USP 797, 795, and 800:
Key Updates, Highlights, and Questions

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797
Compounded Sterile Product Categories Simplified

795
Non-Sterile Compounded Products

800
Hazardous Compounds

797 slides
- New CSP categories
- Hand washing
- Garbing and sterile bunny suits
- Sinks
- Carts
- Certification for Sterile Compounding Spaces
- Cleaning Requirements and Frequencies
- Surface sampling from packet Box 6-2 Ipa
- In-Use Times
- BUD's

795 NONSTERILE NONHAZARDOUS
- Scope: Non-Sterile Compounding and Preparations
- Personnel Preparation and Hand Hygiene
- Cleaning and Sanitation
- BUD Documentation in Tricky Situations

800
- Gloves, Gowns, Shoes
- Scrubs
- Deactivating Cleaning Decontaminating Disinfecting

- Major Changes
  - Compounded Sterile Product Categories Simplified
  - Removed section of hazardous drugs and put into 800
  - Removed section of radiopharmaceuticals and put into 825
- 797 slides
  1) New CSP categories
  2) Hand washing
  3) Garbing and sterile bunny suits
  4) Sinks
  5) Carts
  6) Certification for Sterile Compounding Spaces
  7) Cleaning Requirements and Frequencies
  8) Surface sampling from packet Box 6-2 Ipa
  9) In-Use Times
  10) BUD's

CSP CATEGORIES:

BEFORE:

~~Low~~	~~Medium~~	~~High~~
• 48 hrs room temp • 14 days refrigerated • 45 days frozen	• 30 hrs room temp • 9 days refrigerated • 45 days frozen	• 24 hrs room temp • 3 days refrigerated • 45 days frozen

❖ **Immediate Use CSPS**

- (BUD<4 hours)
- are **NOT** subject to category 1 & 2 requirements as long as certain conditions met (conditions in section 1.3)

NOW:

Category 1	Category 2
•**BUD is:** **12** hours room temperature or **24** hours refrigerated •**PREP** • Cleanroom Suite (see right) or • Segregated Compounding Area	• **BUD is:** • **>12** hours room temperature or • **>24** hours refrigerated • **PREP:** • Cleanroom Suite (buffer with anteroom)

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In the previous guidelines, 25 or more containers of high risk compounds required sterility testing. New regulations have gotten rid of high risk (now only category 1 and category 2). Can you make more than 25 containers under new regulations without a sterility test?

A. Yes
B. No

- Order of hand hygiene and garbing is determined by **placement of the sink,** which may be inside or outside of the cleanroom suite or the segregated compounding area:
  - Order ***must*** be described in facility SOPs
  - Order ***must*** minimize the risk of contaminating hands if performed in unclassified areas
- Personnel ***must*** wash hands and forearms with soap and water **up to elbows** for at least 30 seconds:
  - Sink ***should*** enable hands-free operation
  - **BRUSHES *MUST NOT* BE USED**
  - Hand dryers ***must not*** be used
  - A **closed system** soap dispenser ***must*** be in close proximity to sink

- Low-lint **garment** that fits snugly around the wrists and neck:
  - Garment may be re-used within same shift if stored in classified area or within SCA
- Low-lint, disposable **shoe covers**
- Low-lint, disposable **head covers** that cover the hair and eyes and, if applicable, disposable cover for facial hair
- **Face mask**
- Sterile **powder-free gloves** (disposable)

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Sterile bunny suits are not a must.

Should we use them?
Why or Why Not?

Sink Cleaning:

– All sinks must be cleaned and disinfected on days that compounding is occurring and sporicidal agents applied monthly.

– Order of hand hygiene and garbing depend on sink placement and must be described in facility SOP

Sink Location

Cleanroom suites:

– Buffer room must not contain plumbed water sources or floor drains

– Ante room must not contain floor drains

– Sink may be on either clean or dirty side of ante room

– Sink may be outside of cleanroom suite but must be in a clean place

- Carts in classified areas must be non-porous and have **wheels and casters that are easily cleanable**
- Must be cleaned entirely before crossing from dirty to clean side of ante room

- Before compounding Category 1 or 2 CSPs, Cleanroom suites and PEC's ***must*** be certified according to the Controlled Environment Testing Association (CETA) or equivalent:

  - Initially
  - Every **6 months**
  - After there are **changes** to the room (redesign, construction, PEC moved)

- Certification/Recertification Testing must include:
  - Airflow testing (Air Changes per Hour from HVAC, PEC, and total)
  - HEPA filter integrity testing
  - Total particle count testing
  - (~~In situ~~) **Dynamic smoke visualization studies**

Microbiological Air Sampling

- Required every **6 months**
- Impact collection device must be used (no settling plates)
- Reputable certifiers will be able to interpret and advise on results
- Results that exceed action levels must be investigated, organisms identified at the level of genus, and corrective action plans initiated and evaluated for success
- Action levels for (~~400-1000 L~~) **1000** L of air: see table
- Air is sampled through (~~settling plates~~) viable impact monitoring

Microbiological Surface Sampling

- Required every **30 days** for all classified areas and pass-through spaces
- Must occur at the end of the compounding shift BEFORE cleaning and disinfecting
- Sampling sites: For PEC, interior and equipment, staging or work area(s) near the PEC, frequently touched surfaces
- Results that exceed action levels **MUST** be investigated, organisms identified at the level of genus, and corrective action plans initiated and evaluated for success
- Surfaces are sampled with a surface sampling device.

Site	Cleaning	Disinfecting	Applying Sporicidal
PEC(s) and equipment and all interior surfaces inside the PEC(s)	Daily or when contamination is known or suspected	Daily or when contamination is known or suspected Additionally: sterile 70% IPA to the horizontal work surface every 30 minutes. Do not disrupt compounding process to apply IPA.	Monthly
Removable work tray of the PEC	Daily - Top surface of tray Monthly - Underneath tray	Daily - Top surface of tray Monthly - Underneath tray	Monthly
Pass-through(s)	Daily	Daily [b]	Monthly
Work surface(s) outside the PEC	Daily	Daily [b]	Monthly
Floor(s)	Daily	Daily [b]	Monthly
Wall(s), door(s), and door frame(s)	Monthly	Monthly [b]	Monthly
Ceiling(s)[c]	Monthly	Monthly [b]	Monthly
Storage shelving and bins	Monthly	Monthly [b]	Monthly
Equipment outside the PEC(s)	Monthly	Monthly [b]	Monthly

[a] Many disinfectants registered by the EPA are one-step cleaning and disinfecting agents, which means that the disinfectant has been formulated to be effective in the presence of light to moderate soiling without a separate cleaning step.
[b] Ceilings of the SCA are required to be cleaned, disinfected, and applied with sporicidal agent only when visibly soiled and/or when surface contamination is known or suspected.

- Remove the cover from the surface sampling device. Using a rolling motion, firmly press the media surface onto the surface to be sampled.
- The surface sampling device will leave a residue of growth media on the sample site**. AFTER SAMPLING, REMOVE THE RESIDUE FROM THE SURFACE USING STERILE 70% IPA.**
- Cover each surface sampling device. Store media devices during incubation to prevent condensate from dropping onto the agar and affecting the accuracy of the cfu reading (e.g., invert plates).
- Incubate the surface sampling devices at 30°–35° for no less than 48 hours. Examine for growth. Record the total number of discrete colonies of microorganisms on each device as cfu per sample on an environmental sampling form based on sample type (i.e., surface), sample location, and sample date.
- Incubate the surface sampling device at 20°–25° for no less than 5 additional days. Examine the device for growth. Record the total number of discrete colonies of microorganisms on each media device (cfu per sample) on the environmental sampling record based on sample type (i.e., surface), sample location, and sample date.
- Alternatively, to shorten the overall incubation period, two samples may be collected for each sample location and incubated concurrently.
  - Both samples could be TSA or one sample could be TSA and the other fungal media (e.g., MEA or SDA).
  - Incubate each sample in a separate incubator. Incubate one sample at 30°–35° for no less than 48 hours, and incubate the other sample at 20°-25° for no less than 5 days.
    - If fungal media are used as one of the samples, incubate the fungal media sample at 20°–25° for no less than 5 days.
  - Count the total number of discrete colonies of microorganisms on each sample, and record these results as cfu per sample.
  - Record the results

ISO Class	Actionable Surface Sampling CFU per device or swab
5	>3
7	>5
8	(~~>100~~) **>50**
Required	Every 30 days

In Use Times:

- Components used to prepare CSPs *must* be used only for a specified time after initial entry or puncture.

Components	In-Use Time
Conventionally Manufactured Sterile Products	
Single-Dose Container	12 hours in ISO 5
Multiple-Dose Container	28 days
Pharmacy Bulk Package	As specified by manufacturer in ISO 5
CSPs	
Single-Dose Container	12 hours* in ISO 5
Multiple-Dose Container	28 days*
Compounded Stock Solutions	12 hours* in ISO 5
* Or assigned BUD if shorter	

797: In Use Times

How will the new BUD on stock solutions affect TriMix? Thoughts?

CATEGORY 2 BUD's:

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 one or more nonsterile starting component(s): 1 day	Prepared from one or more nonsterile starting component(s): 4 days	Prepared from one or more nonsterile starting 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

CATEGORY 2 BUD's: Extra Provisions for MULTIDOSE CONTAINERS

- ✓***Must*** be prepared in Cleanroom Suites as Category 2 CSPs
- ✓Are assigned BUDs based on how they are sterilized and whether sterility testing has been performed
- ✓***Must*** pass **container closure integrity test *once*** for each formulation (*USP* <1207>), usually:
  - Microbial immersion test
  - Dye ingress test
- ✓***Must*** prevent microbial growth throughout their BUDs, usually accomplished by adding a preservative agent
- ✓***Must*** demonstrate antimicrobial effectiveness (*USP* <51>) **once** for each formulation in a specific container closure system by **one** of the following methods:
  - **Contracted by the facility** in the designated container closure system
  - Derived from *USP* <51> testing results provided by **an FDA-registered facility**
  - *USP* <51> results published in **peer-reviewed literature sources**; CSP ***must*** be exactly the same as those tested
  - Derived from **bracketed <51> testing results** for a concentration in the range of high and low concentrations tested
- ✓ ***Must*** be **discarded 28 days after initial**

797: BUDs

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New regulations for MULTIDOSE CONTAINERS require USP 51 testing as well as USP 1207 testing.

Has anyone done these?

Thoughts?

- ▶795
  1) Scope: Non-Sterile Compounding and Preparations
  2) Personnel Preparation and Hand Hygiene
  3) Cleaning and Sanitation
  4) BUD Documentation in Tricky Situations

Compounded nonsterile preparations:

A preparation intended to be nonsterile created by combining, admixing, diluting, pooling, reconstituting other than as provided in the manufacturer's labeling ,or otherwise altering of a drug or bulk drug substance

Examples of **CNSP's:**

- ✓ Solid oral preparations
- ✓ Liquid oral preparations
- ✓ Rectal preparations
- ✓ Vaginal preparations
- ✓ Otic preparations
- ✓ **Nasal and sinus preparations intended for local application**
  - i.e. nasal sprays and nasal irrigation
- ✓ Topical preparations
  - i.e., creams, gels, ointments

Personnel Preparation

- ***Must*** maintain hand hygiene and cleanliness required for the type of compounding performed. At a minimum, remove:
  - Personal outer garments
  - **Jewelry** that can interfere with garbing or hand hygiene
    - E.g.: jewelry, piercings, watches and rings
  - Earbuds or headphones

Hand Hygiene

- **When entering the compounding area, compounders must:**
  - Wash hands and forearms up to the elbows with soap and water for at least 30 seconds
  - Dry hands and forearms to the elbows completely with disposable towels or wipers
  - Allow hands and forearms to dry thoroughly before donning gloves

- **Alcohol hand sanitizers alone are not sufficient for hand hygiene**

Cleaning and Sanitizing

- All surfaces must be cleaned and sanitized:
  - On a regular basis at the frequencies specified in table on right
  - Before initiating compounding, if compounding is not performed daily
  - After a spill
  - When surfaces are visibly soiled
- When cleaning and sanitizing are performed as separate steps, cleaning must be the first step
- Must consider compatibility, effectiveness and minimizing residue when selecting cleaning and sanitizing agents

SITE	FREQUENCY of CLEANING and SANITIZING
Work Surfaces	• At the **beginning** and **end** of **each shift**, after spills and when surface contamination is known or suspected • Clean and sanitize work surfaces **between compounding CNSPs with different components**
Floors	• **Daily**, after spills and when surface contamination (e.g., splashes) is known or suspected
Walls	• ~~(Monthly)~~ → **Every 3 months**, after spills and when surface contamination (e.g., splashes) is known or suspected
Ceilings	• ~~(Monthly)~~ → When visibly soiled and when surface contamination is known or suspected
Storage Shelving	• ~~(Monthly)~~ → **Every 3 months**, after spills and when surface contamination (e.g., splashes) is known or suspected

How to document BUD in the Absence of:

- A *USP–NF* Compounded Preparation Monograph

  OR

- CNSP-Specific Stability Information

Type of Preparation	BUD (days)	Storage Temperature
• Non-preserved aqueous dosage forms	**14**	Refrigerator
• Preserved aqueous dosage forms	**35**	Controlled room temperature or refrigerator
• Nonaqueous dosage forms	**90**	Controlled room temperature or refrigerator
• Solid dosage forms	**180**	Controlled room temperature or refrigerator

- Must have a stability-indicating study
  - **Average cost is approximately $13,000 - $25,000**
- PCCA stability indicating studies on file
  - **Must use PCCA bases and chemicals**
  - **If PCCA changes the manufacturer of an API, is their study still valid?**

▶ 800

1) Gloves, Gowns, Shoes
2) Scrubs
3) Deactivating Cleaning Decontaminating Disinfecting
   a) Deactivation
   b) Decontamination
   c) Cleaning

Gloves

- Chemotherapy gloves ***must*** meet ASTM **D6978 standards**
- Activities
  - 1 pair recommended for administration of intact tablet/capsule
  - 2 pairs recommended for all other activities (i.e. compounding)
- Gloves **SHOULD** be changed:
  - Every 30 min unless otherwise recommended by manufacturer
  - When torn, punctured, contaminated
- Hands ***must*** be washed with soap and water before and after removing gloves

Gowns

- ***Must*** be disposable!
- ***Must*** be shown resistant to permeability by HDs
- **Should** be made of polyethylene-coated polypropylene or other laminated material
- ***Must*** close in the back (no open front)
- ***Must*** be long sleeved
- ***Must*** have elastic or knit closed cuffs
- ***Must*** be changed:
  - Per manufacturer's information for permeation
  - Every 2-3 hours if no permeation information
  - Immediately after spill/splash

Shoe Covers

- 2 pairs required for HD compounding

See USP 800 Section 7.2 for further information

"Cloth laboratory coats, surgical scrubs isolation gowns, or other absorbent materials…may also retain HD residue from contact, and may transfer to other health care workers or various surfaces. Washing of non-disposable clothing contaminated with HD residue should only be done according to facility policy as drug residue may be transferred to other clothing. Potentially contaminated clothing **MUST NOT BE TAKEN HOME** under any circumstances."

Cleaning Step	Purpose	Agents	Comments

Deactivating	• Render compound inert or inactive	• EPA-registered oxidizing agents
		  • Sodium hypochlorite ~2% (household bleach b/w 3-5%)
		  • Peroxide formulations
			• There is no one proven method for deactivating
			• Beware of surface compatibility. Untreated bleach will corrode stainless steel surfaces
			  • neutralize bleach w sodium thiosulfate or by following w agent to remove sodium thiosulfate

Decontamination	• Remove HD residue (once its deactivated in step above) from non-disposable surfaces and transfer to absorbent disposable materials	• Includes alcohol, water, peroxide, or sodium hypochlorite	• Do not spray HD containers directly
			  • spraying aerosolizes the HD
			  • Instead, apply agent to disposable wipe and wipe containers down

Cleaning	• Remove organic and inorganic material	• water • detergents (properly diluted and germicidal) • surfactants • solvents/other	• Cleaning agents used on compounding equipment should not introduce microbial contamination. • No cleaning may be performed when compounding activities are occuring
Disinfecting	• Destroy microorganisms	• EPA registered sterile disinfectant • sterile isopropyl alcohol	• Before disinfection can begin, surfaces must be cleaned according to 3 steps above

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Detergents and Cleaning: Any Ideas??? Who has found a detergent?

2% bleach can be used, but must be neutralized to avoid damage to equipment.

FOOD FOR THOUGHT:

Will new regulations affect public perception of your pharmacy?

- X **Different answers from different pharmacies**
- X **Contradicting what we've always said about BUDs**
- X **Limiting patient care**
- X **Increase in prices**

THANK YOU!

Please contact me for further information

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