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USP <797>

KEY CHANGES

The following represents key changes from the currently enforceable version of USP Chapter <797> (last major revision in 2008) to the revised USP Chapter <797> (official as of November 1, 2023). The following are the major changes and are not meant to be an exhaustive list of the entirety of all changes made. Some changes will be reported as direct text excerpts from the respective chapter (notated by quotation marks), while others will be reported as a general comment describing the text or change. *Note: Bolding has been added to the text below for emphasis.*

Category	USP <797>, 2008[1]	USP <797>, 2023[2]
01. INTRODUCTION AND SCOPE		
"The use of technologies, techniques, materials, and procedures other than those described in this chapter … "	" … not prohibited so long as they have been proven to be equivalent or superior with statistical significance to those described herein."	" … not prohibited as long as they are **noninferior** to those described herein **and validated for the intended purpose" (e.g., USP <1223>, <1225>)**
Compounded sterile preparations (CSPs) affected	" … irrigations for wounds and body cavities … " " … aqueous bronchial and nasal inhalations … "	" … Irrigations for **internal** body cavities … [NOTE—irrigations for the mouth, rectal cavity, and sinus cavity **are not required to be sterile**.]" "Nasal dosage forms intended for local application are **not required to be sterile**."
Hazardous drugs	Covered within the chapter under section Hazardous Drugs as CSPs Allows preparation of a "low volume of hazardous drugs" outside of a negative pressure space as long as two tiers of containment are used (closed-system transfer device with containment primary engineering control)	Removed from chapter and references to follow USP <800> No longer allows preparation of a low volume of hazardous drugs outside of a negative pressure space.
Radiopharmaceuticals	Covered within the chapter under section Radiopharmaceuticals as CSPs	Removed from chapter and references to follow USP <825>
Personnel and settings affected	Largely refers to and addresses only compounding personnel	**"Any person entering a sterile compounding area**, *whether preparing a CSP or not*, must meet the requirements in **3. Personal Hygiene and Garbing."**
The designated person(s)	Not addressed	"The compounding facility must designate one or more individuals (i.e., **the designated person(s)) 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." A complete list of the designated person responsibilities has been provided as a separate resource.

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Administration	Standards do not pertain to the clinical administration of CSPs to patients (e.g., implantation, infusion, inhalation)	"For the purposes of this chapter, 'administration' means the direct application of a sterile product or preparation to a single patient by injecting, infusing, or otherwise providing a sterile product or preparation in its final form."
Immediate-use CSPs	"Administration begins not later than 1 hour following the start of the preparation … " Does not involve > 3 commercially manufactured packages of sterile nonhazardous products	"Administration begins **within 4 h following the start of preparation.**" "The preparation involves **not more than 3 different sterile products.**" "Personnel are trained and demonstrate competency in aseptic processes as they related to assigned tasks and the facility's SOPs."
Preparation per approved labeling	Strictly following the manufacturers' approved labeling (product package inserts) is considered a CSP and the requirements of the chapter apply	"**Compounding does not include** mixing, reconstituting, or other such acts that are **performed in accordance with directions contained in approved labeling or supplemental materials** provided by the product's manufacturer." "The product is prepared as a **single dose** for an **individual patient** … " "Approved labeling includes information for the diluent, the resultant strength, the container closure system, and storage time."
Proprietary bag and vial system	Does not mention BUDs other than following the manufacturer's instructions for handling and storing	Docking of the proprietary bag and vial system for **future activation** • This is **considered compounding** and must be performed in accordance with this chapter (ISO Class 5 environment) • BUDs must not be longer than the manufacturer's labeling
CSP microbial categories	CSP Categories • Low Risk • Low Risk with 12-h BUD • Medium Risk • High Risk Factors that determine CSP Category • Type of manipulation • Complexity and length of preparation • If any nonsterile ingredient, component, or equipment is used • Number of sterile products and packages • Number of transfers into any single container • Number of doses being prepared • Following proper garbing • Exposure to lower than ISO class 5 air and duration	CSP Categories • Category 1 • Category 2 • Category 3 Factors that determine CSP Category • Primarily based on environment/conditions of where the CSP is compounded • Level of garbing • Environmental testing and monitoring • Frequency of application of a sporicidal • Based on BUD assignment "Category 1, Category 2, and Category 3 CSPs can be compounded by using only sterile starting ingredients, or by using some or all nonsterile starting ingredients." One (or more) component is non-sterile: sterility of the compound must be achieved through a sterilization process (e.g., terminal sterilization) and must be maintained if it is subsequently manipulated

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02. PERSONNEL TRAINING AND EVALUATION		
Who needs to be trained and how often	"Personnel who prepare CSPs shall be trained … " How often: • Low- and medium-risk level: at least annually • High-risk level: semi-annually	Compounders and those who have direct oversight of compounders • Initially and at least every 6 or 12 months (depends on the individual) Personnel who do not compound nor have direct oversight of compounders, but are associated with other tasks **(e.g., restock or clean/disinfect the SCA, only compound immediate-use CSPs)**: • Defined by facility SOPs
Initial garbing competency evaluations	Compounders need to pass garbing competency evaluations before beginning to prepare CSPs	Garbing competency evaluations include: • Visual observation • Gloved fingertip and thumb sampling (GFT) of both hands Compounders and those who have direct oversight of compounders • " … must complete an initial garbing competency evaluation **no fewer than 3 separate times. The 3 successful completions must be in succession** … " Remediation of failed competency • " … failure of any of the 3 initial garbing competency evaluations r**equires repeat testing until personnel successfully completes 3 evaluations in a row.**"
Ongoing garbing competency evaluations	Visual observation of hand hygiene and garbing • At least annually Gloved fingertip and thumb sampling • Low/medium risk – at least annually • High-risk – at least semiannually	Compounders • Category 1 and 2: **at least every 6 months** • Category 3: **at least every 3 month**s Those who have direct oversight of compounders • At least every 12 months
Initial aseptic manipulation competency evaluations	Compounders need to pass media-fill testing of aseptic manipulation skills before beginning to prepare CSPs	Aseptic manipulation evaluations include: • Visual observation • Media-fill testing with post-GFT • Surface sampling Compounders and those who have direct oversight of compounders • Must complete 1 successful aseptic manipulation competency evaluation Remediation of failed competency • "A failure in the media fill, gloved fingertip and thumb sampling, or surface sample constitutes an overall failure of the aseptic manipulation competency."

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Ongoing aseptic manipulation competency evaluations	Each person authorized to compound in a low-risk or medium-risk level environment: At least annually Each person authorized to compound in a high-risk level environment: At least semiannually	Compounders Category 1 and 2: **at least every 6 months** Category 3: **at least every 3 months** Those who have direct oversight of compounders: At least every 12 months
Gloved fingertip and thumb sampling incubation standards	Incubate sample at 30-35 C for 2-3 days	"Incubate the media device at 30-35 C for no less than 48 h **and** then at 20-25 C for no less than 5 additional days."
Media-fill testing incubation standards	Incubate sample at 20-25 C or 30-35 C for 14 days	"Incubate the final containers at 20-25 C **and** 30-35 C for a minimum of 7 days at each temperature band … " "The order of the incubation temperatures must be described in the facility's SOPs"
Action levels for gloved fingertip and thumb sampling	0 cfu	After garbing: >0 cfu After media-fill testing: >3 cfu Action levels based on total cfu count **from both hands**
03. PERSONAL HYGIENE AND GARBING		
Order of handwashing and garbing	Gave a specific order for garbing and handwashing Sterile gloves could be donned in the buffer room	Order of handwashing and garbing is determined by the placement of the sink Order of garbing must be described by facility's SOPs "Donning and doffing garb should not occur in the same area at the same time" "Sterile gloves must be donned in a classified room or SCA"
Hand hygiene	Allows use of hand dryers Does not mention soap containers	Hand dryers **must not** be used Disposable soap containers **must not** be refilled or topped off – need to be replaced
Sanitizing hands	" … perform antiseptic hand cleansing with an alcohol-based surgical hand scrub with persistent activity."	Do not need an agent with persistent killing
Reusing garb	Allows gown to be reused if used on the same work day	Category 1 and Category 2 • " … gowns may be reused within the **same shift by the same person** if the gown is **maintained in a classified area or adjacent to, or within, the SCA in a manner that prevents contamination.**" • Other garb cannot be reused and should be discarded or laundered before reuse Category 3 • "Disposable garbing items **must not be reused**, and laundered garb **must not be reused without being laundered and resterilized with a validated cycle.**" • "The facility's SOPs must describe disinfection procedures for reusing goggles, respirators, and other reusable equipment."

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Garbing for category 3	Not applicable	"If the facility compounds Category 3 CSPs, **additional garbing requirements must be continuously met in the buffer room in which Category 3 CSPs are prepared."** • No exposed skin (I.e., face and neck must be covered) • All low-lint outer garb must be sterile • Disposable garb cannot be reused • Laundered garb cannot be reused until it is laundered and re-sterilized • Facility's SOPs describe disinfection procedures for reusing goggles, respirators, and other reusable equipment
04. FACILITIES AND ENGINEERING CONTROLS		
ISO classification of particulate matter	Particle count listed as m^3 and ft^3	Particle count is only listed as **m^3**
Use of isolators	PECs shall be located within a restricted access ISO Class 7 buffer area, with exceptions for CAI/CACI which would allow for BUD's equivalent to a full cleanroom suite in a segregated compounding area when certain conditions are met	The exception for CAI/CACI's has been removed; to obtain Category 2 CSP BUD's, the CAI/CACI must be placed in an ISO Class 7 buffer room located within a cleanroom suite Alternatively, a pharmaceutical isolator (different type of engineering control than a CAI/CACI) can be placed in an ISO Class 8 environment without the need for an anteroom
Air exchange requirements	Does not address ISO Class 8 ACPH requirements	ISO Class 8 room: >20 ACPH
Cleanroom	Not addressed	Term to describe ISO-classified anteroom and buffer room
Cleanroom suites: access doors and seals	Not addressed	Seals should not be installed at doors between buffer rooms and anterooms Access doors should be hands-free
Precision and accuracy of pressure differentials	Listed as 0.02 (two decimal places), broad	Listed as 0.020 (three decimal places), narrow
Humidity requirements	Does not mention humidity	"… should be maintained at … a relative humidity of 60% or below … "
05. CERTIFICATION AND RECERTIFICATION		
Certification of PEC and SEC	"Certification procedures such as those outlined in the CETA Certification Guide for Sterile Compounding Facilities shall be used."	All professional organizations have been removed: " … independently certified using the requirements in this chapter and when applicable, manufacturer specifications."
06. MICROBIOLOGICAL AIR AND SURFACE MONITORING		
Viable air sampling – timing and locations	At least every 6 months for all compounds	Category 1 and Category 2: • At least every 6 months Category 3 • Within 30 days before the start of any Category 3 compounding • At least monthly

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Viable air sampling – incubation standards	TSA: • 30-35 C for 48 to 72 h Fungal media: • 26-30 C for 5 to 7 days	Incubate at 30-35 C for no less than 48 h then incubate at 20-25 C for no less than 5 additional days **"To shorten overall incubation period, two sampling media devices may be collected for each sample location and incubated concurrently"** • Incubate one at 30-35 C for no less than 48 h and the other at 20-25 C for no less than 5 days
Surface sampling – timing and locations	"Surface sampling shall be performed in all ISO classified areas on a **periodic** basis"	Locations: • Equipment contained within the PEC • Staging or work area(s) near the PEC • Frequently touched surfaces Category 1 and 2 • At least monthly Category 3 • At least weekly • Prior to assigning a BUD longer than the limits established for Category 2 CSPs
Surface sampling – action levels	Action levels • ISO Class 5: >3 • ISO Class 7: >5 • ISO Class 8 or worse: >100	Action levels • ISO Class 5: >3 • ISO Class 7: >5 • ISO Class 8: **>50**
Identifying microorganisms and Corrective Actions	Identification of microorganisms (at least the genus level) is required regardless of cfu count Mention of **highly pathogenic microorganisms** (e.g., gram-negative rods, coagulase *Staphylococcus*, molds and yeasts) must be immediately remedied regardless of cfu count	If action levels specified for air and surface sampling are exceeded, **" … an attempt must be made to identify any microorganism recovered to the genus level … "** Does not mention highly pathogenic microorganisms "The extent of the investigation should be consistent with the deviation and should include an evaluation of trends" "Data collected in response to corrective actions must be reviewed to confirm that the actions taken have been effective." "The corrective action plan must be dependent on the cfu count and the microorganism recovered."
07. CLEANING, DISINFECTING, AND APPLYING SPORICIDAL DISINFECTANTS AND STERILE 70% IPA		
Minimum frequency for cleaning and disinfecting surfaces	Does not split up minimum frequency based on method (e.g., cleaning, disinfecting)	Minimum frequency for cleaning is broken down by cleaning, disinfecting, and applying sporicidal disinfectant

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Cleaning/disinfecting supplies	Does not specify the type of material	Cleaning and disinfecting supplies (e.g., wipers, sponges, pads, mop heads) • Must be low-lint • Should be disposable • Reusable cleaning tools must be dedicated for use and not be removed from classified areas or SCA and be made of cleanable materials (e.g., not wood or any other porous material) "Cleaning, disinfecting and sporicidal agents used within the PEC **must be sterile**." Sterile water must be used when diluting concentrated agents for use in the PEC.
08. INTRODUCING ITEMS INTO THE SEC AND PEC		
No major changes	--	--
09. EQUIPMENT, SUPPLIES, AND COMPONENTS		
No major changes	--	--
10. STERILIZATION AND DEPYROGENATION		
Biological indicators	Steam Heat – *Bacillus stearothermophilus* Dry Heat – *Bacillus subtilis*	Steam Heat – *Geobacillus stearothermophilus* Dry Heat – *Bacillus atrophaeus*
11. MASTER FORMULATION AND COMPOUNDING RECORDS		
Master formulation records (MFR)	Specific requirements not listed	• Must be created for all CSPs prepared for more than one patient or when using non-sterile components • Any changes or alterations must be approved and documented based on facility's SOPs • Requirements for MFR are listed out in section
Compounding records (CR)	Specific requirements not listed	• Must be created for all Category 1, Category 2, and Category 3 CSPs and for immediate-use CSPs when prepared for more than one patient • Requirements for CR are listed out in section
12. RELEASE INSPECTIONS AND TESTING		
Maximum batch size	Not addressed	"The maximum batch size for all CSPs **requiring sterility testing** must be limited to **250 final yield units.**"
Sterility testing	"A method not described in the *USP* may be used if verification results demonstrate that the alternative is at least as effective and reliable … "	Specifies a *USP* chapter "… or a **validated alternative method (see <1223>) that is noninferior to <71> testing."**
Number of CSPs needed to send for sterility testing	Does not specify number of CSPs needed to be sent for sterility testing	Number of CSPs sent for sterility testing depends on **number of CSPs to be compounded in a single batch** • 1-39 CSPs – must send 10% of the number of CSPs prepared, rounded up to the next whole number • >40 CSPs – must use sample sizes specified in *<71>*, Table 3

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Sterility testing requirements	Required for high-risk level CSPs under certain circumstances: • >25 identical individual single-dose packages • Multiple-dose vials for administration to multiple patients • Exposed longer than 12 h at 2-8 C and longer than 6 h at warmer than 8 C before they are sterilized	Category 1 – not required Category 2 – based on BUD Category 3 – required
13. LABELING		
Compounding notification on label	Not addressed	**"The labeling on the CSP should indicate that the preparation is compounded."**
14. ESTABLISHING BEYOND-USE DATES		
Establishing a BUD for a CSP	Factors that determine a BUD for risk categories • Storage conditions • Information gathered from professional sources (e.g., sterility studies)	Factors that determine Category 1 BUDs • Storage conditions (e.g., controlled room temperature, refrigerator) Factors that determine Category 2 BUDs • Compounding method (e.g., aseptic process, terminally sterilized) • If sterility testing is performed • Starting component of compound (e.g., sterile, nonsterile) • Storage conditions Additional requirements needed for longer BUDs in Category 3 CSPs for: • Increase use of sporicidal disinfectants • Increase of environmental monitoring • Use of sterile garb • Stability determination • Personnel qualification
Non-preserved topical ophthalmic CSPs	Not addressed	"The beyond-use-date of a multiple-dose, aqueous, non-preserved CSP intended for topical, including **topical ophthalmic**, administration may be **assigned in accordance with *14.5 Multiple-Dose CSPs.***" Requirement for passing antimicrobial effectiveness testing in accordance with <51> is not required only if the preparation is: • Prepared as a Category 2 or Category 3 CSP • For use by a single patient • Labeled to indicate that once opened, it must be discarded after 24 h stored at controlled room temp or 72 h stored under refrigeration

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15. USE OF CONVENTIONALLY MANUFACTURED PRODUCTS AS COMPONENTS		
Use of conventionally manufactured single-dose containers	"Single-dose vials exposed to ISO Class 5 or cleaner may be used up to **6 h** after initial needle puncture."	"If a single-dose vial is entered or punctured only in an ISO Class 5 or cleaner air, **it may be used up to 12 h after initial entry or puncture as long as the labeled storage requirements during that 12-h period are maintained**."
Use of conventionally manufactured pharmacy bulk package	Not addressed	"The pharmacy bulk package must be used according to the manufacturer's labeling (see *<659>, General Definitions, Injection Packaging Systems*). The pharmacy bulk package must be entered or punctured only in an ISO Class 5 PEC."
16. USE OF CSPS AS COMPONENTS		
Use of compounded multiple-dose CSPs	Not addressed	When used as a component to compound additional CSPs • Required to meet criteria for antimicrobial effectiveness testing and requirements in *14.5* • Must be stored in conditions the BUD is based (e.g., refrigerator) • After punctured, must not be used longer than assigned BUD or 28 days, whichever is shorter. Remainder must be discarded
Use of compounded single-dose CSPs and CSP stock solutions	Not addressed	When used as a component to compound additional CSPs • Must be entered or punctured in ISO Class 5 or cleaner air • Must be stored in conditions the BUD is based (e.g., refrigerator) • May be used for sterile compounding up to **12 h** or its assigned BUD, whichever is shorter. Remainder must be discarded
17. SOPS		
Who needs training based on facilities SOPs	Not addressed	"All personnel who perform or oversee compounding or support activities must be trained in the SOPs"
18. QUALITY ASSURANCE AND QUALITY CONTROL		
Notification and recall of CSPs with out-of-specification limits	Not addressed except for notifying the patient and physician of potential risk	SOP for recall of out-of-specification limits must contain procedures • To determine severity of problem and urgency for implementation and completion of the recall • To determine distribution of any affected CSP • To identify patients who received the CSP • For disposal and documentation of recalled CSP • To investigate and document reason for failure
Redispensed CSPs	Unopened, unused, returned CSPs may be redispensed when certain conditions are met to ensure the CSP is sterile, pure, and stable	Not specifically addressed; however does not prohibit this practice. Would need to refer to state board of pharmacy for guidance.
19. CSP HANDLING, STORAGE, PACKAGING, SHIPPING, AND TRANSPORT		
No major changes	--	--

Category	USP <797>, 2008[1]	USP <797>, 2023[2]
20. DOCUMENTATION		
No major changes	--	--
21. COMPOUNDING ALLERGENIC EXTRACTS		
Compounding allergenic extract prescription sets	No mention of training or competency evaluation needed for compounders making allergenic extracts	Requirements for personnel who prepare allergenic extracts • Training must be done initially prior to compounding independently and annually • Gloved fingertip and thumb sampling on both hands no fewer than 3 separate times needs to be done prior to compounding independently and at least every 12 months • Sterile technique of compounders needs to be evaluated at least every 12 months • Personnel that have not compounded in 6 months need to be evaluated in all core competencies before resuming their duties

References

1. United States Pharmacopeial Convention. General chapter <797> pharmaceutical compounding—nonsterile preparations. USP43-NF38. Rockville, MD: U.S. Pharmacopeial Convention; 2019.

2. United States Pharmacopeial Convention. General chapter <797> pharmaceutical compounding—sterile preparations. USP-NF 2023, Issue 1, November 1, 2022, official as of November 1, 2023.

Special acknowledgment to **Sarah Hall, PharmD (candidate)**, *UNC Eshelman School of Pharmacy, and* **Kevin Hansen, PharmD, MS, BCSCP**, *Director of Pharmacy, Compounding Services and Data Analytics, Cone Health, for the development of this resource, and to* **Patricia Kienle, RPh, MPA, BCSCP, FASHP**, *Director, Accreditation and Medication Safety, Cardinal Health, and* **Michael Ganio, PharmD, MS, BCSCP, FASHP**, *Senior Director, Pharmacy Practice and Quality, ASHP, for peer-review.*

Kevin and Patti are members of the USP Compounding Expert Committee, but this resource is not affiliated with or endorsed by USP.