USP <797> Review
With a Mention of USP <800>

JOHN DOUGLAS
MONTANA BOARD OF PHARMACY, INSPECTOR
Disclosure

I have no actual or potential conflict of interest in relation to this presentation
Pre-test questions:

1. Which of the following are required when compounding sterile products?
   a. **sterile** isopropyl alcohol
   b. **sterile** gloves
   c. both a & b
   d. neither a or b

2. Which of the following are true for CSPs prepared in LAFWs located in non-classified “room” air?
   a. assigned 12-hour beyond use date
   b. limited to low- and medium-risk
   c. do not require re-certification every 6 months
   d. only a & b
   e. a, b, & c
References


Rationale for Compliance

Administrative Rules of Montana (ARM)
24.174.841 Sterile Products

Centers for Medicare & Medicaid Services (CMS)
Conditions of Participation
(9) The board expects pharmacies/pharmacists engaged in compounding to have policies and procedures to adhere to those guidelines that apply to their practice setting and in all situations to comply with the spirit of United States Pharmacopeia (USP) Chapter 795 "Compounding Nonsterile Preparations" and USP Chapter 797 "Pharmaceutical Compounding-Sterile Preparations."
Compounding

All compounding of medications used or dispensed by the facility must be performed consistent with accepted professional principles which are equivalent to or more stringent than those described in the compounding-related chapters in the USP/NF, which are recognized as authoritative standards regarding minimum standards of safe practice applicable to both sterile and non-sterile compounding.

The definition of compounding as that term is used in the USP is found in USP Chapter <795> and <797>
## Beyond-Use Dates

<table>
<thead>
<tr>
<th>Risk Category</th>
<th>Room Temperature</th>
<th>Refrigeration</th>
<th>Frozen ($\leq 10 , ^\circ \text{C}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immediate-Use</td>
<td>1 hour</td>
<td>1 hour</td>
<td>N/A</td>
</tr>
<tr>
<td>Low-Risk</td>
<td>48 hours</td>
<td>14 days</td>
<td>45 days</td>
</tr>
<tr>
<td>Low-Risk with 12-hour BUD</td>
<td>12 hours</td>
<td>12 hours</td>
<td>N/A</td>
</tr>
<tr>
<td>Medium-Risk</td>
<td>30 hours</td>
<td>9 days</td>
<td>45 days</td>
</tr>
<tr>
<td>High-Risk</td>
<td>24 hours</td>
<td>3 days</td>
<td>45 days</td>
</tr>
</tbody>
</table>
SOPs Written to Address the Following Categories:

- Personnel
- Facilities
- Equipment
- Supplies
- Compounding Procedures
- Safety
- Quality Assurance
- Administration
1) Personnel

- Training
- Education
- Skills
- Competency
- Evaluations
- Responsibilities
Training & Education

• “Conscientiously and skillfully” by expert personnel
• Multi-media instructional sources
• Professional publications
• Didactic training
• Completed and documented “before any personnel begin to prepare CSPs for human or animal use”.
Skills & Competency

- “Highly motivated to perform flawless aseptic manipulations”
- Hand hygiene
- Garbing
- Media-fill testing
- Gloved fingertip sampling
- Cleaning and disinfecting procedures
- Aseptic work practices
Evaluations

• Written competence assessments
• Skill assessment using observational audit tools
• Media-fill testing initially and at least annually (semiannually for high-risk level compounding)
• Gloved fingertip testing
• Routine performance evaluation
• Failed written tests, observational audits, or media-fill tests showing visible growth shall be re instructed and re-evaluated by expert compounding staff prior to resuming compounding sterile preps
Personnel Prohibited from Sterile Compounding:

- Rashes, sunburn, weeping sores
- Conjunctivitis
- Active respiratory infections
- Cosmetics
- Artificial nails
- Hand, wrist, and body jewelry that can interfere with fit of gloves or gowns
- Visible body piercings above the neck
2) Facilities & Equipment

- Environmental quality and control
- Facility design
- Cleaning and disinfecting the sterile compounding area
Environmental Quality and Control & Facility Design

• Viable environmental sampling
• Environmental nonviable particle testing
• Pressure differential monitoring
• Air pattern analysis
• Air changes per hour
• Air Velocities
• Placement of primary engineering controls
• Room design
Viable Particle Sampling

- **Volumetric** collection of airborne microorganisms
- 400-1000 liters of air samples at each location
- Performed in locations prone to contamination
- Semiannually as part of PEC re-certification
- Incubation period guidelines
- Action level guidelines and response

### Table 2. Recommended Action Levels for Microbial Contamination

<table>
<thead>
<tr>
<th>Classification</th>
<th>Air Sample†</th>
</tr>
</thead>
<tbody>
<tr>
<td>ISO Class 5</td>
<td>&gt; 1</td>
</tr>
<tr>
<td>ISO Class 7</td>
<td>&gt; 10</td>
</tr>
<tr>
<td>ISO Class 8 or worse</td>
<td>&gt; 100</td>
</tr>
</tbody>
</table>

* (cfu per cubic meter [1000 liters] of air per plate)
Environmental Nonviable Particle Testing

• Intended to directly measure the performance of the engineering controls
• Used to assign ISO classes
• Every 6 months (and following any servicing of the equipment, in response to identified problems, or when a CSP is being considered a source of patient-related infection)
Pressure Differential Monitoring

- Pressure differential monitored between the buffer area and the ante-area, and between the ante-area and general environment
- Documented in a log at least daily, or by a continuous recording device
Primary Engineer Controls--PEC

• Provide unidirectional airflow
• Velocity sufficient to prevent airborne particles from contacting critical sites
• Smoke studies must be conducted to demonstrate unidirectional flow
• Personnel must understand the concept of HEPA-filtered unidirectional airflow
• Located out of traffic patterns and away from room air currents
Placement of Primary Engineering Controls

- Located in ISO Class 8 environment—“Buffer Room” (ISO 7 for hazardous CSPs)
- Isolators must be located in ISO 8 (or 7) environment
- CSPs prepared in isolators located outside ISO Class 8 environments limited to low-risk, non-hazardous products with a 12-hour BUD
- LAFW (traditional hoods) located in non-classified environment limited to preparation of low-risk CSPs assigned a 12-hour BUD
3) Supplies

- No shipping cartons may be taken into the buffer area
- Supplies and equipment removed from shipping cartons and wiped with sterile IPA
- All cleaning materials (wipes, sponges, mops) must remain in ante- and compounding areas and not removed except for disposal
- Floor mops may be used in both buffer and ante-area, but only in that order
- Foil sealed, 70% sterile IPA swabs are preferred for disinfecting entry points on bags and vials (vs. sterile IPA spray)
- IPA wetted gauze pads should never be used to disinfect entry points
- Pharmacy must maintain control of selection and storage of legend product
- IV solutions that contain medications (e.g., KCl, heparin, dopamine, dextran, mannitol) and high-risk agents (e.g., sterile water, > 0.9% NaCl, and parenteral nutrition components) should be stored in and distributed by the pharmacy
4) Compounding Procedures

- BUDs appropriately assigned based on risk level and compounding environment
- Point of Care Activation Systems: assembled in ISO 5 conditions and activated just prior to administration; BUDs of assembled device based on manufacturer recommendations.
- Ampules: always SDV and always filtered (5 micron)
- Single dose vials: intended to be used for a single dose for a single patient (provisions for single dose vial contents repackaged for multiple patients). Cannot be stored
- Pharmacy Bulk Packages: can be stored for 6 hours in ISO 5 environment
- Multi-dose vials: 28 day BUD (or shorter per manufacturer); must be labeled with a “use by” rather than the opening date
<table>
<thead>
<tr>
<th>Site</th>
<th>Minimum Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>ISO Class 5 PEC</td>
<td>Beginning of each shift &lt;br&gt;Before each batch &lt;br&gt;Every 30 minutes when compounding &lt;br&gt;After spills &lt;br&gt;When surface contamination is known or suspected</td>
</tr>
<tr>
<td>Counters and easily cleanable work surfaces</td>
<td>Daily</td>
</tr>
<tr>
<td>Floors</td>
<td>Daily</td>
</tr>
<tr>
<td>Walls</td>
<td>Monthly</td>
</tr>
<tr>
<td>Ceilings</td>
<td>Monthly</td>
</tr>
<tr>
<td>Storage shelving</td>
<td>Monthly</td>
</tr>
</tbody>
</table>
5) Safety

- Handing and compounding of hazardous drugs to be addressed in USP <800>
- NIOSH list of hazardous drugs
6) Quality Assurance

- Review of compounding procedure
- Visual inspection of final product for particulate and intact containers and seals
- Media-Fill test procedure should mimic risk level of final CSPs (e.g., High-risk compounding personnel should be tested with non-sterile growth media)
- All filters used to sterilize CSPs must undergo filter integrity (bubble-point) testing
7) Administration

- SOP development
- Ensure personnel are properly trained, educated, trained, and evaluated
- Development of action levels
- Record keeping
- Results of monitoring and measurements should be reported within and outside the department to committees such as Infection Control and CQI
Post-test Questions

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   b. sterile gloves
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