

USP <797>: Understanding Changes with Sterile Compounding in Hospitals

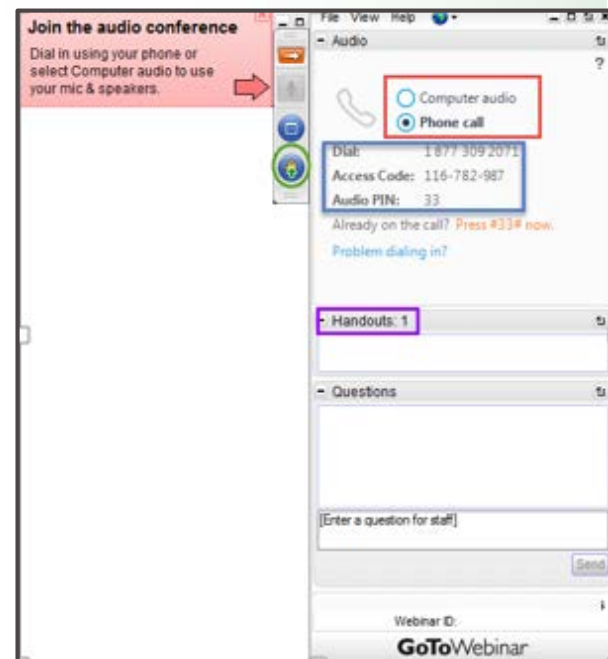
Missouri Hospital Association
Nathan Hanson, PharmD, MS, BCPS
Division Director of Pharmacy Operations
HealthTrust Purchasing Group
8/15/2019



Welcome to the webinar.

The presentation will begin shortly.

- You may listen via phone or via computer audio if your computer has speakers.
- This webinar will be in a “listen only” mode with opportunity to ask questions at the end of the presentation as time allows.
- All lines have been muted. Please enter any questions via the question feature in your control panel.
- If you wish to communicate via phone during the question session please use the “raise your hand” feature in the control panel and your individual line will be unmuted. You must enter the audio PIN for the line to be unmuted.
- Please do not place your line on hold. If you need to step away, please hang-up and redial when you are able to rejoin the call.
- Slides will be placed on the MHA website following the webinar.
- Thank you for your participation!



This research was supported (in whole or in part) by HCA Healthcare and/or an HCA Healthcare affiliated entity. The views expressed in this publication represent those of the author(s) and do not necessarily represent the official views of HCA Healthcare or any of its affiliated entities.



Outline

- What is sterile compounding and what is the USP?
- Why is this important?
 - What has changed?
 - Why is this a focus?
- Review of changes
 - Physical plant – is construction needed? Do you have a cleanroom suite or a segregated compounding area? What hoods do you use?
 - Processes – what policies need to be adjusted? Do you do monthly surface sampling? What BUDs do you need? How detailed is your record keeping?
 - People – what training must be added? Who is your Designated Person? How comprehensive are your training records?



Sterile Compounding Overview

- Some Intravenous (IV) medications do not come from the manufacturer ready to administer.
- They must be compounded
 - Antibiotics, pain medications, medications for the ICU
- Missouri hospitals regulatory and accreditation considerations
 - Department of Health and Senior Services
 - CMS Conditions of Participation
 - Joint Commission (some hospitals)
- The United States Pharmacopeia (USP) creates standards for drugs and compounded preparations



History of Sterile Compounding Focus

- 1995 – MO Department of Health Sterile Compounding rules
- 2004 – USP Chapter <797> published
- 2008 – MO Department of Health Sterile Compounding rules
- 2012 - New England Compounding Center (NECC) tragedy
- 2013 – Federal law creates 503B Registered Outsourcing Facilities
- 2015 – CMS added USP <797> to the State Operations Manual
- 2018 – The Joint Commission announces it is focusing on sterile compounding
- 12/1/2019 – Effective date of revised USP <795> and USP <797>, and new USP <800>

<https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/press-releases/january-31-2018-new-england-compounding-center-pharmacist-sentenced-role-nationwide-fungal>



CMS Change

CMS Manual System

Pub. 100-07 State Operations Provider Certification

Transmittal- 151

**Department of Health &
Human Services (DHHS)
Centers for Medicare &
Medicaid Services (CMS)**

Date: November 20, 2015

SUBJECT: Revisions to State Operations Manual (SOM), Appendix A -Survey Protocol, Regulations and Interpretive Guidelines for Hospitals

I. SUMMARY OF CHANGES: We are clarifying our interpretive guidance in Appendix A for existing regulations in 42 CFR Part 482, concerning preparation and administration of drugs as well as pharmacy requirements and accepted standards of practice for drug compounding. We are taking this opportunity to make clarifications and updates to existing guidance.

NEW/REVISED MATERIAL -

EFFECTIVE DATE: November 20, 2015

IMPLEMENTATION DATE: November 20, 2015



CMS State Operations Manual Appendix A (SOMA) Change – 11/20/2015

- Tag 405: §482.23(c) Standard: Preparation and Administration of Drugs.
- Tag 501: §482.25(b)(1) Pharmaceutical Services

“The applicable standards of practice for safe sterile compounding are, at a minimum, the standards published in The United States Pharmacopeia National Formulary Chapter <797> (“Pharmaceutical Compounding – Sterile Preparations”) and other relevant USP/NF Chapters (USP <797>).”

“Hospitals must ensure that they meet all currently accepted standards for safe preparation and administration for CSPs, whether they are the type of CSP that must be compounded in an aseptic pharmacy location that meets USP standards for low, medium or high-level risk CSPs or are ‘immediate-use CSPs’ prepared outside of the pharmacy.”



The Joint Commission (TJC)

- “As of January 1, 2018, The Joint Commission began enhancing our on-site evaluation of sterile medication compounding in hospitals, critical access hospitals and home care organizations.”
- “What’s Changed? Compounding is a high-risk and complex process and deserves a comprehensive assessment. Hospitals and critical access hospitals can expect additional dialogue in tracer activities, including the *Life Safety Code*® Surveyor Document Review, Medication Management System Tracer, Infection Control System Tracer and Competency Assessment System Tracer. Additional surveyor time also will be spent in the compounding area itself for observation of compounding processes. For home care organizations, the new ‘Medication Compounding’ standards chapter will be utilized to evaluate compliance.”

https://jointcommission.new-media-release.com/2018_411_part1/#sterilemeds



TJC – Why Now?

- “Sterile medication compounding is a very technical process that can lead to patient harm when performed incorrectly or in an incorrect environment. Even with increased regulations, illness and death associated with contaminated compounded products continue to make headlines and therefore requires additional focus.”

4-1-1 on Survey Enhancements



https://jointcommission.new-media-release.com/2018_411_part1/#sterilemeds

What Will Joint Commission Do Next?

Accreditation and Certification

[Download This Issue \(PDF\)](#)

June 12, 2019

More to come: The Joint Commission reviewing revisions to USP General Chapter <797>

The United States Pharmacopeial Convention (USP) [published revisions](#) on June 1 to its General Chapter <797> Pharmaceutical Compounding – Sterile Preparations. These revisions will become “official” – meaning when affected organizations will need to be able to meet the new requirements – on Dec. 1.

The Joint Commission is evaluating the impact of the revisions, and plans to release guidance and updated survey activity information in the coming months.

On its [website](#), USP has several resources and tools to aid in the adoption of the revised standards:

- Free digital access to the revised chapter, from June 1, 2019-Jan. 1, 2020.
- Education courses, both live and recorded, with implementation tips.
- Tools such as the HazRx® Mobile App and HazRx® Data Set.

[Learn more](#) about sterile compounding on our 4-1-1 on Survey Enhancements webpage.

[← Back](#)



Drug and Hospital Infections in the News

[6/28/2019] FDA is warning patients and health care professionals not to use products intended to be sterile produced by Pacifico National Inc., doing business as AmEx Pharmacy, Melbourne, Florida, due to a lack of sterility assurance. These drugs may pose a safety risk to patients.

Seattle Children's cited for safety violations after mold leaves 1 patient dead

[Ayla Ellison](#) ([Twitter](#) | [Google+](#)) - 2 days ago [Print](#) | [Email](#)

2 DMC hospitals at risk of losing Medicare contracts over infection control issues

[Megan Knowles](#) - Tuesday, January 29th, 2019 [Print](#) | [Email](#)



Hospital Infections in the News

June 19, 2019 11:26 AM

Premier Pharmacy Labs recalls drugs after FDA inspection

JESSICA KIM COHEN 

PharMEDium recalls 45 lots of hydromorphone tainted with allergen

[Alia Paavola](#) - 2 days ago [Print](#) | [Email](#)

[6/21/2019] The U.S. Food and Drug Administration is alerting healthcare professionals and patients of a voluntary [recall](#) of all unexpired compounded drugs intended to be sterile produced by Infusion Options, Inc. of Brooklyn, N.Y., due to lack of sterility assurance and other significant quality issues. These drugs may pose a safety risk to patients.



Definitions



What is Compounding?

- From USP 797: “Sterile compounding is defined as combining, admixing, diluting, pooling, reconstituting, repackaging, or otherwise altering a drug or bulk drug substance to create a sterile medication.”
- Sterile compounding does not include:
 - Assembling proprietary bag and vial connecting systems for a single patient
 - Reconstitution of a vial according to label instructions for a single patient
 - The process of administering a drug to a single patient



Definitions – Primary Engineering Controls (PEC)

- Restricted Access Barrier System (RABS)
 - Compounding Aseptic Containment Isolator (CACI)
 - Compounding Aseptic Isolator (CAI)
- Open Front Hoods
 - Biological Safety Cabinet (BSC)
 - Class II A2 – Recirculates some air before exhausting
 - Class II B2 – No recirculation of air before exhausting
 - Others
 - Laminar Airflow Workbench (LAFW)
 - Horizontal – HEPA filtered air flows horizontally
 - Vertical – HEPA filtered air flows vertically
- Pharmaceutical Isolator: contains a decontamination system
 - Rarely used in current practice



Definitions – Secondary Engineering Controls (SEC)

- Segregated Compounding Area (SCA)
 - SCA: Area for compounding non hazardous sterile medications that is marked off from the rest of the pharmacy by a visual perimeter
 - Containment SCA (C-SCA): Area for compounding hazardous sterile medications - must be a separate room
- Cleanroom Suite
 - Anteroom – the room where hand hygiene, garbing activities occur
 - Buffer Room – the room where sterile compounding occurs. Entry to this room is through the anteroom.



ISO Definitions

Category	Particles/m ³	Particles/ft ³	Example
ISO 5	3,520	100	Hood (PEC)
ISO 6	35,200	1,000	
ISO 7	352,000	10,000	Buffer Room (SEC)
ISO 8	3,520,000	100,000	



Beyond Use Date (BUD)

- A sterile compound must begin infusing before the BUD
- Changed to
 - Immediate use without a PEC: **4hrs**
 - PEC, without a compounding suite: **12hrs** at room temperature and **24hrs** in the refrigerator
 - PEC with a compounding suite: **4 days** at room temperature and **10 days** in the refrigerator
- Note: Gloveboxes/RABS are no longer exempt from the cleanroom suite requirement
- Note: Some sterile compounds are not stable for as long as their BUD



Physical Plant



Cleanroom Suite: Non-Hazardous

Ante Room

Positive Pressure to
pharmacy (0.02" w.c.)

20 ACPH

ISO 8

**<68 degrees and
<60% humidity
(recommendation)**

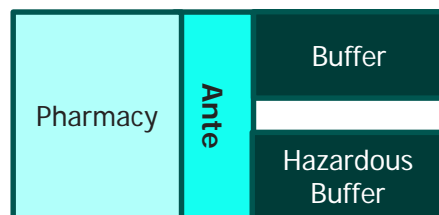
Non-Hazardous Buffer Room

Positive Pressure to Ante
Room (0.02" w.c.)

30 ACPH

ISO 7

**<68 degrees and <60%
humidity
(recommendation)**



Cleanroom Suite: Hazardous

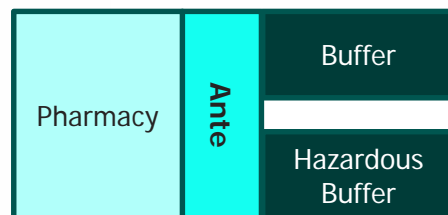
Ante Room

Positive Pressure to
pharmacy (0.02" w.c.)

30 ACPH

ISO 7

<68 degrees and
<60% humidity
(recommendation)



Hazardous Buffer Room

Negative Pressure to Ante
Room (-0.01 to -0.03"
w.c.)

30 ACPH

Externally Vented

ISO 7

<68 degrees and <60%
humidity
(recommendation)



Physical Plant – Cleanroom Suite

- Humidity and temperature controls, daily review, and retrievable log
- Pressure differential controls, visual indicators, retrievable logs
- Low air returns, unless smoke studies prove compliance *
- HEPA filters must be mounted in ceiling
- Install aerosol injection ports in ductwork
- Detailed, extensive cleaning requirements

* Could be on the ceiling previously



Physical Plant – Cleanroom Suite

- Surfaces should be resistant to damage by cleaning and sanitizing agents
- Surfaces of ceilings, walls, floors, doors, door frames, fixtures, shelving, work surfaces, counters and cabinets in the cleanroom suite must be smooth, impervious, free from cracks and crevices and non-shedding
- All cracks and junctures must be sealed
- Tacky mats are no longer allowed in classified rooms



Ceilings and Floors

- Ideally hard ceiling, not drop ceiling. If a drop ceiling:
 - Ceiling tiles must be caulked and secured around each panel to seal them to the support frame.
 - Ceiling panels must be washable, scrubbable and soil resistant, and designed for use in a cleanroom environment
- Sprinkler heads recessed and covered (preferred) and easily cleanable (required)
- Ideally not vinyl composite tile which requires ongoing maintenance
- Smooth, seams heat welded, impervious
- Line of demarcation in anteroom (required) and in the HD buffer room (preferred-could be the doorway) and in a SCA




Other Requirements

- Walls
 - Epoxy paint or smooth paneling (heavy gauge polymer, glass, etc.)
 - No ledge at the base where the floor comes up, or caulked to reduce/remove the horizontal surface
 - Easily cleaned at the junction with the ceiling
 - If overhangs or ledges are present, they must be easily cleanable
- Doors
 - Not wood
 - Equipped with hands free opening (preferred)
 - Interlocked (Preferred)
- Light fixtures
 - Easily cleanable: smooth, mounted flush, and sealed
 - Easy to replace



Other Requirements

- Sinks
 - At least 1 meter from HD Buffer room door opening (1 meter from PEC in an SCA)
 - Should be large enough and deep enough to prevent splashing
 - Hands free is preferred
 - Appropriate soap dispenser, not refillable
 - No floor drains or water supply in buffer room. No floor drain in anteroom.
 - Eye wash station readily available (for hazardous drugs)
 - Pass-throughs:
 - Cleanable and only open one side at a time (interlocking preferred)
 - Consider HEPA filtration for pass-through from non-classified into classified negative space
 - Appropriate hands-free alcohol dispenser
 - Power: Consider uninterruptable power supply and/or generator power for hoods, lights, HVAC, and controls. Or downtime procedures should be developed.
- 

Physical Plant – Segregated Compounding Area (SCA)

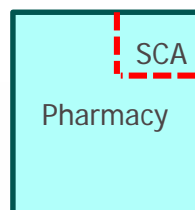
SCA

Within the pharmacy area

Visible perimeter

Cleanable design

Away from contaminants



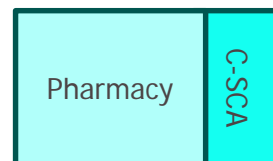
C-SCA

Physically separate room

Negative Pressure to pharmacy (-0.01 to -**0.03"** w.c.)

12 ACPH

Externally Vented



Physical Plant – Segregated Compounding area (SCA)

- No anteroom or buffer room requirement
- Allowable BUD: 12 hours at room temperature and 24 hours refrigerated
- Must be located away from unsealed windows, doors that connect to the outdoors, traffic flow, restrooms, warehouses, and food preparation areas
- A visible perimeter must establish the SCA boundary
- Same requirements for physical cleanability, cleaning processes, garbing, training, and product handling



Physical Plant – Containment Segregated Compounding area (C-SCA)

- For hazardous drug sterile compounding
- Must be a physical room, not an area of a larger room
- External ventilation requirements to contain hazardous drugs



Physical Plant – Hazardous Drugs

Receiving Room

Physically separate
Neutral or Negative
Pressure

Storage Room

Physically Separate
Negative Pressure
12 ACPH
Externally vented
Dedicated refrigerator in
storage room



PEC – Check Your Hood

LAFW/CAI – Non Hazardous

ISO 5

BSC or CACI

Externally vented

ISO 5

- Updated recertification standards
- Gloveboxes are not allowed the longer BUD unless they are in a cleanroom suite
- Must be able to clean behind the PEC



Processes



Processes: Labels, Records, and SOPs

- Specific, detailed Master Formulation Record Requirements ('Recipe')
- Specific, detailed Compounding Record requirements
- Specific, detailed Label requirements
- Standard Operating Procedures (SOPs) and policies reviewed every 12 months
- Specific processes for preparing allergenic extracts



Processes: Cleaning and Disinfection

- Cleaning: Removal of residues
- Disinfection: Destruction of fungi, viruses, and bacteria
- Sporocidal Disinfectant: Class of disinfectants active against bacterial and fungal spores
- Very detailed requirements for cleaning and disinfecting activities that must occur monthly, daily, and throughout each shift
 - Areas
 - Supplies
 - Products
- Example: Water, then cleaning agent, then alcohol.
- Example: EPA registered 1 step cleaning agent, then alcohol



Processes: Surface Sampling

- Required **monthly***
- Calibrated, temperature controlled incubator
- Include these areas
 - Pass through chambers
 - Equipment contained in the PEC
 - Staging/work areas near the PEC
 - Frequently touched surfaces

* Previously was “periodically,” usually done every 6 months



Processes: Monitoring

- Temperature and humidity maximums are recommendations
- Requirements
 - Daily monitoring and documentation of temperature and humidity
 - Cleanroom Suite or SCA
 - Medication storage areas
 - Annual calibration of sensors (or per manufacturer recommendations)
 - Daily documentation of pressure monitoring for cleanroom suite and C-SCA
 - Documentation of cleaning processes
- Documents retrievable for 3 years



Processes: Certification Requirements

- Twice annually
 - Airflow, including air velocity and air volume, ACPH, pressure differentials
 - HEPA Filter leak testing
 - Particle counts
 - Smoke pattern testing
 - Airborne viable particle monitoring
- Usually outsourced to vendor
- New/Changed Requirements
 - Document the PEC ACPH that contribute to the room ACPH
 - Leak test HEPA filters
 - Dynamic airflow smoke pattern test



Processes: Immediate Use Compounding

- Infusion must begin within 4 hours
- May only be a combination of 3 different sterile products or fewer
- For 1 patient
- Follow written aseptic processes “to minimize the potential for contact with nonsterile surfaces, introduction of particulate matter or biological fluids, and mix-ups with other conventionally manufactured products or CSPs.”
- May be prepared outside of the PEC and SEC



Immediate Use Compounding – Cautions

- Should be the exception
- Competencies developed and documented
- Infection Control and Hand Hygiene
- Many other standards to consider
 - Training
 - Documentation
 - Double checks
 - Labeling
 - High Alert



People



Designated Person

- The facility must “designate one or more individuals...to be responsible and accountable for the performance and operation of the facility and personnel in the preparation of CSPs and for performing other functions as described in this chapter”
- Responsible for
 - Training
 - Policy development and implementation
 - Quality Assurance and Quality Control
 - Quality Improvement and Corrective Actions



Training

- Written training program
- Includes people who handle CSPs and/or enter the compounding area
- Demonstrated proficiency in 11 core competency areas every 12 months
- Garbing and fingertip testing: 3 times initially, and every 6 months*
- Compounding and media fill tests: initially and every 6 months *
- Immediate Use Compounding personnel

* Changed from annually for low/medium risk, and every 6 months only for high risk compounding



Garbing

- The person in the room is the primary source of contamination
- Very detailed requirements for garbing products to use and processes to follow: Shoe covers, hair cover, mask, gown, sterile gloves
- No cleaning brushes for hand hygiene allowed, but nail pick is required
- Thorough training
- Accountability to follow processes
- Applicable to cleanroom suites and segregated compounding areas



Summary

- Sterile Compounding is now an area of focus
- 12/1/2019 enforcement date
- Download the standards (www.usp.org/compounding)
- Consider impact on workload, workflow, and staffing needs
- Assign a Designated Person
- Create a Sterile Compounding Taskforce: Facilities Management, Pharmacy, Nursing, HR, Quality, Regulatory Compliance
 - Physical plant – is construction needed? Do you have a cleanroom suite or a segregated compounding area? What hoods do you use?
 - Processes – what policies need to be adjusted? Do you do monthly surface sampling? What BUDs do you need? How detailed is your record keeping? When is Immediate Use preparation acceptable, and how is it managed safely?
 - People – what training must be added? Who is your Designated Person? How comprehensive are your training records?



Helpful Resources

- <https://www.usp.org/compounding>
- USP 797, 795, 800 Guidelines, United States Pharmacopeia, Chapter 797, Chapter 795, Chapter 800, Rockville, MD, www.nim.nih.gov
- [Joint Commission 4-1-1 on Sterile Compounding](#)
- [TJC Accreditation and Certification June Issue](#)
- https://www.jointcommission.org/datetime_tjc/surveyors_increasing_on-site_focus_on_medication_compounding/
- https://www.jointcommission.org/at_home_with_the_joint_commission/certification_reports_of_compounding_hoods_and_rooms_affecting_accreditation_decisions/



USP <797>: Understanding Changes with Sterile Compounding in Hospitals

Missouri Hospital Association
Nathan Hanson, PharmD, MS, BCPS
Division Director of Pharmacy Operations
HealthTrust Purchasing Group
8/15/2019

