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Tony Evers, Governor
Dan Hereth, Secretary

VIRTUAL/TELECONFERENCE
PHARMACY RULES COMMITTEE
of the
PHARMACY EXAMINING BOARD
Virtual, 4822 Madison Yards Way, Madison, WI
Contact: Brad Wojciechowski (608) 266-2112
June 15, 2023

Notice: The following agenda describes the issues that the Committee plans to consider at the meeting. At the time of the meeting, items may be removed from the agenda. ***A quorum of the Board may be present during any committee meetings.***

AGENDA

9:00 A.M.

OPEN SESSION – CALL TO ORDER

A. Approval of Agenda

B. Administrative Rule Matters – Discussion and Consideration

1) Phar 15, Relating to Compounding Pharmaceuticals **(Additional Materials)**
2) Pending or Possible Rulemaking Projects

C. Public Comments

ADJOURNMENT

NEXT MEETING: AUGUST 31, 2023

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MEETINGS AND HEARINGS ARE OPEN TO THE PUBLIC, AND MAY BE CANCELLED WITHOUT NOTICE.

Times listed for meeting items are approximate and depend on the length of discussion and voting. All meetings are held virtually unless otherwise indicated. In-person meetings are typically conducted at 4822 Madison Yards Way, Madison, Wisconsin, unless an alternative location is listed on the meeting notice. In order to confirm a meeting or to request a complete copy of the board's agenda, please visit the Department website at https:\\dsps.wi.gov. The board may also consider materials or items filed after the transmission of this notice. Times listed for the commencement of disciplinary hearings may be changed by the examiner for the convenience of the parties. Requests for interpreters for the hard of hearing, or other accommodations, are considered upon request by contacting the Affirmative Action Officer, or reach the Meeting Staff by calling 608-267-7213.

What's New with *USP* General Chapters ⟨795⟩ and ⟨797⟩?

Brenda Jensen, CPhT, CNMT, MBA

Brian Serumaga, PhD, M Pharm, MPH

May 11, 2023

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Financial Disclosures

- Our speaker Brian Serumaga declares that he does not have a relevant affiliation or financial arrangement with any ineligible companies that may have a direct interest in the subject matter of this continuing pharmacy education (CPE) activity within the past 24 months.
- Our speaker Brenda Jensen declares that she has a current affiliation or financial arrangement with an ineligible company as an owner of Compounding Consultants, LLC.
- Brian Serumaga is employed by USP, and Brenda Jensen is chair of the 2020-2025 Compounding Expert Committee.
- Additionally, NABP staff involved in the planning of this activity do not have an affiliation or financial arrangement with any ineligible companies that may have a direct interest in the subject matter of NABP's CPE program within the past 24 months.
- All relevant financial relationships have been mitigated.

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Learning Objectives

1. Describe the revisions to General Chapter ⟨795⟩ *Pharmaceutical Compounding—Nonsterile Preparations*, including updates to the beyond-use dates
2. Describe the revisions to General Chapter ⟨797⟩ *Pharmaceutical Compounding—Sterile Preparations*, including updates to the beyond-use dates
3. Explain the difference between requirements and recommendations in the *USP* General Chapters

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Assessment Questions

1. When do USP standards become official?

A. As soon as they are published in the *Pharmacopeial Forum*

B. Generally, six months after being published in the *Pharmacopeial Forum*

C. As soon as they are published in the *USP–NF*

D. Generally, six months after being published in the *USP–NF*

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Assessment Questions

2. The current official version of USP ⟨797⟩ was last revised in

A. 2008

B. 2015

C. 2019

D. 2022

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Assessment Questions

3. Category 1 compounded sterile preparations (CSPs) in USP ⟨797⟩ are restricted to

A. Sterile to sterile compounding only

B. CSPs that are assigned a BUD of no more than 6 hours when stored at room temperature

C. CSPs that are assigned a BUD of no more than 24 hours when stored under refrigeration

D. Non-hazardous CSPs only

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Assessment Questions

4. Which of the following standards are available for compounders in the Compounding Compendium?

A. General Chapter ⟨795⟩ *Pharmaceutical Compounding—Nonsterile Preparations*

B. General Chapter ⟨797⟩ *Pharmaceutical Compounding—Sterile Preparations*

C. USP Compounded Preparation Monographs

D. All of the above

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USP Overview

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2020 – 2025 Compounding Expert Committee

Chair: Brenda Jensen, MBA, Owner and Compounding Pharmacy Consultant, Compounding Consultants, LLC
Vice Chair: Vanessa Pinheiro, MS, BS Pharm, Pharmacist and Consultant, Medisca and LP3 Network

EC Member	Affiliation
Lisa Ashworth, BS Pharm	Compounding Specialist and Clinical Pharmacist, Children's Health System of Texas
Phil Ayers, PharmD	Chief, Clinical Pharmacy Services, Mississippi Baptist Medical Center
Gus Bassani, PharmD	Chief Scientific Officer, PCCA
Suzanne Blevins, BSc	Laboratory Director, Aerobiology Laboratory
Brett Cordes, DVM	Veterinarian, Private Practice
Gigi Davidson, BS Pharm	Veterinary Pharmacy Consultant, VetPharm Consulting, LLC
Edmund Elder, PhD, BS Pharm	Director, Zeeh Pharmaceutical Experiment Station, University of Wisconsin-Madison
Kevin Hansen, PharmD, MS	Assistant Director of Pharmacy, Cone Health
Patricia Kienle, MPA, BS Pharm	Director, Accreditation and Medication Safety, Cardinal Health
Elizabeth Rebello, MD, BS Pharm	Professor and Anesthesiologist, University of Texas MD Anderson Cancer Center
Rick Rhoads, PharmD	Director of Compounding, University Compounding Pharmacy
Robert Shrewsbury, PhD	Associate Professor, UNC Eshelman School of Pharmacy
Connie Sullivan, BS Pharm	President and CEO, National Home Infusion Association

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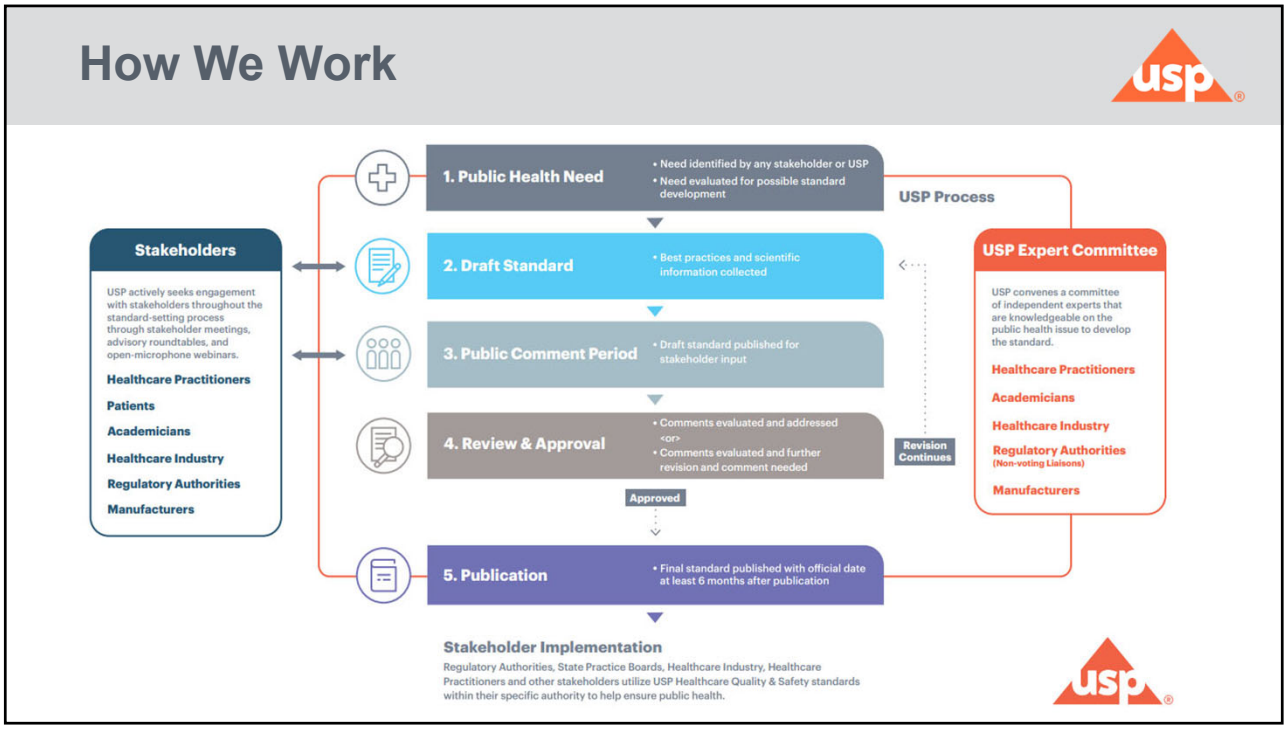
How We Work
Stakeholders
USP actively seeks engagement with stakeholders throughout the standard-setting process through stakeholder meetings, advisory roundtables, and open-microphone webinars.
Healthcare Practitioners
Patients
Academicians
Healthcare Industry
Regulatory Authorities
Manufacturers
1. Public Health Need
• Need identified by any stakeholder or USP
• Need evaluated for possible standard development
2. Draft Standard
• Best practices and scientific information collected
3. Public Comment Period
• Draft standard published for stakeholder input
4. Review & Approval
• Comments evaluated and addressed <or>
• Comments evaluated and further revision and comment needed
Approved
5. Publication
• Final standard published with official date at least 6 months after publication
USP Process
Revision Continues
USP Expert Committee
USP convenes a committee of independent experts that are knowledgeable on the public health issue to develop the standard.
Healthcare Practitioners
Academicians
Healthcare Industry
Regulatory Authorities
(Non-voting Liaisons)
Manufacturers
Stakeholder Implementation
Regulatory Authorities, State Practice Boards, Healthcare Industry, Healthcare Practitioners and other stakeholders utilize USP Healthcare Quality & Safety standards within their specific authority to help ensure public health.

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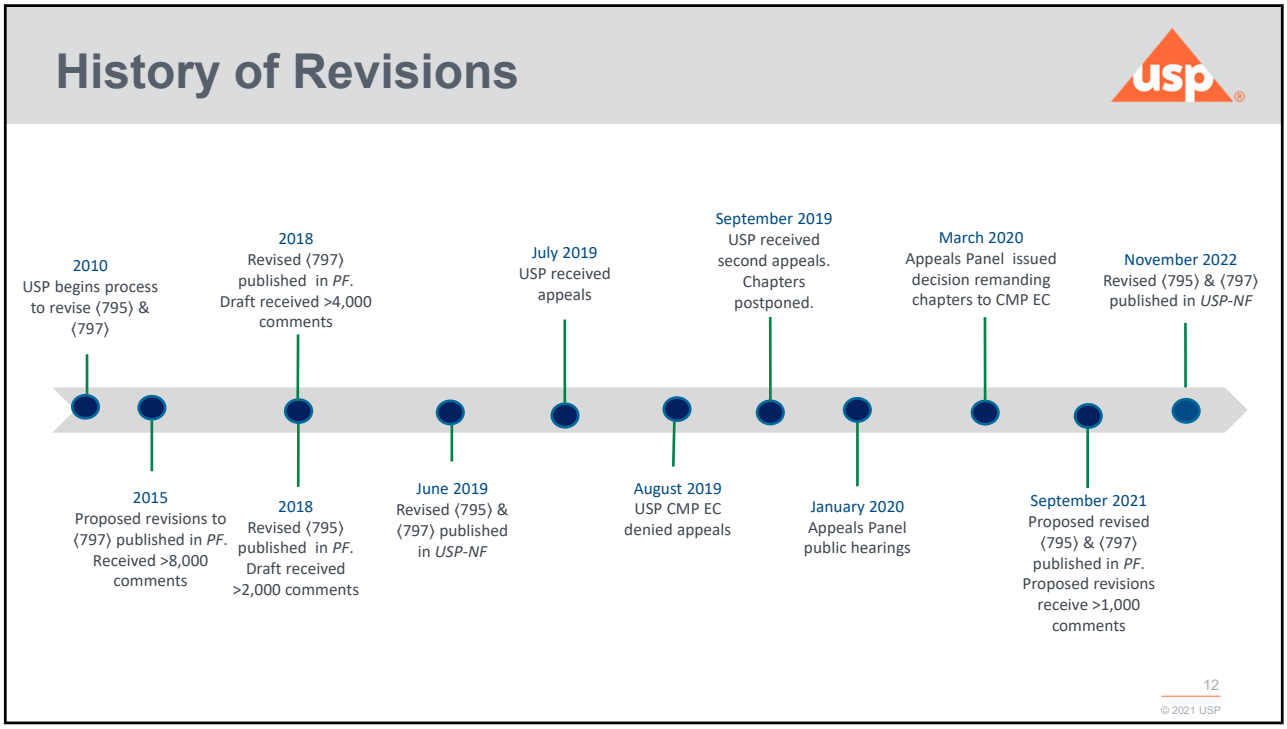
History of Revisions
2010
USP begins process to revise ⟨795⟩ & ⟨797⟩
2015
Proposed revisions to ⟨797⟩ published in PF. Received >8,000 comments
2018
Revised ⟨797⟩ published in PF. Draft received >4,000 comments
2018
Revised ⟨795⟩ published in PF. Draft received >2,000 comments
June 2019
Revised ⟨795⟩ & ⟨797⟩ published in USP-NF
July 2019
USP received appeals
August 2019
USP CMP EC denied appeals
September 2019
USP received second appeals. Chapters postponed.
January 2020
Appeals Panel public hearings
March 2020
Appeals Panel issued decision remanding chapters to CMP EC
September 2021
Proposed revised ⟨795⟩ & ⟨797⟩ published in PF. Proposed revisions receive >1,000 comments
November 2022
Revised ⟨795⟩ & ⟨797⟩ published in USP-NF
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Approach to Revisions

- Stakeholder Engagement
  - Reviewed feedback, including *PF* public comments and issues raised in the appeals
  - Held stakeholder semi-structured interviews (May 2020)
  - Roundtable session (July 28, 2020)
  - Open forum (September 15, 2020)
- Identified key stakeholder engagement discussion topics as a framework
- Also had general considerations throughout the review process
  - Scientifically robust, risk-based approach to assigning beyond-use dates (BUDs)
  - Physical and chemical stability considerations
  - Sterility assurance in ⟨797⟩
  - Operational implications
  - Balancing the need for patient access to cost-effective compounded preparations with rigorous quality standards
  - Implications on regulatory oversight and enforcement

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Overview of Revised General Chapter ⟨795⟩ *Pharmaceutical Compounding—Nonsterile Preparations*

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⟨795⟩ Overview

Chapter Outline

1. Introduction and Scope
2. Personnel Training and Evaluation
3. Personal Hygiene and Garbing
4. Buildings and Facilities
5. Cleaning and Sanitizing
6. Equipment and Components
7. Master Formulation and Compounding Records
8. Release Inspections and Testing
9. Labeling
10. Establishing Beyond-Use Dates
11. SOPs
12. Quality Assurance and Quality Control
13. CNSP Packaging and Transporting
14. Documentation

- Glossary

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⟨795⟩ Revisions

Section 1. Introduction and Scope

- Scope
  - Added information on types of Compounded Nonsterile Preparations (CNSPs)
- Hazardous Drugs
  - Removed all information on handling of hazardous drugs and added references to General Chapter ⟨800⟩ *Hazardous Drugs—Handling in Healthcare Settings*
- Affected Personnel and Settings
  - Added roles and responsibility of the designated person
    - Designated person = One or more individuals assigned to be responsible and accountable for the performance and operation of the facility and personnel as related to the preparation of CNSPs

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Flavoring

- Nonsterile compounding is defined as combining, admixing, diluting, pooling, reconstituting other than as provided in the manufacturer's labeling, or otherwise altering a drug product or bulk drug substance to create a nonsterile preparation
- Adding components (such as flavors) not stipulated in the labeling to conventionally manufactured products is compounding as defined in ⟨795⟩ and has been within the scope of ⟨795⟩ since the chapter was first published in 2004
- Flavors are organic chemicals with reactive functional groups including acids, alcohols, aldehydes, amides, amines, esters, ketones, and lactams
- The effect of adding these substances, even in very small quantities or concentrations, to conventionally manufactured products is unpredictable due to the potential for a variety of chemical reactions
- USP Resource: "⟨795⟩: Adding Flavor to Conventionally Manufactured Nonsterile Products"

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⟨795⟩ Revisions

Section 2. Personnel Training and Evaluation

- Added guidance on training and core competencies
- Included steps in training procedures

Section 3. Personal Hygiene and Garbing

- Added Box on Hand Hygiene Procedures
- Included description of garb and glove requirements
  - Gloves are required for all compounding activities
  - Other garb must be used as appropriate for the type of compounding

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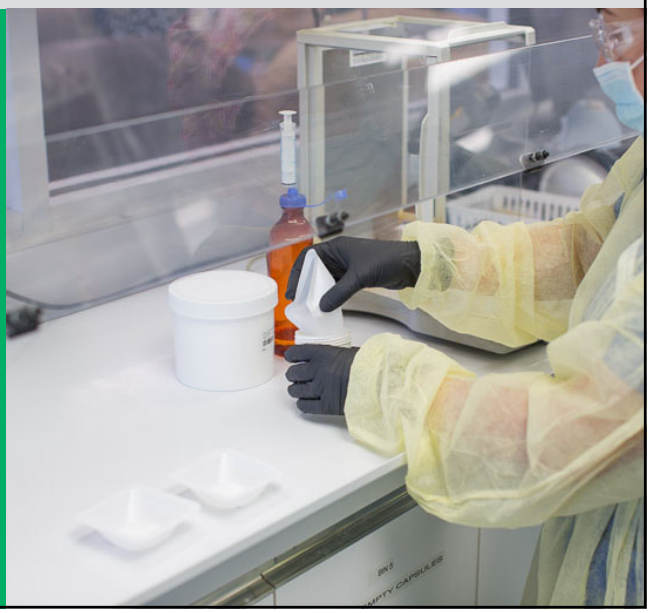
⟨795⟩ Revisions

Section 4. Buildings and Facilities

- Added requirement for a designated area for nonsterile compounding
- Area must be well lit and be maintained in a clean, orderly, sanitary condition and in a good state of repair

Section 5. Cleaning and Sanitizing

- New table on minimum frequencies for cleaning and sanitizing surfaces in nonsterile compounding areas, including:
  - Work surfaces
  - Floors
  - Walls
  - Ceilings
  - Storage Shelving



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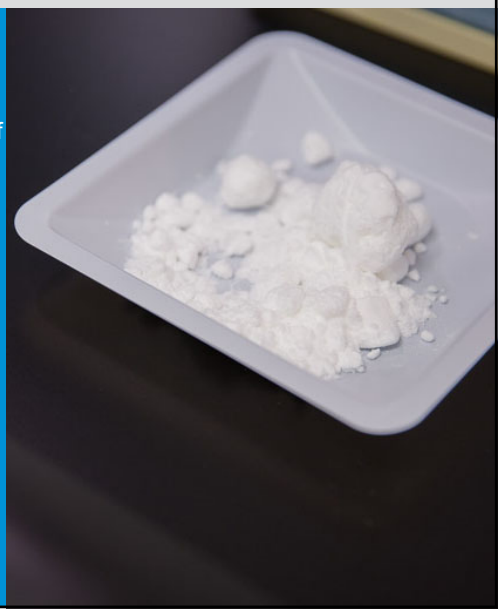
⟨795⟩ Revisions

Section 6. Equipment and Components

- Weighing, measuring, or otherwise manipulating components that could generate airborne chemical particles (eg, APIs, added substances, and conventionally manufactured products) must be evaluated to determine if these activities must be performed in a closed-system processing device
  - Containment ventilated enclosures (CVEs) and biological safety cabinets (BSCs) must be cleaned and sanitized
  - CVE or BSC must be certified at least annually
- Components
  - In the United States, active pharmaceutical ingredients (APIs) must be manufactured by an FDA-registered facility
    - Each API must be accompanied by a valid Certificate of Analysis (COA)
  - In the United States, all components other than APIs should be obtained from an FDA-registered facility
  - Packaging systems of components that lack a vendor's expiration must not be used after 3 years from the date of receipt



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⟨795⟩ Revisions

Section 7. Master Formulation And Compounding Records

- Boxes include required elements of Master Formulation Records and Compounding Records

Section 8. Release Inspections and Testing

- Confirm CNSP and labeling match Compounding Records
- Visual inspections to determine if physical appearance is as expected
- Other tests to ensure quality (eg, pH, assays)

Section 9. Labeling

- Requirements for *labels* (labeling on the immediate container)
- Requirements for *labeling* (all matter on container or in any packaging system or wrapper)

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⟨795⟩ Revisions

Section 10. Establishing Beyond-Use Dates

- Terminology
  - Expiration Date applies to conventionally manufactured drug products
  - BUD applies to CNSPs calculated in terms of hours, days, or months
- Parameters to consider
  - Water activity (a_w)
  - Chemical and physical stability
  - Compatibility of container closure system
  - Degradation of container closure system
  - Potential for microbial proliferation
  - Deviations from essential compounding steps and procedures

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⟨795⟩ Revisions

Section 10. Establishing Beyond-Use Dates

- *Table 4. BUD Limit by Type of Preparation in the **Absence** of a USP–NF Compounded Preparation Monograph or CNSP-Specific Stability Information* [a]

Type of Preparation	BUD (days)	Storage Temperature [b]
Aqueous Dosage Forms ($a_w \geq 0.60$)		
Nonpreserved aqueous dosage forms [c]	14	Refrigerator
Preserved aqueous dosage forms [c]	35	Controlled room temperature or refrigerator
Nonaqueous Dosage Forms ($a_w < 0.60$)		
Oral liquids (nonaqueous) [d]	90	Controlled room temperature or refrigerator
Other nonaqueous dosage forms [e]	180	Controlled room temperature or refrigerator

a A shorter BUD must be assigned when the physical and chemical stability of the CNSP is less than the BUD limit stated in the table (see *10.4 CNSPs Requiring Shorter BUDs*).
b See *Packaging and Storage Requirements* ⟨659⟩.
c An aqueous preparation is one that has an a_w of ≥ 0.6 (eg, emulsions, gels, creams, solutions, sprays, or suspensions).
d A nonaqueous oral liquid is one that has an a_w of < 0.6.
e Other nonaqueous dosage forms that have an a_w of < 0.6 (eg, capsules, tablets, granules, powders, nonaqueous topicals, suppositories, and troches or lozenges).

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⟨795⟩ Revisions

Nonaqueous Dosage Forms: $a_w < 0.6$			Aqueous Dosage Forms: $a_w \geq 0.6$		
Dosage Form	Description	a_w	Dosage Form	Description	a_w
Animal treat	Animal treat (oil flavor)	0.507	Animal treat	Animal treat with 15%–18% aqueous flavor	0.716
Capsule (oil filled)	Olive oil encapsulated	0.468	Cream	Cream vehicle (oil in water emulsion, petrolatum free)	0.968
Capsule (powder filled)	Powder base encapsulated	0.435	Cream	Emollient cream (petrolatum and mineral oil)	0.984
Gel (glycol based)	Propylene glycol, ethoxy diglycol, or hydroxypropyl cellulose gel	0.056	Cream	Cream (oil in water emulsion with natural oils)	0.989
Lollipop (sorbitol based)	Sorbitol-based lollipop	0.460	Foam	Foaming surfactant solution	0.983
Ointment	Hydrophilic petrolatum	0.396	Gel (water based)	Alcohol-free aqueous gel	0.990
Ointment	Polyethylene and mineral oil gel base	0.459	Gel (water based)	Hydroxypropyl methylcellulose (HPMC) gel	1.000
Oral solution (glycol based)	20% Polyethylene glycol and 80% propylene glycol	0.009	Lotion	Lotion (oil in water emulsion)	0.986
Oral solution (oil based)	Medium chain triglycerides oil	0.338	Nasal spray	Nasal spray	0.991
Oral suspension (fixed oil)	Fixed oil with thickener	0.403	Oral solution (water based)	Low-sucrose syrup vehicle	0.906
Powder for inhalation	Encapsulated powder for inhalation	0.402	Oral solution (water based)	90% Water and 10% glycerin	0.958
Stick	Lip balm	0.181	Oral suspension (water based)	Oral suspension base	0.992
Suppository	Polyethylene glycol base	0.374	Rinse	Polymer gel with 30% water	0.960
Suppository	Fatty acid base	0.385	Shampoo	Shampoo	0.976
Tablet (compressed)	Compressed tablet	0.465	Simple syrup	Simple syrup	0.831
Tablet (triturate)	Tablet triturate (lactose and/or sucrose)	0.427	-	-	-
Troche or lozenge (gelatin based)	Gelatin troche or lozenge with NMT 3% aqueous flavor	0.332	-	-	-
Troche or lozenge (glycol based)	Polyethylene glycol troche or lozenge with NMT 3% aqueous flavor	0.571	-	-	-

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⟨795⟩ Revisions

2008 Currently Official Chapter	Revised Chapter
Water-containing oral formulations = **14 days** Water-containing topical/dermal and mucosal liquids and semisolid formulations = **30 days** Nonaqueous formulations = **6 months**	Nonpreserved aqueous dosage forms ($a_w \geq 0.60$) = **14 days** Preserved aqueous dosage forms ($a_w \geq 0.60$) = **35 days** Oral liquids (nonaqueous) ($a_w < 0.60$) = **90 days** Other nonaqueous dosage forms ($a_w < 0.60$) = **180 days**

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⟨795⟩ Revisions

Section 10. Establishing Beyond-Use Dates

- In the **Presence** of CNSP-Specific Stability Information
  - BUD may be extended up to a maximum of 180 days
  - Stability-indicating analytical method for the API(s), CNSP formulation, and material of composition of the container closure that will be used
  - An aqueous CNSP must be tested for ⟨51⟩ antimicrobial effectiveness at the end of the BUD
    - Bracketing can be utilized to provide flexibility
  - If compounding from a *USP–NF* compounded preparation monograph, the BUD must not exceed the BUD specified in the monograph
- Shorter BUDs may be required
  - If components have an earlier expiration date or BUD
  - If ingredients are known to be susceptible to decomposition

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⟨795⟩ Revisions

Section 11. SOPs

Section 12. Quality Assurance and Quality Control

- Quality Assurance = set of written processes that, at a minimum, verifies, monitors, and reviews the adequacy of the compounding process
- Quality Control = observation of techniques and activities that demonstrate that requirements are met
- SOPs for complaint receipt, acknowledgement, and handling
- Review of adverse events

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⟨795⟩ Revisions

Section 13. CNSP Packaging and Transporting

Section 14. Documentation

Glossary

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Overview of Revised General Chapter ⟨797⟩ *Pharmaceutical Compounding—Sterile Preparations*

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⟨797⟩ Revisions

Chapter Outline

1. Introduction and Scope
2. Personnel Training and Evaluation
3. Personal Hygiene and Garbing
4. Facilities and Engineering Controls
5. Certification and Recertification
6. Microbiological Air and Surface Monitoring
7. Cleaning, Disinfecting, and Applying Sporicidal Disinfectants and Sterile 70% IPA
8. Introducing Items into the SEC and PEC
9. Equipment, Supplies, and Components
10. Sterilization and Depyrogenation
11. Master Formulation and Compounding Records
12. Release Inspections and Testing
13. Labeling
14. Establishing Beyond-Use Dates
15. Use of Conventionally Manufactured Products as Components
16. Use of CSPs as Components
17. SOPs
18. Quality Assurance and Quality Control
19. CSP Handling, Storage, Packaging, Shipping, and Transport
20. Documentation
21. Compounding Allergenic Extracts

- Glossary

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⟨797⟩ Intent

- Serve as the minimum standards for the preparation of compounded sterile preparations (CSPs) for human and animal drugs
- To minimize harm, including death, from:
  - Microbial contamination (nonsterility)
  - Excessive bacterial endotoxins
  - Variability from the intended strength of correct ingredients
  - Physical and chemical incompatibilities
  - Chemical and physical contaminants
  - Use of ingredients of inappropriate quality
- Requires aseptic techniques, processes, and procedures when preparing any sterile medication to minimize:
  - Contact with nonsterile surfaces
  - Introduction of particulate matter or biological fluids
  - Mix-ups with other products or CSPs

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⟨797⟩ Revisions

Administration is out of the scope of the chapter

- Sterile compounding is defined as:
  - Combining,
  - Admixing,
  - Diluting,
  - Pooling,
  - Reconstituting,
  - Repackaging, or
  - Otherwise altering a drug or bulk drug substance to create a sterile preparation

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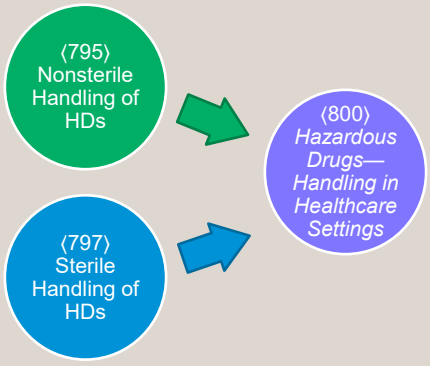
⟨797⟩ Revisions

Scope

- *Removes* provisions for handling of hazardous drugs
  - Compounded sterile hazardous drugs *are subject to* ⟨800⟩



- *Removes* provisions for radiopharmaceuticals
  - Compounding radiopharmaceuticals *are subject to* ⟨825⟩ *Radiopharmaceuticals—Preparation, Compounding, Dispensing, and Repackaging*

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⟨797⟩ Revisions

Alternative Technologies

- The use of technologies, techniques, materials, and procedures other than those described in this chapter is not prohibited as long as they are noninferior to those described herein and validated for the intended purpose (eg, *Validation of Alternative Microbiological Methods* ⟨1223⟩ and *Validation of Compendial Procedures* ⟨1225⟩).

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⟨797⟩ Revisions

Immediate-Use CSPs

Requirements for Immediate-Use CSPs
Aseptic techniques, processes, and procedures are followed, and written SOPs are in place to minimize the potential for contact with nonsterile surfaces, introduction of particulate matter or biological fluids, and mix-ups with other conventionally manufactured products or CSPs.
Personnel are trained and demonstrate competency in aseptic processes as they relate to assigned tasks and the facility's SOPs.
The preparation is performed in accordance with evidence-based information for physical and chemical compatibility of the drugs (eg, approved labeling, stability and compatibility studies).
The preparation involves not more than 3 different sterile products.
Any unused starting component from a single-dose container must be discarded after preparation is complete. Single-dose containers must not be used for more than one patient.
Administration begins within 4 hours following the start of preparation. If administration has not begun within 4 hours following the start of preparation, it must be promptly, appropriately, and safely discarded.
Unless directly administered by the person who prepared it or administration is witnessed by the preparer, the CSP must be labeled with the names and amounts of all active ingredients, the name or initials of the person who prepared the preparation, and the 4-hour time period within which administration must begin.

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⟨797⟩ Revisions

Preparation Per Approved Labeling

- Clarifies that 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
- Preparing a conventionally manufactured sterile product in accordance with the directions in the manufacturer's approved labeling is out of scope of this chapter only if:
  - The product is prepared as a single dose for an individual patient; and
  - The approved labeling includes information for the diluent, the resultant strength, the container closure system, and storage time
- Proprietary bag and vial systems
  - Docking and activation in accordance with the manufacturer's labeling for *immediate* administration to an individual patient is not considered compounding and may be performed outside of an ISO Class 5 environment
  - Docking for *future activation* and administration is considered compounding and must be performed in accordance with this chapter, with the exception of *14. Establishing Beyond-Use Dates*. BUDs for proprietary bag and vial systems must not be longer than those specified in the manufacturer's labeling

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⟨797⟩ Revisions

Categories of CSPs

- High-Risk
- Medium-Risk
- Low-Risk
- Low-Risk With 12-Hour BUD

Category 1 CSPs	Category 2 CSPs	Category 3 CSPs
• Must be prepared in a PEC that may be located in an unclassified segregated compounding area • Assigned a BUD of ≤ 12 hours at controlled room temperature or ≤ 24 hours when refrigerated	• Must be prepared in a cleanroom suite • May be assigned a BUD of > 12 hours at controlled room temperature or > 24 hours if refrigerated	• Have additional requirements that must be met at all times • May be assigned a BUD longer than established for Category 2 CSPs, up to 180 days

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⟨797⟩ Revisions

Assigning Longer BUDs Than in the Chapter*

2008 Last Official Chapter	2015 Revision Proposed in *PF*	2018 Revision Proposed in *PF*	2019 Revision Published in *USP-NF* (subsequently remanded)	Revised Chapter
BUDs could be assigned up to the duration indicated by appropriate information sources for the same or similar formulations and by personal experience	The ability to assign longer BUDs was not described	BUDs could be assigned up to a maximum of 90 days if supported by stability data	BUDs could only be assigned up to the limits described in the chapter	Category 3 describes the requirements a compounding site must ensure at all times for assigning longer BUDs than those established for Category 2 CSPs, up to a maximum of 180 days

* If there is a compounded preparation monograph for a particular CSP formulation, the BUD in the monograph can be assigned if the CSP is prepared according to the monograph and all monograph requirements are met, including sterility testing.

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⟨797⟩ Revisions

Personnel Training and Evaluation

Knowledge and Competency of Core Skills

Garbing Competency Evaluation

- Visual observation
- Gloved fingertip and thumb sampling of both hands

Aseptic Manipulation Competency Evaluation

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

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⟨797⟩ Revisions

Personnel Qualifications

	2008 Last Official Chapter	2015 Revision Proposal	2018 Revision Proposal	2019 Remanded Chapter	Revised Chapter
Visual observation of hand hygiene and garbing	Annually	Every 3 months	Every 6 months	Every 6 months	**Category 1 & 2:** Every 6 months **Category 3:** Every 3 months for personnel who compound Category 3 CSPs
Gloved fingertip and thumb sampling	**Low/Medium-Risk CSPs:** Annually **High-Risk CSPs:** Semi-annually	Every 3 months	Every 6 months	Every 6 months	**Category 1 & 2:** Every 6 months **Category 3:** Every 3 months for personnel who compound Category 3 CSPs as part of garbing competency and aseptic competency
Media-fill testing	**Low/Medium-Risk CSPs:** Annually **High-Risk CSPs:** Semi-annually	Every 3 months	Every 6 months	Every 6 months	**Category 1 & 2:** Every 6 months **Category 3:** Every 3 months for personnel who compound Category 3 CSPs

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⟨797⟩ Revisions

Minimum Garbing Requirements

2008 Last Official Chapter	2015 Revision Proposal	2018 Revision Proposal	2019 Remanded Chapter	Revised Chapter
• Gown • Dedicated shoes or shoe covers • Head and facial hair covers • Face masks • Sterile gloves	Determined based on: • Category • Type of PEC Included: • Gown or coveralls • Disposable covers for shoes • Disposable covers for head and facial hair • Sterile gowns or sleeves • Sterile gloves	• Gown • Disposable covers for shoes • Disposable covers for head and facial hair • Face mask • Sterile gloves If using RABS → disposable gloves inside of gauntlet gloves	• Gown • Disposable covers for shoes • Disposable covers for head and facial hair • Face mask • Sterile gloves If using RABS → disposable gloves inside of gauntlet gloves	• Low-lint garment with sleeves that fit snugly around the wrists and an enclosed neck (eg, 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 RABS, (ie, a CAI or 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

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Minimum Garbing Requirements

Revised Chapter – Category 3
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. The following additional garbing requirements must be followed in the buffer room where Category 3 CSPs are prepared for all personnel regardless of whether Category 3 CSPs are compounded on a given day: 1. Do not allow any exposed skin in the buffer room (ie, face and neck must be covered). 2. All low-lint outer garb must be sterile, including the use of sterile sleeves over gauntlet sleeves when a RABS is used. 3. Disposable garbing items must not be reused, and laundered garb must not be reused without being laundered and resterilized with a validated cycle. 4. The facility's SOPs must describe disinfection procedures for reusing goggles, respirators, and other reusable equipment.

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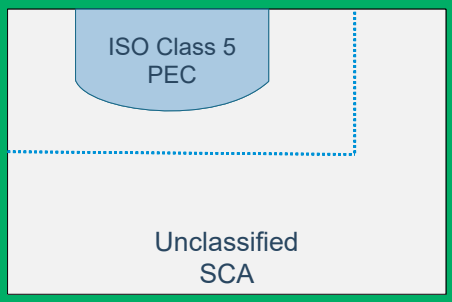
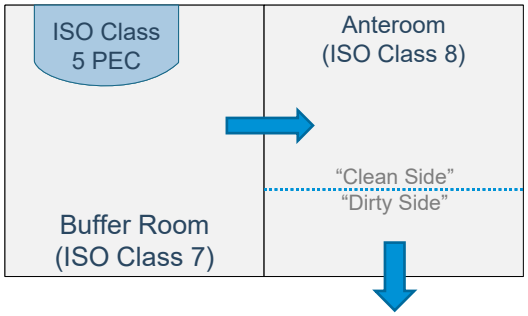
Minimum PEC Placement

Category 1 CSPs



Category 2 or 3 CSPs



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Certification and Recertification

- During dynamic operating conditions
- Required every 6 months
- Includes:
  - Airflow testing
  - HEPA filter integrity testing
  - Total particle count testing
  - Dynamic airflow smoke pattern test

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Microbiological Air and Surface Monitoring

	2008 Last Official Chapter	2015 Revision Proposal	2018 Revision Proposal	2019 Remanded Chapter	Revised Chapter
Viable air sampling	Every 6 months	Monthly	Every 6 months	Every 6 months	**Category 1 & 2:** Every 6 months **Category 3:** Monthly
Surface sampling	Periodically	Monthly	Monthly	Monthly	**Category 1 & 2:** Monthly **Category 3:** Weekly

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

- Frequencies specified for separate activities
  - Cleaning
  - Disinfecting
  - Applying a sporicidal disinfectant
- Cleaning and disinfecting supplies (eg, wipers, sponges, pads, and mop heads)
  - Must be low-lint
  - Should be disposable
  - Reusable cleaning tools must be dedicated for use

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

- Cleaning, disinfecting, and sporicidal agents used within the PEC must be sterile
- Cleaning and disinfecting supplies used in the PEC must be sterile with the exception of tool handles and holders, which must be cleaned and disinfected prior to use in a PEC
- Reusable cleaning tools must be made of cleanable materials (eg, handles should not be made of wood or any other porous material) and must be cleaned and disinfected before and after each use

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Component Selection

- Conventionally manufactured sterile products should be used when available and appropriate for the intended CSP
- Active pharmaceutical ingredients:
  - Must comply with the criteria in the *USP–NF* monograph, if one exists
  - Must have a COA that includes the specifications (eg, compendial requirements for quality) and that test results for the component show that the API meets expected quality
  - In the United States, must be manufactured by an FDA-registered facility
  - Outside of the United States, must comply with the laws and regulations of the applicable regulatory jurisdiction
- Components other than APIs:
  - Must comply with the criteria in the *USP–NF* monograph, if one exists
  - Must be accompanied by documentation (eg, COA, labeling) that includes the specifications and test results and shows that the component meets the specifications
  - In the United States, should be manufactured by an FDA-registered facility
  - Outside of the United States, must comply with the laws and regulations of the applicable regulatory jurisdiction

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Terminal Sterilization Methods and Aseptic Processing

- A CSP may be prepared by the following methods:
  - Terminal sterilization is the preferred method of sterilization
    - Steam
    - Dry heat
    - Irradiation

    Probability of a nonsterile unit (PNSU) of 10^{-6}
  - Aseptic processing
    - Compounding with only sterile starting ingredient(s), or
    - Compounding with nonsterile ingredient(s) followed by sterilization by filtration

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Master Formulation and Compounding Records

Master Formulation Record

- Required for
  - All CSPs prepared from nonsterile ingredient(s)
  - CSPs prepared for more than one patient

Compounding Record

- Required for
  - All Category 1, Category 2, and Category 3 CSPs
  - Immediate-use CSPs prepared for more than one patient
- May be in the form of a prescription or medication order or label
- May be stored electronically through an ACD, workflow management system, or other similar equipment
  - As long as it is retrievable and contains the required information

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Release Inspections and Testing

Visual Inspection

Sterility Testing

- Required for **Category 2** CSPs assigned a BUD that requires sterility testing, and for all **Category 3** CSPs
- **The maximum batch size for all CSPs requiring sterility testing must be limited to 250 final yield units**
- If the number of CSPs to be compounded in a single batch is less than the number of CSPs needed for testing as specified in *USP* ⟨71⟩, *Table 3*, additional units must be compounded to perform sterility testing
  - If between 1 and 39 CSPs, test a number of units equal to 10% of CSPs prepared
  - If >40 CSPs, test based on *USP* ⟨71⟩, *Table 3*
- If an alternative method is used for sterility testing, the method must be validated (see ⟨1223⟩) and demonstrated to be suitable for that CSP formulation

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Release Inspections and Testing

Bacterial Endotoxins Testing

- Required for
  - **Category 2** injectable CSPs compounded from one or more nonsterile component(s) and assigned a BUD that requires sterility testing
  - **Category 3** injectable CSPs compounded from one or more nonsterile component(s)
- **Category 2** CSPs assigned a BUD that does not require sterility testing but compounded from one or more nonsterile component(s) **should** be tested

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Establishing Beyond-Use Dates

Quality factors

- Chemical and physical stability properties of the drug and/or its formulation
- Materials of composition of the container closure system and compatibility of the container closure system with the final preparation (eg, leachables, interactions, adsorption, and storage conditions)

Sterility factors

- Conditions of the environment in which the CSP is prepared
  - Cleanroom suite or SCA
- Aseptic processing and sterilization method
- Starting components
  - Sterile or nonsterile starting ingredients
- Whether or not sterility testing is performed
- Storage conditions
  - Packaging and temperature

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Category 1 CSP BUD Limits

Storage Conditions	
Controlled Room Temperature (20°–25°)	Refrigerator (2°–8°)
≤ 12 hours	≤ 24 hours

2008 Last official ⟨797⟩

Low-Risk Level CSP in SCA — **12 hours**

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Category 2 CSP BUD Limits

Preparation Characteristics		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): 1 day	Prepared from one or more nonsterile starting component(s): 4 days	Prepared from one or more nonsterile starting component(s): 45 days

2008 Last official ⟨797⟩

High-Risk Level CSPs	1 day	3 days	45 days

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Category 2 CSP BUD Limits

Preparation Characteristics		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 only sterile starting components: 4 days	Prepared from only sterile starting components: 10 days	Prepared from only sterile starting components: 45 days

2008 Last official ⟨797⟩

Medium-Risk Level CSPs	30 hours	9 days	45 days
Low-Risk Level CSPs	48 hours	14 days	45 days

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Category 2 CSP BUD Limits

Preparation Characteristics		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): 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

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Category 3 CSP BUD Limits

Preparation Characteristics	Storage Conditions		
Compounding Method	Controlled Room Temperature (20°–25°)	Refrigerator (2°–8°)	Freezer (-25°–10°)
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

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Additional Requirements for Category 3 CSPs

- Category 3 CSPs undergo sterility testing, supplemented by endotoxin testing when applicable, and have more requirements than Category 2 CSPs for
  - Personnel qualification
  - Use of sterile garb
  - Frequency of applying sporicidal disinfectants
  - Frequency of environmental monitoring
  - Stability determination
- The maximum batch size for all CSPs requiring sterility testing must be limited to 250 final yield units

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Multiple-Dose CSPs

- A multiple-dose CSP must be prepared as a Category 2 or Category 3 CSP
- For preserved aqueous multiple-dose CSPs, antimicrobial effectiveness testing must be passed in accordance with *USP* ⟨51⟩
- Time within which multiple-dose preserved CSPs must be used:
  - Whichever is shorter:
    - BUD limit assigned based on if CSP is compounded as Category 2 or Category 3
    - Up to 28 days after container is initially entered or punctured, if supported by ⟨51⟩ testing
- Time within which multiple-dose, nonpreserved, aqueous topical, and topical ophthalmic CSPs must be used:
  - BUD limit assigned based on if CSP is compounded as Category 2 or Category 3, and
  - Discarded 24 hours after first opening if stored at room temperature, or 72 hours if refrigerated

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Use of Conventionally Manufactured Products as Components

- Addresses the time within which an entered or punctured conventionally manufactured product must be used

Type of Container	Time within which product must be used
Single-Dose Container	ISO Class 5 → 12 hours
Multiple-Dose Container	28 days
Pharmacy Bulk Package	As specified by the manufacturer

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Use of CSPs as Components

- Addresses the use of CSPs (eg, multiple-dose CSPs, single-dose CSPs, and compounded stock solutions) as components to prepare final CSPs

Type of Container	Time within which product must be used
Single-Dose CSP and CSP Stock Solution	ISO Class 5 → 12 hours
Multiple-Dose CSP	28 days

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Notification and Recall

- If a CSP is dispensed or administered before the results of release testing are known, the facility must have procedures in place to:
  - Immediately notify the prescriber
  - Recall any unused dispensed CSPs and quarantine any stock remaining
  - Investigate if other lots are affected and recall if necessary
- An SOP for recall must contain procedures:
  - To determine the severity and the urgency
  - To determine the distribution of any affected CSP
  - To identify patients who have received the CSP
  - For disposal and documentation of the recalled CSP
  - To investigate and document the reason for failure

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Compounding Allergenic Extracts

Licensed allergenic extracts:

- Section applicable only when:
  - The compounding process involves transfer via sterile needles and syringes of conventionally manufactured sterile allergen products and appropriate conventionally manufactured sterile added substances; and
  - Manipulations are limited to penetrating stoppers on vials with sterile needles and syringes and transferring sterile liquids in sterile syringes to sterile vials

Provisions include:

- Personnel Qualifications
  - Gloved fingertip and thumb sampling every 12 months
  - Media-fill testing every 12 months
- Facilities
  - ISO Class 5 PEC
  - Dedicated allergenic extract compounding area (AECA)
- Establishing BUDs
  - No later than the earliest expiration date of any component
  - Must not exceed 1 year
- Documentation
  - Compounding records

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Next Steps

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Next Steps

- The Compounding Expert Committee decided to delay the implementation of the revised chapters until November 1, 2023
- Sign up for updates to ⟨795⟩, ⟨797⟩, and other topics related to USP Healthcare Quality and Safety Standards
  - *https://www.usp.org/hqs-signup-form*
- Attend the Compounding Expert Committee's Official Meetings
  - *https://callforcandidates.usp.org/node/32481*

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Assessment Questions

1. When do USP standards become official?

A. As soon as they are published in the *Pharmacopeial Forum*

B. Generally, six months after being published in the *Pharmacopeial Forum*

C. As soon as they are published in the *USP–NF*

D. Generally, six months after being published in the *USP–NF*

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Assessment Questions

2. The current official version of USP ⟨797⟩ was last revised in

A. 2008

B. 2015

C. 2019

D. 2022

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Assessment Questions

3. Category 1 compounded sterile preparations (CSPs) in USP ⟨797⟩ are restricted to

A. Sterile to sterile compounding only

B. CSPs that are assigned a BUD of no more than 6 hours when stored at room temperature

C. CSPs that are assigned a BUD of no more than 24 hours when stored under refrigeration

D. Non-hazardous CSPs only

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Assessment Questions

4. Which of the following standards are available for compounders in the Compounding Compendium?

A. General Chapter ⟨795⟩ *Pharmaceutical Compounding – Nonsterile Preparations*

B. General Chapter ⟨797⟩ *Pharmaceutical Compounding – Sterile Preparations*

C. USP Compounded Preparation Monographs

D. All of the above

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Email questions to CompoundingSL@USP.org

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