Open Forum Session

Revisions to *USP* General Chapter 〈795〉
*Pharmaceutical Compounding – Nonsterile Preparations*

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

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<th>Welcome</th>
<th>Selma Mitiche, Senior Scientist II, Personalized Medicines</th>
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<td>• USP Overview</td>
<td>Brenda Jensen, Chair, Compounding Expert Committee</td>
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<td>• Background</td>
<td>Gus Bassani, Chair, 〈795〉 Subcommittee</td>
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| • Overview of Revised General Chapter 〈795〉  
*Pharmaceutical Compounding – Nonsterile Preparations* | |

### 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
- Monographs 1–6: Peptides & Oligonucleotides
  - Michael De Felippe

Small Molecules
- Monographs 6–16: Proteins
  - Wendy Saffill-Clemmer
- Monographs 17–22: Complex Biologics & Vaccines
  - Elad Ziblackis

Excipients
- Monographs 23–33: Biologics
  - Matthew Borra

General Chapters
- Monographs 34–44: Advanced Therapies
  - Mehrdad Aalai

Healthcare Quality & Safety
- Monographs 45–55: Nomenclature & Labeling
  - Stephanie Crawford
- Monographs 56–66: Healthcare Safety & Quality
  - Melody Ryan

Dietary Supplements & Herbal Medicines
- Monographs 67–77: Compounding
  - Branda Jensen
- Monographs 78–83: Healthcare Information & Technology
  - Jeanine Tuttle

Dietary Supplements Admission
- Monographs 84–90: Botanical Dietary Supplements
  - Robin Mares
- Monographs 91–97: Non-botanical Dietary Supplements
  - Guido F. Pauli

Food Ingredients
- Monographs 98–100: Evaluation & Labeling
  - Tammie Low Dog
- Monographs 101–103: 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

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How we work

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
   - Comments evaluated and further revision and comment needed

5. Publication
   - Final standard published with official date at least 6 months after publication

Stakeholder Implementation

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
Academics
Healthcare Industry
Regulatory Authorities (Non-voting Liaisons)
Manufacturers

Stakeholders
USP actively seeks engagement with stakeholders throughout the standard-setting process through stakeholder meetings, advisory roundtables, and open-microphone webinars.

Healthcare Practitioners
Patients
Academics
Healthcare Industry
Regulatory Authorities
Manufacturers
History of 〈795〉

- **First Nonsterile Compounding Standard**

- **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

2010
USP begins process to revise (795) & (797)

2015
Proposed revisions to (797) published in PF. Received >8,000 comments

2018
Revised (797) published in PF. Draft received >4,000 comments

2018
Revised (795) published in PF. Draft received >2,000 comments

2018
Revised (795) & (797) published in USP-NF

2019
June 2019
USP received appeals

2019
August 2019
USP CMP EC denied appeals

2019
September 2019
USP received second appeals. Chapters postponed.

2020
March 2020
Appeals Panel issued decision remanding chapters to CMP EC

2021
November 2021
Proposed revised (795) & (797) published in USP-NF

2022
September 2021
Proposed revised (795) & (797) published in PF. Proposed revisions receive >1,000 comments
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

- 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〉
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
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
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
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
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
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)
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
### 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**

<table>
<thead>
<tr>
<th>Type of Preparation</th>
<th>BUD (days)</th>
<th>Storage Temperature</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Aqueous Dosage Forms ($a_w \geq 0.60$)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonpreserved aqueous dosage forms $^c$</td>
<td>14</td>
<td>Refrigerator</td>
</tr>
<tr>
<td>Preserved aqueous dosage forms $^c$</td>
<td>35</td>
<td>Controlled room temperature or refrigerator</td>
</tr>
<tr>
<td><strong>Nonaqueous Dosage Forms ($a_w &lt; 0.60$)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral liquids (nonaqueous) $^d$</td>
<td>90</td>
<td>Controlled room temperature or refrigerator</td>
</tr>
<tr>
<td>Other nonaqueous dosage forms $^e$</td>
<td>180</td>
<td>Controlled room temperature or refrigerator</td>
</tr>
</tbody>
</table>

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$a$ 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 $\geq 0.6$ (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).
## Nonaqueous Dosage Forms: $a_w < 0.6$

<table>
<thead>
<tr>
<th>Dosage Form</th>
<th>Description</th>
<th>$a_w$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Animal treat</td>
<td>Animal treat (oil flavor)</td>
<td>0.507</td>
</tr>
<tr>
<td>Capsule (oil filled)</td>
<td>Olive oil encapsulated</td>
<td>0.468</td>
</tr>
<tr>
<td>Capsule (powder filled)</td>
<td>Powder base encapsulated</td>
<td>0.435</td>
</tr>
<tr>
<td>Gel (glycol based)</td>
<td>Propylene glycol, ethoxy diglycol, or hydroxypropyl cellulose gel</td>
<td>0.056</td>
</tr>
<tr>
<td>Lollipop (sorbitol based)</td>
<td>Sorbitol-based lollipop</td>
<td>0.460</td>
</tr>
<tr>
<td>Ointment</td>
<td>Hydrophilic petrolatum</td>
<td>0.396</td>
</tr>
<tr>
<td>Oral solution (glycol based)</td>
<td>20% Polyethylene glycol and 80% propylene glycol</td>
<td>0.009</td>
</tr>
<tr>
<td>Oral solution (oil based)</td>
<td>Medium chain triglycerides oil</td>
<td>0.338</td>
</tr>
<tr>
<td>Oral suspension (fixed oil)</td>
<td>Fixed oil with thickener</td>
<td>0.403</td>
</tr>
<tr>
<td>Powder for inhalation</td>
<td>Encapsulated powder for inhalation</td>
<td>0.402</td>
</tr>
<tr>
<td>Stick</td>
<td>Lip balm</td>
<td>0.181</td>
</tr>
<tr>
<td>Suppository</td>
<td>Polyethylene glycol base</td>
<td>0.374</td>
</tr>
<tr>
<td>Suppository</td>
<td>Fatty acid base</td>
<td>0.385</td>
</tr>
<tr>
<td>Tablet (compressed)</td>
<td>Compressed tablet</td>
<td>0.465</td>
</tr>
<tr>
<td>Tablet (triturate)</td>
<td>Tablet triturate (lactose and/or sucrose)</td>
<td>0.427</td>
</tr>
<tr>
<td>Troche or lozenge (gelatin based)</td>
<td>Gelatin troche or lozenge with NMT 3% aqueous flavor</td>
<td>0.332</td>
</tr>
<tr>
<td>Troche or lozenge (glycol based)</td>
<td>Polyethylene glycol troche or lozenge with NMT 3% aqueous flavor</td>
<td>0.571</td>
</tr>
</tbody>
</table>

## Aqueous Dosage Forms: $a_w \geq 0.6$

<table>
<thead>
<tr>
<th>Dosage Form</th>
<th>Description</th>
<th>$a_w$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Animal treat</td>
<td>Animal treat with 15%–18% aqueous flavor</td>
<td>0.716</td>
</tr>
<tr>
<td>Cream</td>
<td>Cream vehicle (oil in water emulsion, petrolatum free)</td>
<td>0.968</td>
</tr>
<tr>
<td>Cream</td>
<td>Emollient cream (petrolatum and mineral oil)</td>
<td>0.984</td>
</tr>
<tr>
<td>Cream</td>
<td>Cream (oil in water emulsion with natural oils)</td>
<td>0.989</td>
</tr>
<tr>
<td>Foam</td>
<td>Foaming surfactant solution</td>
<td>0.983</td>
</tr>
<tr>
<td>Gel (water based)</td>
<td>Alcohol-free aqueous gel</td>
<td>0.990</td>
</tr>
<tr>
<td>Gel (water based)</td>
<td>Hydroxypropyl methylcellulose (HPMC) gel</td>
<td>1.000</td>
</tr>
<tr>
<td>Lotion</td>
<td>Lotion (oil in water emulsion)</td>
<td>0.986</td>
</tr>
<tr>
<td>Nasal spray</td>
<td>Nasal spray</td>
<td>0.991</td>
</tr>
<tr>
<td>Oral solution (water based)</td>
<td>Low-sucrose syrup vehicle</td>
<td>0.906</td>
</tr>
<tr>
<td>Oral solution (water based)</td>
<td>90% Water and 10% glycerin</td>
<td>0.958</td>
</tr>
<tr>
<td>Oral suspension (water based)</td>
<td>Oral suspension base</td>
<td>0.992</td>
</tr>
<tr>
<td>Rinse</td>
<td>Polymer gel with 30% water</td>
<td>0.960</td>
</tr>
<tr>
<td>Shampoo</td>
<td>Shampoo</td>
<td>0.976</td>
</tr>
<tr>
<td>Simple syrup</td>
<td>Simple syrup</td>
<td>0.831</td>
</tr>
<tr>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
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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 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
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
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
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Email questions to CompoundingSL@USP.org

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