Sterile Compounding / USP 797

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Disclosures

I “Lucas Kraemer” declare no conflicts of interest, real or apparent, and no financial interests in any company, product, or service mentioned in this program, including grants, employment, gifts, stock holdings, and honoraria.”

I “Brenda Jensen” am a consultant to compounding facilities.

Learning Objectives

At the conclusion of this program, the participating pharmacist or technician will be able to:

1. Describe practices within and outside the scope of USP <797>
2. Explain major changes to USP <797> including facility, personnel, and documentation
3. Review BUD limits for compounded sterile preparations

USP Overview

The 2020 – 2025 Council of Experts

Biologics

Biologics Monographs 1–Peptides & Oligonucleotides
Michael De Felippis

Biologics Monographs 2–Proteins
Wendy Saffell-Clemmer

Biologics Monographs 3–Complex Biologics & Vaccines
Earl Zablackis

Biologics Monographs 4–Antibiotics
Matthew Borer

Biologics Monographs 5–Advanced Therapies
Mehrshid Alai

Small Molecules

Small Molecules 1
Mary Selbel

Small Molecules 2
Justin Pennington

Small Molecules 3
Eric Kesslen

Small Molecules 4
Kim Huynh-Ba

Small Molecules 5
Amy Karren

Over-the-Counter (OTC) Methods & Approaches
Raphael Omaf

Excipients

Simple Excipients
Eric Munson

Complex Excipients
Otilia Koo

Excipients Test Methods
Chris Moreton

General Chapters

General Chapters–Dosage Forms
Martin Coffey

General Chapters–Chemical Analysis
Nancy Lewen

General Chapters–Microbiology

General Chapters–Packaging & Distribution
Renaud Janssen

General Chapters–Measurement & Data Quality
Jane Weitzel

General Chapters–Statistics
Charles Tan

General Chapters–Physical Analysis
Xiaorong He

Healthcare Quality & Safety

Nomenclature & Labeling
Stephanie Crawford

Healthcare Safety & Quality
Melody Ryan

Compounding
Brenda Jensen

Healthcare Information & Technology
Jeanne Tuttle

Dietary Supplements & Herbal Medicines, Food Ingredients

Botanical Dietary Supplements & Herbal Medicines
Robin Marles

Non-botanical Dietary Supplements
Guido F Pauli

Dietary Supplements Admission Evaluation & Labeling
Tieraona Low Dog

Food Ingredients
Jon DeVries

2020 – 2025 Compounding Expert Committee

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Vice Chair: Vanessa Pinheiro, M.S., B.S. Pharm., Pharmacist and Consultant, Medisca and LP3 Network

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

USP Standards for Compounding

USP provides 3 types of public standards for compounding

USP General Chapters

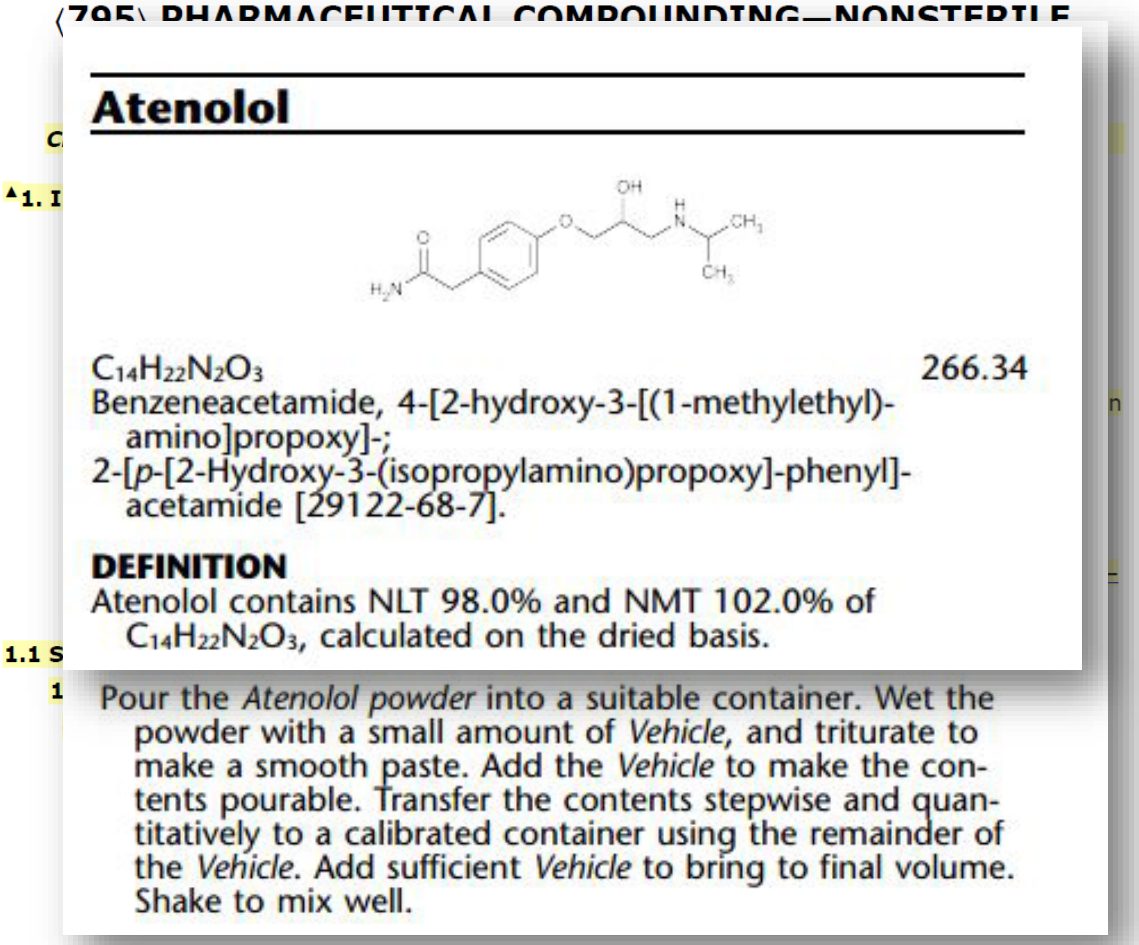
- Establish practice standards to help ensure the quality of compounded preparations

USP Compounded Preparation Monographs

- Contain formulations for specific preparations for which there is no suitable commercially available product

USP Monographs for Bulk Drug Substances and Other Ingredients

- Provide standards for identity, quality, purity, strength, packaging and labeling for bulk substances and other ingredients that may be used in compounded preparations



Atenolol

$C_{14}H_{22}N_2O_3$ 266.34

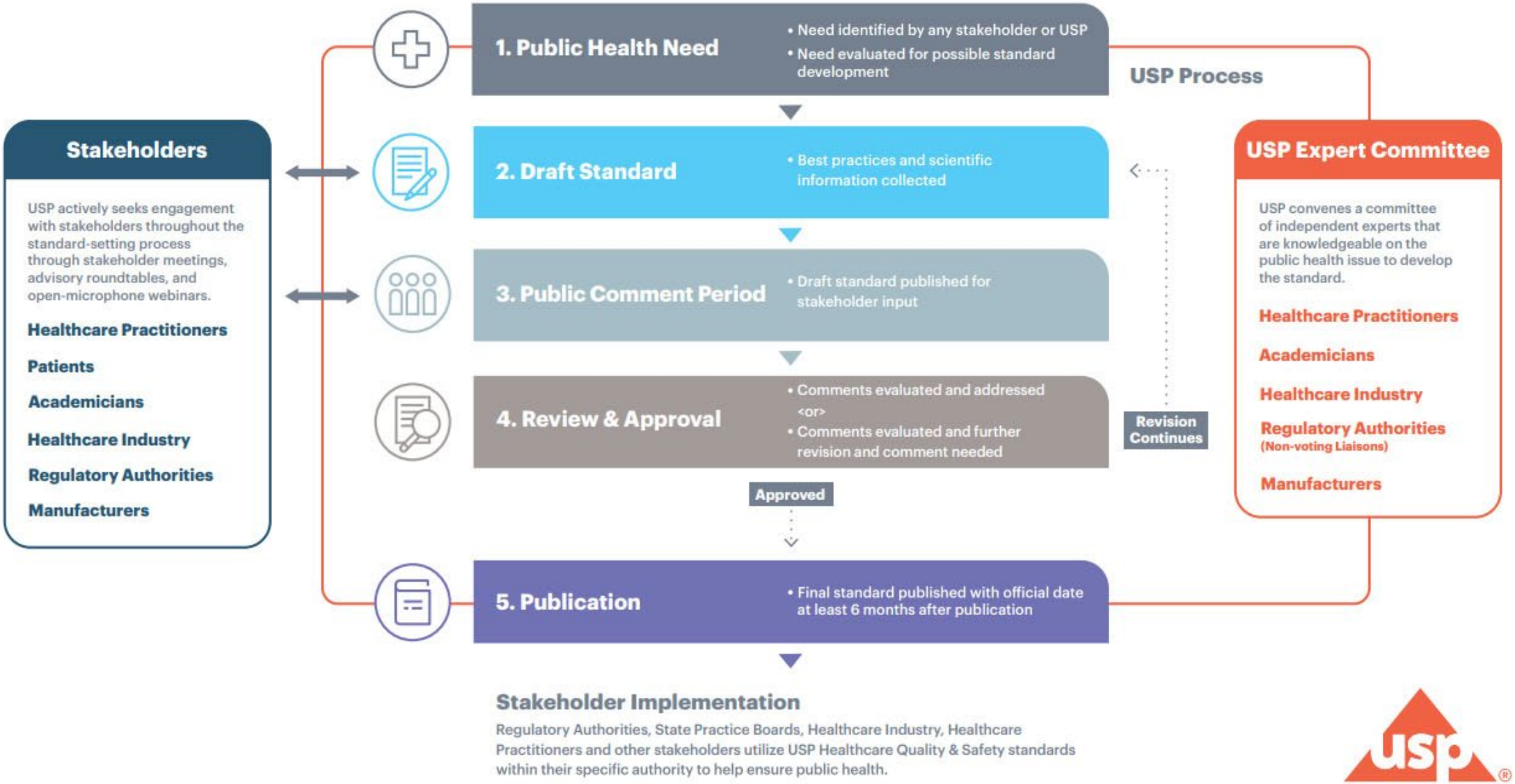
Benzeneacetamide, 4-[2-hydroxy-3-[(1-methylethyl)-amino]propoxy]-;
2-[*p*-[2-Hydroxy-3-(isopropylamino)propoxy]-phenyl]-acetamide [29122-68-7].

DEFINITION

Atenolol contains NLT 98.0% and NMT 102.0% of $C_{14}H_{22}N_2O_3$, calculated on the dried basis.

Pour the *Atenolol powder* into a suitable container. Wet the powder with a small amount of *Vehicle*, and triturate to make a smooth paste. Add the *Vehicle* to make the contents pourable. Transfer the contents stepwise and quantitatively to a calibrated container using the remainder of the *Vehicle*. Add sufficient *Vehicle* to bring to final volume. Shake to mix well.

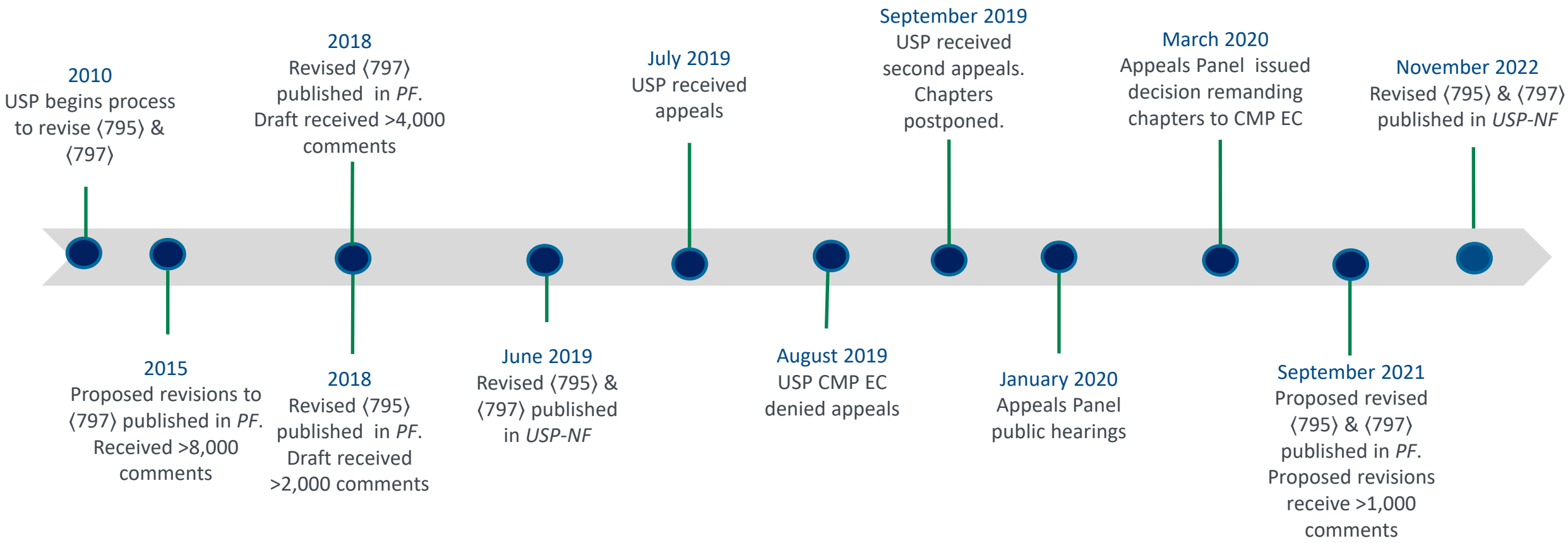
How We Work


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
Revision Continues
Approved
5. Publication
• Final standard published with official date at least 6 months after publication
USP Process
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.

History of ⟨797⟩

- **First Sterile Compounding Standard**
  - ⟨1074⟩ *Dispensing Practices for Sterile Drug Products Intended for Home Use* **(1992)**
  - ⟨1206⟩ *Sterile Drug Products for Home Use* **(1995)**
- **General Chapter ⟨797⟩**
  - Published in USP27-NF22 **(2004)**
    - Incorporated ⟨1206⟩
  - Revised in USP USP31-NF26 2S **(2008)**

History of Revisions



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 BUDs
  - Physical and chemical stability considerations
  - Sterility assurance
  - Operational implications
  - Balancing the need for patient access to cost-effective CSPs with rigorous quality standards
  - Implications on regulatory oversight and enforcement

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

⟨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

⟨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

⟨797⟩ Revisions

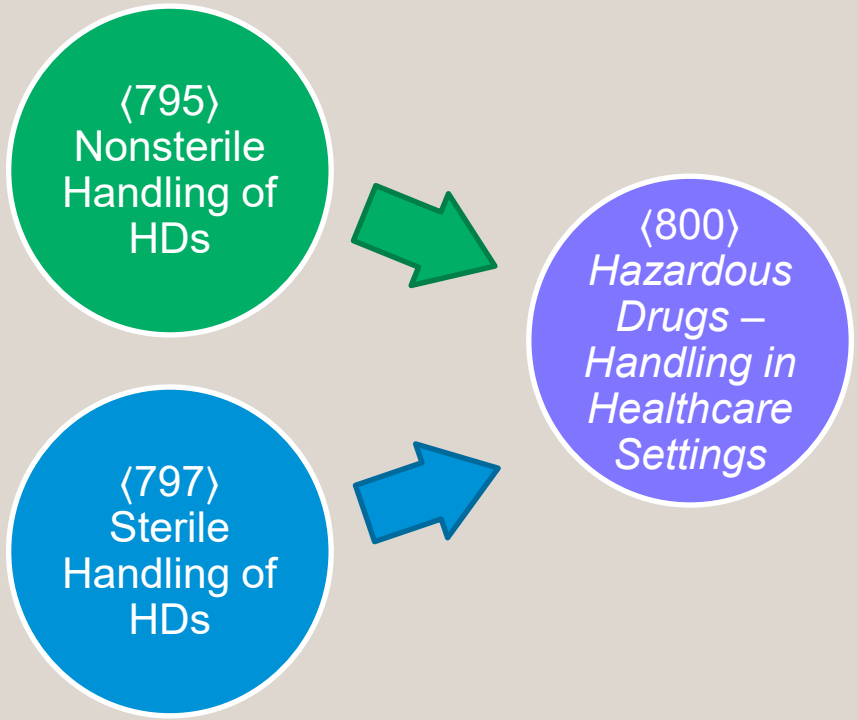
Administration is out of the scope of the chapter

- 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

⟨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*

⟨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 (e.g., *Validation of Alternative Microbiological Methods* ⟨1223⟩ and *Validation of Compendial Procedures* ⟨1225⟩).

⟨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 (e.g., 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.

⟨797⟩ Revisions

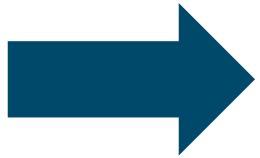
Preparation Per Approved Labeling

- 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

⟨797⟩ Revisions

Categories of CSPs

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



Category 1 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

Category 2 CSPs

- Must be prepared in a cleanroom suite
- May be assigned a BUD of > 12 hours at controlled room temperature or > 24 hours if refrigerated

Category 3 CSPs

- 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

⟨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.

⟨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

⟨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 (e.g., gown or coverall) • Low-lint covers for shoes • Low-lint cover for head that covers the hair and ears, and if applicable, cover for facial hair • Low-lint face mask • Sterile powder-free gloves • If using a RABS, (i.e., 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

⟨797⟩ Revisions

Minimum Garbing Requirements

Revised Chapter – Category 3

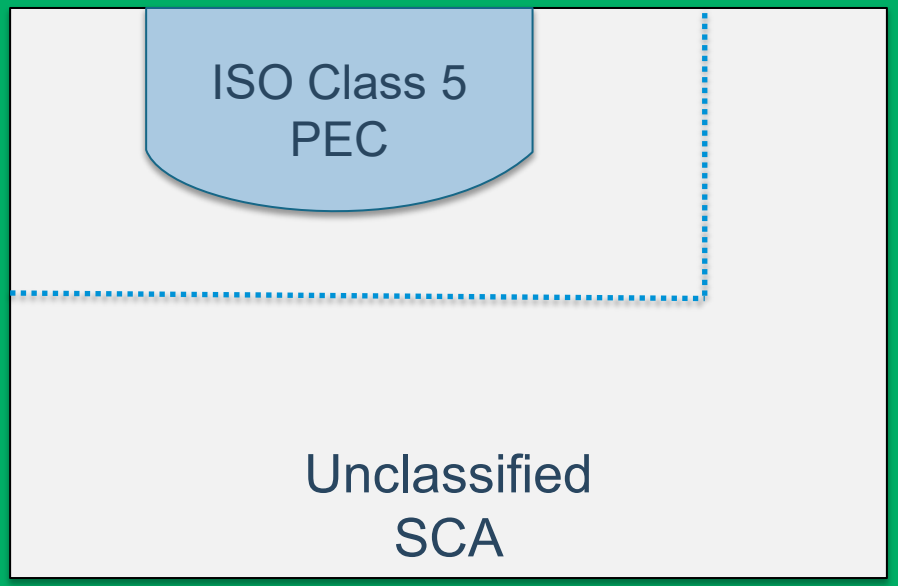
If the facility compounds Category 3 CSPs, additional garbing requirements must be continuously met in the buffer room in which Category 3 CSPs are prepared. The following additional garbing requirements must be followed in the buffer room where Category 3 CSPs are prepared for all personnel regardless of whether Category 3 CSPs are compounded on a given day:

1. Do not allow any exposed skin in the buffer room. (i.e., 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.

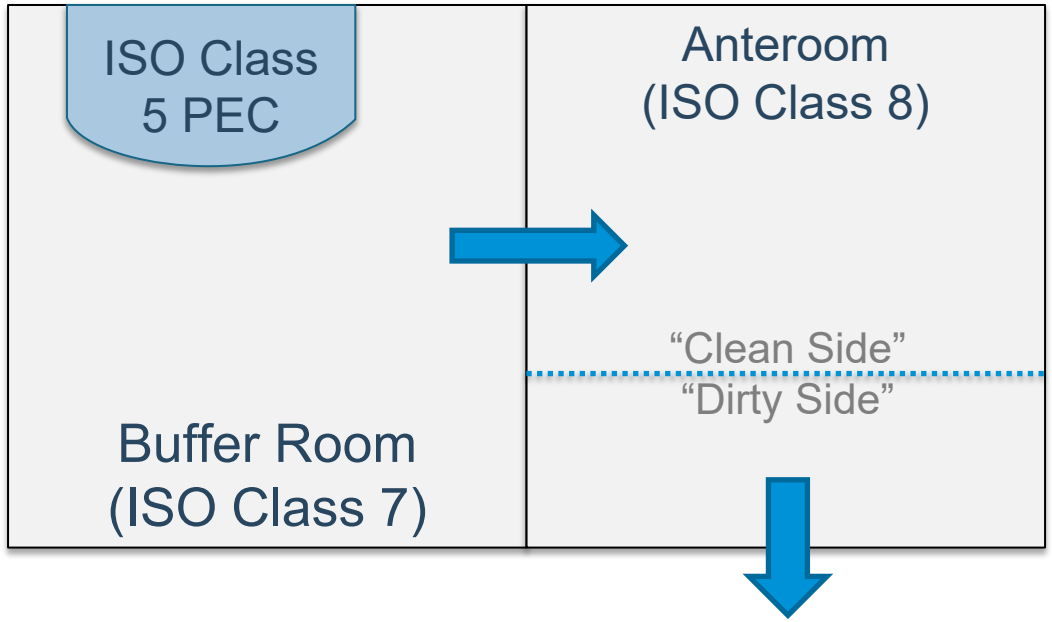
⟨797⟩ Revisions

Minimum PEC Placement

Category 1 CSPs



Category 2 or 3 CSPs



⟨797⟩ Revisions

Facility Requirements

- **For Category 1 CSPs**
  - All PECs may be placed in an unclassified SCA
- **For Category 2 and Category 3 CSPs**
  - LAFS and RABS must be placed in an ISO Class 7 positive-pressure buffer room with an ISO Class 8 positive-pressure anteroom

Laminar airflow system (LAFS)	Laminar airflow workbench (LAFW) Integrated vertical laminar flow zone (IVLFZ) Class II Biological safety cabinet (BSC)
Restricted-access barrier system (RABS)	Compounding aseptic isolator (CAI) Compounding aseptic containment isolator (CACI)

  - Isolators must be placed in an ISO Class 8 or better positive-pressure room

⟨797⟩ Revisions

Facility Requirements

- Added clarifications on **Air Exchange Requirements**
  - HEPA filters must be located in the ceiling
  - Returns must be low on the wall

Compounding Area	ACPH Requirement
Unclassified SCA	No requirement
ISO Class 7 room(s)	≥ 30 ACPH
ISO Class 8 room(s)	≥ 20 ACPH

- **Water Sources**
  - Sink may be placed inside or outside the anteroom
  - Buffer room must not contain water sources

⟨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

⟨797⟩ Revisions

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

⟨797⟩ Revisions

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 (e.g., wipers, sponges, pads, and mop heads)
  - Must be low-lint
  - Should be disposable
  - Reusable cleaning tools must be dedicated for use

⟨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 (e.g., handles should not be made of wood or any other porous material) and must be cleaned and disinfected before and after each use

⟨797⟩ Revisions

Component Selection

- Conventionally manufactured sterile products should be used when available and appropriate for the intended CSP
- Active pharmaceutical ingredients (APIs):
  - Must comply with the criteria in the *USP–NF* monograph, if one exists
  - Must have a certificate of analysis (COA) that includes the specifications (e.g., 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 (e.g., 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

⟨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

⟨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

⟨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

⟨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

⟨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 (e.g., 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

⟨797⟩ Revisions

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**

⟨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

⟨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**

⟨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
		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

⟨797⟩ Revisions

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

⟨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

⟨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

⟨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

⟨797⟩ Revisions

Use of CSPs as Components

- Addresses the use of CSPs (e.g., 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

⟨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

⟨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

Next Steps

Next Steps

- 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

Thank You

The standard of trust