OBJECTIVES

- Recognize USP chapters related to medication compounding
- Describe the scope and purpose of USP 797
- Identify key factors in meeting or exceeding the purpose of USP 797
- Recognize key areas where infection prevention professionals may
  - Assist organizations in meeting USP requirements
  - Audit performance of the organization in complying with USP 797
  - Identify opportunities for performance improvement
WHAT IS USP

• United States Pharmacopoeial Convention
  • Our Mission
    • To improve global health through public standards and related programs that help ensure the quality, safety, and benefit of medicines and foods.
    • No enforcement nor regulatory authority
    • Standards are developed and revised by more than 800 volunteer experts
  • Chapters below 1000 are considered to be standards and are considered enforceable by regulatory bodies
ARCRONYMS

• USP – United States Pharmacopeial Convention
• CSP – Compounded Sterile Product
• BUD – Beyond Use Date
• PEC – Primary Engineering Control (ISO class 5 or better)
• SEC – Secondary Engineering Control (ISO class 7 or better)
• SCA – Segregated Compounding Area
USP CHAPTERS APPLICABLE TO PHARMACEUTICAL COMPOUNDING

• USP 795
  • Pharmaceutical Compounding - Non-sterile Preparations
• USP 797
  • Pharmaceutical Compounding - Sterile Compounding
• USP 800
  • Hazardous Drug – Handling in Health Care Settings
• USP 825
  • Radiopharmaceuticals
• USP 71, 49.....
USP 797 SCOPE AND PURPOSE

• Sterile compounding
  • Combining, admixing, diluting, pooling, reconstituting, repackaging or other alterations of a drug or bulk drug substance to create a sterile compound

• Purpose of the chapter is to minimize harm

• Aseptic technique must be followed

• Administration is out of scope
  • Preparation for administration is within scope
    • IV bag spiking in 2016 edition was called out not specific in 2019, but likely fall under Immediate Use
IMMEDIATE USE

• Compounding of CSPs for direct and immediate administration to a patient
  1. Aseptic processes
  2. The preparation is performed in accordance with evidence-based information for physical and chemical compatibility of the drugs (e.g., FDA-approved labeling, stability studies).
  3. Not more than 3 different sterile products.
  4. Any unused starting component from a single-dose container must be discarded after preparation for the individual patient is complete. Single-dose containers must not be used for more than 1 patient.
  5. Administration begins within 4 hours following the start of preparation.
  6. CSP properly labeled

(The United States Pharmacopeial Convention USP Compounding Compendium, 2019)
CSP CATEGORIES

• Category 1 CSP
  • Prepared within a ISO Class 5 environment
  • BUD
    • 12 hours or less stored at room temp
    • 24 hours or less stored under refrigeration

• Category 2 CSP
  • Prepared within an ISO Class 5 environment that is within an ISO Class 7 buffer room
  • BUD is determined by compounding method, sterility testing and storage conditions
## CSP CATEGORY 2 BUD

<table>
<thead>
<tr>
<th>Preparation Characteristics</th>
<th>Storage Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Controlled Room Temperature (20°-25°)</td>
</tr>
<tr>
<td>Aseptically processed CSPs</td>
<td>Prepared from 1 or more non-sterile component(s): 1 day</td>
</tr>
<tr>
<td></td>
<td>Prepared from only sterile starting components: 4 days</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Terminally sterilized CSPs</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
</tr>
</tbody>
</table>
KEY SECTIONS OF USP 797

• Personnel training and evaluation
• Personal hygiene and garbing
• Facilities and engineering controls
• Certification and recertification
• Microbiological air and surface sampling
• Cleaning, disinfecting and applying sporicidal agents in compounding areas
PERSONNEL TRAINING AND PERSONAL HYGIENE AND GARBING

• Gloved fingertip and thumb sampling
  • Chapter provides a detailed sampling procedure
  • Initial
    • 3 separate times
    • Action level > 0 cfu
  • Subsequent and every 6 months after media fill
    • Action level > 3 cfu

• Media fill
  • Must mimic most complicated procedure personnel expected to perform

• Garbing
  • Minimum hair cover, mask, shoe cover, gown and sterile gloves
  • Properly donning and doffing
ASEPTIC TECHNIQUE

• Handling of material prior to entry into ISO class 5 PEC
• Hand sanitization
• Sanitizing of critical site
  • Use of sterile alcohol wipe in same direction 3 times
    • Physical removal of spores
• Use of first air
  • Horizontal flow
  • Vertical flow
• Minimizing equipment and impact on unidirectional airflow
  • Smoke studies
FACILITIES AND ENGINEERING CONTROLS

- Clean room suited vs. SCA (C-SCA)

(CriticalPoint, LLC, 2018)
FACILITIES AND ENGINEERING CONTROLS

• Secondary Engineering Controls (SEC)
  • Air Exchanges
    • ISO Class 8 minimum 20
    • ISO Class 7 minimum 30 (suggest 45-50)
  • Terminally HEPA filtered air

• Primary Engineering Controls (PEC)
  • Horizontal flow hood
  • Vertical flow hood
    • Hazardous drug preparation
WATER SOURCES

- Outside buffer room
  - Ante-room clean/dirty
  - Outside ante-room
- Must be 1 meter from PEC in SCA
- At least 1 meter from entrance to hazardous drug compounding buffer room
- Integrated eye wash
  - Avoid the need for hose on floor or additional cleaning surface
- Sink should be scrub size
  - Proper hand hygiene
  - Reduce splash
  - Should cover plumbing
CERTIFICATION AND RECERTIFICATION

- SEC and PEC by CETA (Control Environment Testing Association) certified professional
  - Initially
  - Every 6 months
- Includes
  - ISO classification, Particle counts both viable and non-viable, surface sampling
  - HEPA filter functioning
  - Air exchanges
- Certify to CAG (CETA Application Guide) 003
  - Will ensure meets all USP requirements
MICROBIOLOGICAL AIR AND SURFACE SAMPLING

• Purpose
  • Proper practices being followed
  • Proper disinfecting and cleaning
  • Maintaining environmental quality

• Viable air sampling must be completed every 6 months
  • Will be a part of certification
  • Suggest doing self sampling between certifications for trending

• Surface sampling
  • Monthly

• Completed under dynamic conditions
**ACTION LEVELS**

**MICROBIOLOGICAL SAMPLING**

- Identify to genus level
- Develop corrective action plan
- Involve infection control colleagues
- Evaluate trends
- Resample

<table>
<thead>
<tr>
<th>ISO Class</th>
<th>Air Sampling Action Levels (cfu per cubic meter (1000 liters) of air per plate)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>&gt;1</td>
</tr>
<tr>
<td>7</td>
<td>&gt;10</td>
</tr>
<tr>
<td>8</td>
<td>&gt;100</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ISO Class</th>
<th>Surface Sampling Action Levels (cfu/device or swab)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>&gt;3</td>
</tr>
<tr>
<td>7</td>
<td>&gt;5</td>
</tr>
<tr>
<td>8</td>
<td>&gt;50</td>
</tr>
</tbody>
</table>
CLEANING AND DISINFECTING

• What products should we use
  • Must be compatible with equipment
  • Minimize co-worker exposure
  • Should products be rotated
• Continuous
  • Sanitizing work surface with sterile IPA
  • Minimum every 30 minutes or between products
• Daily
  • Cleaning and disinfecting
• Monthly
  • Application of sporicidal
• USP 800 must add step for deactivation/decontamination
## Minimum Frequency for Classified Areas and SCA

<table>
<thead>
<tr>
<th>Site</th>
<th>Cleaning</th>
<th>Disinfecting</th>
<th>Sporicidal</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEC and equipment inside</td>
<td>Daily and when contamination</td>
<td>• Daily and when contamination</td>
<td>Monthly</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Sterile 70% IPA every 30</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>minutes</td>
<td></td>
</tr>
<tr>
<td>Removable work tray</td>
<td></td>
<td>• Work surface daily</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• All surfaces and underneath</td>
<td></td>
</tr>
<tr>
<td>Pass-throughs</td>
<td>Daily</td>
<td>Daily</td>
<td>Monthly</td>
</tr>
<tr>
<td>Work surface outside PEC</td>
<td>Daily</td>
<td>Daily</td>
<td>Monthly</td>
</tr>
<tr>
<td>Floors</td>
<td>Daily</td>
<td>Daily</td>
<td>Monthly</td>
</tr>
<tr>
<td>Walls, doors, door frame</td>
<td>Monthly</td>
<td>Monthly</td>
<td>Monthly</td>
</tr>
<tr>
<td>Ceilings</td>
<td>Monthly</td>
<td>Monthly</td>
<td>Monthly</td>
</tr>
<tr>
<td>Storage shelving and bins</td>
<td>Monthly</td>
<td>Monthly</td>
<td>Monthly</td>
</tr>
<tr>
<td>Equipment outside PEC</td>
<td>Monthly</td>
<td>Monthly</td>
<td>Monthly</td>
</tr>
</tbody>
</table>
CLEANING AND DISINFECTING PROCESS

• Dedicated equipment
  • Hazardous drug area separate from non-hazardous
• Low-linting disposable mop heads and wipes
• Cleanest to dirtiest
• Top to bottom
• No spray
  • Damage hoods HEPA filters
  • Aerosolize hazardous drug
DOCUMENTATION

• SOPs
• Education, training and competency
  • Competency demonstrated at least every 12 months
  • Observed hand hygiene and garbing every 6 months
  • Gloved fingertip and media fill every 6 months
• Deactivation, decontamination, cleaning and disinfecting
  • Daily and monthly
• Certification
  • Signed by Designated Person
• Equipment records
• Air and surface sampling records
SUMMARY

• All about infection prevention and quality
• Requires collaboration with multi-disciplinary groups
  • Facilities and engineering requirements
  • Processes and procedures
  • Environmental monitoring
• Infection prevention
  • Review policy and procedures
  • Consultation for cleaning, and disinfecting products
  • Assess compliance
  • Help develop remediation plans
QUESTIONS

References: