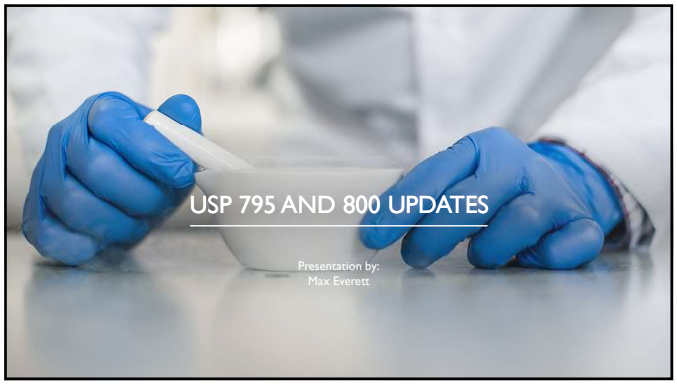


1

ABOUT ME

- B.S. in Mechanical Engineering.
- M.S. in Regulatory Affairs and Quality Assurance.
- Have worked as a pharmacy compounding technician in both 503A and 503B facilities.
- Commissioned 503A and 503B inspections with regulatory agencies, BOPs and the FDA.
- Currently serve as the Director of Quality for Olympia Pharmaceuticals 503B Outsourcing Facility.

2

AGENDA

- USP 795 UPDATES
- USP 800 UPDATES
- TAKE AWAY TOOLS
- LEARNING OBJECTIVE: DESCRIBE KEY USP REGULATIONS
- LEARNING OBJECTIVE: APPLY FUNDAMENTALS OF USP 795 AND USP 800

3

USP 795: UPDATES

4

USP 795: WHAT IS IT?

- USP 795 is the general chapter provided by US pharmacopeia that provides standards for compounding quality nonsterile preparations and medications.
- Establishes the basis for nonsterile compounding and the requirements for compounding.
- New updates include specified dosage forms, designated person(s), and references to USP <800>

Category	USP <795>, 2014[1]	USP <795>, 2023[2]
01. INTRODUCTION AND SCOPE		
CNSPs subject to the requirements in this chapter	Did not specify specific dosage forms Includes reconstituting or manipulating conventionally manufactured products per manufacturer labeling.	Added information on types of CNSPs: solid oral, liquid oral, rectal, vaginal, topical (i.e., creams, gels, and ointments), nasal and sinus intended for local application (i.e., nasal sprays and nasal irrigation), otic (excluding use in perforated eardrums) Excludes reconstitution of a conventionally manufactured product per manufacturer labeling.
The designated person	Not addressed	"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."
Hazardous drugs	Covered throughout the chapter	Removed from chapter and references to follow USP <800>

5

USP 795: 6 KEY AREAS

1. Training and Documentation of Competency
2. Compounding Ingredients and BUDs
3. Facilities
4. Equipment used in Compounding
5. Pharmacy Documentation
6. Quality Control and Error Prevention

6

USP 795: TRAINING AND DOCUMENTATION OF COMPETENCY

- Skilled staff are essential to safe nonsterile compounding.
- Displaying competency for tasks performed is critical.
- Expertise is not a "one and done" event, education must be a part of qualification and normal routine.
- New USP 795 states at least annually, includes understanding of 795, SDS and COA, and facility SOPs related to compounding.

Category	USP <795>, 2014[1]	USP <795>, 2023[2]
02. PERSONNEL TRAINING AND EVALUATION		
Training and competencies	Was not specific on what was required for training	"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 ..."** List of core competencies
Steps of training procedure	Did not include what steps needed to be taken in the training procedure	Includes three steps that need to be included in the training procedures: 1. Understand requirements of Chapter <795> 2. Understand and interpret safety data sheets and certificates of analysis (if applicable) 3. Read/understand procedures related to compounding duties

[1] Pharmaceutical compounding—nonsterile preparations. USP. Accessed April 5, 2024. https://www.usp.org/compounding/general-chapter-795.

7

USP 795: TRAINING AND DOCUMENTATION OF COMPETENCY

- Training must be done initially, then repeated at a minimum of annually and provided by designated person or assigned trainer.
- Core competencies include:
  - Hand, Hygiene, Garbing
  - Cleaning, Sanitizing
  - Handling, transporting components and CNSPs
  - Documentation of the process (MFR, Compounding Record)
  - Understanding of 795, SDS, COA
  - Facility SOPs

Category	USP <795>, 2014[1]	USP <795>, 2023[2]
03. PERSONAL HYGIENE AND GARBING		
Risk of contamination	Not addressed	Prior to entering the compounding area, personnel who have a risk of contamination (e.g., rashes, oozing sores, recent tattoos) must notify the designated person Designated person is responsible to evaluate any risk of contamination
Hand hygiene procedures	Not addressed	Added a box on hand hygiene procedures
Garb and glove requirements	"As needed"	Gloves are required 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"

- "The trainer must also be trained!"

8

LEARNING ASSESSMENT

- **True or False:**

The trainer or designated person can receive an abbreviated training that covers all of the core competencies listed in USP 795.

9

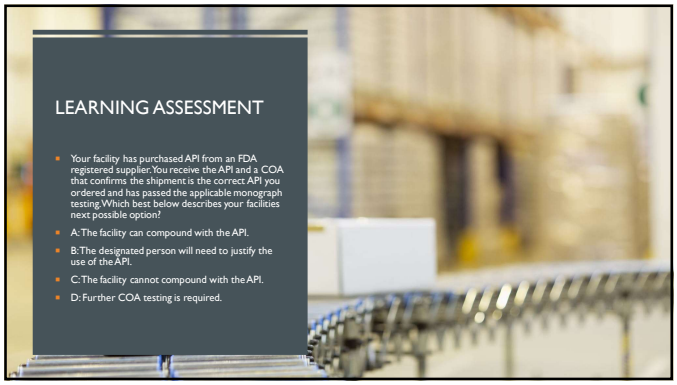
USP 795: COMPOUNDING INGREDIENTS

Category	USP <795>, 2014[1]	USP <795>, 2023[2]
Components	Not addressed	APIs must be manufactured by an FDA-registered facility and must be accompanied by a valid certificate of analysis

- Component Update: Requirement for API to be manufactured in FDA facility.
- Source API and Ingredients from FDA registered manufacturer. Not to be confused with the supplier/vendor.
- Avoid "Chemical grade", "not for human use", "research grade" material.
  - These materials can land the facility in regulatory trouble.
- Maintain control of components and reject unacceptable components.
- API and Excipients
  - Must comply with USP-NF monographs and have Compendial COA that displays expected quality.
  - Manufactured in FDA registered facility.
  - Excipient ONLY: If an excipient cannot be obtained from an FDA registered facility, designated person to determine selection based on suitability for intended use. (Must have justification!)
- Water
  - Purified or WFI must be used for compounding NS formulations that include the use of water.

10

LEARNING ASSESSMENT



- Your facility has purchased API from an FDA registered supplier. You receive the API and a COA that confirms the shipment is the correct API you ordered and has passed the applicable monograph testing. Which best below describes your facilities next possible option?
- A: The facility can compound with the API.
- B: The designated person will need to justify the use of the API.
- C: The facility cannot compound with the API.
- D: Further COA testing is required.

11

USP 795: BUDS

- Must consider chemical and physical properties of the drug and compatibility with the container closure system.
- Potential for microbial proliferation i.e. aqueous based, non-aqueous etc.
  - Determined through water activity testing.
- Non-preserved and Aqueous dosage forms.
  - 14 Days BUD and must be refrigerated
- Preserved Aqueous dosage forms
  - 35 Days BUD at CRT
- Oral Liquids (non-aqueous)
  - 90 Days BUD at CRT
- Other Non-Aqueous forms (Capsules, Tablets)
  - 180 Days BUD at CRT
- If extending beyond these ranges, AET testing, and stability testing is required

Category	USP <795>, 2014[1]	USP <795>, 2023[3]
10. ESTABLISHING BEYOND-USE DATES		
BUDs	Used the term "water-containing" to help determine BUDs	Eliminated the term "water-containing" Now uses water activity levels to help determine BUDs. Parameters to consider when assigning BUDs: water activity, 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

12

USP 795: FACILITIES

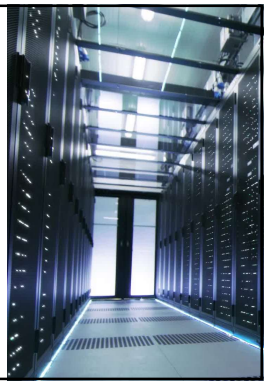
Category	USP <795>, 2014[1]	USP <795>, 2023[2]
04. BUILDINGS AND FACILITIES		
Compounding area	Not addressed	Requires a designated area for nonsterile compounding
Storage area	Not addressed	Temperature in storage area(s) should be monitored at least daily

- Ingredients and Training can be compromised if the facility is not a suitable environment.
- Think "the environment must be suitable for the intended use".
  - Update: Designated area for nonsterile compounding. Avoid "double duty" areas i.e. mixing of different operations/activities.
- Must be well lit, maintained, orderly, and sanitary. NO CARPET!
- Minimize potential for "Cross Contamination".
- Temperature control within compounding and storage areas
  - Update: Manual documentation at least once daily during hours of business.
  - Continuous monitored equipment recommended to catch excursions.
    - Must be retrievable, annual calibration.
    - Ensures the MOST confidence in temperature control!

13

LEARNING ASSESSMENT

- Your facility contains a continuous monitoring software to monitor the temperature of the nonsterile API storage area.
- **True or False:**
- Your facility does not need to continuously monitor the storage area for temperature on the weekends because the facility is closed.



14

USP 795: FACILITIES

Table 1. Minimum Frequency for Cleaning and Sanitizing in Nonsterile Compounding Area(s)—Surfaces

Site	Minimum Frequency
Work surfaces	• At the beginning and end of each shift on days when compounding occurs, after spills, and when surface contamination (e.g., from splashes) is known or suspected • Between compounding CNSPs with different components
Floors	• Daily on days when compounding occurs, after spills, and when surface contamination (e.g., from splashes) is known or suspected
Walls	• When visibly soiled, after spills, and when surface contamination (e.g., from splashes) is known or suspected
Ceilings	• When visibly soiled and when surface contamination (e.g., from splashes) is known or suspected

- Facility Update: Cleaning and Sanitizing
- Added detail on the requirements for frequency of cleaning NS areas.
- Work Surfaces: Clean prior to shift, end of shift and between compounding CNSPs.
- Floors: Daily when compounding
- Walls + Ceilings: Suspected Spills or contamination
- These are the minimum requirements, cleaning and sanitizing should be routine and established based on facility use and risk.

15

USP 795: EQUIPMENT

Category	USP <795>, 2014[1]	USP <795>, 2023[2]
06. EQUIPMENT AND COMPONENTS		
Equipment	Not addressed	"... components that could generate airborne chemical particles must be evaluated to determine if these activities must be performed in a closed-system processing device ... " Containment ventilated enclosures must be certified at least every 12 months
Components	Not addressed	APIs must be manufactured by an FDA-registered facility and must be accompanied by a valid certificate of analysis

- Must be suitable for intended compounding process – Common theme!
- Equipment must not adversely impact the quality of the CNSP, and disposable or dedicated equipment is recommended!
- Equipment must be maintained and cleaned so as to prevent cross contamination.
- Must be inspected prior to use and verified to accuracy every 12 months i.e. annual calibration.
- Containment ventilated enclosure (CVE) or Biological Safety Cabinets must be certified at least every 12 months or by other applicable regulatory jurisdiction.
  - Differs state to state, some require 6-month certifications

Pharmaceutical compounding - sterile preparations. USP. Accessed April 5, 2024. https://www.usp.org/compounding/general-chapter-795.

16

USP 795: DOCUMENTATION

Category	USP <795>, 2014[1]	USP <795>, 2023[2]
07. MASTER FORMULATION AND COMPOUNDING RECORDS		
Master formulation record and compounding record	A MFR **should** be created before compounding a preparation for the first time. A CR **should** be completed each time a preparation is compounded Should = **recommended**	A MFR **must** be created for each unique formulation of a CNSP. A CR **must** be created for all CNSPs. Must = **required**

- "If it wasn't documented, it didn't happen!"
- Update: Master Formulation Record must be created fir each unique formulation of CNSP.
  - Think of this as your recipe for baking a cake, must be controlled and consistent! State what drugs to use.
- Update: Compounding Record must be created for all compounded CNSP.
  - Think of this as your instructions for using the cake recipe, documenting each step along the way! State what manufacturer, lots, quantities of drugs to use.
- Maintain control of forms, records, and other documentation critical to compounding to preserve data integrity.

USP 795&797 key changes. Accessed April 5, 2024. https://www.ashp.org/-/media/assets/pharmacy-practice/resources-centers-compounding/docs/USP-795-Key-Changes.pdf.
Pharmaceutical compounding - sterile preparations. USP. Accessed April 5, 2024. https://www.usp.org/compounding/general-chapter-795.

17

USP 795: QUALITY CONTROL AND ERROR PREVENTION

Category	USP <795>, 2014[1]	USP <795>, 2023[2]
08. RELEASE INSPECTIONS AND TESTING		
Visual inspection	Not addressed	Before releasing and dispensing, the CNSP must be visually inspected

- "Build quality into the product" – this is done by taking every opportunity to prevent potential problems before they happen.
- Completed through training, education, facilities, SOPs and more.
- Quality is separate from the operations team – removes bias!
- Inspect and approve the final product, as well as review the performance of the procedures and equipment used in the process.
- Update: Requirement of visual inspection of CNSP prior to release
  - Inspect CNSP for Color, Texture, Uniformity
  - Inspect labeling on CNSP matches the Compounding Record
  - If inspection does not pass, a deviation is opened to investigate and provide CAPA.
- Monitor Complaints and nonconformances as a part of CQI to further prevent error!

USP 795&797 key changes. Accessed April 5, 2024. https://www.ashp.org/-/media/assets/pharmacy-practice/resources-centers-compounding/docs/USP-795-Key-Changes.pdf.

18

USP 800: UPDATES

19

USP 800: WHAT IS IT?

- USP 800 is the general chapter provided by US pharmacopeia that provides standards for compounding quality hazardous preparations and medications.
- Establishes the basis for hazardous compounding and the requirements for hazardous compounding.
- Applies to handling of hazardous (HDs) drugs where there is a risk of exposure to patients, healthcare workers and the environment.
- Became official on December 01, 2019, and became compendially applicable on November 01, 2023.
- Covers decontamination, spill control, cleaning, deactivation, facility and engineering controls, medical surveillance, and handling of hazardous drugs.
- USP 800 is to be used in conjunction with 795, 797

20

USP 800: KEY AREAS

1. RESPONSIBILITY OF PERSONNEL HANDLING HAZARDOUS DRUGS AND TRAINING
2. PERSONAL PROTECTIVE EQUIPMENT (PPE)
3. FACILITY, ENVIRONMENTAL AND ENGINEERING CONTROLS
4. COMPOUNDING REQUIREMENTS
5. RECEIPT, STORAGE, DISPOSAL
6. DEACTIVATING, DECONTAMINATING, CLEANING AND DISINFECTING

21

USP 800: RESPONSIBILITY OF PERSONNEL HANDLING HAZARDOUS DRUGS AND TRAINING

Skilled, educated and trained staff are essential to safe hazardous compounding.

Designated person must ensure compliance with USP 800 and competency on the risks associated with hazardous compounding. All facility personnel responsible for safety!

Training must be role specific i.e. receipt, storage, compounding, dispensing.

Training must include, at a minimum:

- Facility list of HD drugs and their risks
- Facility SOPs related to HDs
- PPE and proper use of equipment
- Spill and disposal of HDs
- Response to suspected HD exposure

Must be completed initially and repeated annually.

22

USP 800: PERSONAL PROTECTIVE EQUIPMENT

- Provides worker protection to reduce exposure to HDs.
- Gowns, head, hair, shoe covers, and two pairs of chemotherapy gloves are <u>required</u> for sterile and nonsterile compounding.
- PPE <u>must</u> be worn when handling HDs during:
  - Receipt, storage and transport
  - Compounding, deactivation, cleaning and disinfecting
  - Spill control and waste disposal
- Additional PPE may be required based on <u>RISK</u>.
  - Eye, face respiratory protection may be included based on the type of drug or compound.

23

USP 800: FACILITY, ENVIRONMENTAL AND ENGINEERING CONTROLS

Table 3. Engineering Controls for Sterile HD Compounding

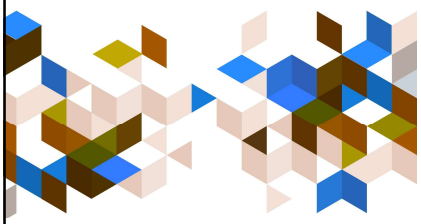
Configuration	C-PEC	C-SEC	Maximum BUD
ISO Class 7 buffer room with an ISO Class 7 ante-room	• Externally vented • Examples: Class II BSC or CACI	• Externally vented • 30 ACPH • Negative pressure between 0.01 and 0.03 inches of water column relative to adjacent areas	As described in ‹797›
Unclassified C-SCA	• Externally vented • Examples: Class II BSC or CACI	• Externally vented • 12 ACPH • Negative pressure between 0.01 and 0.03 inches of water column relative to adjacent areas	As described in ‹797›; for CSPs prepared in a segregated compounding area

- HDs must be handled under conditions to promote safety and environmental protection.
- Signs designating the hazard must be displayed before the entrance to an HD area and access must be restricted to authorized, qualified personnel.
- Designated areas must be available for:
  - <u>Receipt and unpacking</u>: Must be done in a neutral or negative pressure room. Cannot be done within the sterile compounding area.
  - <u>Storage of HDs</u>: Best practice – separate hazardous and nonHD API. HD API must be kept in negative pressure, 12 ACH.
  - Nonsterile and sterile compounding: must be separate! CPEC/CSEC must be externally vented.
- Primary HD cleanrooms (C-SEC) must be externally vented and meet the requirement of negative pressure of 0.01 to 0.03 inches of water with respect to adjacent areas.

24

USP 800: FACILITY, ENVIRONMENTAL AND ENGINEERING CONTROLS

- Environmental wipe sampling for HD surface residue should be performed routinely to verify containment of HDs.
  - Recommended at least every 6 months utilizing an Environmental wipe kit that aids in identifying HD markers.
  - Includes performing a wipe sample within:
    - Pass through chambers, Interior of C-PEC, staging areas or contact surfaces near C-PEC.
  - Goal: to show absence of cross contamination of HDs into unwanted, uncontrolled areas.
- Note: There is currently no standard for acceptable limits for HD surface contamination.
  - Would be developed with risk management strategies.
  - Provides added level of assurance in preventing cross contamination.



LEARNING ASSESSMENT

- **True or False:**
- Environmental wipe sampling is required to be performed every 6 months per USP 800 to monitor the absence of cross contamination.

USP 800: COMPOUNDING REQUIREMENTS

- Personnel involved in compounding HDs must be compliant with USP 795 and 797.
- As mentioned, Compounding must be done in proper engineering controls.
  - C-PEC: Externally vented
  - C-SEC: Negatively pressured 01 – 03 inches of water
- Compounding components are recommended to be single use and disposable – best practice!
  - If single use is not available, dedicated tools and equipment must be assigned.
- Powdered HDs must be handled under a C-PEV to protect from exposure.
  - Due to particle generating activities.

USP 800: RECEIPT, STORAGE AND DISPOSAL

Table 4. Summary of Requirements for Receiving and Handling Damaged HD Shipping Containers

If the shipping container appears damaged	• Seal container without opening and contact the supplier • If the unopened package is to be returned to the supplier, enclose the package in an impervious container and label the outer container "Hazardous" • If the supplier declines return, dispose of as hazardous waste
If a damaged shipping container must be opened	• Seal the container in plastic or an impervious container • Transport it to a C-PEC and place on a plastic-backed preparation mat • Open the package and remove undamaged items • Wipe the outside of the undamaged items with a disposable wipe • Enclose the damaged item(s) in an impervious container and label the outer container "Hazardous" • If the supplier declines return, dispose of as hazardous waste • Deactivate, decontaminate, and clean the C-PEC (see *Deactivating, Decontaminating, Cleaning, and Disinfecting*) and discard the mat and cleaning disposables as hazardous waste

- HDs should be received from the supplier in impervious plastic to reduce the potential of exposure and to allow for the facility to conduct the internal transfer process. Once received, HDs must be placed within a segregated HD receiving/quarantine area.
- HDs must not be unpacked from their external shipping containers in sterile compounding areas or in positive pressure areas.
- PPE shall be worn based on risk and type of exposure of the HD being received, as established by facility SOPs.
  - At a minimum: Chemotherapy gloves must be worn.
- Facility must establish policies for receipt that thoroughly assess the initial inspection of the shipment at receipt.
  - Must document any visible signs of damage, leakage, rips, tears, holes, or sounds of broken glass.
- Damaged packages or shipments must be considered spills and be reported to the designated person. These shipments must be managed according to the facilities established procedures.
- Spill Kits must be readily available in the receiving area.

28

USP 800: RECEIPT, STORAGE AND DISPOSAL

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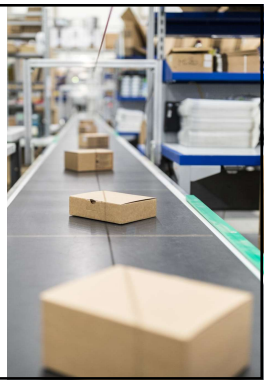
- HDs must be stored in a manner that prevents spillage or breakage.
- HDs must be stored separately from nonHDs, and within negative pressure rooms that are externally vented at 12 ACH.
- Nonsterile and Sterile HDs may be stored together, but HDs used for NS compounding should not be stored in areas designated for sterile compounding to minimize traffic in the area – reduce potential contamination!
- All personnel who perform routine custodial waste removal and cleaning activities in HD handling areas must be trained in appropriate procedures to protect themselves and the environment to prevent HD contamination.
- Disposal of all HD waste, including, but not limited to, unused HDs and trace-contaminated PPE and other materials, must comply with all applicable federal, state, and local regulations.

29

LEARNING ASSESSMENT

- **True or False:**
- It is okay to store nonHD and HD APIs within the same storage room as long as they are both stored within a negatively pressured room that is externally vented with at least 12 air changes per hour.



30

USP 800: DEACTIVATING, DECONTAMINATING, CLEANING AND DISINFECTING

- All areas where HDs are handled and all reusable equipment and devices must be deactivated, decontaminated, and cleaned.
  - Sterile compounding areas must be subsequently disinfected.
- Facilities must establish procedures for Deactivating, Decontaminating, Cleaning and Disinfecting and personnel must be trained on the facility process.
- Agents selected must be appropriate for the type of HD contaminant(s), location, and surface materials. The products used must be compatible with the surface material.
- Cleaning should be applied through the use of wipes wetted with appropriate solution and not delivered by a spray bottle to avoid spreading HD residue.
- "There is no one proven method for deactivating all compounds."

31

USP 800: DEACTIVATING, DECONTAMINATING, CLEANING AND DISINFECTING

- **When Should Decontamination Occur?**
- The work surface of the C-PEC must be decontaminated between compounding different hazardous drugs
- At least once daily (when being used)
- Any time there is a spill
- Before and after certification
- Every 30 minutes while compounding
- Any time voluntary interruption occurs
- If the ventilation tool is moved
- When surface contamination is suspected

Cleaning Steps		
Cleaning Step	Purpose	Example Agents
Deactivation	Render compound inert	As listed in the HD labeling or other agents that may incorporate EPA registered oxidizers (i.e. peroxide formulations, sodium hypochlorite, etc.)
Decontamination	Remove all HD residue	Materials that have been validated to be effective for HD decontamination, or using other materials proven to be effective through testing, which may include alcohol, water, peroxide or sodium hypochlorite
Cleaning	Remove organic and inorganic materials	Germicidal detergent
Disinfection (for sterile manipulations)	Destroy microorganisms	EPA-registered disinfectant and/or sterile alcohol as appropriate for use

32

THANK YOU

- Take Away Tools:
- **795** - 795 Key Changes
- **795** - FAQs for USP 795
- **800** - FAQs for USP 800

33