Welcome

The standard of trust

Open Forum Session

Revisions to *USP* General Chapter ⟨795⟩ *Pharmaceutical Compounding – Nonsterile Preparations*

November 8, 2022
10:00 AM - 12:00 PM ET

General Chapter ⟨795⟩ Open Forum

NOTICE TO PARTICIPANTS:

- Please note this session is currently being recorded and will be made available on the USP website
- Disclaimer
  - This open forum is for informational purposes only

Agenda

Session Overview	Speakers
Welcome	Selma Mitiche, Senior Scientist II, Personalized Medicines
• USP Overview • Background • Overview of Revised General Chapter ⟨795⟩ *Pharmaceutical Compounding – Nonsterile Preparations*	Brenda Jensen, Chair, Compounding Expert Committee Gus Bassani, Chair, ⟨795⟩ Subcommittee
Next Steps	Selma Mitiche, Senior Scientist II, Personalized Medicines
Question & Answer Session	**Moderator:** Selma Mitiche, Senior Scientist II, Personalized Medicines **Panelists:** Compounding Expert Committee

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 Seibel

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 Ornaf

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
Donald Singer

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

Chair: Brenda Jensen, MBA, Owner and Compounding Pharmacy Consultant, Compounding Consultants, LLC
Vice Chair: Robert Shrewsbury, Ph.D., Associate Professor, UNC Eshelman School of Pharmacy

EC Member	Affiliation
Lisa Ashworth, B.S. Pharm.	Compounding Specialist and Clinical Pharmacist, Children's Health System of Texas
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
Vanessa Pinheiro, M.S., B.S. Pharm.	Pharmacist and Consultant, Medisca and LP3 Network
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
Connie Sullivan, B.S. Pharm.	President and CEO, National Home Infusion Association

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

USP Process

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 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

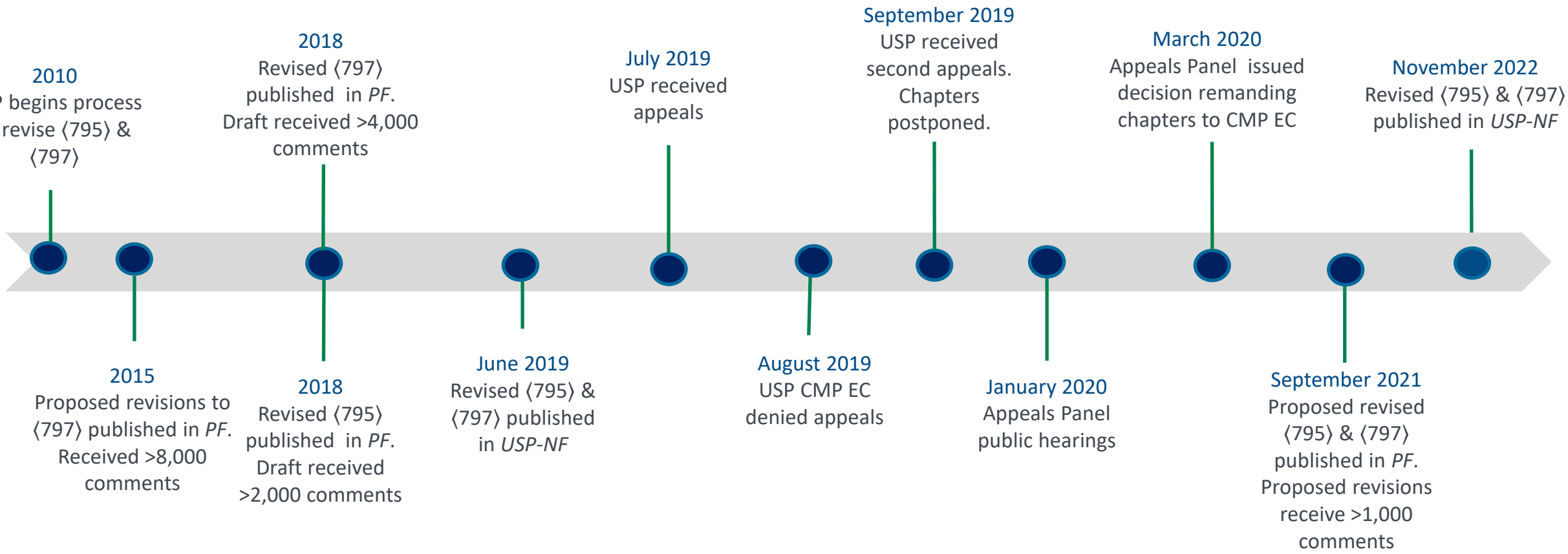
Stakeholder Implementation

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 ⟨795⟩

- **First Nonsterile Compounding Standard**
  - *USP* ⟨1161⟩ *Pharmacy Compounding Practices* **(1996)**
- **General Chapter ⟨795⟩**
  - Published in USP 24–NF 19 **(2000)**
  - Revised in USP 27–NF 22 **(2004)**
  - Revised in USP 34–NF 29 **(2011)**
    - Incorporated *USP* ⟨1075⟩ *Good Compounding Practices*
  - Revision Bulletin **(2014)**
    - Clarified that the BUDs in ⟨795⟩ are specific for nonsterile preparations and do not apply to sterile preparations

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
  - Operational implications
  - Balancing the need for patient access to cost-effective CNSPs with rigorous quality standards
  - Implications on regulatory oversight and enforcement

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

Purpose of Current Revision

- **Purpose of Current Revision**
  - To review latest science and best practices
  - To respond to stakeholder input received throughout the last cycle and after the 2019 appeals
  - To clarify topics that are frequently queried and misconstrued
  - To align with published ⟨800⟩ and revisions for ⟨797⟩

- **Previous ⟨795⟩ and 2019's Remanded Revisions Served as Templates for this Revision**
  - Many sections were "summary" statements and were expanded to add clarity and additional information
  - Revision was modeled alongside the revisions for ⟨797⟩

⟨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

⟨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

⟨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

⟨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

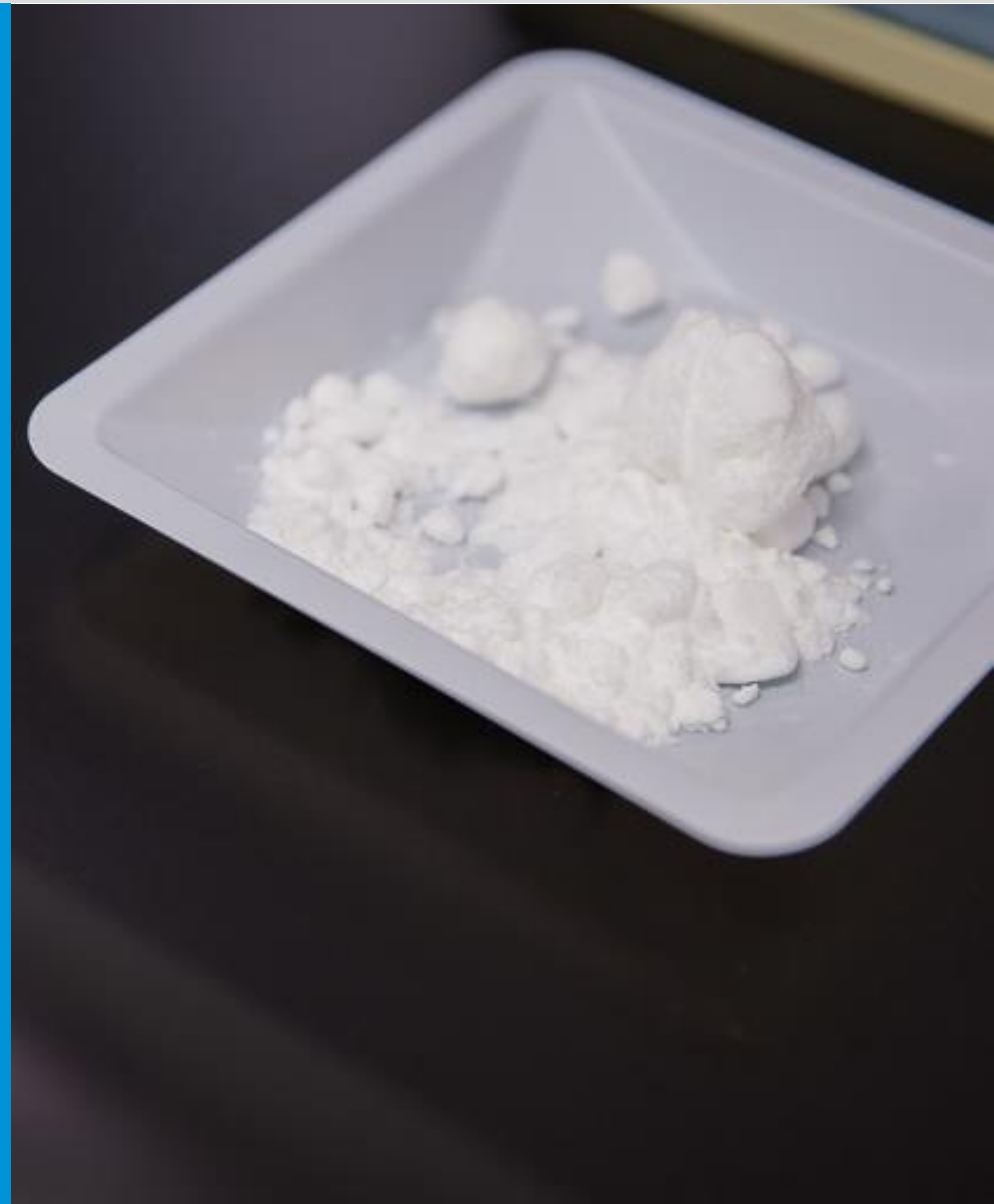
Section 5. Cleaning and Sanitizing

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

⟨795⟩ Revisions

Section 6. Equipment and Components

- Weighing, measuring, or otherwise manipulating components that could generate airborne chemical particles (e.g., 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 Enclosure (CVE) must be cleaned and sanitized
  - CVE must be certified at least annually
- Components
  - In the United States, APIs must be manufactured by an FDA-registered facility
    - Each API must be accompanied by a valid 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



⟨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 (e.g., 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)

⟨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

⟨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 (e.g., 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 (e.g., capsules, tablets, granules, powders, nonaqueous topicals, suppositories, and troches or lozenges).

⟨795⟩ Revisions

Nonaqueous Dosage Forms: a_w < 0.6		
Dosage Form	**Description**	**a_w**
Animal treat	Animal treat (oil flavor)	0.507
Capsule (oil filled)	Olive oil encapsulated	0.468
Capsule (powder filled)	Powder base encapsulated	0.435
Gel (glycol based)	Propylene glycol, ethoxy diglycol, or hydroxypropyl cellulose gel	0.056
Lollipop (sorbitol based)	Sorbitol-based lollipop	0.460
Ointment	Hydrophilic petrolatum	0.396
Ointment	Polyethylene and mineral oil gel base	0.459
Oral solution (glycol based)	20% Polyethylene glycol and 80% propylene glycol	0.009
Oral solution (oil based)	Medium chain triglycerides oil	0.338
Oral suspension (fixed oil)	Fixed oil with thickener	0.403
Powder for inhalation	Encapsulated powder for inhalation	0.402
Stick	Lip balm	0.181
Suppository	Polyethylene glycol base	0.374
Suppository	Fatty acid base	0.385
Tablet (compressed)	Compressed tablet	0.465
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

Aqueous Dosage Forms: a_w ≥ 0.6		
Dosage Form	**Description**	**a_w**
Animal treat	Animal treat with 15%–18% aqueous flavor	0.716
Cream	Cream vehicle (oil in water emulsion, petrolatum free)	0.968
Cream	Emollient cream (petrolatum and mineral oil)	0.984
Cream	Cream (oil in water emulsion with natural oils)	0.989
Foam	Foaming surfactant solution	0.983
Gel (water based)	Alcohol-free aqueous gel	0.990
Gel (water based)	Hydroxypropyl methylcellulose (HPMC) gel	1.000
Lotion	Lotion (oil in water emulsion)	0.986
Nasal spray	Nasal spray	0.991
Oral solution (water based)	Low-sucrose syrup vehicle	0.906
Oral solution (water based)	90% Water and 10% glycerin	0.958
Oral suspension (water based)	Oral suspension base	0.992
Rinse	Polymer gel with 30% water	0.960
Shampoo	Shampoo	0.976
Simple syrup	Simple syrup	0.831
-	-	-
-	-	-
-	-	-

⟨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

⟨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

⟨795⟩ Revisions

Section 13. CNSP Packaging and Transporting

Section 14. Documentation

Glossary

Next Steps

Next Steps

- The Compounding Expert Committee decided to delay the implementation of the ⟨795⟩ revision until November 1, 2023
- USP Compounding Workshop
  - February 7, 2023, 8:00 AM – 5:30 PM ET
  - February 8, 2023, 8:00 AM – 3:30 PM ET
- 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://www.usp.org/events-training/search?type%5B0%5D=event_types%3AExpert%20Committee/Panel%20Meeting

Question and Answer Session

2020 – 2025 Compounding Expert Committee

EC Member	Affiliation
Brenda Jensen, MBA	Owner and Compounding Pharmacy Consultant, Compounding Consultants, LLC
Robert Shrewsbury, Ph.D.	Associate Professor, UNC Eshelman School of Pharmacy
Lisa Ashworth, B.S. Pharm.	Compounding Specialist and Clinical Pharmacist, Children's Health System of Texas
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
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Rick Rhoads, Pharm.D.	Director of Compounding, University Compounding Pharmacy
Connie Sullivan, B.S. Pharm.	President and CEO, National Home Infusion Association

Alan Parr, Pharm.D., Ph.D. (*advisor*)	Director of Biopharmaceutics, BioCeutics, LLC
Brenda Yuzdepski, B.S. Pharm. (*advisor*)	Owner and CEO, Medical Arts Pharmacy

Thank You

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Sign up for updates: https://www.usp.org/hqs-signup-form

Email questions to CompoundingSL@USP.org

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