

## What's New with *USP* General Chapters <795> and <797>?

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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.
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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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## What's New With USP General Chapters <795> and <797>?


# The 2020 – 2025 Council of Experts



| Biologics   | Small Molecules   | Excipients  | General Chapters  | Healthcare Quality & Safety   | Dietary Supplements & Herbal Medicines, Food Ingredients   |
|---|---|---|---|---|--|
|    |    |    |    |    |   |
| <b>Biologics Monographs 1-<br/>Peptides &amp; Oligonucleotides</b><br>Michael De Felippis<br><br><b>Biologics Monographs 2-<br/>Proteins</b><br>Wendy Saffell-Clemmer<br><br><b>Biologics Monographs 3-<br/>Complex Biologics &amp; Vaccines</b><br>Earl Zablackis<br><br><b>Biologics Monographs 4-<br/>Antibiotics</b><br>Matthew Borer<br><br><b>Biologics Monographs 5-<br/>Advanced Therapies</b><br>Mehrshid Alai | <b>Small Molecules 1</b><br>Mary Seibel<br><br><b>Small Molecules 2</b><br>Justin Pennington<br><br><b>Small Molecules 3</b><br>Eric Kessler<br><br><b>Small Molecules 4</b><br>Kim Huynh-Ba<br><br><b>Small Molecules 5</b><br>Amy Kamen<br><br><b>Over-the-Counter (OTC)<br/>Methods &amp; Approaches</b><br>Raphael Omaf | <b>Simple Excipients</b><br>Eric Munson<br><br><b>Complex Excipients</b><br>Otilia Koo<br><br><b>Excipients Test Methods</b><br>Chris Moreton | <b>General Chapters- Dosage Forms</b><br>Martin Coffey<br><br><b>General Chapters-<br/>Chemical Analysis</b><br>Nancy Lewan<br><br><b>General Chapters- Microbiology</b><br><br><b>General Chapters-<br/>Packaging &amp; Distribution</b><br>Renaud Janssen<br><br><b>General Chapters-<br/>Measurement &amp; Data Quality</b><br>Jane Weitzel<br><br><b>General Chapters- Statistics</b><br>Charles Tan<br><br><b>General Chapters-<br/>Physical Analysis</b><br>Xiaorong He | <b>Nomenclature &amp; Labeling</b><br>Stephanie Crawford<br><br><b>Healthcare Safety &amp; Quality</b><br>Melody Ryan<br><br><div style="border: 2px solid orange; padding: 2px;"><b>Compounding</b><br/>Brenda Jensen</div><br><b>Healthcare Information<br/>&amp; Technology</b><br>Jeanne Tuttle | <b>Botanical Dietary Supplements<br/>&amp; Herbal Medicines</b><br>Robin Marles<br><br><b>Non-botanical Dietary<br/>Supplements</b><br>Guido F Peuli<br><br><b>Dietary Supplements Admission<br/>Evaluation &amp; Labeling</b><br>Tiersons Low Dog<br><br><b>Food Ingredients</b><br>Jon DeVries |

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# 2020 – 2025 Compounding Expert Committee



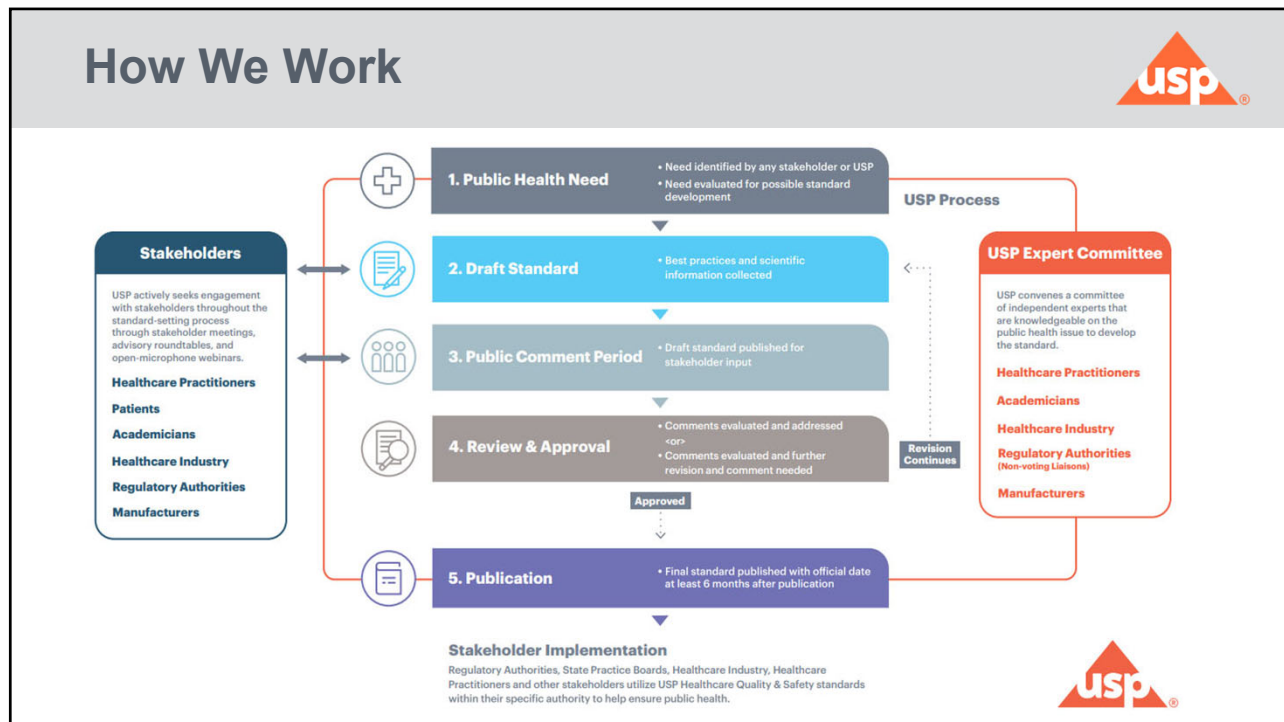
**Chair:** Brenda Jensen, MBA, Owner and Compounding Pharmacy Consultant, Compounding Consultants, LLC  
**Vice Chair:** Vanessa Pinheiro, MS, BS Pharm, Pharmacist and Consultant, Medisca and LP3 Network

| 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                             |

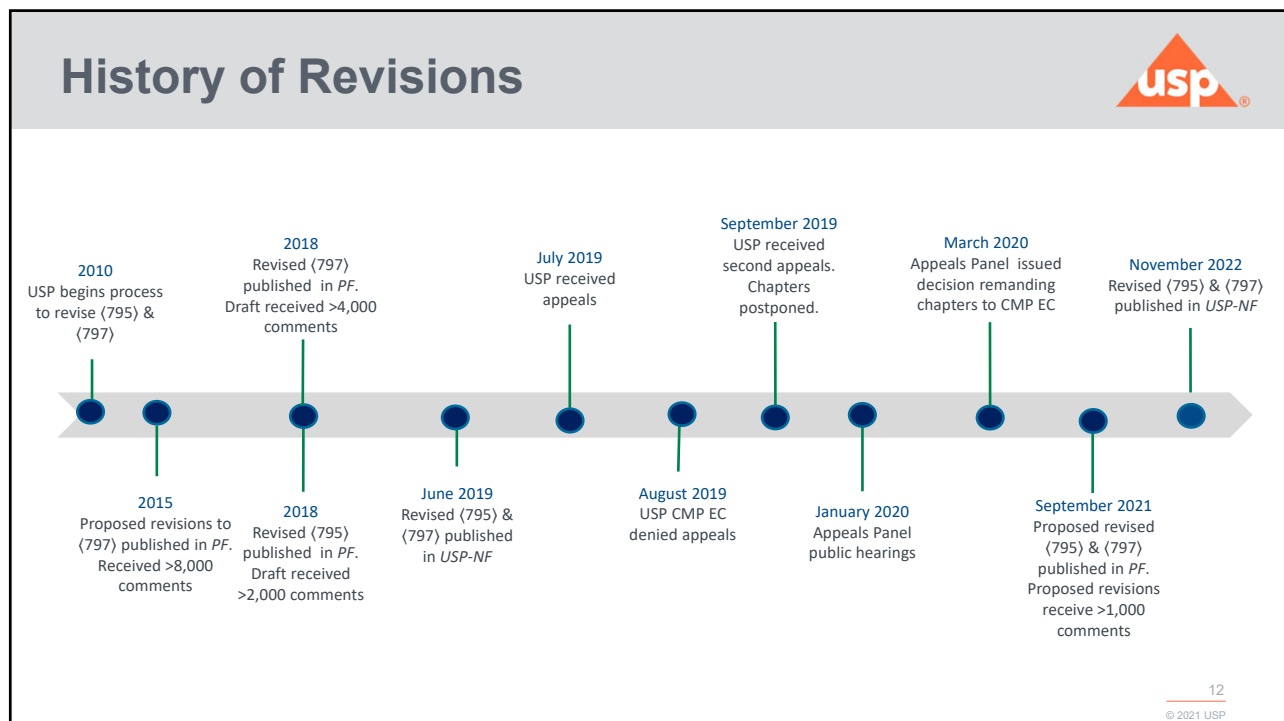
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## What's New With USP General Chapters <795> and <797>?



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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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## What's New With USP General Chapters <795> and <797>?

### <795> Overview



#### Chapter Outline

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

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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

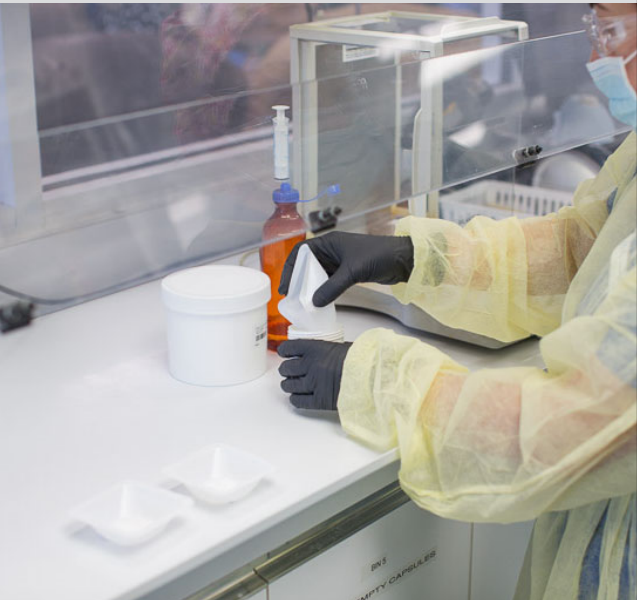


### Section 4. Buildings and Facilities

- ▶ 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 <sup>a</sup>**

| Type of Preparation   | BUD (days) | Storage Temperature <sup>b</sup>            |
|---|------------|---|
| <b>Aqueous Dosage Forms (<math>a_w \geq 0.60</math>)</b>    |            |   |
| Nonpreserved aqueous dosage forms <sup>c</sup>              | 14         | Refrigerator                                |
| Preserved aqueous dosage forms <sup>c</sup>                 | 35         | Controlled room temperature or refrigerator |
| <b>Nonaqueous Dosage Forms (<math>a_w &lt; 0.60</math>)</b> |            |   |
| Oral liquids (nonaqueous) <sup>d</sup>                      | 90         | Controlled room temperature or refrigerator |
| Other nonaqueous dosage forms <sup>e</sup>                  | 180        | Controlled room temperature or refrigerator |

<sup>a</sup> 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).  
<sup>b</sup> See *Packaging and Storage Requirements* (659).  
<sup>c</sup> An aqueous preparation is one that has an  $a_w$  of  $\geq 0.6$  (eg, emulsions, gels, creams, solutions, sprays, or suspensions).  
<sup>d</sup> A nonaqueous oral liquid is one that has an  $a_w$  of  $< 0.6$ .  
<sup>e</sup> 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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## What's New With USP General Chapters <795> and <797>?


| <div> &lt;795&gt; Revisions <div>usp</div> </div>   |  |
|---|--|
| 2008 Currently Official Chapter   | Revised Chapter  |
| Water-containing oral formulations = <b>14 days</b>   | Nonpreserved aqueous dosage forms ( $a_w \geq 0.60$ ) = <b>14 days</b> |
| Water-containing topical/dermal and mucosal liquids and semisolid formulations = <b>30 days</b> | Preserved aqueous dosage forms ( $a_w \geq 0.60$ ) = <b>35 days</b>    |
| Nonaqueous formulations = <b>6 months</b>   | Oral liquids (nonaqueous) ( $a_w < 0.60$ ) = <b>90 days</b>            |
|   | Other nonaqueous dosage forms ( $a_w < 0.60$ ) = <b>180 days</b>       |

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| <div> &lt;795&gt; Revisions <div>usp</div> </div>  |
|--|
| <p><b>Section 10. Establishing Beyond-Use Dates</b></p> <ul style="list-style-type: none"> <li>▶ In the <b>Presence</b> of CNSP-Specific Stability Information <ul style="list-style-type: none"> <li>– BUD may be extended up to a maximum of 180 days</li> <li>– Stability-indicating analytical method for the API(s), CNSP formulation, and material of composition of the container closure that will be used</li> <li>– An aqueous CNSP must be tested for &lt;51&gt; antimicrobial effectiveness at the end of the BUD <ul style="list-style-type: none"> <li>• Bracketing can be utilized to provide flexibility</li> </ul> </li> <li>– If compounding from a <i>USP–NF</i> compounded preparation monograph, the BUD must not exceed the BUD specified in the monograph</li> </ul> </li> <li>▶ Shorter BUDs may be required <ul style="list-style-type: none"> <li>– If components have an earlier expiration date or BUD</li> <li>– If ingredients are known to be susceptible to decomposition</li> </ul> </li> </ul> |


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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  | 12. Release Inspections and Testing                           |
| 2. Personnel Training and Evaluation   | 13. Labeling  |
| 3. Personal Hygiene and Garbing  | 14. Establishing Beyond-Use Dates                             |
| 4. Facilities and Engineering Controls   | 15. Use of Conventionally Manufactured Products as Components |
| 5. Certification and Recertification   | 16. Use of CSPs as Components                                 |
| 6. Microbiological Air and Surface Monitoring  | 17. SOPs  |
| 7. Cleaning, Disinfecting, and Applying Sporocidal Disinfectants and Sterile 70% IPA | 18. Quality Assurance and Quality Control                     |
| 8. Introducing Items into the SEC and PEC  | 19. CSP Handling, Storage, Packaging, Shipping, and Transport |
| 9. Equipment, Supplies, and Components   | 20. Documentation   |
| 10. Sterilization and Depyrogenation   | 21. Compounding Allergenic Extracts                           |
| 11. Master Formulation and Compounding Records                                       | ▶ 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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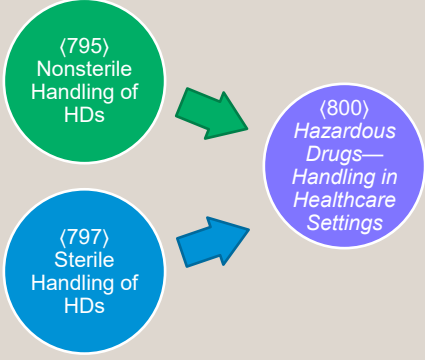
## What's New With USP General Chapters <795> and <797>?

### <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

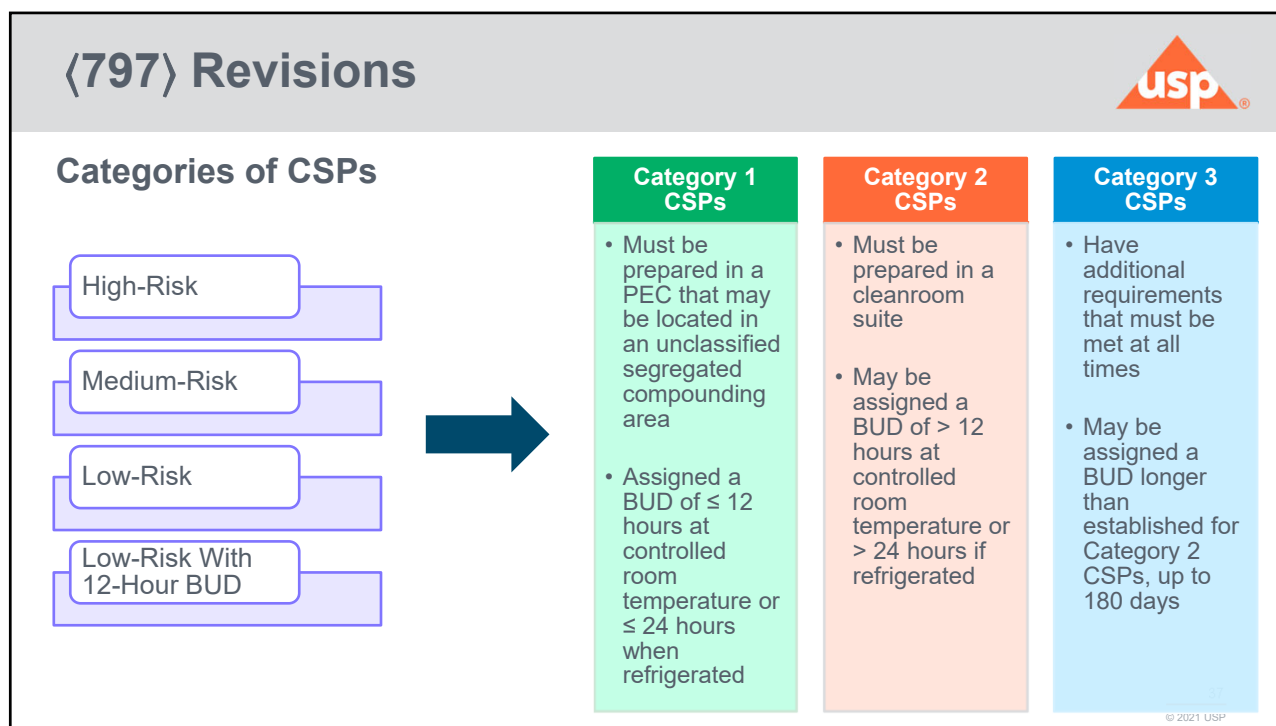
- ▶ Clarifies that compounding does not include mixing, reconstituting, or other such acts that are performed in accordance with directions contained in approved labeling or supplemental materials provided by the product's manufacturer
- ▶ Preparing a conventionally manufactured sterile product in accordance 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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## What's New With USP General Chapters <795> and <797>?



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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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## What's New With USP General Chapters <795> and <797>?

### <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        | <b>Category 1 &amp; 2:</b> <u>Every 6 months</u><br><b>Category 3:</b> <u>Every 3 months</u> for personnel who compound Category 3 CSPs  |
| Gloved fingertip and thumb sampling            | <b>Low/Medium-Risk CSPs:</b> <u>Annually</u><br><br><b>High-Risk CSPs:</b> <u>Semi-annually</u> | Every 3 months         | Every 6 months         | Every 6 months        | <b>Category 1 &amp; 2:</b> <u>Every 6 months</u><br><b>Category 3:</b> <u>Every 3 months</u> for personnel who compound Category 3 CSPs as part of garbing competency and aseptic competency |
| Media-fill testing                             | <b>Low/Medium-Risk CSPs:</b> <u>Annually</u><br><br><b>High-Risk CSPs:</b> <u>Semi-annually</u> | Every 3 months         | Every 6 months         | Every 6 months        | <b>Category 1 &amp; 2:</b> <u>Every 6 months</u><br><b>Category 3:</b> <u>Every 3 months</u> for personnel who compound Category 3 CSPs  |

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## What's New With USP General Chapters <795> and <797>?

| <div> <div>&lt;797&gt; Revisions</div>  </div>   |   |   |   |   |
|---|---|---|---|---|
| Minimum Garbing Requirements  |   |   |   |   |
| 2008 Last Official Chapter  | 2015 Revision Proposal  | 2018 Revision Proposal  | 2019 Remanded Chapter   | Revised Chapter   |
| <ul style="list-style-type: none"> <li>Gown</li> <li>Dedicated shoes or shoe covers</li> <li>Head and facial hair covers</li> <li>Face masks</li> <li>Sterile gloves</li> </ul> | <p>Determined based on:</p> <ul style="list-style-type: none"> <li>Category</li> <li>Type of PEC</li> </ul> <p>Included:</p> <ul style="list-style-type: none"> <li>Gown or coveralls</li> <li>Disposable covers for shoes</li> <li>Disposable covers for head and facial hair</li> <li>Sterile gowns or sleeves</li> <li>Sterile gloves</li> </ul> | <ul style="list-style-type: none"> <li>Gown</li> <li>Disposable covers for shoes</li> <li>Disposable covers for head and facial hair</li> <li>Face mask</li> <li>Sterile gloves</li> </ul> <p>If using RABS → disposable gloves inside of gauntlet gloves</p> | <ul style="list-style-type: none"> <li>Gown</li> <li>Disposable covers for shoes</li> <li>Disposable covers for head and facial hair</li> <li>Face mask</li> <li>Sterile gloves</li> </ul> <p>If using RABS → disposable gloves inside of gauntlet gloves</p> | <ul style="list-style-type: none"> <li>Low-lint garment with sleeves that fit snugly around the wrists and an enclosed neck (eg, gown or coverall)</li> <li>Low-lint covers for shoes</li> <li>Low-lint cover for head that covers the hair and ears, and if applicable, cover for facial hair</li> <li>Low-lint face mask</li> <li>Sterile powder-free gloves</li> <li>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</li> </ul> |


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| <div> <div>&lt;797&gt; Revisions</div>  </div>   |
|---|
| Minimum Garbing Requirements  |
| <div> <div>Revised Chapter – Category 3</div> <p>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:</p> <ol style="list-style-type: none"> <li>Do not allow any exposed skin in the buffer room (ie, face and neck must be covered).</li> <li>All low-lint outer garb must be sterile, including the use of sterile sleeves over gauntlet sleeves when a RABS is used.</li> <li>Disposable garbing items must not be reused, and laundered garb must not be reused without being laundered and resterilized with a validated cycle.</li> <li>The facility's SOPs must describe disinfection procedures for reusing goggles, respirators, and other reusable equipment.</li> </ol> </div> |

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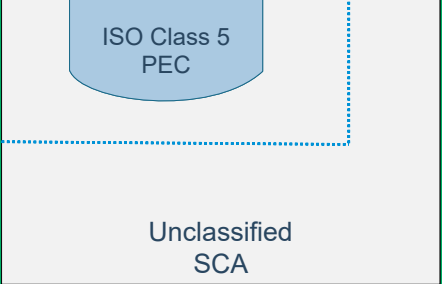
## What's New With USP General Chapters <795> and <797>?

### <797> Revisions

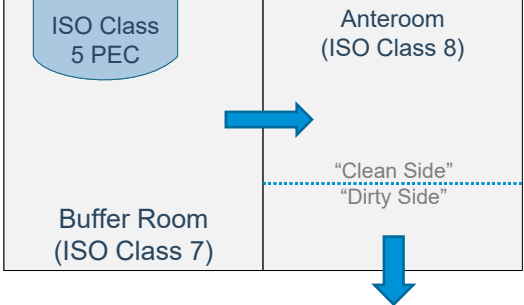


#### Minimum PEC Placement

Category 1 CSPs




Category 2 or 3 CSPs



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### <797> Revisions



#### 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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## What's New With USP General Chapters <795> and <797>?

| <div> <div>&lt;797&gt; Revisions</div> <div>usp®</div> </div> |                            |                        |                        |                       |   |
|---|----------------------------|------------------------|------------------------|-----------------------|---|
| 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        | <b>Category 1 &amp; 2:</b><br><u>Every 6 months</u><br><b>Category 3:</b><br><u>Monthly</u> |
| Surface sampling  | Periodically               | Monthly                | Monthly                | Monthly               | <b>Category 1 &amp; 2:</b><br><u>Monthly</u><br><b>Category 3:</b> <u>Weekly</u>            |

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| <div> <div>&lt;797&gt; Revisions</div> <div>usp®</div> </div>  |
|--|
| <b>Cleaning, Disinfecting, and Applying Sporicidal Disinfectants and Sterile 70% IPA</b> <ul style="list-style-type: none"> <li>▶ Frequencies specified for separate activities <ul style="list-style-type: none"> <li>– Cleaning</li> <li>– Disinfecting</li> <li>– Applying a sporicidal disinfectant</li> </ul> </li> <li>▶ Cleaning and disinfecting supplies (eg, wipers, sponges, pads, and mop heads) <ul style="list-style-type: none"> <li>– Must be low-lint</li> <li>– Should be disposable</li> <li>– Reusable cleaning tools must be dedicated for use</li> </ul> </li> </ul> |

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## <797> Revisions



### 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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## <797> Revisions



### 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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## <797> Revisions



### 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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## <797> Revisions



### 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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## <797> Revisions



### 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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## <797> Revisions




### 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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**<797> Revisions** 

### 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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**<797> Revisions** 

### Category 1 CSP BUD Limits

| Storage Conditions                       |                         |
|--|-------------------------|
| Controlled Room Temperature<br>(20°–25°) | Refrigerator<br>(2°–8°) |
| ≤ 12 hours                               | ≤ 24 hours              |

**2008 Last official <797>**

Low-Risk Level CSP in SCA

→


12 hours

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## What's New With USP General Chapters <795> and <797>?

### <797> Revisions



#### 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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### <797> Revisions



#### 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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## What's New With USP General Chapters <795> and <797>?

| <b>&lt;797&gt; Revisions</b>       |   |   |  |   |
|------------------------------------|---|---|--|---|
| <b>Category 2 CSP BUD Limits</b>   |   |   |  |   |
| <b>Preparation Characteristics</b> |   | <b>Storage Conditions</b>   |  |   |
| <b>Compounding Method</b>          | <b>Sterility Testing Performed &amp; Passed</b> | <b>Controlled Room Temperature (20°–25°)</b>                      | <b>Refrigerator (2°–8°)</b>  | <b>Freezer (–25° to –10°)</b>                                       |
| 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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| <b>&lt;797&gt; Revisions</b>  |  |  |                             |                           |
|---|--|--|-----------------------------|---------------------------|
| <b>Category 3 CSP BUD Limits</b>  |  |  |                             |                           |
| <b>Preparation Characteristics</b>  |  | <b>Storage Conditions</b>                    |                             |                           |
| <b>Compounding Method</b>   |  | <b>Controlled Room Temperature (20°–25°)</b> | <b>Refrigerator (2°–8°)</b> | <b>Freezer (–25°–10°)</b> |
| 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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## <797> Revisions



### 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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## <797> Revisions



### 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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## <797> Revisions



### 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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## <797> Revisions



### 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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## <797> Revisions



### 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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## <797> Revisions



### 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



- ▶ 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



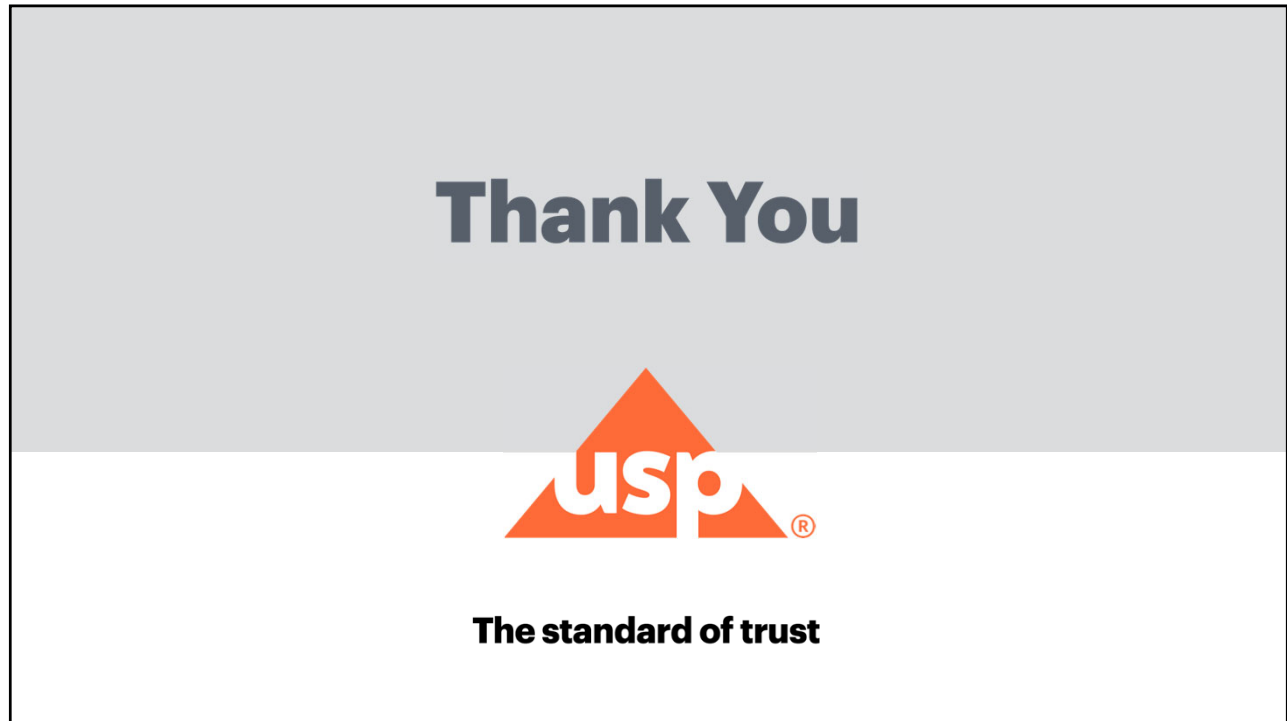
### 4. Which of the following standards are available for compounders in the Compounding Compendium?

- 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

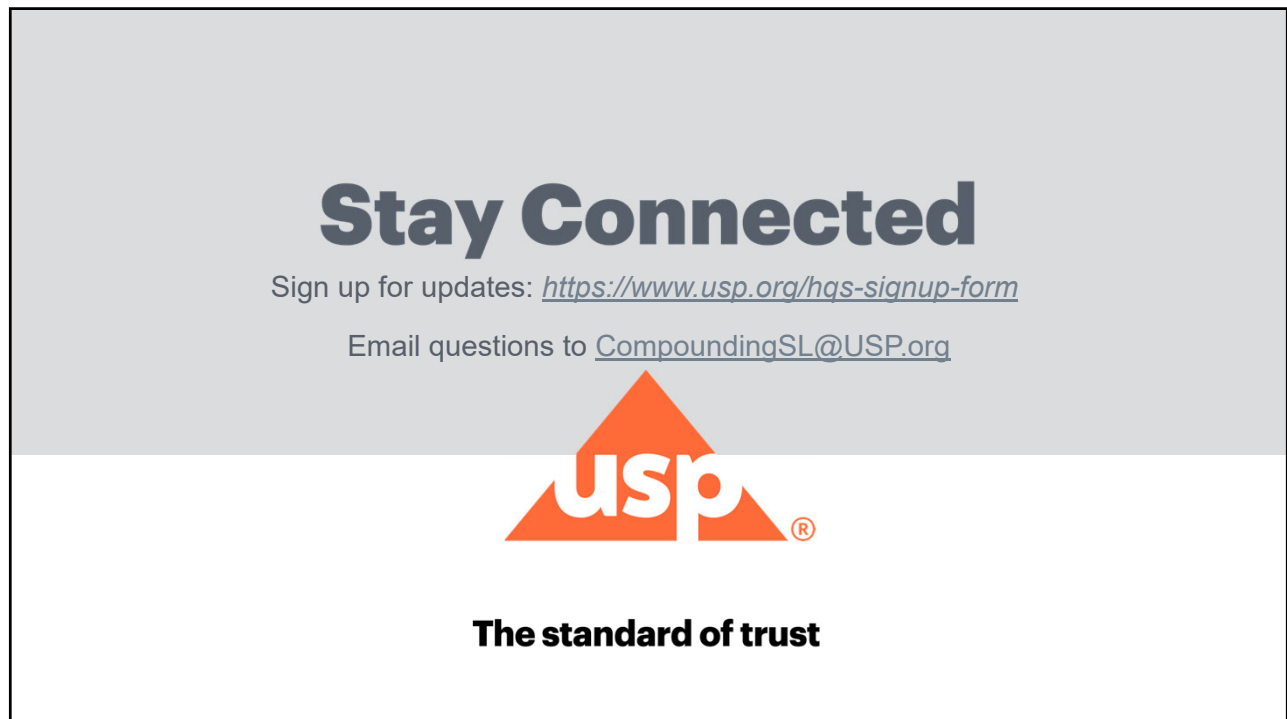
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