



Missouri Board Of Pharmacy

An Update on Sterile Compounding Regulations

August 9, 2016

Katie DeBold, PharmD
Inspector

Webinar Design

- * All participants are muted, "listen only" mode
- * Listen by telephone option



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- * Board-approved for one hour (0.1 CEU) of live pharmacist continuing education
- * Must be officially signed up and logged on via your computer
- * **CE credit will not be issued to those listening via the phone only**
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Handouts and Recordings

- Handouts posted on Board's website
- Recording of webinar
 - Videos/Webinars under "Publications/Resources" on the Board's website

Videos/Webinars #

- 2015 Legislation and Regulation Update #
- 2015 DEA Update With Scott Collier #
- 2015 Inspector Tips for Your Next Inspection #
- 2014 Pharmacist Administration Regulation Review and Update #
- 2014 BNDD Update #

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How to Ask a Question




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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:

- * 1. 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
- * Injectables, intravenous solutions, parenteral solutions
- * Implantable devices 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 stratification is mostly unchanged. Administration time is no longer included within the storage/beyond use parameters

Risk Level	Current Rule	Emergency/Amended Rule
Risk Level 1	<ul style="list-style-type: none"> 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 	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
Risk Level 2	Any product stored >48 hours at room temp, >7 days under refrigeration, >30 days frozen or administered beyond 48 hours after preparation.	Room temp: BUD >48 hours Fridge storage: BUD >7 days Frozen: BUD >30 days
Risk Level 3: N/A	Risk level 3 is determined via sterility of compounding ingredients (Non-sterile to sterile compounding)	

* Removal of administration time may allow pharmacies 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

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

* 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.

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



Section 5: Facilities & Equipment

- 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.



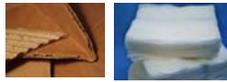
Section 6: Primary Engineering Controls (PEC)

- * 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 line of demarcation to designate the area used for sterile compounding
 - * Must be clean, well-lit, free of infestation by insects and rodents
 - * Trash disposed of at least daily
 - * Furniture, carts, supplies and equipment cleaned and disinfected with sterile alcohol 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
 - * Tacky mats
 - * Food, gum, eating, drinking, smoking
 - * Particle shedding items such as: pencils, corrugated cardboard paper towels, cotton items (ex: gauze pads)
 - * Shipping or other external cartons
 - * Non-essential supplies or equipment



Section 8: Garbing & Hand Hygiene

Risk Level	Current Rule	Emergency/Amended Rule
Risk Level 1	No garbing required	Non-shedding gowns, hair cover, face mask, beard cover and gloves
Risk Level 2	Hair cover, beard cover, gown, mask, & gloves	Non-shedding gowns, hair cover, face mask, beard cover, shoe covers, and sterile gloves
Risk Level 3	Hair cover, beard cover, gown, mask, gloves, & shoe covers	Non-shedding gowns, hair cover, face mask, beard cover, shoe covers, and sterile gloves

- * 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 9: 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 garbing
 - * 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 (ex-risk level changes)



Media Fills

- * Policy and procedure required for media fill testing
- * Media fill testing shall comply with USP Chapter 797's procedures and methods
- * Process must simulate the most challenging or stressful conditions encountered
- * During initial media fill testing, a minimum of 3 media-fill tests must be completed.
- * More details in later webinar



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 in USP Chapter 71
 - * Pyrogen testing must be conducted according to USP Chapter 151
 - * 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

Site	Frequency
ISO Class 5 - PEC	<ul style="list-style-type: none"> Daily cleaning: germicidal agent followed by sterile alcohol Frequent disinfection throughout the day (prior to compounding, between batches and after spills/surface contamination): sterile alcohol
Counters & Work Surfaces	Daily
Floors	Daily
Walls	Monthly
Ceilings	Monthly
Storage Shelving	Monthly

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

Classification	Air Sample (cfu per 1000 L of air per plate)	Classification	Surface Sample (cfu per plate)
ISO Class 5	>1	ISO Class 5	>3
ISO Class 7	>10	ISO Class 7	>5
ISO Class 8 or worse	>100	ISO Class 8 or worse	>100

- * 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



Continuing Education

- * Post Webinar Survey
 - Do not close web browser window
 - Click Close on "The webinar has ended" screen
 - Survey will then open
 - Phones and tablets may not receive survey
- * 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.

Future Webinars

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