Missouri Board Of Pharmacy
An Update on Sterile Compounding Regulations
August 9, 2016
Katie DeBold, PharmD
Inspector

Webinar Design
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- Listen by telephone option

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  - No CE credit for watching recording.

How to Ask a Question

Missouri Board Of Pharmacy
An Update on Sterile Compounding Regulations
August 9, 2016
Katie DeBold, PharmD Inspector
Webinar Objectives

- Review updated requirements of the emergency rule (effective 08/04/16):
  - 20 CSR 2220-2.200: Sterile Compounding
- Review updated requirements of the amended rule (effective 03/2017):
  - 20 CSR 2220-2.200: Sterile Compounding
- Answer questions

Introduction

- Why now?
- Did the board adopt USP 797?
- Emergency vs Amended Rule. What’s the difference?
- Future plans?

Overview of the Major Changes

- No changes to facility or structural design
- Major changes:
  - Training & media fill testing
  - Garbing
  - Clarification regarding controlled areas vs buffer areas
  - Increased cleaning & disinfection requirements
  - Environmental Sampling (eventually)
  - Remedial Investigations

Compounding Definition

- Compounded sterile medications may include, but are not limited to:
  - Compounded biologics, diagnostics, drugs, nutrients, and radiopharmaceuticals that must be sterile when they are administered to patients, including, but not limited to the following dosage forms:
  - Baths and soaks for live organs and tissues
  - Epidural and intrathecal solutions
  - Bladder/wound solutions
  - Injectable, intravenous solutions, parenteral solutions
  - Implantable device and dosage forms
  - Inhalation solutions
  - Irrigation solutions
  - Ophthalmic preparations
  - Repackaged sterile preparations
  - Assembly of point-of-care systems

Terminology Changes

- Replaced Class 100 & Class 10,000 terminology with ISO classifications
- Addition of buffer area definition – ISO Class 7 or better area where the primary engineering control (PEC) is physically located.
- Clarification of controlled area definition
  - Controlled area refers to pharmacies that do not have an ISO classified area for the placement of their PEC
  - A room or area designated for sterile compounding. The area is separated from other activities/operations by a line of demarcation.

Terminology Changes

- Removal of “isolator” terminology
  - Isolator is a type of PEC with an automated system for built in decontamination.
  - RABS = Restricted Access Barrier System
  - New terminology for the types of PECs that people currently refer to as “gloveboxes” and “isolators”. Includes CAI & CACI
  - CAI: Compounding Aseptic Isolator
  - Used for non-hazardous compounding
  - CACI: Compounding Aseptic Containment Isolator
  - Used for hazardous compounding
### Risk Levels

- Risk Level identification is mostly unchanged. Administration time is no longer included within the storage/beyond use parameters.

<table>
<thead>
<tr>
<th>Risk Level</th>
<th>Current Rule</th>
<th>Emergency/Amended Rule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk Level 1</td>
<td>Product stored at room temp and completely administered within 48 hours after prep. Stored in the fridge for 7 days or less before complete administration to a patient over a period not to exceed 48 hours. Frozen storage for 30 days or less and complete administration not to exceed 48 hours.</td>
<td>Room temp: assigned a beyond-use date (BUD) of ≤48 hours or less. Fridge storage: BUD of ≤7 days or less. Frozen: BUD of ≤30 days or less.</td>
</tr>
<tr>
<td>Risk Level 2</td>
<td>Any product stored &gt;48 hours at room temp, &gt;7 days under refrigeration, &gt;30 days frozen or administered beyond ≤48 hours after preparation.</td>
<td></td>
</tr>
<tr>
<td>Risk Level 3 (NA: Risk level 3 is determined via stability of compounding ingredients (Non-sterile to sterile compounding))</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Removal of administration time may allow pharmacy to change risk levels.

### Section 2: Policies & Procedures

- No changes within this section.
- Specific policy and procedure requirements are referenced throughout the rest of the rule
- Annual review of sterile compounding policy is still required

### Section 3: Personnel Education, Training, and Evaluation

<table>
<thead>
<tr>
<th>Risk Level</th>
<th>Current Rule</th>
<th>Emergency/Amended Rule</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Risk Levels</td>
<td>Suitable didactic and experiential training</td>
<td>Specific competencies and assessments. Reference Section 10: Aseptic Technique Skill Assessment</td>
</tr>
<tr>
<td>Risk Level 2</td>
<td>Assessment of competency in all risk level 2 procedures</td>
<td>No change</td>
</tr>
<tr>
<td>Risk Level 3</td>
<td>Specific education in risk level 3 procedures such as sterilization, aseptic processing, end preparation testing etc.</td>
<td>No change</td>
</tr>
</tbody>
</table>

- Additional training required for changes in risk level or compounding methods
- Policy and procedure is required for staff training and assessment

### Section 4: Storage & Handling

- Minor changes for all risk levels:
  - Addition of daily incubator temperature documentation, if applicable
  - Reference to section (21) regarding recall procedures

### Section 5: Facilities & Equipment

- Facility requirements clarified. No changes to physical structure or room design.

<table>
<thead>
<tr>
<th>Risk Level</th>
<th>Emergency/Amended Rule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk Level 1</td>
<td>Preparations must be prepared in a PEC located in a controlled area defined by a line of demarcation</td>
</tr>
<tr>
<td>Risk Level 2</td>
<td>Preparations must be prepared in a PEC located in an ISO Class 7 buffer area or in a RABS located within a controlled area</td>
</tr>
<tr>
<td>Risk Level 3</td>
<td>Preparations must be prepared in a PEC located in an ISO Class 7 buffer area or in a RABS located within a controlled area</td>
</tr>
</tbody>
</table>

- All cleaning requirements moved to Section (17): General Cleaning and Disinfection Requirements
  - Risk Level 3 preparations shall at a minimum remain Risk Level 3 for the life of the preparation. Same is true for Risk Level 2 preps
  - Automated compounding device calibration:
    - Calibration to occur prior to initial and daily use. Test results shall be reviewed by the pharmacist and documented in the pharmacy's records.
  - Pressure differential monitoring: No requirement to install a pressure monitoring device. However, if the pharmacy currently has one installed, the results must be monitored and documented daily.
Section 5: Facilities & Equipment (Certification)

- Frequency of certification is unchanged - All PEC and ISO classified areas certified initially and every 6 months
- Re-certification must occur when:
  - Any major changes or service to PEC or ISO classified area
  - PEC or room is relocated or the physical structure of the ISO classified area has been altered
- Certification results must be reviewed by a pharmacist and documented in the pharmacy’s records
- Deficiencies or failures shall be investigated and corrected prior to further compounding which may include recertification of the PEC/ISO classified area.
- Corrections may include, but are not limited to, changes in the use of the affected PEC or ISO classified area or initiating a recall.

Section 6: Primary Engineering Controls (PEC)

- New section to provide guidance on proper usage of PECs
- PEC placement: must be located out of traffic patterns and away from conditions that could adversely affect their operation or disrupt intended airflow patterns (e.g., ventilation systems or cross-drafts)
- PECs shall maintain ISO Class 5 or better conditions and provide unidirectional flow
- Establish a recovery time for PECs and identify it in the pharmacy policies and procedures

Section 7: Controlled Area

Controlled area requirements:
- For non ISO classified areas - a box of demarcation to designate the area used for sterile compounding
- Must be clean, well lit, free of irritation by insects and rodents
- Trash disposed of at least daily
- Furniture, carts, supplies and equipment cleaned and disinfected with sterile draped before entering ISO classified areas.
- All personnel entering controlled and buffer areas need to be appropriately garbed (see Section 8)

- Items PROHIBITED in the controlled/buffer areas
  - Tissue paper
  - Food, gum, eating, drinking, smoking
  - Particle shedding items such as: pencils, corrugated cardboard paper towels, cotton tips (2x gauge pads)
  - Dipping or other external cartons
  - Non-essential supplies or equipment

Section 8: Garbing & Hand Hygiene

<table>
<thead>
<tr>
<th>Risk Level</th>
<th>Current Rule</th>
<th>Emergency/demand rule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk Level 1</td>
<td>No garbing required</td>
<td>Non-shedding gowns, hair cover, face mask, beard cover and gloves</td>
</tr>
<tr>
<td>Risk Level 2</td>
<td>Hair cover, beard cover, gown, mask, &amp; gloves</td>
<td>Non-shedding gowns, hair cover, face mask, beard cover, shoe covers, and sterile gloves</td>
</tr>
<tr>
<td>Risk Level 3</td>
<td>Hair cover, beard cover, gown, mask, gloves, &amp; shoe covers</td>
<td>Non-shedding gowns, hair cover, face mask, beard cover, shoe covers, and sterile gloves</td>
</tr>
</tbody>
</table>

- All Risk Levels: Gloves shall be disinfected before use and frequently thereafter
- No exemptions for RABS. Garb is donned according to risk level.
- Risk Level 2 & 3: if using a RABS, sterile gloves must be donned over the RABS gloves

Section 9: Aseptic Technique & Preparation

- Specific requirements for handwashing:
  - Hands and forearms washed for 30 seconds with warm water
  - Debris removed from underneath fingernails.
    - Amended rule will require a disposable nail cleaner
  - Risk Level 3: sterilization methods need to be USP recognized

Section 10: Aseptic Technique & Preparation

- In Use Time: the time/date before which a conventionally manufactured product or a CSP must be used after it has been opened or needle-punctured.
- All vials/containers must be dated/timed after initial needle puncture.
- Single dose vials/containers – Maximum in-use time is 6 hours unless otherwise specified by the manufacturer
- Multiple dose vials/containers – Maximum in-use time of 28 days unless otherwise specified by the manufacturer
- Ampules must be used immediately and cannot be stored
**Section 10: Aseptic Technique Skill Assessment**
- Aseptic technique skill assessment consists of:
  - Media fill testing
  - Direct visual observation of the following competencies:
    - Proper aseptic technique and work practices
    - Cleaning/disinfection
    - Hand hygiene, gloving, and gaiting
    - Identifying, weighing, and measuring of ingredients
    - Labeling and inspecting preparations
- Who needs the assessment? All sterile compounding personnel
- How often?
  - Risk Levels 1 & 2: Prior to initial compounding and every 12 months thereafter
  - Risk Level 3: Prior to initial compounding and every 6 months thereafter
  - All Risk Levels: Reassessment when appropriate (as risk level changes)

**Section 11: Record Keeping**
- Few additions/clarifications
  - Training records must include the dates and results of the aseptic technique skill assessment and media fill testing
  - Incubator temperatures need to be recorded (if applicable)
  - Certification records for both PEC and ISO classified area
  - Pressure recordings (if applicable)
    - If a continuous monitoring system is used, the system must be able to maintain pressure recordings and alerts. These need to be reviewed and documented daily
  - All records/reports need to be kept for 2 years

**Section 12: Labeling**
- Section 13: Beyond-Use Dating
- Section 18: Cytotoxic Drugs
- One label change:
  - Label must include a designation indicating hazardous drugs if applicable
- No changes to beyond-use dating section other than clarifications
- One recommendation added to cytotoxic drug section:
  - The use of a closed system transfer device

**Section 14: End-Preparation Evaluation**
- Risk Level 1 & 2: No changes
- Risk Level 3: Addition of USP Chapters
  - Sterility testing must be conducted according to USP Chapter 71
  - Pyrogen testing must be conducted according to USP Chapter 123
  - Endotoxin testing must be conducted according to USP Chapter 85
  - All sterile preparations must be tested for sterility
  - All parenteral sterile preps must be tested for pyrogens
  - Potency testing required for sterile preps with BUD >30 days
  - Emergency dispensing:
    - Risk level 3 compounded prep is dispensed prior to sterility/pyrogen test results
    - Requires physician authorization for each emergency dispensing. This authorization and the need for the emergency dispense must be documented in the prescription record

**Section 16: Point of Care Assembled Systems**
- Assembly of point of care assembled systems is considered Risk Level 1 sterile compounding.
  - Examples: addEase, ADD-Vantage, Mini-Bag Plus, Vial-Mate, Vial2Bag, etc.
  - All systems that are assembled by the pharmacy shall be assigned two beyond-use dates. Both dates need to be recorded in the compounding log.
  - BUD for the non-activated state according to the manufacturer.
    - If no manufacturer documentation, beyond use date is limited to 15 days
  - BUD for the activated state according to drug stability. (Risk Level 1 maximums apply)
Section 17: General Cleaning & Disinfection

Cleaning & Disinfection of controlled and buffer areas shall be performed according to Chapter 797.

<table>
<thead>
<tr>
<th>Site</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>ISO Class 5 - PEC</td>
<td>Monthly</td>
</tr>
<tr>
<td>Counters &amp; 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>

Section 17: General Cleaning & Disinfection

- If compounding occurs less frequently than the specified timeframes, cleaning/disinfection must occur prior to each compounding session.
- Policy and procedure required for all aspects of cleaning/disinfection.
- All cleaning tools must be low-lint and dedicated for use in the controlled or buffer area.
- Sterile water for irrigation must be used for dilution of germicidal agents that will be used in the PEC.

Environmental Sampling

Emergency Rule: No changes

- Risk levels 2 & 3: Applicable environmental monitoring of air and surfaces must be conducted.

Amended Rule: New Section (18)

- Air Sampling:
  - All risk levels: must occur every 6 months
  - Surface sampling:
    - Risk Level 2: must occur every 6 months
    - Risk Level 3: must occur every 30 days

Section 20: Remedial Investigations

- Remedial investigation is required if:
  - Any required sampling or testing results in a CFU count that exceeds 797 action levels.
  - The pharmacy detects a highly pathogenic microorganism in any preparation or ISO classified area.
  - Ex: Gram-negative rods, coagulase positive staph, molds, fungus/yeast
  - Microorganism identification is NOT mandatory. However, if a pharmacy chooses to conduct this testing, a remedial investigation needs to occur for highly pathogenic microorganisms.

Section 20: Remedial Investigations

- CSPs and any ingredients that are part of the remedial investigation shall be quarantined.
- All affected areas shall be resampled prior to further compounding.
- Pharmacy shall notify the Board in writing within 7 days if any preparation or environmental monitoring detects a highly pathogenic microorganism, regardless of CFU count.

Section 21: Recalls

A recall is required when:

- A CSP is deemed to be misbranded or adulterated
- A CSP is non-sterile
- End-preparation testing results are out of specification

Actions required by the pharmacy:

- Notify the prescriber
- If CSP has the potential to harm the patient, notify all patients
- Any recall shall be reported to the board, in writing, within 3 business days
- Document all activities related to the recall.
Questions

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• Click Close on “The webinar has ended” screen
• Survey will then open
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• Survey must be submitted within 48 hours to receive CE credit
• Certificates will be mailed in 30 days
• Questions: compliance@pr.mo.gov

A link to a recording of this webinar for viewing will be available on the Board’s website within 30 days.

Continuing Education

Future Webinars

• August 17, 2016, 12 noon: Sterile Compounding: Garbing & Cleaning
• August 25, 2016, 10 am: TBA