Kentucky Board of Pharmacy
Sterile Compounding Inspection Process

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Kentucky Board of Pharmacy

Disclosures & Accreditation

Mr. Daniels has reported that he has nothing to disclose with regard to potential conflicts of interest for this activity.

Learning Objectives

1. Discuss the Kentucky Board of Pharmacy current sterile compounding regulation and USP 797 standards including regulation requirements, compound waivers, and corrective action plans requirements.
2. Outline requirements for each section of the sterile compounding inspection form including compounding procedures, compound records, and primary and secondary engineering controls.
3. Describe compliance issues in each of the inspection areas and corrective actions.

Kentucky Board of Pharmacy

SERVES THE COMMONWEALTH TO PROMOTE, PRESERVE, AND PROTECT THE PUBLIC HEALTH, SAFETY, AND WELFARE THROUGH EFFECTIVE REGULATION OF THE PRACTICE OF PHARMACY.

Pre-presentation Question 1

True or False:

Effective January 1, 2018, all sterile compounded preparations shall be compounded pursuant to USP 797 version 2008, unless specified portions submitted by a pharmacist have been waived by the Board.

Pre-presentation Question 2

Which of the following areas are included in the sterile compounding inspection form:

A. Policies and Procedures

B. Training and Garbing

C. Environment Ante and Buffer Rooms

D. B and C

E. All of the above

Pre-presentation Question 3

True or False:

High Risk sterile compounders are only required to document training annually.

Pre-presentation Question 4

True or False:

Sterile compound batching is consider low risk compounding allowing for a BUD of 14 days refrigerated.

Pre-presentation Question 5

Which of the following BUDs apply to a medium risk sterile compounded preparation:

A. Room Temperature: 30 hours

B. Refrigeration: 9 days

C. Frozen: 45 days

D. A and C

E. All of the above

USP 797 in Kentucky

- 201 KAR 2:076 Compounding Regulation
- Compounding Waivers
- Plan of Correction

201 KAR 2:076. Compounding

- Effective January 1, 2018, all sterile compounded preparations shall be compounded pursuant to USP 797, unless specified portions submitted by a pharmacist have been waived by the Board
- Must comply with June 1, 2008 version of USP Chapter 797

Compounding Waivers

- After January 1, 2018, all written waiver requests submitted by a pharmacist shall be considered by the Board at its next regularly scheduled meeting
- The Board, upon a showing of good cause and in balancing the best interest of the public health, safety and welfare, may waive the requirement of any specified portion of USP 795 or 797

Board Approved Waiver

- Board has not addressed USP Chapter 800
- Hazardous drugs are addressed in USP Chapters 795 and 797
- Board approved one waiver for a hospital pharmacy to comply with USP Chapter 800

Plan of Correction

- Newsletter June 2018 ***Compounding Inspections***

…drug inspectors will be issuing a letter to the pharmacist-in-charge requesting that a corrective action plan be submitted to the inspector within seven days addressing any noncompliance issues. If there are substantial noncompliance issues, the pharmacy may be reinspected for compliance.

KENTUCKY BOARD OF PHARMACY

Matt Bevin
Governor

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Date
Hospital Pharmacy
Address
Citry, Kentucky Zip code
Permit#
PIC:

PIC Name,

Based on the inspection performed on [redacted] you were found to be non-compliant with 201 KAR 2:076 Section 2 (2). Please submit a corrective action plan or submit proof of completed correction. An example of a corrective action plan has been provided that you may use, attaching documentation as needed. This will need to be submitted to the Pharmacy and Drug Inspector within 7 days of the date of inspection. As pharmacist-in-charge you are required to respond to the Kentucky Board of Pharmacy regarding any identified violations or deficiencies per 201 KAR 2:205 Section 2(3)(f).

Thank you for help in resolving this matter.

Paul Daniels RPh.

Plan of Correction

- PIC has 7 days to respond with documentation of correction unless working with inspector
  - 201 KAR 2:205 Section 2(3)(f) - PIC responsible for responding to BOP

Plan of Correction Example

- **Category** - Training, PnP, Environment, etc.
- **Task** - Compliance requirements
- **Comments** – Plans to reach compliance
- **Responsible Party** - Names of persons responsible
- **Due Date** – Date of compliance completion
- **Status** – In progress, Completed

USP Chapter 797 Inspection

Inspection Form

- Policies and Procedures
- Training and Garbing
- Garbing
- Environment Ante and Buffer Rooms
- Cleaning

Inspection Form Continued

- Environment Monitoring: Certifications of Rooms
- Environment Monitoring: Certifications of Equipment
- Compounding Procedures
- Continuous Quality Improvement
- Sterile Compounding of Hazardous Drugs
- 12 Hour BUD

Inspection Form Continued

- Immediate Use
- CAI not located in ISO Class 7 Room
- High Risk
- Extended BUD and Sterility Testing
- Transporting CSP Outside of the Facility
- Board Approved Waivers

USP Chapter 797 Inspection

- Policies and Procedures
- Training
  - Low/Medium Risk – annually
  - High Risk – every 6 months
  - Didactic
  - Competencies
  - Media Fill Testing (MFT)
  - Gloved Finger Sampling (GFS)

USP Chapter 797 Inspection

- Training
  - Competencies
    - Cleaning
    - Handwashing, Gowning and Garbing
    - Aseptic Technique
  - Media Fill Testing (MFT)
    - Most Challenging conditions
    - Involve any equipment used

USP Chapter 797 Inspection

- Training
  - Gloved Fingertip Sampling
    - Initial – done once before starting to compound
      - Both hands
      - Zero growth
      - Proves person can put on sterile gloves correctly
    - Annually/every 6 months – done at conclusion of MFT
      - Both hands
      - 3 colony forming units (CFUs) between both hands
      - Validates aseptic technique

USP Chapter 797 Inspection

- Garbing in ante room
  - Don hair, face, beard covers and shoe covers (in any order) then stepping over line of demarcation
  - Hand washing up to elbows for at least 30 seconds
  - Use nail pick
  - Don gown
  - Use waterless, alcohol based surgical scrub with persistent activity

USP Chapter 797 Inspection

- Garbing – Sterile Gloves
  - Donned without contaminating
  - Used in Compounding Aseptic Isolator (CAI) or Compounding Aseptic Containment Isolator (CACI) over isolator gloves
    - Changed when compounding personnel leave the isolator
    - Cannot be laid on isolator deck and reused

USP Chapter 797 Inspection

- Environment
  - Contained
  - No traffic
  - Cleaned
    - Cleaning procedures – daily and monthly
  - Pressures
  - Temperatures
  - Humidity

USP Chapter 797 Inspection

- Environmental Monitoring
  - Nonviable Particle Counts
    - Every 6 months
    - ISO classification
  - Viable Air Particle Counts
    - Every 6 months
  - Surface Sampling
    - Periodically

USP Chapter 797 Inspection

- Environmental Monitoring
  - Be familiar with certifier
  - Watch certifier
  - Certification done under dynamic conditions
  - Review results

USP Chapter 797 Inspection

- Compounding Procedures
  - Inspectors to observe compounding
  - Aseptic technique
    - Vertical versus horizontal air flow
    - Using first air
    - Spraying gloves with sterile IPA 70%
  - Pharmacist supervision and checking

USP Chapter 797 Inspection

- Compound Record
  - Not detailed
  - Traceability
    - Who
    - What
    - When

UPS Chapter 797 Inspection

- Beyond Use Dates (BUD)
  - Low Risk
    - 48 hours room temperature
    - 14 days refrigerated
    - 45 days frozen
  - Medium Risk
    - 30 hours room temperature
    - 9 days refrigerated
    - 45 day frozen

USP Chapter 797 Inspection

- BUD
  - High
    - 24 hours room temperature
    - 3 days refrigerated
    - 45 days frozen
  - Depends on sterility and stability, if stability less than USP BUDs, must use lesser time
  - If extend BUD, must have stability data and sterility test

USP Chapter 797 Inspection

- Continuous Quality Improvement
  - Near errors and errors
  - Environmental monitoring

USP 797

Sterile Compounding Compliance Issues

Policies and Procedures (PnP)

- Polices and Procedures need to reflect operations in your pharmacy and the equipment used
  - Pharmacy has isolators and only has PnPs for laminar flow hoods or vice versa
- Packaging , Handling , Security, Storage, Disposal, Destruction, Transport and Return of CSPs and Supplies
  - Lack of PnP for transporting CSP
  - Lack of PnP for Returning CSP
-

Training and Garbing

- Visually observed and appropriately documented competencies of cleaning and disinfecting, initially and at the completion of media fill test, and including environmental services, if applicable and when appropriate
  - Lack of documented training for environmental services
  - Lack of documented training for pharmacist
- Written policy personnel cannot compound if have sunburn, illness , open sores, etc.
  - No written policy

Garbing

- Garb from dirtiest to cleanest, using the line of demarcation appropriately
  - Personnel ignoring line of demarcation
- Sterile gloves donned appropriately
  - Fewer incidents but still observed

Environment: Ante and Buffer Rooms

- Pressure is recorded each shift, a minimum of daily
  - Lack of pressures recorded
- Temperature is recorded daily
  - Lack of temperature records
- Controlled storage areas for room temperature is 68 to 77 F or 20 to 25 C
  - HVAC systems fails to maintain temperature within range

Cleaning

- Personnel appropriately garbed when cleaning
  - Not garbing when opening and cleaning isolators
- Cleaning and disinfecting agent appropriate for bacteria, viruses, fungi
  - Personnel not knowing the correct use or dwell time of the cleaning agent being utlized

Environment Monitoring: Certifications of Rooms

- Smoke test performed in PEC in direct compounding area to demonstrate unidirectional airflow under dynamic conditions
  - No video of smoke test available (highly recommended)
- Differential pressure measured to be at least negative 0.01 inch water column from buffer room to positive pressure ISO 7 ante room with door closed
  - No certification for the negative pressure room

Environment Monitoring: Certifications of Rooms Continued

- Documentation of viable air and surface sampling shall include sampling locations
  - No locations or times provided
    - Know the sample locations, usually a diagram provided by certifier. The results can provide a picture of a possible issue.
- Documentation of surface sampling shall include size of surface sampled, 24-30 cm2
  - Know what size plates you are using and how to use them correctly

Environment Monitoring: Certifications of Rooms Continued

- All CFUs analyzed down to the genus with mold, yeast, coagulase positive Staph, gram negative rods require immediate Investigation
  - Not Performed
    - The type and location of the organism gives you information
    - Review your test results

Environment Monitoring: Certifications of Rooms Continued

- Exceeded action levels should prompt a re-evaluation of adequacy of personnel work practices, cleaning, operational procedures and/or air efficiency and require an investigation into the source of contamination
  - Not Investigated
  - Not Documented

Environment Monitoring: Certifications of Equipment

- Air Changes per Hour (ACPH) requirement **not** met
  - ISO Class 7 ante room, minimum of 30 ACPH
  - ISO Class 8 ante room, recommended 20 ACPH
  - ISO Class 7 non-hazardous buffer, minimum 30 ACPH with at 15 from outside source
  - ISO Class 7 hazardous buffer room, minimum 30 ACPH

Environment Monitoring: Certifications of Equipment Continued

- Pressures **not** maintained as outline in the requirements
  - Differential pressure measured to be at least positive 0.02 inch water column from ante room to general pharmacy with door closed
  - Differential pressure measured to be at least positive 0.02 inch water column from non-hazardous buffer room to ante room with door closed
  - Differential pressure measured to be at least negative 0.01 inch water column from hazardous buffer room to positive pressure IS0 7 ante room with door closed

Environment Monitoring: Certifications of Equipment Continued

- Smoke Test **not** performed in the PEC in direct compounding area to demonstrate unidirectional airflow under dynamic conditions
- HEPA Filters **not** tested
  - Room HEPA filters leak tested and repaired if needed
  - Hood HEPA filters leaks tested and repaired if needed

Environment Monitoring: Certifications of Equipment Continued

- Viable Air and Surface Sampling **not** completely documented

Documentation of sampling shall include:

1. Date and Time of Sampling
2. Sample Locations
3. Method of Collection & Volume of Air Sampled (For Viable Air)
4. Frequency of Sampling & Action levels
5. Time of Day, in relationship to compounding

Environment Monitoring: Certifications of Equipment Continued

- Viable air microbial actions documented but review under the wrong volume of air
  - Viable Air sampling performed using active impaction device with appropriate growth media to support bacteria and for high risk compounding fungus, at least every 6 months in all ISO classified area using 400-1000 L of air per sample
    1. 1000 L: ISO Class 5 > 1 CFU/m3 or 400 L: > 1 CFU/m3
    2. 1000 L: ISO Class 7 > 10 CFU/m3 or 400 L: > 4 CFU/m3
    3. 1000 L: ISO Class 8 > 100 CFU/m3 or 400 L: > 40 CFU/m3

Environment Monitoring: Certifications of Equipment Continued

- Surface microbial action levels exceeded requirements due to confusion concerning room classification
    1. ISO Class 5, less than 3 CFU/m3
    2. ISO Class 7, less than 5 CFU/m3
    3. ISO Class 8, less than 100 CFU/m3

Environment Monitoring: Certifications of Equipment Continued

- All CFUs NOT analyzed down to the genus level
  - All CFUs analyzed down to the genus level with mold, yeast, coagulase positive Staph., gram negative rods require immediate investigation
- No documentation when action levels exceeded
  - Exceeded action levels should prompt a re-evaluation of adequacy of personnel work practices, cleaning, operational procedures and/or air efficiency and require an investigation into the source of contamination

Compounding Procedures

- Using **regular/non-sterile IPA** to wipe down supplies
  - Required supplies wiped down with 70% sterile IPA (sIPA)
- **Not** wiping stoppers prior to use
  - Rubber stoppers of vials/bottles and ampules disinfected with 70% sIPA prior to introducing needle or breaking an ampule
- Opening supplies in **non-classified rooms**
  - Syringes, needles, tubing opened only in ISO Class 5 PEC.
- **Not** disinfecting sterile gloves after touching non-sterile objects

Compounding Procedures Continued

Sterile compounded preparations **using low risk BUD dating**

-Batching is Medium Risk

1. Room Temp: 30 hours
2. Refrigerated: 9 days
3. Frozen: 45 days

Compound Record **not** completed for each batch

-Traceability – Patient record to the batch record

Continuous Quality Improvement (CQI)

- CQI **not** formalized in writing
  - Track and trend data
  - Track complaints from patients and practitioners
- **Not** sharing data with staff
  - Share data with Staff – will ask how often?
  - Identification of appropriate follow-up mechanisms when action limits or thresholds are exceeded

Sterile Compounding of Hazardous Drugs (HD)

- HD training **not** completed annually for all staff involve in compounding
  - Personnel who handle, dispose, or compound HD are trained and competency is assessed prior to handling HD and annually thereafter. Training shall be a didactic overview and verified by testing specific HD preparation techniques.
- **No** written confirmation by all compounding personnel of reproductive capability that they understand the risks

Sterile Compounding of Hazardous Drugs Continued

- HD **not** stored separately from other inventory
- CACI **not** located in a negative pressure room with at least 12 ACPH
- **Not** recording all pressures at least daily

12 Hour BUD

- Personnel **not** gowning and garbing the same as for a cleanroom

- ISO Class 5 LAWF is segregated compounding area, **near** garbage can, sink, window, or door

Immediate Use

- Immediate use CSP not labeled completely
  - CSP is immediately and completely administered by compounder or witnessed by compounder, if not must be labeled with:

  1. Patient identifier
  2. Names and amounts of all ingredients
  3. Name/initials of compounder
  4. Exact 1 hour BUD and time

CAI not located in ISO Class 7 Room

- Unable to provide documentation for CAI
  - Documentation from CAI manufacturer the ISO Class 5 environment is maintained under dynamic conditions when not located in an ISO Class 7 environment
  - Documentation from CAI manufacturer compounder is exempt from garbing

Extended BUD and Sterility Testing

- Sterility testing not performed according to USP Chapter 71
  - Sterility testing is done using membrane filtration or direct inoculation per USP Chapter 71
- CSP not quarantined until results received
  - CSP quarantined until results of sterility and endotoxin tests received
  - Patient and prescriber notified of potentially contaminated CSP and potential risks

Transporting CSP Outside of the Facility

- Not monitoring temps during transit
  - –Ascertain temperature of CSP during transit
- No directions if temp exceeded
  - –Specific handling packed with the CSP

Board Approved Waivers

- Waivers obtained from the Board prior to inspections
- Provide complete documentation in the waiver request
- Suggest a representative be present at the Board Meeting to answer any questions concerning the waiver

Post-presentation Question 1

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Post-presentation Question 2

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Contact Information

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