What's Up With USP Updates?

Looking at updates to USP <795> and <797>

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Conflict of Interest

- The speakers have nothing to disclose.

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Learning Objectives

- Discuss final updates to USP <795> and <797>.
- Identify potential areas for gaps to occur when implementing the new USP chapters.
- Define remedies that will address the common gaps that the new USP chapters will create.

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Poll Question 1

- What is your current area of practice?
  - Pharmacist
  - Pharmacy Technician
  - Pharmacy Intern
  - Pharmacy Leader (Supervisor, Manager, Director, etc.)
  - Other (Academia, Industry, PBM, etc.)

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Background

- United States Pharmacopeia (USP) is an independent, nonprofit organization focused on the safety and quality of medicines
- The organization sets standards for quality, purity, strength, and identity for medicines, food ingredients, and dietary supplements[1]
- Their standards are split up into chapters
  - Chapters less than <1000> are considered enforceable,
  - Chapters greater than or equal to <1000> are considered guidelines
- Our focus will be chapters <795> and <797>, which are *enforceable*

https://qualitymatters.usp.org/what-us-pharmacopeia

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Poll Question 2:
Who Enforces USP <795>/<797>?

1. United States Pharmacopeia
2. Food and Drug Administration (FDA)
3. Deemed Status Organizations (TJC, DNV)
4. Boards of Pharmacy
5. Institutions are expected to self-enforce only

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Who Enforces USP <795>/<797>?

- Although USP creates the chapters, they have no involvement in the enforcement of them
- State Boards of Pharmacy, The Joint Commission, Det Norske Veritas (DNV), and other institutions with *deemed status* from the Centers for Medicare and Medicaid
- These regulatory bodies will reference USP when they are conducting surveys and site visits to ensure compliance
- A lack of compliance can/will lead to citations and potentially loss of reimbursement for services provided

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https://www.jointcommission.org/resources/news-and-multimedia/fact-sheets/facts-about-federal-deemed-status/

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IL State Board of Pharmacy Self-Inspection Form

Pharmaceutical Compounding Standards (Section 1330.640)				
REQUIREMENTS	YES	NO	N/A	AUTHORITY
The minimum standards and technical equipment considered adequate for compounding drugs shall include:				
A storage area separate for materials used in compounding.				68 Administrative Code Section 1330.640(a)
Scales and balances for the compounding done in the pharmacy.				68 Administrative Code Section 1330.640(b)
An area of the pharmacy used for compounding activities.				68 Administrative Code Section 1330.640(c)
A heating apparatus.				68 Administrative Code Section 1330.640(d)
A logbook or record keeping system to track each compounded prescription and the components used.				68 Administrative Code Section 1330.640(e)

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https://idfpr.illinois.gov/content/dam/soi/en/web/idfpr/forms/pdfs/nonsterilecompoundingselfinspectionreport.pdf

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IL State Board of Pharmacy Self-Inspection Form

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https://idfpr.illinois.gov/content/dam/soi/en/web/idfpr/forms/pdfs/sterilecompoundingselfinspectionreport.pdf

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Administrative Code Section 1330.640

ADMINISTRATIVE CODE

TITLE 68: PROFESSIONS AND OCCUPATIONS
CHAPTER VII: DEPARTMENT OF FINANCIAL AND PROFESSIONAL REGULATION
SUBCHAPTER b: PROFESSIONS AND OCCUPATIONS
PART 1330 PHARMACY PRACTICE ACT
SECTION 1330.640 PHARMACEUTICAL COMPOUNDING STANDARDS

Section 1330.640 Pharmaceutical Compounding Standards

All pharmaceutical compounding standards, both sterile and nonsterile, shall be governed by the USP-NF (USP 41-NF 36), as set forth in the United States Pharmacopoeia (USP), 41st Revision and the National Formulary, 36th Edition, Compounding Compendium, with the exception of USP Chapter <800> as it pertains to the handling of hazardous drugs in health care settings. Beginning May 1, 2019, all pharmaceutical compounding standards, both sterile and nonsterile, shall be governed by the USP-NF (USP 42-NF 37), as set forth in the 2019 edition of the USP Compounding Compendium, with the exception of USP Chapter <800> as it pertains to the handling of hazardous drugs in health care settings.

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https://www.ilga.gov/commission/jcar/admincode/068/06801330F064008.html

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Disclaimer

The following are **subjective** key points to consider. Different sites have different needs that require attention. Always make sure to conduct a thorough gap analysis to ensure compliance!

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USP <795>
Pharmaceutical Compounding – Nonsterile Preparations

- Definition: combining, admixing, diluting, pooling, reconstituting other than as provided in the manufacturer's labeling, or otherwise altering a drug product or bulk drug substance to create a nonsterile preparation.
- Application: all persons who prepare compounded nonsterile preparations (CNSPs); all places where CNSPs are prepared for human and animal patients
  - Yes, animals are included too!
  - Pharmacists, technicians, nurses, physicians, dentists, naturopaths, and chiropractors

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United States Pharmacopeial Convention. General chapter <795> pharmaceutical compounding—nonsterile preparations. USP-NF 2023, Issue 1, November 1, 2022, official as of November 1, 2023.

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USP <795>
Pharmaceutical Compounding – Nonsterile Preparations

Poll Question 3

- Which of the following preparations is considered a CNSP under USP <795>?
  1. Reconstituting a bottle of Amoxicillin powder
  2. First Omeprazole Oral Suspension Compounding Kit
  3. Mycophenolate Mofetil for Oral Suspension
  4. Nimodipine Oral Solution using capsules

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USP <795>
Pharmaceutical Compounding – Nonsterile Preparations

- Designated Person

2014 USP <795>	2023 USP <795>
No mention of "designated person"	*"The compounding facility must designate one or more individuals to be responsible and accountable for the performance and operation of the facility and personnel for the preparation of CNSPs."*

- The designated does not have to be a pharmacist or a technician, however both a pharmacist and technician can be designated persons!

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USP <795>
Pharmaceutical Compounding – Nonsterile Preparations

- Responsibilities of the Designated Person(s)
  - SOPs are created and implemented
  - Follow-up: for non compliance and errors
  - Documentation of corrective action
  - Quality Assurance and Quality Control (QA/QC)

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USP <795>
Pharmaceutical Compounding – Nonsterile Preparations

- Training and Competencies

2014 USP <795>	2023 USP <795>
Non-specific	*"All personnel who compound or have direct oversight of compounding CNSPs must be initially trained and qualified by demonstrating knowledge and competency according to the requirements … " "Knowledge and competency must be demonstrated initially and at least every 12 months … "*

- Hand Hygiene was also modified to reflect specific steps, outlined in a text box

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USP <795>
Pharmaceutical Compounding – Nonsterile Preparations

- Hand Hygiene was also modified to reflect specific steps, outlined in a text box

Box 1. Hand Hygiene Procedures

- Wash hands with soap and water for at least 30 s
- Dry hands completely with disposable towels or wipers
- Don gloves

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USP <795>
Pharmaceutical Compounding – Nonsterile Preparations

- Garbing and the need for gloves

2014 USP <795>	2023 USP <795>
"When appropriate"	*"Gloves must be worn for all compounding activities"* *"Other garb must be appropriate for the type of compounding performed and should be worn as needed for the protection of the personnel from chemical exposures and for prevention of CNSP contamination"*

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USP <795>
Pharmaceutical Compounding – Nonsterile Preparations

- Verbiage – especially with respect to Master Formulation Records (MFRs) and Compounding Records (CRs)
- When reviewing USP chapters, recall *"should"* = recommendation
  - "Must" = required!

2014 USP <795>	2023 USP <795>
A MFR should be created before compounding a preparation for the first time *A CR should be completed each time a preparation is compounded*	*"An MFR **must** be created for each unique formulation of a CNSP"* *"A CR **must** be created for all CNSPs. Each CR must be reviewed for completeness before the CNSP is released"*

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USP <795>
Pharmaceutical Compounding – Nonsterile Preparations

- Beyond-Use-Dating (BUDs)
  - Recall: BUDs are NOT the same as expiration dates
  - Utilization of a_w in determination of product and potential BUD
  - An $a_w < 0.6$ will usually indicate a nonaqueous dosage form
    - Capsule, gel (glycol based), ointment (petrolatum), suppository
  - An $a_w \geq 0.6$ will indicate an aqueous dosage form
    - Cream (oil in water), gel (water based), simple syrup

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USP <795>
Pharmaceutical Compounding – Nonsterile Preparations

- In the absence of monograph or preparation-specific stability information:

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

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USP <795>
Pharmaceutical Compounding – Nonsterile Preparations

- Compounding Area

2014 USP <795>	2023 USP <795>
Non Specific	*"An area must be designated for nonsterile compounding. The method of designation must be described in the facility's SOPs."* *"There should not be carpet in the compounding area."* *"Other activities must not be occurring in the compounding area at the same time as compounding."*

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Think, Pair, Share

- Based off of the changes to <795> presented, are you prepared?
- Discuss amongst your groups:
  - Do you have a designated person(s)? Are they specifically spelled out in your SOPs or policies?
  - Do your recipes have accurate BUDs to reflect the changes to USP <795>?
  - Is the necessary garb available to your teammates?
    - Recall, while gloves are a "must", there are is other garb that could be required!
  - Do you have a documentation practice in place for competencies as well as corrective action plans?
    - If so, what is your practice?

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USP <797>
Pharmaceutical Compounding – Sterile Preparations

- Definition: combining, admixing, diluting, pooling, reconstituting, repackaging, or otherwise altering a drug product or bulk drug substance to create a sterile preparation
- Application: all persons who prepare compounded sterile preparations (CSPs); all places where CSPs are prepared for human and animal patients
  - Anyone entering a sterile compounding area, whether preparing a CSP or not, must meet the requirements related to personal hygiene and garbing
- The update to the chapter is more verbose in a multitude of capacities

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USP <797>
Pharmaceutical Compounding – Sterile Preparations

- Immediate-Use Compounded Sterile Preparations

2008 USP <797>	2023 USP <797>
"The compounding process involves simple transfer of not more than three (3) commercially manufactured packages of sterile nonhazardous products…and not more than two entries into any one container or package."	*"Personnel are trained and demonstrate competency in aseptic processes…"*
"Administration begins not later than 1 hour following the start of the preparation of the CSP."	*"The preparation involves not more than 3 different sterile products."*
	"Administration begins within 4 h following the start of preparation."

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Poll Question 4:
Immediate-Use Compounded Sterile Preparations

Under which USP <797> version would the following practice be acceptable?

1. 2008 USP <797>
2. 2023 USP <797>
3. Neither version
4. Both versions

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USP <797>
Pharmaceutical Compounding – Sterile Preparations

- Initial and Ongoing Garbing Competencies

2008 USP <797>	2023 USP <797>
"Compounding personnel shall be evaluated initially prior to beginning compounding CSPs"	*"Before beginning to compound…or having direct oversight of compounding personnel…complete an initial garbing competency evaluation no fewer than 3 separate times."*

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USP <797>
Pharmaceutical Compounding – Sterile Preparations

- Initial and Ongoing Manipulation Competencies aka Media-Fill Testing

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USP <797>
Pharmaceutical Compounding – Sterile Preparations

- Cleaning Supplies and Materials

2008 USP <797>	2023 USP <797>
Specific materials are not explicitly referenced	*"Cleaning, disinfecting, and sporicidal agents used within the PEC must be sterile."*

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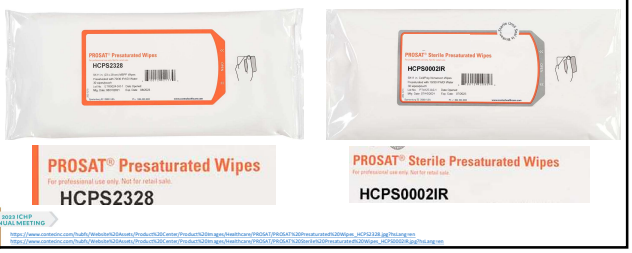
USP <797>
Pharmaceutical Compounding – Sterile Preparations

- Do not forget that products going into the PEC must be sterile



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USP <797>
Pharmaceutical Compounding – Sterile Preparations

Modification from "risk" levels to "categories":

2008 USP <797>	2023 USP <797>
CSP Categories -Low Risk -Medium Risk -High Risk	CSP Categories -Category 1 -Category 2 -Category 3

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USP <797>
Pharmaceutical Compounding – Sterile Preparations

Category 1 CSPs

- Least controlled environmental conditions
- Shortest Beyond-Use Dating (BUD) other than Immediate-Use
- Only category that may be compounded in a segregated compounding area (SCA)

Table 12. BUD Limits for Category 1 CSPs[a]

Storage Conditions	
Controlled Room Temperature (20°–25°)	Refrigerator (2°–8°)
≤12 h	≤24 h

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USP <797>
Pharmaceutical Compounding – Sterile Preparations

Category 2 CSPs

- More environmental control and testing than Category 1
- Simply, products compounded within a Primary Engineering Control (PEC) within a Secondary Engineering Control (SEC) that has

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USP <797>
Pharmaceutical Compounding – Sterile Preparations

Table 13. BUD Limits for Category 2 CSPs[a]

Preparation Characteristics		Storage Conditions		
Compounding Method	Sterility Testing Performed and 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

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Poll Question 5:
Which of the following BUDs would be appropriate for the pictured environment?

1. 4 days at controlled room temperature
2. 10 days under refrigerated conditions
3. 4 hours at controlled room temperature
4. ≤ 12 hours at controlled room temperature

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USP <797>
Pharmaceutical Compounding – Sterile Preparations

Segregated Compounding Area

*The area within 1 m of the PEC should be dedicated only for sterile compounding

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USP <797>
Pharmaceutical Compounding – Sterile Preparations

Incubation Temperatures and Timeframes

2008 USP <797>	2023 USP <797>
Gloved Fingertip Test (GFT): 30°-35°C for 48-72 hours *Media Fill Test (MFT): 20°-25°C or 30-35°C for 14 days OR minimum of 7 days at each temp*	*GFT: "Incubate the media device at 30°-35° for no less than 48 h and then at 20°–25° for no less than 5 additional days. Samples must be incubated in an incubator."* *MFT: "Incubate the final containers at 20°-25° and 30°-35° for a minimum of 7 days at each temperature band to detect a broad spectrum of microorganisms. Final containers must be incubated in an incubator"*

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USP <797>
Pharmaceutical Compounding – Sterile Preparations

Incubation Temperatures and Timeframes

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Resource Recommendations

<795> FAQs

November 1, 2022

2023 USP CHAPTER <797> AND <795> REVISIONS

ASHP has compiled the following documents to help inform pharmacies on the USP <797> and <795> changes and as assets to be used during implementation of the new standards to ensure compliance prior to the November 1, 2023 deadline. Resources accompanied with the lock symbol. 🔒 are exclusively for ASHP members. If you are not currently a member, join today to access these documents.

USP Chapter <797> 🔒
- USP <797> Key Changes [PDF]
- USP <797> List Of Standard Operating Procedures [PDF]

USP Chapter <795> 🔒
- USP <795> Key Changes [PDF]
- USP <795> List Of Standard Operating Procedures [PDF]

Persons Responsibilities 🔒
- USP Designated Persons Responsibilities Chart [PDF]
- USP Designated Persons Responsibilities [PDF]

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