Welcome

The standard of trust

Open Forum Session

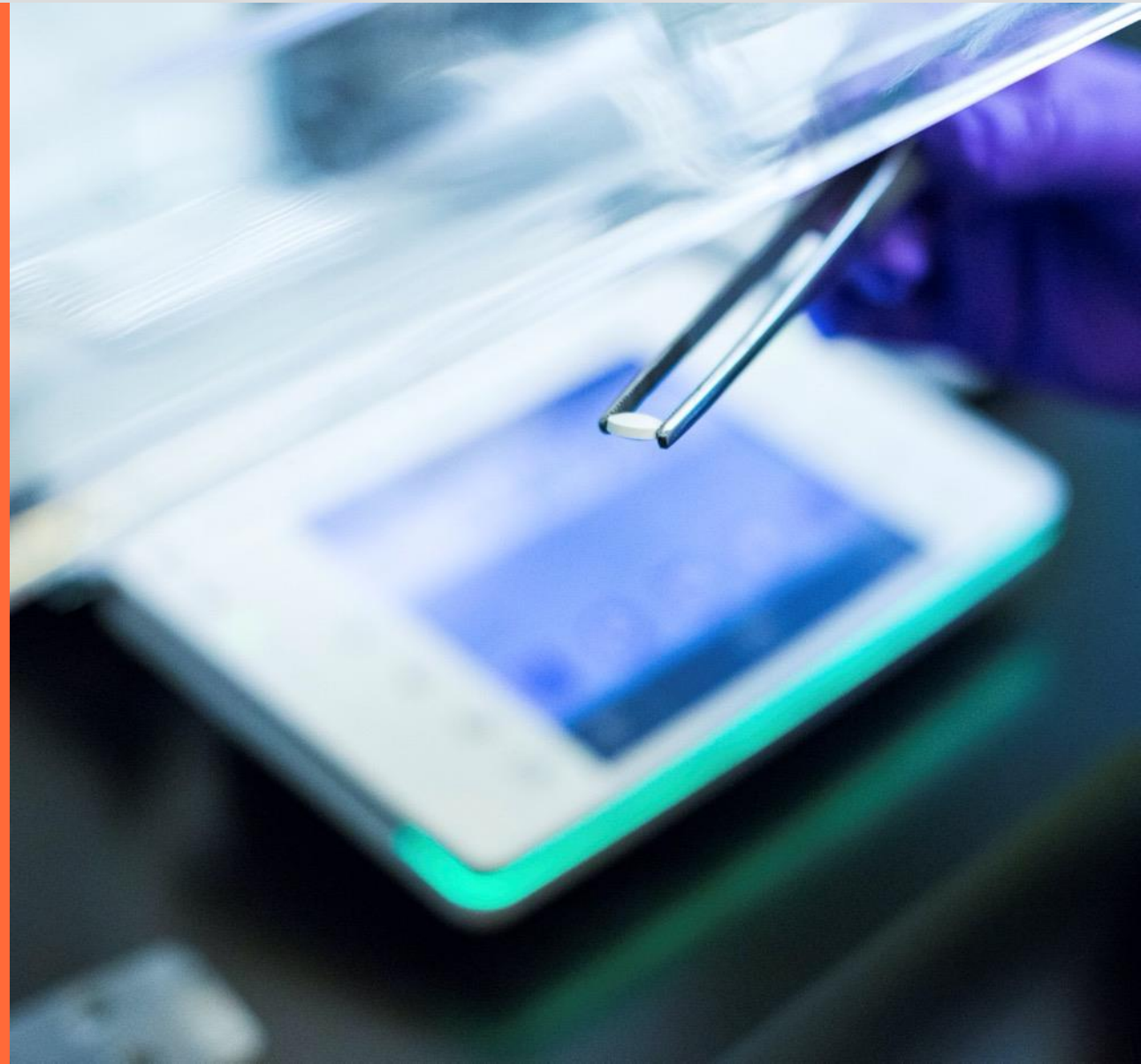
Proposed Revisions to USP General Chapter ⟨795⟩ *Pharmaceutical Compounding – Nonsterile Preparations*

January 12, 2022
10:00 AM - 12:00 PM EDT

General Chapter ⟨795⟩ Open Forum

NOTICE TO PARTICIPANTS:

- To minimize background noise, all lines will be muted upon joining the session
- During the meeting, you may ask questions at any time by using the **Q&A** function
  - Select the Q&A icon on the bottom right-hand column of your WebEx view page
  - Use the text box at the bottom to enter your question, and hit send
- Questions will be collated for the Q&A portion of the session



General Chapter ⟨795⟩ Open Forum

NOTICE TO PARTICIPANTS:

- Please note this session is currently being recorded and will be made available on USP's website at http://www.usp.org/compounding/general-chapter-795
- Disclaimer
  - This open forum is for informational purposes only
  - All comments must also be submitted via the public comment form

Agenda

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

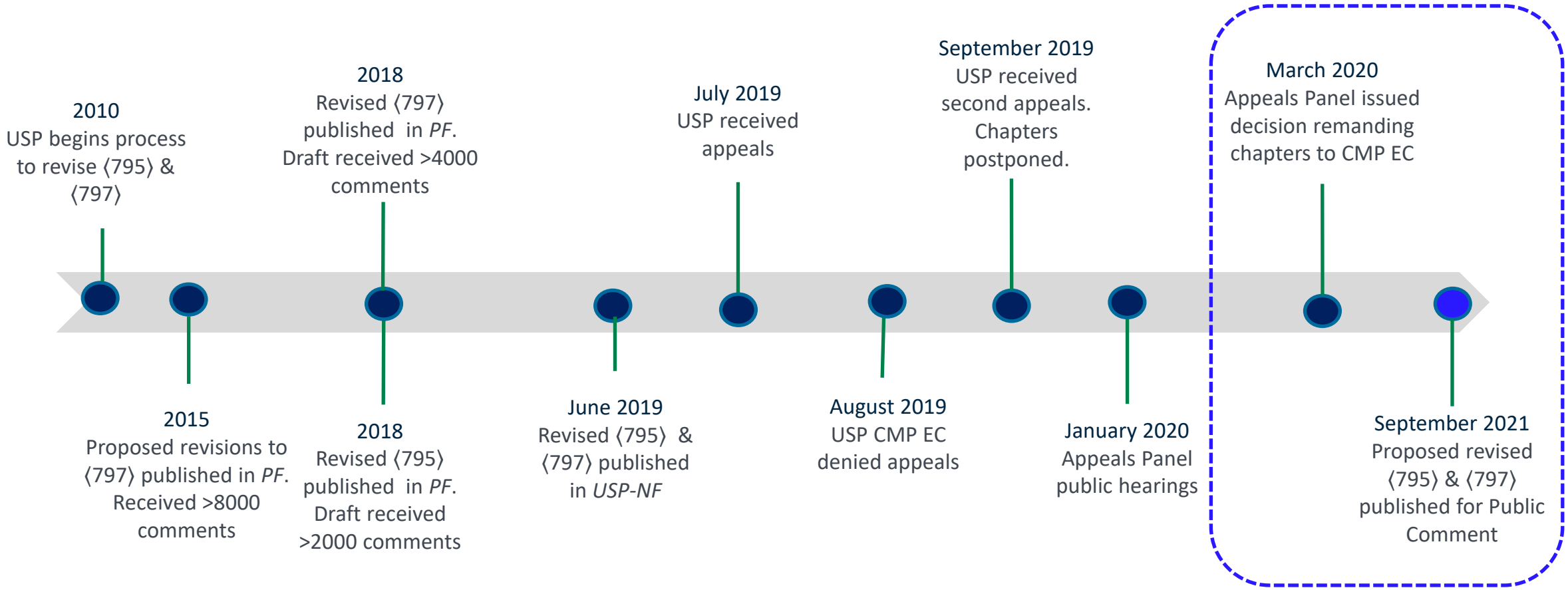
Stakeholder Implementation

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
    - CURRENTLY OFFICIAL

History of Revisions and Appeals



Approach to Revisions after the Appeals

- The Appeals Panel held public hearings in January 2020 regarding the proposed ⟨795⟩ chapter
  - The Appeals Panel remanded the proposed chapter to the Compounding Expert Committee (CMP EC) with a recommendation for further engagement on the issues raised by stakeholders, particularly concerning beyond-use date (BUD) provisions
  - The Appeals Panel did not determine the chapters to require revision, but noted that the issues raised in the appeals warranted additional dialogue and consideration
  - It was left to the purview of the CMP EC to determine the appropriateness of future revisions to the chapter, if any

Approach to Revisions after the Appeals

- 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

- **Proposal 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 revision efforts for ⟨797⟩
- **Current ⟨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 proposal was modeled alongside current revision efforts for ⟨797⟩
- **Inclusion of Supplementary Materials**

⟨795⟩ Overview

Proposed 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
- 9. Labeling
- 10. Establishing Beyond-Use Dates
- 11. SOPs
- 12. Quality Assurance and Quality Control
- 13. CNSP Packaging and Transporting
- 14. Complaint Handling and Adverse Event Reporting
- 15. Documentation
- Glossary

⟨795⟩ Proposed 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 individual responsible and accountable for the performance and operation of the facility and personnel

⟨795⟩ Proposed 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⟩ Proposed Revisions

Section 4. Buildings and Facilities

- Added requirement for a designated space for nonsterile compounding
- Area must be designed and controlled to provide well-lighted comfortable conditions for garbed personnel
- Surfaces in a compounding area must be cleanable and clean

Section 5. Cleaning and Sanitizing

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

⟨795⟩ Proposed Revisions

Section 6. Equipment and Components

- Any weighing, measuring, or other manipulation of an API or added substance in powder form that can generate airborne contamination from drug particles must occur inside a containment device (i.e., powder containment hood).
  - Containment Ventilated Enclosure (CVE) must be cleaned
  - CVE must be certified annually
- Components
  - APIs must be manufactured by an FDA-registered facility
    - Each API must be accompanied by a valid COA
  - Ingredients other than APIs should be obtained from an FDA-registered facility
  - Packages of ingredients that lack vendor expiration must not be used after 1 year from the date of receipt

⟨795⟩ Proposed Revisions

Section 7. Master Formulation And Compounding Records

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

Section 8. Release Inspections

- 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 immediate container)
- Requirements for *labeling* (all matter on container or in package or wrapper)

⟨795⟩ Proposed 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⟩ Proposed Revisions

Section 10. Establishing Beyond-Use Dates

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

Type of Preparation	BUDs (days)	Storage Temperature [a]
Aqueous Dosage Forms ($a_w \geq 0.6$)		
Non-preserved aqueous dosage forms [b]	14	Refrigerator
Preserved aqueous dosage forms [b]	35	Controlled room temperature or refrigerator
Nonaqueous Dosage Forms ($a_w < 0.6$)		
Oral liquids (nonaqueous) [c]	90	Controlled room temperature or refrigerator
Other nonaqueous dosage forms [d]	180	Controlled room temperature or refrigerator

a See *Packaging and Storage Requirements* ⟨659⟩.
b An aqueous preparation is one that has an a_w of ≥ 0.6 (e.g., emulsions, gels, creams, solutions, sprays, or suspensions).
c A nonaqueous liquid is one that has an a_w of < 0.6 .
d Capsules, tablets, granules, powders, nonaqueous topicals, suppositories, troches.

⟨795⟩ Proposed Revisions

Nonaqueous Dosage Forms: a_w < 0.60			Aqueous Dosage Forms: a_w ≥ 0.60		
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	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 (gelatin)	Gelatin troche with NMT 3% aqueous flavor	0.332	-	-	-
Troche (glycol based)	Polyglycol troche with NMT 3% aqueous flavor	0.571	-	-	-

⟨795⟩ Proposed 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 specific API, CNSP, and type of container closure that will be used
  - An aqueous CNSP must first be tested for ⟨51⟩ antimicrobial effectiveness at the end of the proposed BUD
    - Bracketing can be utilized to provide flexibility
  - If compounding from a *USP–NF* compounded preparation monograph, 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

Supplementary Materials

⟨795⟩ Supplementary Materials

DISCLAIMER

- These supplemental documents are **not part of the proposed chapters**, are **not comprehensive overviews** of the proposed chapters, and are **not intended to be used in place** of the proposed chapters

- These documents **do not reflect the CMP EC's opinions on further revisions to the chapters**

- These documents are **not intended to be subject to public comment**
  - Stakeholders are encouraged to submit comments on the proposed chapters for the CMP EC to continue to evaluate revisions to the chapters
  - The CMP EC will consider all comments received on the chapters

- Please note that **neither the proposed chapters nor these documents are official *United States Pharmacopeia – National Formulary* (*USP–NF*) text**, and they are not intended to be enforceable by regulatory authorities
  - Users must refer to the *USP–NF* for official text

⟨795⟩ Supplementary Materials

- BUD Reference for the 2021 Proposed Revisions to ⟨795⟩
  - Resource for assigning proposed BUDs
- CMP EC Responses to Stakeholder Engagement Themes for the 2021 Proposed Revisions to ⟨795⟩
  - Responses and proposed chapter revisions made based on stakeholder engagement
- BUD Scientific Rationale for the 2021 Proposed Revisions to ⟨795⟩
  - Evolution of USP's BUD standards for compounded preparations
  - Rationale for the proposed BUD limits
- Stability Study Reference Document for the 2021 Proposed Revisions to ⟨795⟩ and ⟨797⟩
  - Explanation of the details and purpose of stability studies
  - Resources for conducting a study
- All supplementary resources are posted online with the proposed chapters
  - https://go.usp.org/Proposed_2021_Revisions_795_797

Submitting Comments

Submitting Comments

- All information related to ⟨795⟩ is on the USP Compounding Page
  - http://www.usp.org/compounding/general-chapter-795
- The proposed chapters and supplementary materials are posted online at
  - https://go.usp.org/Proposed_2021_Revisions_795_797
- The ⟨795⟩ electronic submission form is at
  - https://usp.az1.qualtrics.com/jfe/form/SV_3OBK7VUbvver6zs

⟨795⟩ Public Comment Form

Link to the public comment form can also be found in the briefing statement of the chapter

BRIEFING

⟨795⟩ Pharmaceutical Compounding—Nonsterile Preparations. To improve clarity and respond to stakeholder input, the Compounding Expert Committee proposes to revise this chapter with the following major edits:

1. Expand guidance for assigning beyond-use dates (BUDs) for compounded nonsterile preparations (CNSPs) in the absence of stability information.
2. Elaborate on the role of water activity (a_w) in determining BUD limits for preparations.
3. Add a table of commonly compounded dosage forms and their respective a_w values to aid compounders in determining BUD limits for CNSPs.
4. Clarify the requirements for identifying the need for a recall and related procedures.

A copy of this proposal and additional supplementary materials are posted online here.
Please submit comments using the electronic submission form here.
Additionally, minor editorial changes have been made to update this chapter to current *USP* style.

⟨795⟩ Public Comment Form

Public Comments requested through the electronic submission form

Welcome to the electronic form for submitting your comments on USP's proposed **General Chapter <795> *Pharmaceutical Compounding – Nonsterile Preparations.***

USP General Chapter <795> provides standards for compounding quality nonsterile preparations. The chapter describes requirements for the compounding process, facilities, equipment, components, documentation, quality controls, and training.

The USP Compounding Expert Committee proposes to revise General Chapter <795> to improve clarity and respond to stakeholder input. The revision proposal is available at www.uspnf.com/notices/general-chapter-795-proposed-revisions.

If you have any questions, please email CompoundingSL@usp.org.

Please enter your contact information

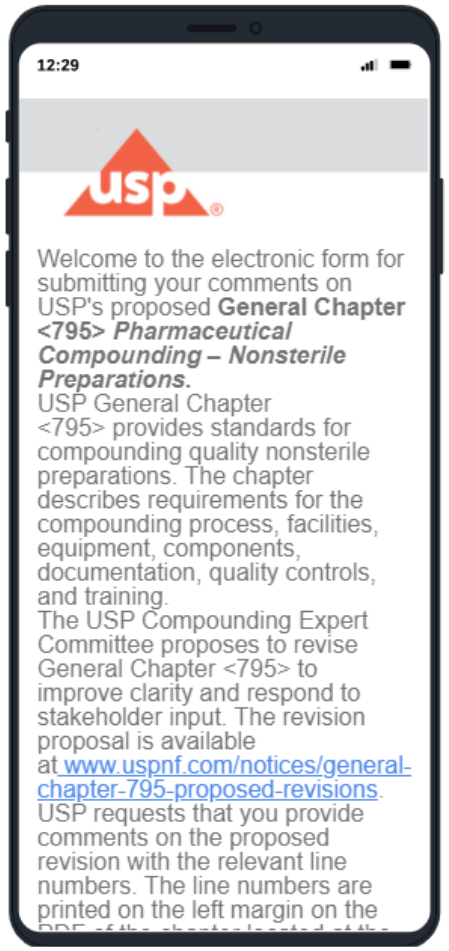
First Name

Last Name

Email

Title

Organization



⟨795⟩ Public Comment Form

Please enter your contact information

First Name

Last Name

Email

Title

Organization

Address

Address 1

Address 2

City

State

Zip

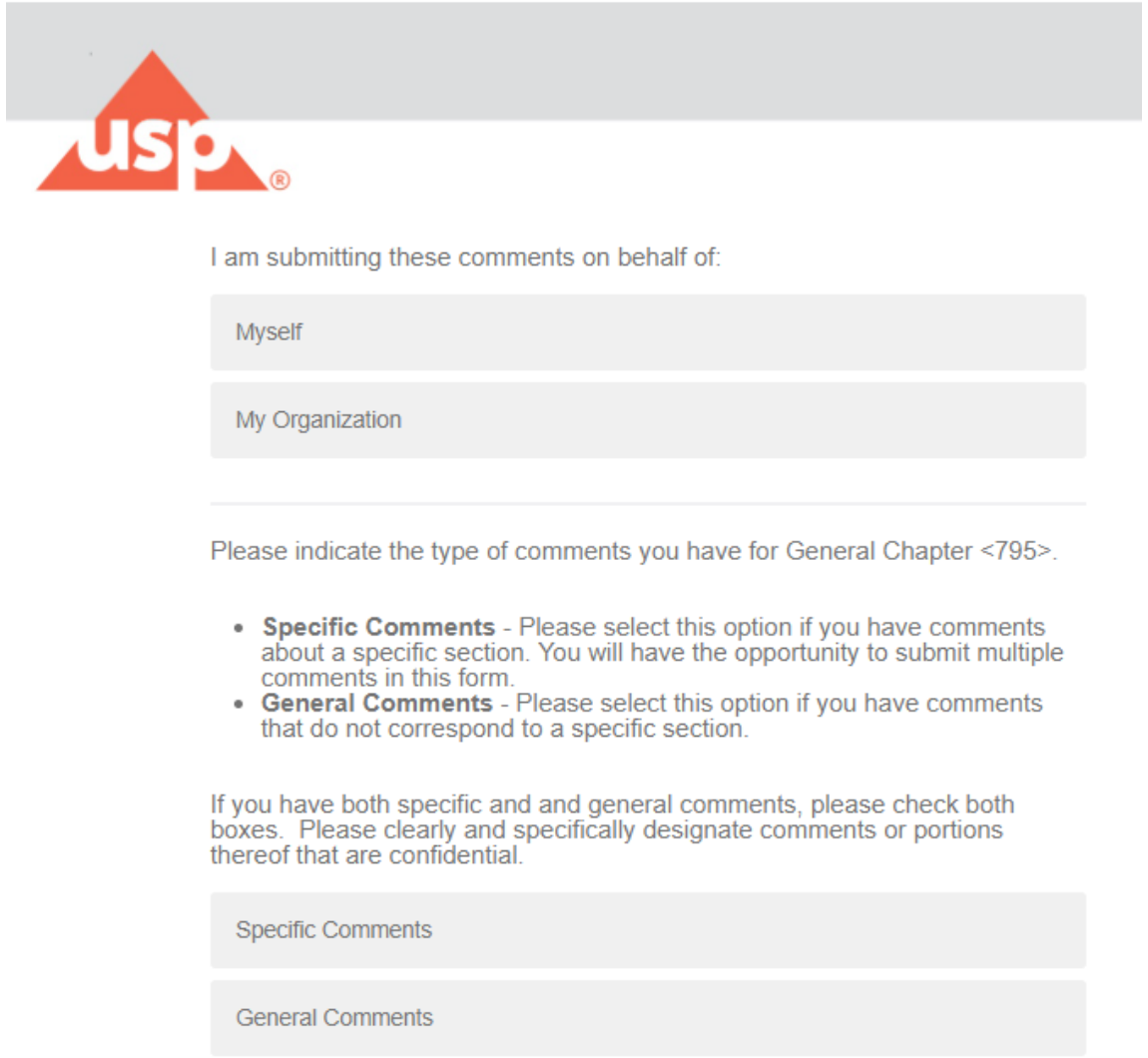
Country

Please select the type of organization that most closely represents where you work

- Government Agency
- Health Plan
- Healthcare Association
- Healthcare Practitioner
- Healthcare Professional Associations
- Patient

→

⟨795⟩ Public Comment Form



I am submitting these comments on behalf of:

Myself

My Organization

Please indicate the type of comments you have for General Chapter <795>.

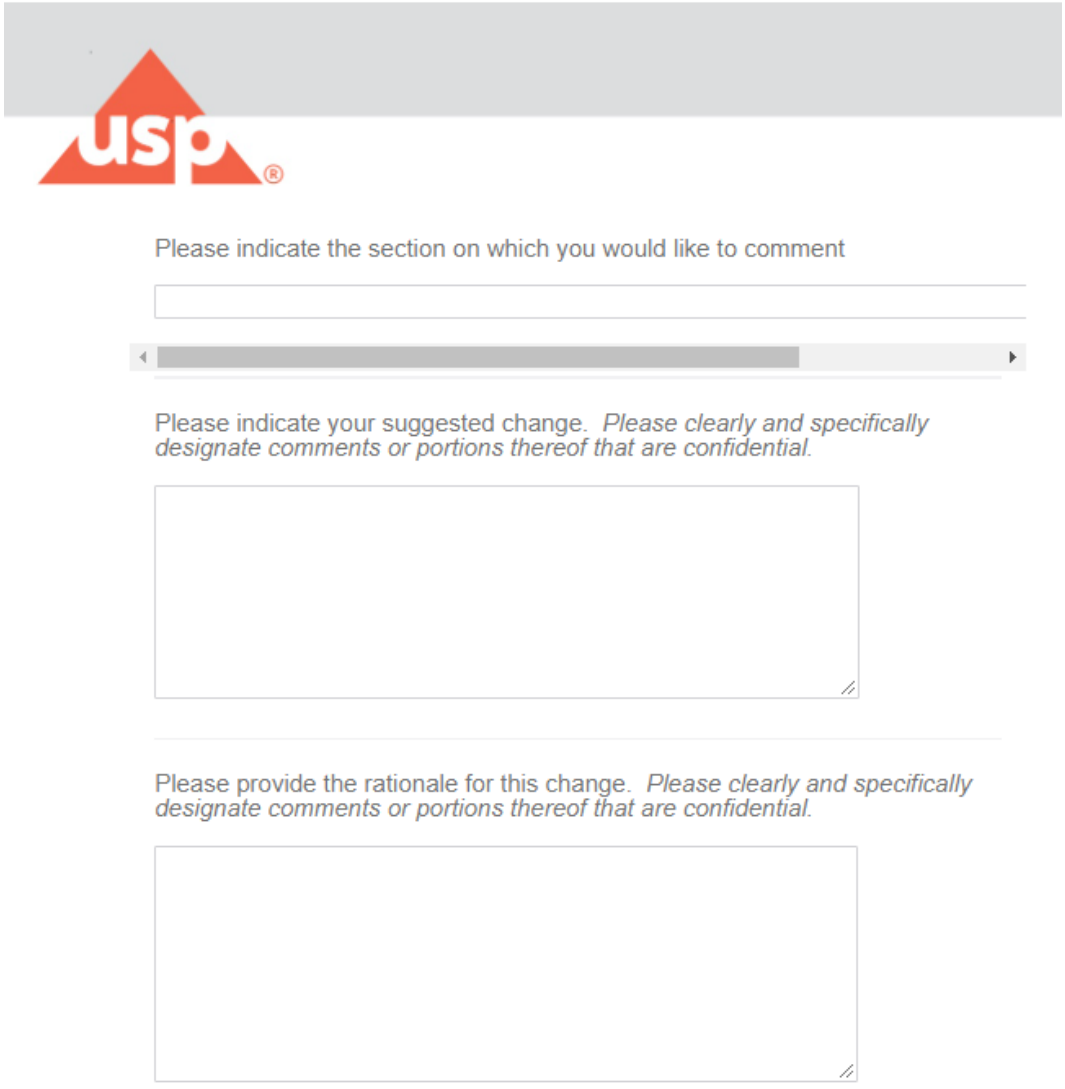
- **Specific Comments** - Please select this option if you have comments about a specific section. You will have the opportunity to submit multiple comments in this form.
- **General Comments** - Please select this option if you have comments that do not correspond to a specific section.

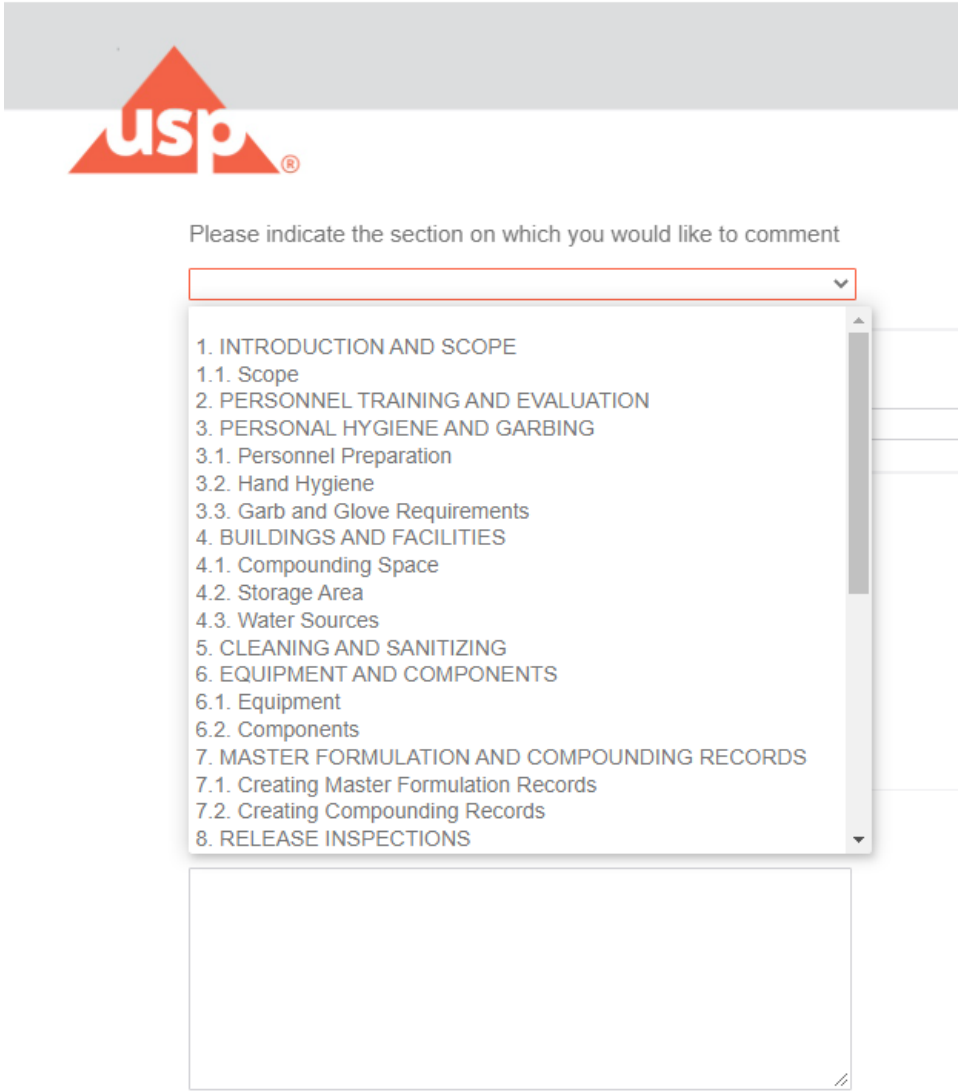
If you have both specific and and general comments, please check both boxes. Please clearly and specifically designate comments or portions thereof that are confidential.

Specific Comments

General Comments

⟨795⟩ Public Comment Form





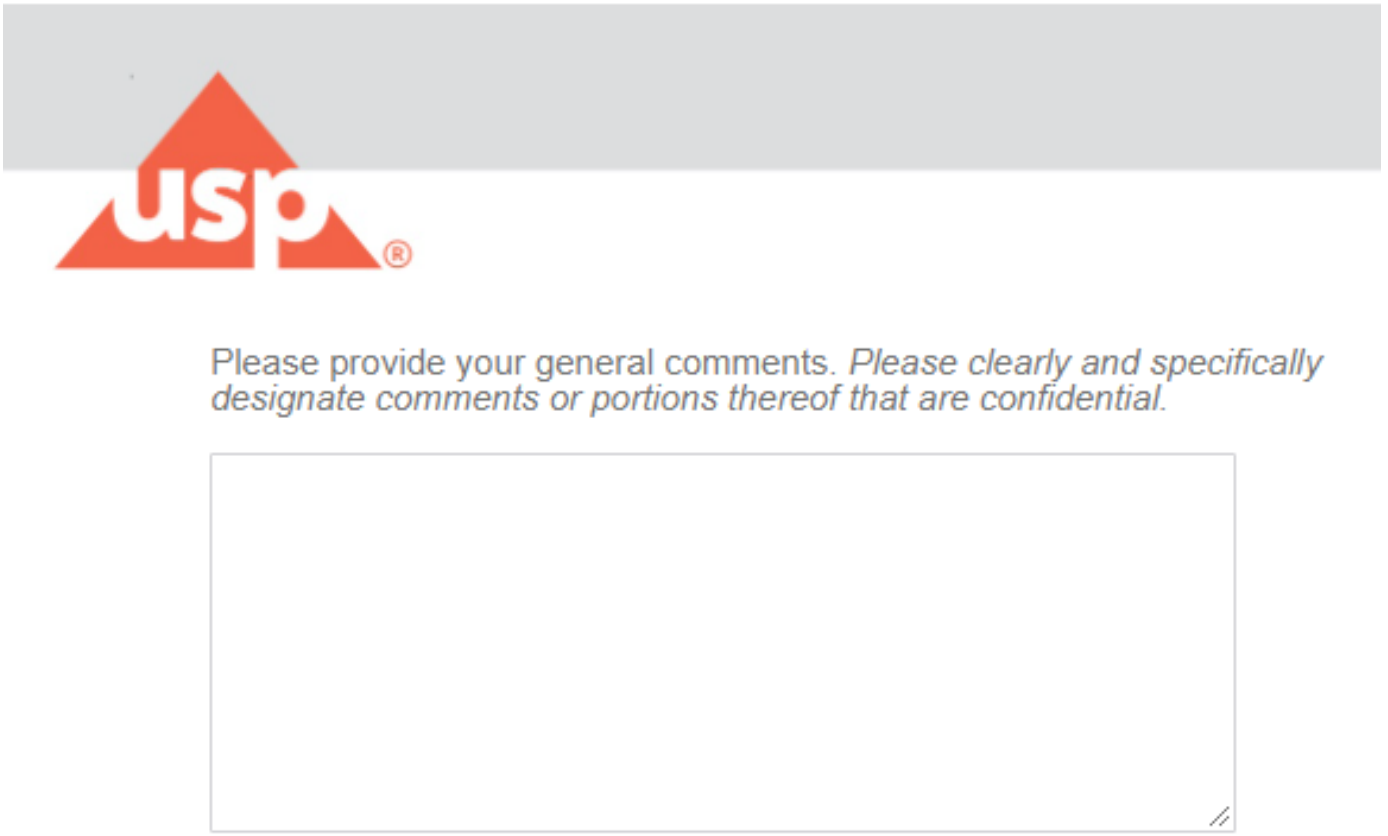
⟨795⟩ Public Comment Form

Do you have additional specific comments you would like to share?

Yes

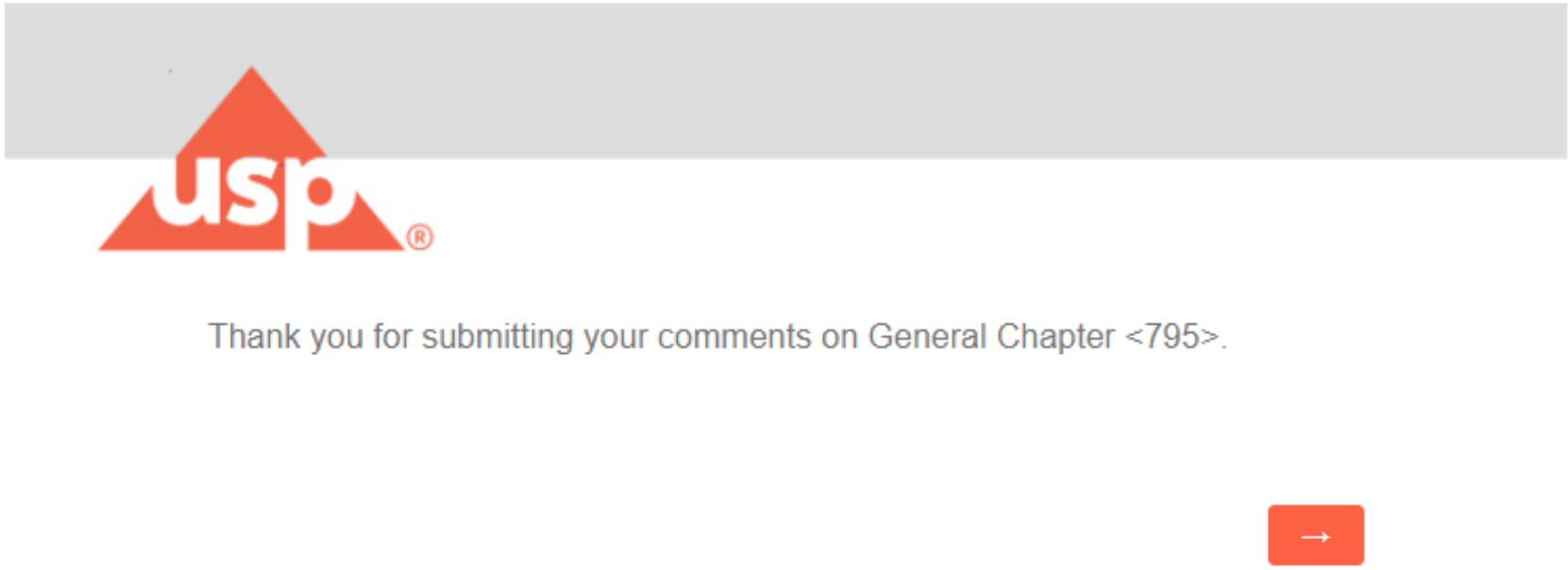
No

⟨795⟩ Public Comment Form



Please provide your general comments. *Please clearly and specifically designate comments or portions thereof that are confidential.*

⟨795⟩ Public Comment Form



Next Steps

⟨795⟩ Revision Proposal

Next Steps

- Stakeholders submit comments for the chapters by January 31, 2022, using the electronic forms
  - The Compounding Expert Committee will review all comments as they consider revisions to the chapters
  - Comments will be addressed through commentary posted on the USP website

- 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
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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

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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Stay Connected

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

Email questions to CompoundingSL@USP.org

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