USP STERILE COMPOUNDING

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OBJECTIVES

- Recognize USP chapters related to medication compounding
- Describe the scope and purpose of USP 797
- Identify key factors in meeting or exceeding the purpose of USP 797
- Recognize key areas where infection prevention professionals may
  - Assist organizations in meeting USP requirements
  - Audit performance of the organization in complying with USP 797
  - Identify opportunities for performance improvement

WHAT IS USP

- United States Pharmacopeial Convention
  - Our Mission
    - To improve global health through public standards and related programs that help ensure the quality, safety, and benefit of medicines and foods.
  - No enforcement nor regulatory authority
  - Standards are developed and revised by more than 800 volunteer experts
- Chapters below 1000 are considered to be standards and are considered enforceable by regulatory bodies

ARCRONYMS

- USP – United States Pharmacopeial Convention
- CSP – Compounded Sterile Product
- BUD – Beyond Use Date
- PEC – Primary Engineering Control (ISO class 5 or better)
- SEC – Secondary Engineering Control (ISO class 7 or better)
- SCA – Segregated Compounding Area

USP CHAPTERS APPLICABLE TO PHARMACEUTICAL COMPOUNDING

- USP 795
  - Pharmaceutical Compounding - Non-sterile Preparations
- USP 797
  - Pharmaceutical Compounding - Sterile Compounding
- USP 800
  - Hazardous Drug – Handling in Health Care Settings
- USP 825
  - Radiopharmaceuticals
- USP 71, 49…..

USP 797 SCOPE AND PURPOSE

- Sterile compounding
  - Combining, admixing, diluting, pooling, reconstituting, repackaging or other alterations of a drug or bulk drug substance to create a sterile compound
- Purpose of the chapter is to minimize harm
- Aseptic technique must be followed
- Administration is out of scope
  - Preparation for administration is within scope
    - IV bag spiking in 2016 edition was called out not specific in 2019, but likely fall under Immediate Use

IMMEDIATE USE

- Compounding of CSPs for direct and immediate administration to a patient
    1. Aseptic processes
    2. The preparation is performed in accordance with evidence-based information for physical and chemical compatibility of the drugs (e.g., FDA-approved labeling, stability studies).
    3. Not more than 3 different sterile products.
    4. Any unused starting component from a single-dose container must be discarded after preparation for the individual patient is complete. Single-dose containers must not be used for more than 1 patient.
    5. Administration begins within 4 hours following the start of preparation.
    6. CSP properly labeled

(The United States Pharmacopeial Convention USP Compounding Compendium, 2019)

CSP CATEGORIES

- Category 1 CSP
  - Prepared within a ISO Class 5 environment
  - BUD
    - 12 hours or less stored at room temp
    - 24 hours or less stored under refrigeration
- Category 2 CSP
  - Prepared within an ISO Class 5 environment that is within an ISO Class 7 buffer room
  - BUD is determine by compounding method, sterility testing and storage conditions

CSP CATEGORY 2 BUD

Preparation Characteristics		Storage Conditions		
Compounding Method	Sterility Testing Performed and Passed	Controlled Room Temperature (20°-25°)	Refrigerator (2°-8°)	Freezer (-25° to -10°)
Aseptically processed CSPs	No	Prepared from 1 or more non-sterile component(s): 1 day	Prepared from 1 or more non-sterile component(s): 4 days	Prepared from 1 or more non-sterile component(s): 45 days
		Prepared from only sterile starting components: 4 days	Prepared from only sterile starting components: 10 days	Prepared from only sterile starting components: 45 days
	Yes	30 days	45 days	60 days
Terminally sterilized CSPs	No	14 days	28 days	45 days
	Yes	45 days	60 days	90 days

(The United States Pharmacopeial Convention USP Compounding Compendium, 2019)

KEY SECTIONS OF USP 797

- Personnel training and evaluation
- Personal hygiene and garbing
- Facilities and engineering controls
- Certification and recertification
- Microbiological air and surface sampling
- Cleaning, disinfecting and applying sporicidal agents in compounding areas

PERSONNEL TRAINING AND PERSONAL HYGIENE AND GARBING

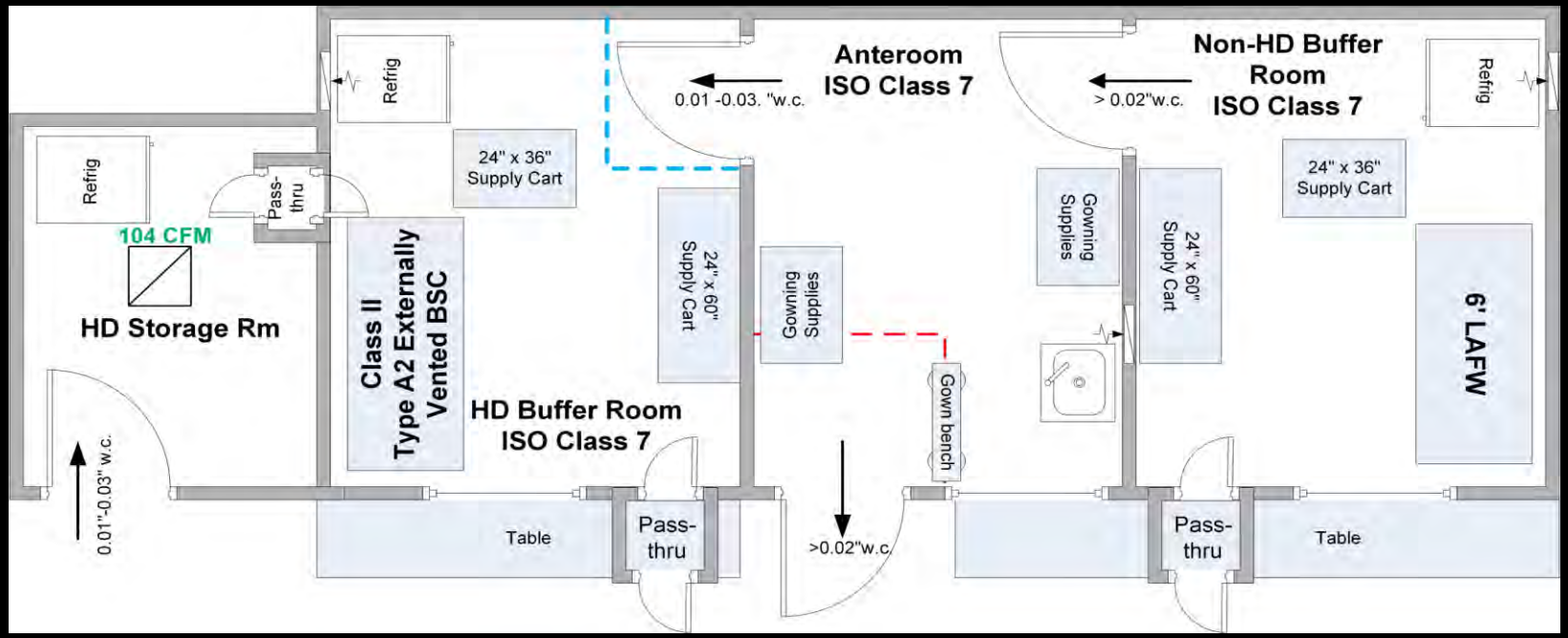
- Gloved finger tip and thumb sampling
  - Chapter provides a detail sampling procedure
  - Initial
    - 3 separate times
    - Action level > 0 cfu
  - Subsequent and every 6 months after media fill
    - Action level >3 cfu
- Media fill
  - Must mimic most complicated procedure personnel expected to perform
- Garbing
  - Minimum hair cover, mask, shoe cover, gown and sterile gloves
  - Properly donning and doffing

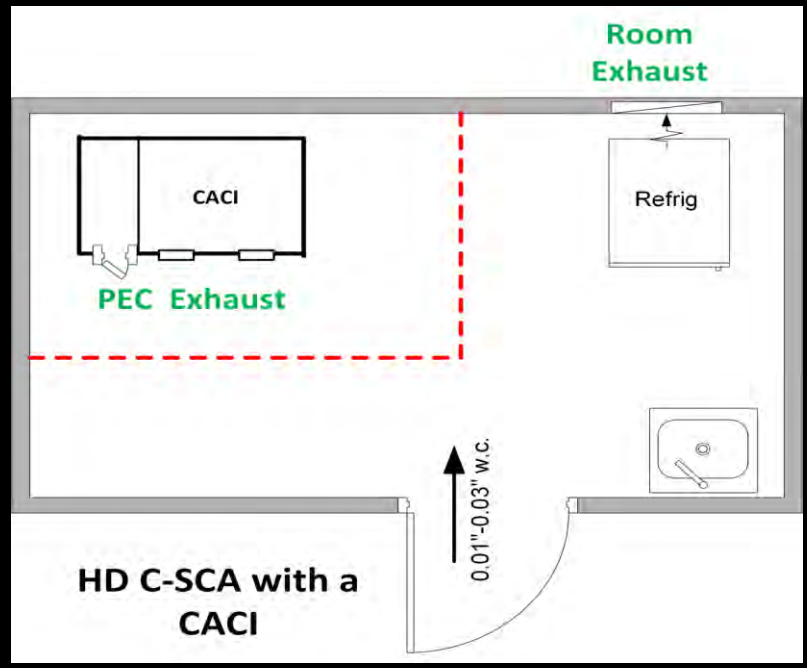
ASEPTIC TECHNIQUE

- Handling of material prior to entry into ISO class 5 PEC
- Hand sanitization
- Sanitizing of critical site
  - Use of sterile alcohol wipe in same direction 3 times
    - Physical removal of spores
- Use of first air
  - Horizontal flow
  - Vertical flow
- Minimizing equipment and impact on unidirectional air flow
  - Smoke studies

FACILITIES AND ENGINEERING CONTROLS

- Clean room suited vs. SCA (C-SCA)





(CriticalPoint, LLC, 2018)

FACILITIES AND ENGINEERING CONTROLS

- Secondary Engineering Controls (SEC)
  - Air Exchanges
    - ISO Class 8 minimum 20
    - ISO Class 7 minimum 30 (suggest 45-50)
  - Terminally HEPA filtered air
- Primary Engineering Controls (PEC)
  - Horizontal flow hood
  - Vertical flow hood
    - Hazardous drug preparation

WATER SOURCES

- Outside buffer room
  - Ante-room clean/dirty
  - Outside ante-room
- Must be 1 meter from PEC in SCA
- At least 1 meter from entrance to hazardous drug compounding buffer room
- Integrated eye wash
  - Avoid the need for hose on floor or additional cleaning surface
- Sink should be scrub size
  - Proper hand hygiene
  - Reduce splash
  - Should cover plumbing

CERTIFICATION AND RECERTIFICATION

- SEC and PEC by CETA (Control Environment Testing Association) certified professional
  - Initially
  - Every 6 months
- Includes
  - ISO classification, Particle counts both viable and non-viable, surface sampling
  - HEPA filter functioning
  - Air exchanges
- Certify to CAG (CETA Application Guide) 003
  - Will ensure meets all USP requirements

MICROBIOLOGICAL AIR AND SURFACE SAMPLING

- Purpose
  - Proper practices being followed
  - Proper disinfecting and cleaning
  - Maintaining environmental quality
- Viable air sampling must be completed every 6 months
  - Will be a part of certification
  - Suggest doing self sampling between certifications for trending
- Surface sampling
  - Monthly
- Completed under dynamic conditions

ACTION LEVELS MICROBIOLOGICAL SAMPLING

- Identify to genus level
- Develop corrective action plan
- Involve infection control colleagues
- Evaluate trends
- Resample

ISO Class	Air Sampling Action Levels (cfu per cubic meter (1000 liters) of air per plate)
5	>1
7	>10
8	>100

ISO Class	Surface Sampling Action Levels (cfu/device or swab)
5	>3
7	>5
8	>50

CLEANING AND DISINFECTING

- What products should we use
  - Must be compatible with equipment
  - Minimize co-worker exposure
  - Should products be rotated
- Continuous
  - Sanitizing work surface with sterile IPA
  - Minimum every 30 minutes or between products
- Daily
  - Cleaning and disinfecting
- Monthly
  - Application of sporicidal
- USP 800 must add step for deactivation/decontamination

MINIMUM FREQUENCY FOR CLASSIFIED AREAS AND SCA

Site	Cleaning	Disinfecting	Sporicidal
PEC and equipment inside	Daily and when contamination	• Daily and when contamination • Sterile 70% IPA every 30 minutes	Monthly
Removable work tray	• Work surface daily • All surfaces and underneath work tray monthly		
Pass-throughs	Daily	Daily	Monthly
Work surface outside PEC	Daily	Daily	Monthly
Floors	Daily	Daily	Monthly
Walls, doors, door frame	Monthly	Monthly	Monthly
Ceilings	Monthly	Monthly	Monthly
Storage shelving and bins	Monthly	Monthly	Monthly
Equipment outside PEC	Monthly	Monthly	Monthly

CLEANING AND DISINFECTING PROCESS

- Dedicated equipment
  - Hazardous drug area separate from non-hazardous
- Low-linting disposable mop heads and wipes
- Cleanest to dirtiest
- Top to bottom
- No spray
  - Damage hoods HEPA filters
  - Aerosolize hazardous drug

DOCUMENTATION

- SOPs
- Education, training and competency
  - Competency demonstrated at least every 12 months
  - Observed hand hygiene and garbing every 6 months
  - Gloved finger tip and media fill every 6 months
- Deactivation, decontamination, cleaning and disinfecting
  - Daily and monthly
- Certification
  - Signed by Designated Person
- Equipment records
- Air and surface sampling records

SUMMARY

- All about infection prevention and quality
- Requires collaboration with multi-disciplinary groups
  - Facilities and engineering requirements
  - Processes and procedures
  - Environmental monitoring
- Infection prevention
  - Review policy and procedures
  - Consultation for cleaning, and disinfecting products
  - Assess compliance
  - Help develop remediation plans

QUESTIONS

References:

CriticalPoint, LLC. (2018). 2018 CriticalPoint Sterile Compounding Boot Camp. Tonitown, NJ.

The United States Pharmacopeial Convention USP Compounding Compendium. (2019, July 18). 2019 USP Compounding Compendium. Rockville, MD, United States. doi:10.6.1.1