WHAT HAPPENS NOW? A REVIEW OF USP CHAPTER <797> REVISIONS

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Topic Overview

The wait is finally over, and revisions to USP General Chapter <797> Pharmaceutical Compounding – Sterile Preparations have been released. This chapter was first published in 2008 by the United States Pharmacopeial Convention as a result of and response to patient harm and death that resulted from compounded sterile preparations (CSPs). Years later, a process of revisions, appeals, and a public comment period resulted in the 2022 updates. These revisions are the culmination of scientific and clinical practice advancements and stakeholder input. This course will review pertinent sections of the revised guidelines and provide guidance for personnel involved with sterile compounding.

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How to Earn Credit: From December 17, 2022, through December 17, 2025, participants must:

1) Read the "learning objectives" and "author and planning team disclosures;"
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3) Complete the Course Test and Evaluation form. The Course Test will be graded automatically. Following successful completion of the Course Test with a score of 70% or higher, a statement of participation will be made available immediately. (No partial credit will be given.)

Learning Objectives: Upon completion of this educational activity, participants should be able to:

1. **Recall** training and evaluation requirements for compounding personnel
2. **Assign** beyond-use dates to compounded sterile preparations (CSPs)
3. **Identify** components of Master Formulation and Compounding Records
4. **Recall** sterility testing and endotoxin requirements

Disclosures

The following individuals were involved in the development of this activity: Liz Fredrickson, PharmD, BCPS, and Susan DePasquale, MSN, PMHNP-BC. There are no financial relationships relevant to this activity to report or disclose by any of the individuals involved in the development of this activity.

Introduction

The new guidelines for the United States Pharmacopeia, General Chapter <797> were released on November 1, 2022. Institutions must now prepare for implementation of these new guidelines, looking to their state boards of pharmacy to understand how to comply with Chapter <797>. Compounding personnel now need to be educated on the changes as well. This course will review pertinent sections of the revised <797> guidelines and provide guidance for individuals involved in sterile compounding.

Where We've Been with USP <797>

United States Pharmacopeia, General Chapter <797>, titled Pharmaceutical Compounding – Sterile Preparations, was first published in 2008 by the United States Pharmacopeial Convention.[1] The purpose of the chapter was to set standards for the safe practice of sterile compounding.[1] In part, this chapter was a result of and response to patient harm and death that resulted from compounded sterile preparations (CSPs).[1] Three years following its publication, a survey found many institutions were unable to comply as a result of financial limitations.[2]

Since that time, the chapter has undergone a process of revisions, appeals, and public comment. Chapter revisions were originally planned for June 2019, but by September 2019, the publication was postponed.[3] In March 2020, a panel issued decisions on appeals to USP <797>, and in September 2020, an open forum for beyond-use dating provisions was held.[3] In September 2021, the revised guidelines were published for review, with a comment period held open until March 2022.[3]

The new guidelines were finally released on November 1, 2022.[3] These revisions are the culmination of scientific and clinical practice advancements and stakeholder input. During the public comment period, USP received more than 1,400 public comments from stakeholders.[4] Compounding personnel may find the <797> commentary provided by USP to be useful as it reviews the

changes to the guidelines. This document includes public comments and the Expert Committee's response on whether to incorporate those comments.[5]

List of Useful Acronyms

- **CAI** = compounding aseptic isolator
- **CACI** = compounding aseptic containment isolator
- **CR** = compounding record
- **CSP** = compounded sterile preparation
- **MFR** = master formulation record
- **RABS** = restricted access barrier system
- **SOP** = standard operating procedure
- **USP** = United States Pharmacopeia
- **USPC** = United States Pharmacopeial Convention

Compounded Sterile Preparations Categories

Previously, CSPs were categorized by risk level of low, medium, or high, which were assigned based on specified criteria and conditions for each level.[4] Compounding personnel should now be familiar with three categories of CSPs: Category 1, Category 2, and Category 3.[6] These categories differ based on three factors:[6]

1. The **environment** in which they are compounded
2. The **probability** for **microbial growth** during the time they will be stored
3. The **time** within which they must be used

Category 1 CSPs are compounded under the least controlled environmental conditions and thus have the shortest beyond-use dates of the three categories.[6] Category 2 CSPs have stricter environmental controls and testing requirements and may be assigned longer beyond-use dates than Category 1 CSPs. Category 3 is the newest category.[6] These CSPs undergo sterility testing and endotoxin testing when applicable.[6] Compared to Category

1 and 2 CSPs, they have more requirements for personnel qualifications, garbing, sporicidal disinfectants, environmental monitoring, and stability determination.[6] When applicable requirements are met, Category 3 CSPs are assigned the longest beyond-use dates of the three categories.[6] Table 1 provides a comparison of the three CSP categories.[6]

Table 1. Comparison of CSP Categories

Category	Criteria	Beyond-use date (BUD)
Category 1	• Must be prepared in an ISO Class 5 or better primary engineering control (PEC) that can be in an unclassified segregated compounding area (SCA)	• Have shortest BUDs
Category 2	• Must be made in a cleanroom suite	• BUD assigned based on risk elements (compounding method, sterility testing, & starting ingredients) • Longer BUDs than Category 1
Category 3	• Undergo sterility testing, supplemented by endotoxin testing when applicable • More requirements than Category 2 CSPs	• BUD assigned based on compounding method and storage conditions • Longest BUDs (up to a maximum of 180 days)

Immediate-use CSPs

Immediate-use CSPs are intended to be directly and immediately administered to a patient.[6] Category 1, 2, and 3 CSPs requirements are not applicable when the following criteria are met:[6]

1. Aseptic techniques, processes, and procedures are followed
2. Written standard operating procedures (SOPs) are in place to minimize contamination and mix-ups with other CSPs
3. Personnel are trained and demonstrate competency in aseptic processes
4. The preparation is compounded using evidence-based information for the physical and chemical compatibility of the drugs
5. No more than **3** different sterile products are used
6. Unused starting components from a single-dose container are discarded after the preparation is complete
7. Single-dose containers are not used for more than one patient
8. Administration begins within **4 hours** following the start of preparation
9. If the administration of the drug or product has not begun within **4 hours** following the start of preparation, it is promptly discarded.
10. The CSP is labeled with the names and amounts of all active ingredients and the name or initials of the compounding pharmacist unless it is directly administered by the person who prepared it or administration is witnessed by the preparer, the CSP

There are notable differences from the previous version of the chapter. Previously, administration of an immediate-use CSP had to begin within one hour following the start of the preparation. Additionally, it is important to note personnel who prepare these types of CSPs now need to demonstrate competency.[7]

Preparation Per Approved Labeling

The newest guidelines state compounding does not include mixing, reconstituting, or performing similar acts *via manufacturer directions*.[6] This information may help in reducing sterile compounding workload for facilities.[7] When a conventionally manufactured sterile product is prepared via manufacturer directions, it is out of the scope of the chapter if: [6]

1. The product is prepared as a single dose for an individual patient, *and*
2. The approved labeling includes information for the diluent, the resultant strength, the container closure system, and storage time

Establishing Beyond-Use Dates

The process of assigning beyond-use dates was significantly revised within the guidelines.[4,6] The USP Compounding Expert Committee utilized the previously published chapter and stakeholder input to revise the BUD limits.[4] Due to the challenge of predicting stability and sterility concerns for all sterile products, these limits were created using a risk-based approach.[4]
Longer BUD limits are permitted in certain specific circumstances based on additional requirements.[4] Tables 2, 3, and 4 detail the BUD limits for Category 1, Category 2, and Category 3 CSPs, respectively.[6]

Table 2. BUD Limits for Category 1 CSPs

Storage Condition	**Controlled Room Temperature (20-25°C)**	**Refrigerator (2-8° C)**
BUD	≤12 hours	≤24 hours

Table 3. BUD Limits for Category 2 CSPs

Preparation Characteristics		**Storage Conditions**		
Compounding Method	**Sterility Testing Performed and Passed**	**Controlled Room Temperature (20 to 25 °C)**	**Refrigerator (2-8 °C)**	**Freezer (-25 to -10 °C)**
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	Prepared from	Prepared from

		starting components: 4 days	only sterile starting components: 10 days	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

Table 4. BUD Limits for Category 3 CSPs

Compounding Method	**Controlled Room Temperature (20-25°C)**	**Refrigerator (2-8°C)**	**Freezer (-25 to -10°C)**
Aseptically processed, sterility tested, and passing all applicable tests for Category 3 CSPs	60 days	90 days	120 days
Terminally sterilized, sterility tested, and passing all applicable tests for Category 3 CSPs	90 days	120 days	180 days

Use of Conventionally Manufactured Products as Components

There have been updates regarding the use of conventionally manufactured products as components within CSPs.[6] These changes are compared to the previous guidelines in Table 5 below.[6]

Table 5. Other Beyond Use Dates

Type	Previous Guidelines	Current Guidelines
Single Dose Vials	• **6** hours if opened in an ISO 5 or cleaner air	• **12** hours if opened or punctured in ISO 5 or cleaner air
Multiple Dose Vials	• 28 days unless otherwise stated by the manufacturer	• 28 days unless otherwise stated by the manufacturer
Read-to-use products	• Per manufacturer instructions	• Per manufacturer instructions
Ampules	• Do not store for any amount of time	• Do not store for any amount of time

Sterility Testing

Sterility testing requirements vary depending on the CSP category.[6] Category 1 CSPs do not require sterility testing. Some Category 2 CSPs may be assigned a BUD that requires sterility testing.[6] All Category 3 CSPs require that testing be performed according to <71> or a validated alternative method that is not inferior to <71>.[6,8] For CSPs that undergo sterility testing, USP <71> specifies the minimum quantity of each container to be tested.[6] The maximum batch size for all CSPs requiring sterility testing is limited to 250 final yield units.

If the number of CSPs compounded in a single batch is less than the number of CSPs needed for testing as specified in Table 3 within USP <71>, additional units must be compounded as noted below:

- **If 1–39 CSPs are compounded in a single batch**: sterility testing must be performed on a number of units equal to 10% of the number of CSPs prepared, rounded up to the next whole number.[6]

- **If 39 CSPs are compounded:** 10% of 39 rounded up to the next whole number would indicate that 4 additional CSPs must be prepared for sterility testing[6]

Endotoxins Testing

Requirements for endotoxins testing also depend on the category of CSPs.[6] Category 1 CSPs do not require testing for bacterial endotoxins.[6] Category 2 CSPs compounded from one or more nonsterile component(s) should be tested for bacterial endotoxins.[6] Category 3 CSPs compounded from one or more nonsterile component(s) also must undergo this testing to ensure that they do not contain excessive bacterial endotoxins.[6]

If an official USP–NF monograph or other CSP formula source does not specify an endotoxin limit, the CSP must not exceed the endotoxin limit calculated as described in Chapter <1085> for the appropriate route of administration for humans.[6,9]

Personnel Training and Evaluation

The concept of the designated person is new within the chapter.[6,10] This individual (or individuals) is responsible for ensuring personnel who enter the sterile compounding area can maintain its environmental quality. Their responsibilities include overseeing daily operations to make sure the facility is USP <797> compliant.[6,10]

The guidelines also include important information regarding compounding personnel.[6,10] Notably, training and evaluation are not limited to individuals who directly compound CSPs.[6,10] Per the guidelines, any personnel involved with compounding CSPs, handling CSPs, or accessing the compounding area must demonstrate competency to maintain the environmental quality and CSP safety.[6] The following individuals must be trained and qualified:

- Compounders

- Personnel who have direct oversight of compounders
- Personnel who perform restocking or cleaning and disinfection duties

The designated person may choose to train personnel themselves or they can assign a trainer. The frequency of training for individuals who compound CSPs differs from those who do not directly compound, and facilities should note these differences in training records and standard operating procedures (SOPs) to make this distinction clear. Personnel who compound or oversee direct compounding must be trained initially and then every 12 months, while those who perform restocking or cleaning duties should complete training as noted within the facility's SOP.[6]

Personnel who directly compound or have oversight of compounding must demonstrate competency in the following areas:[6]

- Hand hygiene and garbing
- Cleaning and disinfection
- Calculations, measuring, and mixing
- Aseptic technique
- Achieving and/or maintaining sterility
- Use of equipment
- Documentation of the compounding process
- Principles of high-efficiency particulate air (HEPA)-filtered unidirectional airflow within the ISO Class 5 area
- Proper use of PECs
- Principles of movement of materials and personnel within the compounding area

Competency in Garbing and Hand Hygiene

Before compounding a Category 1, Category 2, or Category 3 CSP, personnel must complete an initial garbing competency evaluation no fewer three times in a row.[6,10] Prior to each evaluation, personnel should perform a complete hand hygiene and full garb procedure.

United States Pharmacopeia, Chapter <797> provides the gloved fingertip and thumb sampling procedure as described below.[6] To ensure proper pressure is applied during the gloved finger-tip test, experts recommend holding the plate vertically.[6,7]

1. Use one sampling media device (*e.g.*, plates, paddles, or slides) per hand, containing general microbial growth agar (*e.g.*, trypticase soy agar [TSA]) supplemented with neutralizing additives (*e.g.*, lecithin and polysorbate 80) as this agar supports both bacterial and fungal growth.
2. Label each media device with a personnel identifier, right or left hand, and the date and time of sampling.
3. Do not apply sterile 70% isopropyl alcohol (IPA) to gloves immediately before touching the media device because this could cause a false-negative result.
4. Using a separate media device for each hand, collect samples from all gloved fingertips and thumbs from both hands by rolling fingertip pads and thumb pad over the agar surface.
5. Incubate the media device at 30°–35° for no less than 48 hours and then at 20°–25° for no less than 5 additional days. Samples must be incubated in an incubator.
6. Handle and store media devices to avoid contamination and prevent condensate from dropping onto the agar during incubation and affecting the accuracy of the cfu reading (*e.g.*, invert plates).
7. Record the number of cfu per hand (left hand, right hand).
8. Determine whether the cfu action level is exceeded by counting the total number of cfu from both hands

Failure is noted either via visual observation or exceeding action levels of the gloved fingertip and thumb sampling (Table 6).[6] Personnel who fail any of the three evaluations must undergo repeat testing until they can pass three in a row.[6] After initial evaluation, personnel must demonstrate competency at least once every 6 months for Category 1 and Category 2 CSPs and at least once every 3 months for Category 3 CSPs. Designated persons should consider implementing thorough training of personnel prior to competency evaluation to help ensure success.

Competency in Aseptic Technique

In addition to demonstrating competency in garbing, personnel must also complete an aseptic manipulation competency evaluation. This consists of the following:

- Visual observation
- Media-fill testing
- Gloved fingertip and thumb sampling on both hands
- Surface sampling of the direct compounding area.[6]

This evaluation should be done initially and at least once every 6 months for those compounding Category 1 and Category 2 CSPs and at least once every 3 months for those who prepare Category 3 CSPs.[6]

United States Pharmacopeia, Chapter <797> provides the media-fill testing procedure as follows:[6]

1. If all the starting components are sterile, to begin with, manipulate them in a manner that simulates sterile-to-sterile compounding activities, and transfer the sterile soybean–casein digest media into the same types of container closure systems commonly used at the facility. Do not further dilute the media unless specified by the manufacturer.
2. If some of the starting components are nonsterile, to begin with, dissolve a commercially available nonsterile soybean–casein digest powder in nonbacteriostatic water to make a 3% nonsterile solution. Manipulate it in a manner that simulates nonsterile-to-sterile compounding activities. Prepare at least 1 container as the positive control to demonstrate growth promotion, which is indicated by visible turbidity upon incubation.
3. Once the compounding simulation is completed and the final containers are filled with the test media, perform a gloved fingertip and thumb sample on each hand and surface sample of the direct compounding area inside the PEC. Take the samples prior to disinfecting gloves and PEC. Handle and store samples to avoid contamination and prevent

condensate from dropping onto the agar during incubation and affecting the accuracy of the cfu reading (*e.g.*, invert containers).

4. Incubate the final containers at 20°–25° and 30°–35° for a minimum of 7 days at each temperature band to detect a broad spectrum of microorganisms. The order of the incubation temperatures must be described in the facility's SOPs. Final containers must be incubated in an incubator.
5. Failure is indicated by visible turbidity or other visual manifestations of growth in the media in one or more container closure unit(s) on or before 14 days

Failure is indicated by visible turbidity or visual manifestations in the growth media. Gloved fingertip and thumb sampling failure is noted by more than 3 cfu from both hands (Table 6).[6]

Table 6. Action Levels for Gloved Fingertip and Thumb Sampling

Gloved Fingertip and Thumb Sampling	Action Level (cfu total from both hands)
After garbing	>0
After media-fill testing	>3

Tables 7 and 8 are provided within USP <797> and offer useful information related to the requirements for personnel involved with sterile compounding.[6] These beneficial tables can be included within an institution's SOP and designated persons can modify them to include the specific requirements of their facility.

Table 7. Initial Training and Competency

		Required <797> and Supplemented by Facility SOP			
Personnel Function	**Defined by Facility SOPs**	**Training and Competency in Maintaining the Quality of Sterile Compounding Environment**	**Training and Competency in Sterile Compounding Principles and Practices**	**Garbing Competency (Including GFT)**	**Media Fill and Post-GFT and Surface Sampling**

Compounder		X	X	X	X
Designated person and personnel with direct oversight of compounding personnel		X	X	X	X
Personnel who restock or clean and disinfect the sterile compounding area	x				
Personnel who perform in-process checks or final verification of CSPs	x				
Personnel who only compound immediate-use CSPs	x				
Others (*e.g.*, maintenance personnel, certifiers, contractors, inspectors, surveyors)	x				

Table 8. Ongoing Training and Competency

		Required <797> and Supplemented by Facility SOPs		
Personnel Function	**Defined by Facility SOPs**	**Training and Competency in Sterile Compounding Principles and Practices**	**Garbing Competency (including GFT)**	**Media fill with post-GFT and surface sampling**
Compounder		At least every 12 months	Category 1 and 2 at least every 6 months	Category 1 and 2 at least every 6 months Category 3 at least every 3 months

			Category 3 at least every 3 months	
Designated person and personnel with direct oversight of compounding personnel		At least every 12 months	At least every 12 months	At least every 12 months
Personnel who restock or clean and disinfect the sterile compounding area	x			
Personnel who perform in-process checks or final verification of CSPs	x			
Personnel who only compound immediate-use CSPs	x			
Others (*e.g.*, maintenance personnel, certifiers, contractors, inspectors, surveyors)	x			

For facilities compounding Category 3 CSPs, it's important to note specific garbing requirements.[6,11] These are as follows:

- Compounders are not allowed any exposed skin in the buffer room
- All low-lint garb must be sterile
- 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

Facilities and Engineering Controls

Compounding Aseptic Isolators (CAI) and Compounding Aseptic Containment Isolators (CACI) are now referred to as Restricted Access Barrier Systems (RABS) within this section of the guidelines.[6,10] If Category 2 CSPs are being prepared, these systems must be located in a cleanroom suite.[6] Additionally, personnel should note that Category 1, Category 2, and Category 3 CSPs must be compounded in an ISO Class 5 or better primary engineering control (PEC).[6] If a facility only compounds Category 1 CSPs, the PEC may be placed in an unclassified SCA.[6] Table 9 summarizes the minimum requirements related to the placement of PECs when compounding nonhazardous CSPs.[6]

Table 9. Summary of Minimum Requirements for Placement of PECs for Compounding Non-HD CSPs

PEC Type	Device Type	Placement for Category 1 CSPs	Placement for Category 2 and 3 CSPs
LAFS	LAFW	Unclassified SCA	ISO Class 7 positive-pressure buffer room with an ISO Class 8 positive-pressure anteroom
	IVLFZ	N/A b	ISO Class 7 positive-pressure buffer room with an ISO Class 8 positive-pressure anteroom
	BSC	Unclassified SCA	ISO Class 7 positive-pressure buffer room with an ISO Class 8 positive-pressure anteroom

RABS	CAI or CACI	Unclassified SCA	SO Class 7 positive-pressure buffer room with an ISO Class 8 positive-pressure anteroom
Pharmaceutical isolator	Pharmaceutical isolator	Unclassified SCA	ISO Class 8 positive-pressure room

Certification and Recertification

United States Pharmacopeia, Chapter <797> states areas used for compounding must be independently certified. Recertification must be performed at least every 6 months.[6] Certification should meet the requirements of the chapter and manufacturer specifications where applicable. This includes:

- **Airflow testing:** performed to determine acceptability of the air velocity, the room air exchange rate, and the room pressure differential in doorways between adjacent rooms to ensure consistent airflow
- **HEPA filter integrity testing:** filters must be leak tested at the factory and then leak tested again after installation
- **Total particle count testing:** must be performed under dynamic operating conditions using calibrated electronic equipment
- **Dynamic airflow smoke pattern test:** performed for each PEC during dynamic operating conditions to demonstrate unidirectional airflow and sweeping action over and away from the preparation(s)

Cleaning, Disinfecting, and Applying Sporicidal Disinfectants and Sterile 70% IPA

This section includes requirements for cleaning and disinfecting. The minimum frequency for cleaning and disinfecting surfaces is described in Table 10 below. Experts recommended triple-cleaning all equipment before

introducing it into the sterile compounding area. This includes uses an EPA-registered one-step bacterial cleaner first and then using an EPA-registered one-step sporicidal cleaner twice.[7]

Table 10. Minimum Frequency for Cleaning and Disinfecting Surfaces and Applying Sporicidal Disinfectants in Classified Areas and in the SCA

Site	Cleaning	Disinfecting	Applying Sporicidal Disinfectant
PEC(s) and equipment inside the PEC(s)	Equipment and all interior surfaces of the PEC daily on days when compounding occurs and when surface contamination is known or suspected	Equipment and all interior surfaces of the PEC daily on days when compounding occurs and when surface contamination is known or suspected	• Monthly for entities compounding Category 1 and/or Category 2 CSPs • Weekly for entities compounding • Category 3 CSPs
Removable work tray of the PEC when applicable	• Work surface of the tray daily on days when compounding occurs • All surfaces and the area underneath the work tray monthly	• Work surface of the tray on days when compounding occurs • All surfaces and the area underneath the work tray monthly	• Monthly for work surfaces of the tray • Monthly for all surfaces and the area underneath the work tray
Pass-through chamber	Daily on days when compounding occurs	Daily on days when compounding occurs	• Monthly for entities compounding

Work surfaces outside the PEC	Daily on days when compounding occurs	Daily on days when compounding occurs	• Category 1 and/or Category 2 CSPs • Weekly for entities compounding Category 3 CSPs
Floors	Daily on days when compounding occurs	Daily on days when compounding occurs	
Walls, doors, door frames Ceilings Storage shelves and bins Equipment outside the PEC	Monthly	Monthly	Monthly

Sterilization and Depyrogenation

The terms aseptic processing and terminal sterilization are better defined within the newest guidelines.[10] United States Pharmacopeia <797> states terminal sterilization includes compounding with sterile and/or nonsterile starting ingredient(s) and subsequent sterilization with a process intended to achieve a PNSU of 10−6[6] The PNSU is also called the sterility assurance level (SAL), and a PNSU of 10^{-6} is equivalent to a probability that 1 unit in a million is nonsterile.[6] Aseptic processing includes 1) compounding with only sterile starting ingredient(s) or 2) compounding with nonsterile ingredient(s) followed by sterilization by filtration.

Terminal sterilization is noted as the preferred method unless the specific CSP or container closure system cannot tolerate terminal sterilization.[6,7] Steam sterilization is not an option in cases where moisture, pressure, or the temperatures used would degrade the CSP, or if there is insufficient moisture to sterilize the CSP within the final, sealed, container

closure system.[6] Filtration may not be best for CSP preparations with suspended drug particles or emulsions with a significant droplet size.[6]

Records and Labeling

Master Formulation Records

The role of proper record keeping is highlighted within the revised guidelines. This involves the completion of two records: a master formulation records (MFR) and compounding records (CR).[6] An MFR is a detailed record of procedures that describes how to prepare the CSP. An MFR can be thought of like a recipe, and the intent is to ensure repeatable, accurate compounding every time the CSP is prepared. The guidelines state an MFR must be created for any CSP prepared from nonsterile ingredient(s) or for CSPs prepared for more than one patient. Required MFR components include the following:[6]

- Name, strength or activity, and dosage form of the CSP
- Identities and amounts of all ingredients and relevant characteristics of components if applicable
- Type and size of container closure system(s)
- Complete instructions for preparing the CSP, including equipment, supplies, a description of compounding steps, and special precautions
- Physical description of the final CSP
- Beyond-use date and storage requirements
- Reference source to support the stability of the CSP
- Quality control (QC) procedures
- Other information as needed to describe the compounding process and ensure repeatability

Compounding Records

A CR documents the compounding process of each CSP. A medication order or prescription can serve as the CR.[6] United States Pharmacopeia <797> requires a CR be created for all CSP categories.[6] Additionally, a CR must be created for immediate-use CSPs prepared for more than one patient.[6] The

MFR is the basis for preparing the CR. Designated persons could make a copy of the MFR that includes spaces for recording information needed to complete the CR.

Requirements for compounding records include the following:[6]

- Name, strength or activity, and dosage form of the CSP
- Date and time of preparation of the CSP
- Assigned internal identification number (could be a prescription or lot number)
- A method to identify individuals involved in the compounding process and those verifying the final CSP
- Name of each component
- Vendor, lot number, and expiration date for each component for CSPs prepared for more than one patient and for CSPs prepared from nonsterile ingredient(s)
- Weight or volume of each component
- Strength or activity of each component
- Total quantity compounded
- Final yield
- Assigned BUD and storage requirements
- Results of QC procedures
- MFR reference for the CSP (if applicable)
- Calculations (if applicable)

Labeling

Per USP <797>, all categories (Category 1, Category 2, and Category 3) of CSPs must be labeled with appropriate, legible identifying information. This assists with preventing errors during storage, dispensing, and use of these products.[6] The terms "labeling" and "label" differ in their meanings. *Labeling* refers to all labels and other written, printed, or graphic matter on the immediate container or on or inside any package or wrapper in which it is enclosed, except any outer shipping container.[6] *Label* refers to parts of the

labeling that is on the immediate container. More information regarding labeling can be found in USP <7> - Labeling.[6,12]

Labeling must comply with regulatory jurisdictions and should minimally contain the following on the immediate container of the CSP:[6]

- Assigned internal identification number (like a barcode or prescription number)
- Active ingredient(s) with amount(s), activity(ies), or concentration(s)
- Storage conditions if other than controlled room temperature
- BUD
- Dosage form
- Total amount or volume if it is not obvious from the container
- If it is a single-dose container, a statement stating such when space permits
- If it is a multiple-dose container, a statement stating such

The labeling on the CSP must display the following information, as applicable:[6]

- Route(s) of administration
- Special handling instructions
- Warning statements
- Compounding facility name and contact information if the CSP is to be sent outside of the facility or healthcare system in which it was compounded

SOPs and Documentation

Standard Operating Procedures

Facilities that prepare CSPs must develop SOPs for the compounding process and other support activities.[6] These should be prepared in a way that ensures consistency and repeatability and should be written in a user-friendly manner. It has been recommended that facilities utilize Chapter <797> as the

basis for SOP development and then customize it with additional quality elements.[7] SOPs must include the types of CSPs that are prepared.[6] Designated person(s) should ensure SOPs are appropriate and are implemented, and they must follow up to ensure corrective actions are taken if problems, deviations, failures, or errors are identified. If such problems are noted, these must be documented.[6]

Documentation

Documentation, whether written or electronic, is required for all facilities that prepare CSPs.[6] Documentation records must be legible and comply with USP <797>.[6] This documentation must minimally include the following:[6]

- Personnel training, competency assessments, and qualification records including corrective actions for any failures
- Certification reports, including corrective actions for any failures
- Environmental air and surface monitoring procedures and results
- Equipment records (*e.g.*, calibration, verification, and maintenance reports)
- Receipt of components
- SOPs, MFRs (if required), and CRs (if required)
- Release inspection and testing records
- Information related to complaints and adverse events including corrective actions taken
- Results of investigations and corrective actions

Importantly, all documentation must comply with all laws and regulations of the institution's applicable regulatory jurisdiction. Documents must be stored in a way to ensure they are not lost and will not deteriorate, and all documentation must be readily retrievable.[6]

Next Steps for Compounding Personnel

As institutions prepare for the implementation of these newest guidelines, they should highlight important revisions and changes.

Compounding personnel, in particular designated persons, should thoroughly read through the revised guidelines and take notes.[13] These guidelines can serve as an important basis for facility SOPs.[13] Boards of pharmacy may have more stringent requirements than those recommended by USP <797>.[13] An example of additional requirements may include obtaining a certain number of sterile compounding CEUs. This is true for states such as Massachusetts.[14] The deadline for enforcement of USP <797> is November 1, 2023, but state boards could implement an earlier deadline.[6] Importantly, any institution should refer to its state board(s) of pharmacy to ensure they are compliant with those specific regulations.

Summary

The revisions to USP General Chapter <797> Pharmaceutical Compounding – Sterile Preparations have been released. These revisions are the culmination of scientific and clinical practice advancements and stakeholder input. Previously, CSPs were categorized by risk level of low, medium, or high, which were assigned based on specified criteria and conditions for each level. Compounding personnel should now be familiar with three categories of CSPs: Category 1, Category 2, and Category 3. These categories differ based on the environment in which they are compounded, the probability for microbial growth during the time they will be stored, and the time within which they must be used. These guidelines can serve as an important basis for facility SOPs. Boards of pharmacy may have more stringent requirements than those recommended by USP <797>.

Course Test

1. **Individuals who directly compound sterile preparations must complete how many successive garbing competency evaluations prior to compounding CSPs?**

    a. 1
    b. 2
    c. 3
    d. 4

2. **How often should a garbing competency evaluation minimally be completed for individuals who compound Category 2 CSPs?**

    a. Initially and then every 3 months
    b. Initially and then every 6 months
    c. Initially and then every 12 months
    d. Initially and then every 2 years

3. **Which of the following is the action level for gloved fingertip and thumb sampling after media-fill testing?**

    a. 0
    b. >1
    c. >2
    d. >3

4. **Which of the following CSP Categories does not require sterility testing?**

    a. Category 1
    b. Category 2
    c. Category 3
    d. All categories require sterility testing

5. **Which of the following CSP categories may require endotoxin testing?**

    a. Category 1
    b. Category 2
    c. Category 3
    d. Category 2 and Category 3

6. Which of the following best defines a master formulation record?

a. A record of procedures describing how to prepare a CSP
b. A record that documents the process of compounding a CSP
c. A record containing a medication order or prescription for a CSP
d. A record that contains a method to identify individuals involved in compounding and verifying the final CSP

7. Which of the following is a required component of a master formulation record?

a. Date and time the CSP was prepared
b. Assigned internal identification number of the CSP
c. Beyond-use date
d. Total quantity compounded

8. Which of the following beyond-use dates would be assigned to a Category 1 CSP stored at controlled room temperature?

a. ≤ 6 hours
b. ≤ 12 hours
c. ≤ 24 hours
d. ≤ 48 hours

9. Which of the following beyond-use dates would be assigned to a Category 2 CSP that has been aseptically processed, did not pass sterility testing, is prepared from one or more nonsterile starting ingredients, and is stored in the refrigerator?

a. 1 day
b. 4 days
c. 45 days
d. 60 days

10. Of the three CSP categories, which includes the longest beyond-use dates?

a. Category 1
b. Category 2
c. Category 3
d. Categories 1 and 2

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