USP 797 REVISIONS

Top Things to Know

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On November 1, 2022, the United States Pharmacopeia (USP) published revisions to General Chapter 797, *Pharmaceutical Compounding — Sterile Preparations* (CSPs), which becomes official on November 1, 2023. This also changes the status of USP 800, which addresses hazardous drugs, to "compendially applicable" or having the ability to be enforced. Following are key considerations from the revisions to USP 797 that pertain to health systems.

1. IMMEDIATE-USE CSPs

Many CSPs will be prepared under the new Category 1, 2 or 3 system put forth by the revisions to USP 797. However, immediate-use CSPs continue to be an option provided all of the criteria from the revisions to 797 are met. Here are a few of these criteria which deserve specific attention.

- Personnel who prepare immediate-use CSPs are trained and demonstrate competency in aseptic processes as they relate to assigned tasks and the facility's SOPs. This will include personnel beyond the pharmacy.
- The preparation involves not more than 3 different sterile products. "Products" is the key term here as opposed to the number of containers. As explained in greater detail in the USP 797 FAQ, an immediate-use preparation can contain more than 3 containers in total as long as there are only 3 products being used.
- Administration begins within 4 hours following the start of preparation. Note that this is a departure from the 1-hour BUD in the current 797.
- Can you make all CSPs immediate use so the pharmacy doesn't have to do them? No.

2. CSP CATEGORIES

Category 1 CSPs are compounded in an unclassified segregated compounding area under the least controlled environmental conditions and assigned a BUD of 12 hours or less at controlled room temperature or 24 hours or less when refrigerated (see USP 797 revisions for additional requirements). Category 2 CSPs require more environmental controls in a cleanroom suite and may be assigned a BUD of greater than 12 hours at controlled room temperature or more than 24 hours if refrigerated. Category 2 CSP formulations may not exceed BUD limits established in Table 13 of 797 revisions (see next page).

Table 13. BUD Limits for Category 2 CSPs

PREPARATION	STORAGE CONDITIONS			
Compounding Method	**Sterility Testing Performed & 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): 4 days	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 3 CSPs have a number of additional requirements. For example, Category 3 CSPs must be supported by a stability-indicating assay validated using USP 1225, Validation of Compendial Procedures. The sterile preparation must follow the same ingredients and procedures as the stability assay, as well as packaged using the exact container-closure system and made of the same materials used in the study.

Category 3 CSPs, such as injectables or ophthalmic solutions, must pass the appropriate particulate matter test once for each formulation. Injections must pass particulate testing according to USP 788, Particulate Matter in Injections, while ophthalmic solutions must pass particulate testing according to USP 789, Particulate Matter in Ophthalmic Solutions. Additionally, the container-closure systems used for injections and ophthalmic solutions must pass testing according to USP 1207, Package Integrity Evaluation — Sterile Products, for each formulation. Both Category 2 and Category 3 multidose CSPs must pass antimicrobial effectiveness testing in accordance with USP 51.

3. ENDOTOXIN TESTING

Category 1 sterile preparations do not require endotoxin testing. Category 2 sterile injectable preparations compounded from one or more nonsterile components and assigned a BUD that requires sterility testing must be tested for endotoxin content in accordance with USP 85, Bacterial Endotoxins. If a Category 2 sterile preparation is compounded from one or more nonsterile components but is assigned a BUD that does not require sterility testing, endotoxin testing is not required; however, endotoxin testing is suggested. Category 3 sterile injectable preparations compounded from one or more nonsterile component(s) must be tested for endotoxin content.

4. GARBING PRACTICES

The minimum garbing requirements for Category 1 and 2 CSPs in the USP 797 revisions are listed below:

- Low-lint garment with sleeves that fit snugly around the wrists and an enclosed neck (e.g., gown or coverall)
- Low-lint covers for shoes
- Low-lint cover for head that covers the hair and ears, and if applicable, cover for facial hair
- Low-lint face mask
- Sterile, powder-free gloves
- If using a restricted access barrier system (RABS) (i.e., a compounding aseptic isolator (CAI) or compounding aseptic containment isolator (CACI), disposable gloves should be worn inside the gloves attached to the RABS sleeves. Sterile gloves must be worn over the gloves attached to the RABS sleeve.

Health systems should also be aware that the FDA has expressed in numerous 483 observations of compounding facilities preparing CSPs a desire for any gowning component that enters the ISO 5 area to be sterile.[1,2] This is generally mentioned in their Insanitary Conditions Guidance Document as well.

Anyone entering a buffer room where Category 3 CSPs are prepared must follow stricter garbing practices than Categories 1 or 2:

- Compounders are not allowed any exposed skin in the buffer room (e.g., face and neck must be covered).
- All low-lint outer garb must be sterile, including the use of sterile sleeves over gauntlet sleeves when a RABS is used.
- Once a compounder leaves a classified area, disposable garbing items must be discarded and laundered; garb must not be reused without being laundered and re-sterilized with a validated cycle.
- The facility's SOPs must describe disinfection procedures for reusing goggles, respirators and other reusable equipment.

5. ENVIRONMENTAL MONITORING

Personnel compounding Category 1 or 2 sterile preparations are required to perform media fills with glove fingertip sampling and surface sampling of the direct compounding area at least every six months, and those electing for Category 3 CSPs are required to perform media fills every 3 months.

Viable air sampling for classified areas used for either Category 1 or 2 CSPs must be performed with an impaction device at least every six months. For those electing to pursue Category 3 CSPs, the frequency of viable air sampling will be at least monthly and must start at least 30 days prior to Category 3 CSPs being prepared.

Surface sampling of classified areas is required for Category 1 or Category 2 preparations at least monthly. For Category 3 sterile preparations, surface sampling is performed at least weekly and must be performed in the ISO 5 with each batch of a Category 3 CSP unless using a self-enclosed robotic device. Surface sampling must be done in all classified areas and pass-throughs. The sampling must include:

- Each classified area, including each room
- The interior of each ISO Class 5 primary engineering control (PEC)
- Pass-through chambers connecting to classified areas
- Equipment contained within the PEC
- Staging or work area(s) near the PEC
- Frequently touched surfaces

Pharmacies must also conduct viable air sampling and surface sampling:

- When new facilities and equipment are certified
- After servicing any facility or equipment (see Section 4, Facilities and Engineering Controls)
- After identifying any problem (e.g., microbial growth in preparation sterility tests)
- After identifying any problematic trends (e.g., failed fingertip/thumb sampling results, failed media-fill testing, or repeated air or surface contamination)
- Any changes are made to the facility or processes that could impact the compounding environment (e.g., change in cleaning agents)

Pharmacies must also conduct total airborne particle-count testing in all classified areas during dynamic operating conditions at least every six months for all categories of sterile preparations.

With the volume of environmental monitoring being done for at least Category 2 CSPs, health systems will need to determine if they have the capacity or are willing to invest in the capacity to incubate the number of samples taken at the different temperatures required. Another option will be to contract with a third-party lab company who can appropriately incubate the samples, count the colonies grown, and if desired or required, identify the microorganisms grown.

6. CLEANING AND SANITIZING

Cleaning and sanitizing procedures also changed in Chapter 797 revisions. Pharmacies must clean surfaces prior to disinfecting them unless they use EPA-registered one-step disinfectant cleaners that simultaneously clean and disinfect with an appropriate contact time specified by the product.

In a PEC, after cleaning and disinfecting, pharmacies must apply sterile 70% isopropyl alcohol (IPA) to remove any residues of the product(s). Sterile 70% IPA must also be applied immediately before initiating compounding.

Another significant difference exists in the frequency of sporicidal application between Categories 1 and 2 and Category 3 preparations. When pharmacies create Category 3 preparations, they must apply a sporicidal agent to the PEC, including the removable work tray (if applicable), the equipment and work surfaces outside the PEC (pass-throughs and floors) at least weekly. Compounding Categories 1 and 2 preparations require monthly application of a sporicidal agent to all areas.

Along with these changes, the process for cleaning and disinfecting the PEC received more detailed directions. Compounders must:

- If necessary, remove visible particles, debris or residue with an appropriate solution (e.g., Sterile Water for Injection or Sterile Water for Irrigation) using sterile, low-lint wipers.
- Use a sterile low-lint wiper, apply a sterile cleaning agent followed by a sterile EPA-registered disinfectant, or apply a sterile EPA-registered (or equivalent for entities outside the U.S.) one-step disinfectant cleaner to equipment and all PEC interior surfaces.
- Ensure the contact time specified by the manufacturer is achieved.
- Using a sterile low-lint wiper, apply sterile 70% IPA to equipment and all PEC interior surfaces.
- Allow the surface to dry completely before beginning compounding.

PCCA Resources

PCCA offers additional resources to **health system clients that drive compounding success and mitigate risk to patients**, including:

- Live, in-person training for nonsterile, sterile, hazardous and nonhazardous compounding in our state-of-the-art training facility and lab at PCCA's world headquarters in Houston, Texas.
- Customized training to meet your pharmacy's specific compounding needs at your facility, PCCA headquarters or virtually.

Clients with a service agreement have access to our entire formulation database, extended beyond-use date stability data and our Clinical Services team. This team of 20+ clinical compounding pharmacists functions like a drug information center specifically for compounding, helping your team solve their clinical, technical and regulatory questions.

USP Resources

USP offers a number of tools, including:

USP 797 FAQs

USP 7957 Commentary

USP 797 Open Forum Presentation presented and recorded on November 8, 2022

USP 797 Open Forum Slides presented on November 8, 2022

References

[1] **https://www.fda.gov/media/99696/download** *Accessed 07/19/2023*

[2] **https://www.fda.gov/media/104861/download** *Accessed 07/19/2023*

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