivating, decontaminating, and cleaning underneath the work surface of a C-PEC
  • There is a known or suspected airborne exposure to powders or vapors
Proper Disposal of Hazardous Drugs

- Yellow Containers for articles contaminated with hazardous drugs (gloves, tubing, gowns)

- Black Containers for hazardous drugs that are also RCRA Hazardous Waste
**Guide to Pharmaceutical Waste Management**

**Pharmaceutical Waste Identification and Segregation**

### Trace Chemotherapy Waste
- Empty chemotherapy drug containers and packaging immediately in contact with these containers
- “RCRA empty” vials, syringes, IV bags, and tubing
- Gowns, gloves, wipes, and other paraphernalia associated with routine handling, preparation, and administration of chemotherapy

### Non-Hazardous Pharmaceutical Waste
- Pharmaceuticals that do not meet the definition of an Environmental Protection Agency (EPA) hazardous waste
- Fentanyl patches – folded in half
- Unused non-hazardous controlled substances (e.g., tablets, capsules, liquids)

### Municipal Solid Waste
- Empty containers, IVs, vials, bottles, ointment tubes
- Empty IV bags and tubing that contained normal saline, dextrose, and electrolytes

### Bulk Chemotherapy Wastes
- Containers or IV bags that are not empty or are partially full
- Overly contaminated garments and spill cleanup materials

### Corrosivity Characteristic Wastes [D002]
- Strong acids with pH ≤2
- Strong bases with pH ≥12.5

### Reactivity Characteristic Wastes [D003]
- Nitroglycerine**

### Ignitability Characteristic Wastes [D001]
- Amyl nitrite inhalers (for angina pain)
- Androgel
- Benzamycin
- Brevibloc
- Clindamycin (if > 24% alcohol)
- Clrythromycin gel 2%
- Flexible collodion used as a base in wart removers
- Perchlorocap
- Primatene aerosol
- Silver nitrate applicators (for cauterizing)
- Taxol injection
- Texacort solution 1%

### Toxicity Characteristic Wastes
- Barium sulfate [D005]
- Chloroform [D022]
- Dandruff shampoo and mineral preparations with selenium [D010]
- Insulin with m-Cresol [D024]
- Lindane [D003]
- Mineral preparations containing cadmium [D006]
- Mineral preparations containing chromium [D007]
- Silver sulfadiazine cream [D011]
- Vaccines with thimerosal/mercury (e.g., influenza vaccine) [D009]

### Hazardous Waste

#### Chloral hydrate (CIV) [U034]
#### Chlorambucil* [U035]
#### Cyclophosphamide* [U055]
#### Daunomycin* [U059]
#### Dichlorodifluoromethane [U075]
#### Diethylstilbestrol [U089]
#### Hexachlorophene [U132]
#### Lindane [U129]
#### Melphan* [U150]
#### Mercury [U151]
#### Mitomycin C* [U010]

### U-Listed Hazardous Wastes
- Paraldehyde (CIV) [U182]
- Phenol [U188]
- Reserpine [U200]
- Resorcine [U201]
- Saccharin [U202]
- Selenium sulfide [U205]
- Streptozotocin* [U206]
- Trichloromononofluoromethane [U121]
- Uracil mustard* [U237]
- Warfarin ≤0.3% [U248]

### P-Listed Acute Hazardous Waste
- Arsenic trioxide* [P012]
- Epinephrine** [P042]
- Nicotine [P075]
- Nitroglycerine** [P081]
- Physostigmine [P204]
- Physostigmine salicylate [P188]
- Warfarin >0.3% [P001]

Containers or stock bottles that held a pharmaceutical on the P-List and are not “RCRA empty” (e.g., have not been triple rinsed) should be managed as P-Listed Waste

*Use containers no larger than 1 quart to assist in keeping under accumulation quantity limits and facilitate moving full containers within time limits.

### Regulated Medical Waste and Sharps
- Syringes and needles
- Scalpels, razor blades, and lancets
- Fentanyl patches – folded in half
- Unused non-hazardous controlled substances (e.g., tablets, capsules, liquids)
## Summary…
### Facility Design Examples for CSP per USP <800>

<table>
<thead>
<tr>
<th>Compounding Function</th>
<th>PEC</th>
<th>Containment Area</th>
<th>Airflow / Pressure</th>
<th>Max. BUD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compounding sterile HD in a cleanroom</td>
<td>BSC or CACI</td>
<td>ISO Class 7 negative pressure buffer rm with + pressure anteroom</td>
<td>30 ACPH, HEPA supply; exhaust</td>
<td>Per USP &lt;797&gt;</td>
</tr>
<tr>
<td>Sterile HD in CACI (outside a buffer room) per USP &lt;797&gt;</td>
<td>CACI</td>
<td>Containment segregated compounding area (C-SCA)</td>
<td>12 ACPH; exhaust; minimum negative pressure 0.01” water column</td>
<td>Per USP &lt;797&gt;</td>
</tr>
<tr>
<td>LR or MR level sterile HDs</td>
<td>BSC or CACI</td>
<td>Non-ISO Class C-SCA</td>
<td>12 ACPH; exhaust; 0.01 – 0.03” wc negative pressure</td>
<td>12 hours</td>
</tr>
<tr>
<td>HD storage negative room</td>
<td>N/A</td>
<td>Fixed walls; HD APIs &amp; manipulated HDs</td>
<td>Negative 0.01 – 0.03” wc; vented; 12 ACPH</td>
<td>N/A</td>
</tr>
<tr>
<td>Refrigerate HDs separately</td>
<td>N/A</td>
<td>Negative pressure room (buffer room or C-SCA).</td>
<td>Place near room exhaust to compressor</td>
<td>N/A</td>
</tr>
</tbody>
</table>
USP <800> Compliance

• Engineering controls that are used in HD sterile compounding:
  • ISO Class 5
    • Direct compounding area inside of a Containment Primary Engineering Control (C-PEC) such as a BSC or CACI
  • ISO Class 7 buffer room
    • A negative pressure ISO Class 7 hazardous buffer room (Containment Secondary Engineering Control; C-SEC).
    • 30 ACPH; -0.01 to 0.03” wc; HEPA filter at ceiling level and near door
• Anteroom
  • ISO Class 8 anteroom if adjacent to non hazardous buffer area
  • ISO Class 7 positive anteroom if adjacent to hazardous buffer area
  • 30 ACPH; +0.02 to 0.05” wc; HEPA filter at ceiling level and near door
Resources/References


Assessment of Risk Model on Hazardous Drug Handling; VISN 23 Resources.


OSHA Compliance Assistance Quick Start Health Care Industry
https://www.osha.gov/dcsp/compliance_assistance/quickstarts/health_care/index_hc.html

OSHA Controlling Occupational Exposure to Hazardous Drugs
https://www.osha.gov/SLTC/hazardousdrugs/controlling_occex_hazardousdrugs.html

Which direction do we go from here?

On your way home to start a three day weekend?
Thank You...Questions?