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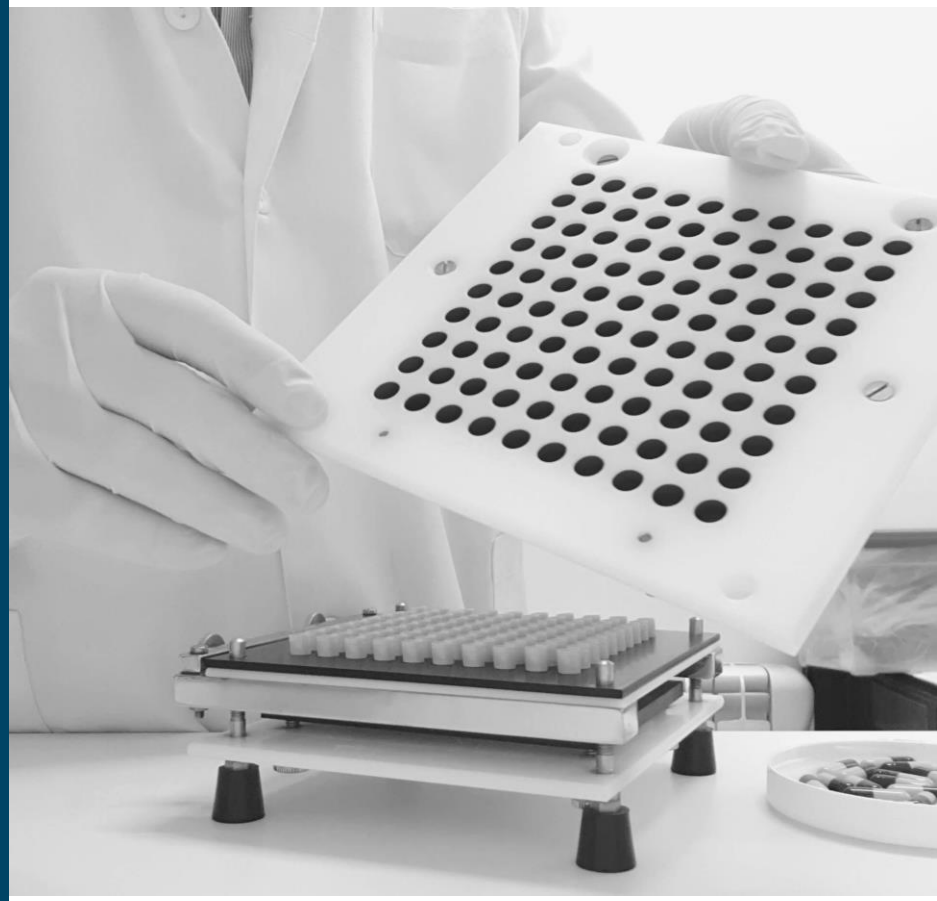
Revised USP<795> and USP<797> Standards



Today's Presenters

- Denise M. Leard, Esq.
  - Brown & Fortunato
- Lisa K. Smith, Esq.
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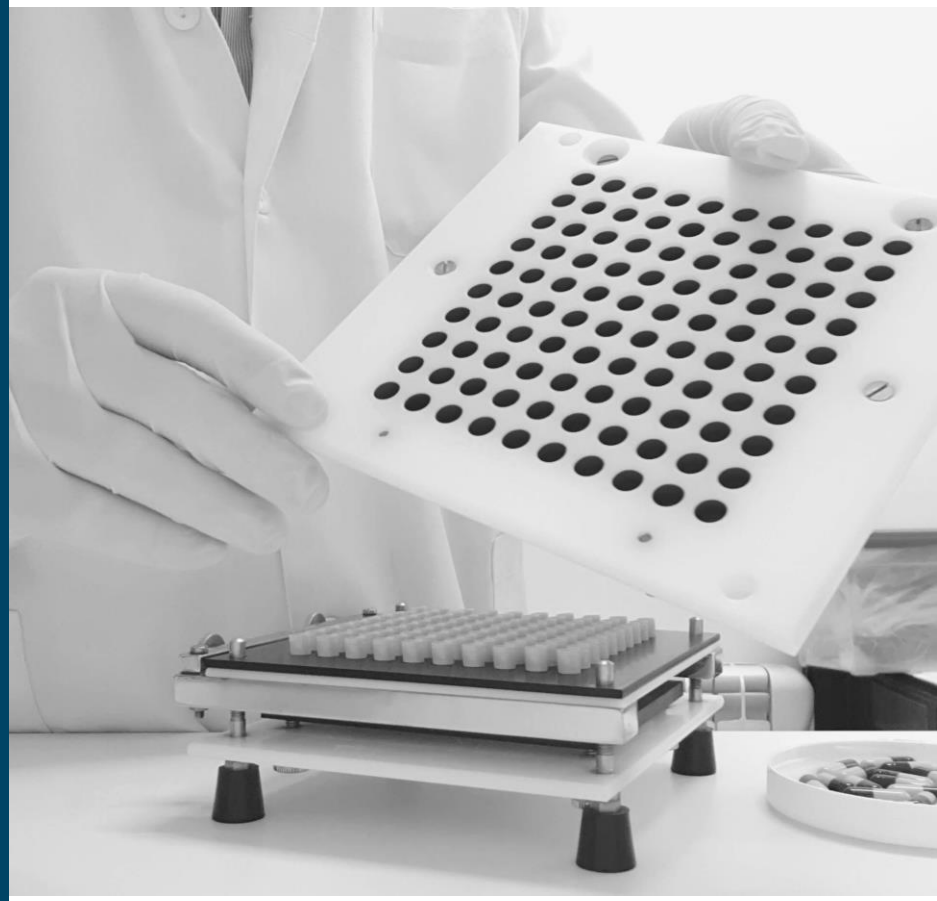
Introduction



Introduction

- On June 1, 2019, USP published revisions to USP<795> and USP<797>. After publication of the revised and new compounding standards, USP received appeals on certain provisions.
- After thoughtful deliberation and evaluation of the record and hearings from the appellants on January 21 and 22, 2020, the Appeals Panel granted the appeals and remanded the chapters to the Compounding Expert Committee (CMP EC) with the recommendation for further engagement on the issues raised.

Introduction

- On September 1, 2021, USP published revisions to USP<795> and USP<797>.
- After considering input from more than 1,400 public comments received during the public comment period from September 2021 to March 2022, on November 1, 2022, USP published revised versions of USP<795> and USP<797>.
- The effective date for these revised chapters is **November 1, 2023.**

Introduction

- Almost every state board of pharmacy has adopted, in whole or in part, the provisions of USP<795> and USP<797> as standards for pharmacy compounding.

Introduction

- There are many changes made in the revised versions of USP<795> and USP<797>. Due to time constraints, during this webinar we will focus on the following few areas:
  - Change in compounding categories
  - Cleaning/disinfecting requirements
  - Training/competency requirements
  - Beyond-use dating

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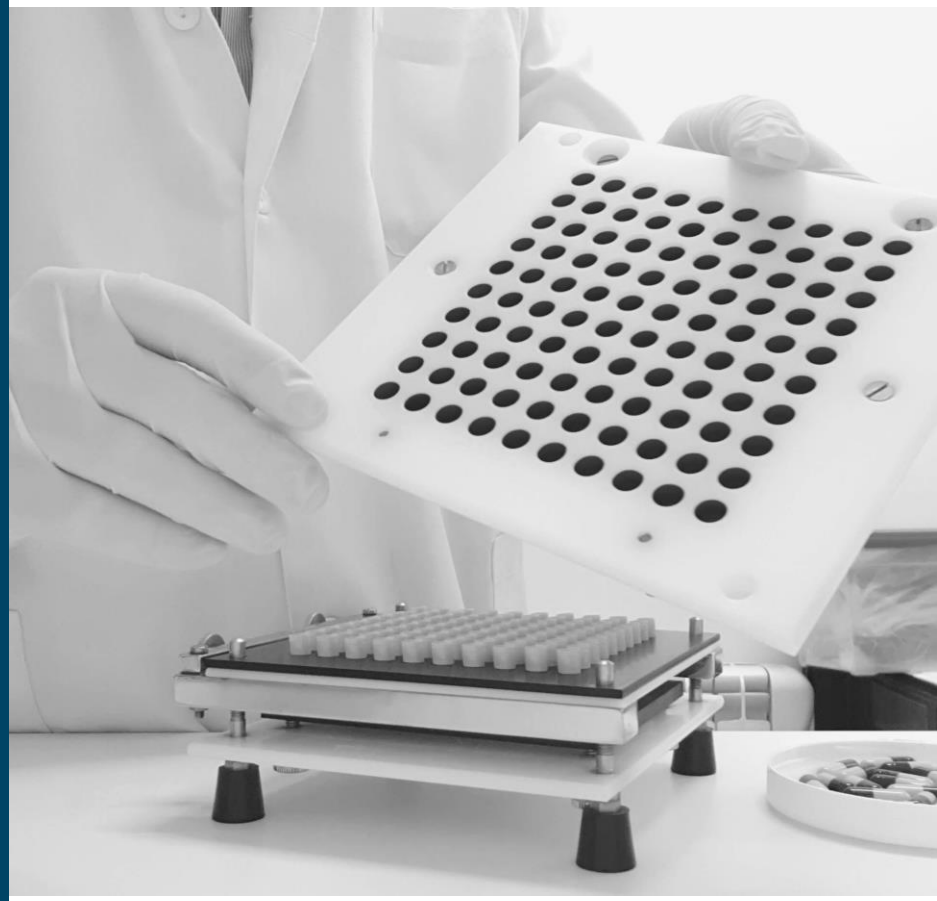
USP<795> Revisions



Compounded Non-Sterile Products (CNSPs) Subject to USP<795>

- 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.

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. Responsibilities include but are not limited to:
  - Overseeing training program to ensure competency of personnel involved in compounding, handling, and preparing CNSPs
  - Selecting components
  - Monitoring and observing compounding activities and taking immediate corrective action if deficient practices are observed
  - Ensuring that SOPs are fully implemented and that follow-up is carried out if problems, deviations or errors are identified
  - Establishing, monitoring and documenting procedures for handling and storage of CNSPs and/or components of CNSPs

Training and Competencies

- 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

Training and Competencies

- List of core competencies:
  - Hand hygiene
  - Garbing
  - Cleaning and sanitizing
  - Handling and transporting components and CNSPs
  - Measuring and mixing
  - Proper use of equipment and devices selected to compound CNSPs
  - Documentation of the compounding process (e.g. Master Formulation Records and Compounding Records)

Training Procedure Steps

- 3 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 and understand procedures related to compounding duties

Hand Hygiene Procedures

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

Garb and Glove Requirements

- 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

Minimum Frequency for Cleaning and Sanitizing

- Work Surfaces
  - At the beginning and end of each shift on days when compounding occurs
  - After spills
  - When surface contamination is known or suspected (e.g., from splashes)
  - Between compounding CNSPs with different components

Minimum Frequency for Cleaning and Sanitizing

- Floors
  - Daily on days when compounding occurs
  - After spills
  - When surface contamination is known or suspected (e.g., from splashes)

Minimum Frequency for Cleaning and Sanitizing

- Walls
  - When visibly soiled
  - After spills
  - When surface contamination is known or suspected (e.g., from splashes)

Minimum Frequency for Cleaning and Sanitizing

- Ceilings
  - When visibly soiled
  - When surface contamination is known or suspected (e.g., from splashes)

Minimum Frequency for Cleaning and Sanitizing

- Storage shelving
  - Every 3 months
  - After spills
  - When surface contamination is known or suspected (e.g., from splashes)

Minimum Frequency for Cleaning and Sanitizing

- Containment ventilated enclosure (CVE)
  - At the beginning and end of each shift on days when compounding occurs
  - After spills
  - When surface contamination is known or suspected (e.g., from splashes)
  - Clean and sanitize the horizontal work surface of the CVE between compounding CNSPs with different components

Minimum Frequency for Cleaning and Sanitizing

- Biological Safety Cabinet (BSC)
  - At the beginning and end of each shift on days when compounding occurs
  - After spills
  - When surface contamination is known or suspected (e.g., from splashes)
  - Clean and sanitize the horizontal work surface of the BSC between compounding CNSPs with different components
  - Clean and sanitize under the work surface at least monthly

Minimum Frequency for Cleaning and Sanitizing

- Other equipment and devices used in compounding operations
  - Before first use and thereafter in accordance with the manufacturer's recommendations
  - If no recommendation is available, between compounding CNSPs with different components

Master Formulation Record (MFR) and Compounding Record (CR)

- A MFR must be created for each unique formulation of a CNSP.
- A CR must be created for all CNSPs.
- Required elements for both MFR and CR are listed in section

Beyond Use Dates (BUDs)

- Eliminated the term “water-containing”
- Now uses water activity levels (a_w) to help determine BUDs

Beyond Use Dates (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
  - Significant deviations from essential compounding steps and procedures

Beyond Use Dates (BUDs)

- Aqueous Dosage Forms ($a_w \geq 0.60$)
  - Nonpreserved aqueous dosage forms — 14 days in refrigerator
  - Preserved aqueous dosage forms — 35 days in controlled room temp or refrigerator
- Nonaqueous Dosage Forms ($a_w < 0.60$)
  - Oral liquids (nonaqueous) — 90 days in controlled room temp or refrigerator
  - Other nonaqueous dosage forms — 180 days in controlled room temp or refrigerator

Beyond Use Dates (BUDs)

- USP<795> contains a table showing the water activity (a_w) of common compounded nonsterile dosage forms for reference

Beyond Use Dates (BUDs)

- Provisions also included for when a shorter BUD is required or when a longer BUD is allowed

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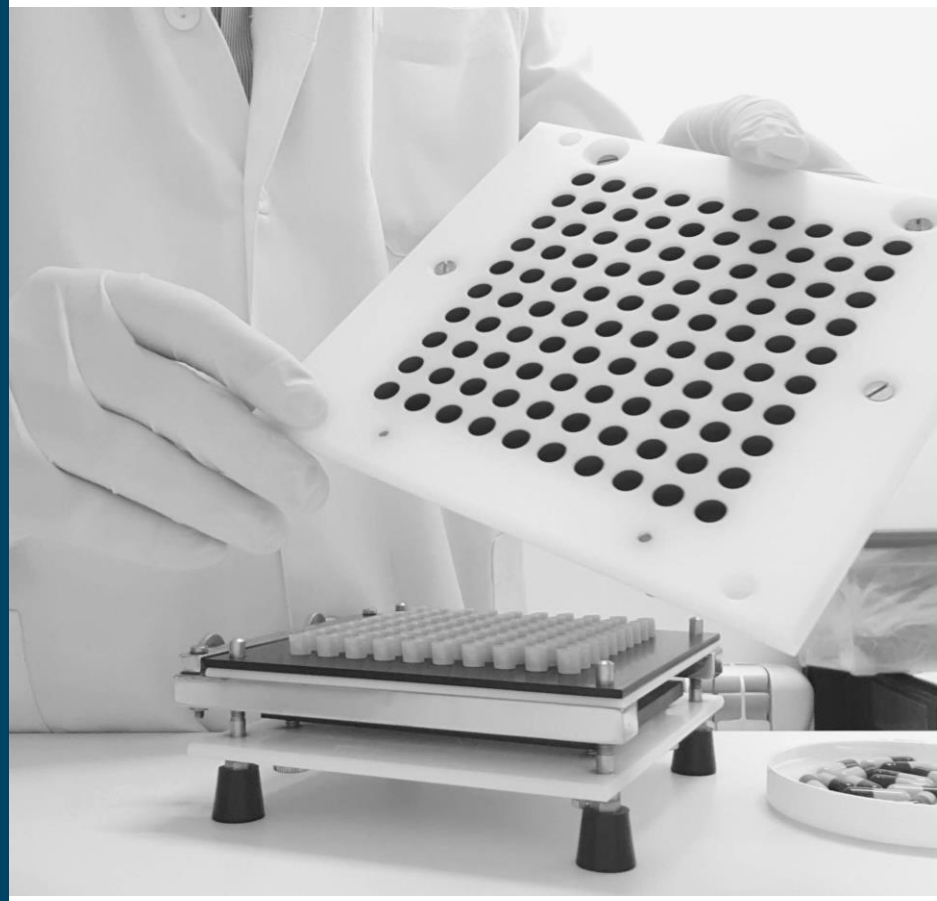

Compounded Sterile Preparations (CSPs) Affected

- Injections, including infusions
- Irrigations for internal body cavities not normally exposed to environment outside the body (e.g. bladder cavity, peritoneal cavity)
  - NOTE— irrigations for the mouth, rectal cavity, and sinus cavity are not required to be sterile
- Aqueous preparations for pulmonary inhalation
  - NOTE— Nasal dosage forms intended for local application are not required to be sterile
- Ophthalmic dosage forms
- Baths and soaks for live organs and tissues
- Implants

Personnel and Settings Affected

- Any person entering a sterile compounding area, whether preparing a CSP or not, must meet the Personal Hygiene and Garbing requirements set out in Section 3 of USP<797>.

Designated Person(s)

- The compounding facility must designate one or more individuals (i.e., the designated person(s)) to be responsible and accountable for the performance and operation of the facility and personnel in the preparation of CSPs and for performing other functions as described in this chapter.

CSP Microbial Risk Categories

- Change from low, medium, high to:
  - Category 1
  - Category 2
  - Category 3

CSP Microbial Risk Categories

- Category 1, 2, and 3 CSPs can be compounded by using only sterile starting ingredients, or by using some or all nonsterile starting ingredients.
- If one (or more) component is non-sterile, sterility of the compound must be achieved through a sterilization process (e.g., terminal sterilization) or sterilizing filtration, and then sterility must be maintained if the CSP is subsequently manipulated.

Personnel Training

- Compounders and those who have direct oversight of compounders
  - Initially and at least every 6 or 12 months (depends on the individual)
- Personnel who do not compound nor have direct oversight of compounders, but are associated with other tasks (e.g., restock or clean/disinfect the segregated compounding area):
  - Defined by facility SOPs

Personnel Training

- List of core competencies:
  - Hand hygiene
  - Garbing
  - Cleaning and disinfection
  - Calculations, measuring and mixing
  - Aseptic technique
  - Achieving and/or maintaining sterility (and apyrogenicity if compounding with nonsterile components
  - Use of equipment
  - Documentation of the compounding process (e.g., Master Formulation Records and Compounding Records)
  - Principles of HEPA-filtered unidirectional airflow with the ISO 5 Class area
  - Proper use of PECs
  - Principles of movement of materials and personnel within the compounding area

Initial Garbing Competency Evaluations

- Garbing competency evaluations include:
  - Visual observation
  - Gloved fingertip and thumb sampling (GFT) of both hands
- Compounders and those who have direct oversight of compounders
  - Must complete an initial garbing competency evaluation no fewer than 3 separate times. The 3 successful completions must be in succession.
- Remediation of failed competency
  - Failure of any of the 3 initial garbing competency evaluations requires repeat testing until personnel successfully completes 3 evaluations in a row.

Ongoing Garbing Competency Evaluations

- Compounders
  - Category 1 and 2: at least every 6 months
  - Category 3: at least every 3 months
- Those who have direct oversight of compounders
  - At least every 12 months

Initial Aseptic Manipulation Competency Evaluations

- Aseptic manipulation evaluations include:
  - Visual observation
  - Media-fill testing with post-GFT
  - Surface sampling
- Compounders and those who have direct oversight of compounders
  - Must complete 1 successful aseptic manipulation competency evaluation
- Remediation of failed competency
  - A failure in the media fill, gloved fingertip and thumb sampling, or surface sample constitutes an overall failure of the aseptic manipulation competency

Ongoing Aseptic Manipulation Competency Evaluations

- Compounders
  - Category 1 and 2: at least every 6 months
  - Category 3: at least every 3 months
- Those who have direct oversight of compounders:
  - At least every 12 months

Action Levels for Gloved Fingertip and Thumb Sampling

- After garbing: >0 cfu
- After media-fill testing: >3 cfu
- Action levels based on total cfu count **from both hands**

Order of Handwashing and Garbing

- Order of handwashing and garbing is determined by the placement of the sink
- Order of garbing must be described by facility's SOPs
- Donning and doffing garb should not occur in the same area at the same time
- Sterile gloves must be donned in a classified room or segregated compounding area

Reusing Garb

- Category 1 and Category 2
  - Gowns may be reused within the same shift by the same person if the gown is maintained in a classified area or adjacent to, or within, the SCA in a manner that prevents contamination.
- Other garb cannot be reused and should be discarded or laundered before reuse

Garbing for Category 3

- If the facility compounds Category 3 CSPs, additional garbing requirements must be continuously met in the buffer room in which Category 3 CSPs are prepared.
  - No exposed skin (I.e., face and neck must be covered)
  - All low-lint outer garb must be sterile
  - Disposable garb cannot be reused
  - Laundered garb cannot be reused until it is laundered and re-sterilized
  - Facility's SOPs describe disinfection procedures for reusing goggles, respirators, and other reusable equipment

Surface Sampling – Timing and Locations

- Category 1 and 2
  - At least monthly
- Category 3
  - At least weekly
  - Prior to assigning a BUD longer than the limits established for Category 2 CSPs

Minimum Frequency for Cleaning and Disinfecting Surfaces

- Minimum frequency for cleaning is broken down by cleaning, disinfecting, and applying sporicidal disinfectant
- Cleaning:
  - Daily on days when compounding occurs and when surface contamination is known or suspected:
    - Equipment inside the PEC and all interior surfaces of the PEC
  - Daily on days when compounding occurs:
    - Work surface of removable work tray of the PEC, pass-through chambers, work surfaces outside the PEC, floors
  - Monthly:
    - Walls, doors, door frames, ceilings, storage shelving and bins, equipment outside the PEC, all surfaces and area underneath the removable work tray of the PEC

Minimum Frequency for Cleaning and Disinfecting Surfaces

- Disinfecting:
  - Daily on days when compounding occurs and when surface contamination is known or suspected:
    - Equipment inside the PEC and all interior surfaces of the PEC
  - Daily on days when compounding occurs:
    - Work surface of removable work tray of the PEC, pass-through chambers, work surfaces outside the PEC, floors
  - Monthly:
    - Walls, doors, door frames, ceilings, storage shelving and bins, equipment outside the PEC, all surfaces and area underneath the removable work tray of the PEC

Minimum Frequency for Cleaning and Disinfecting Surfaces

- Applying Sporicidal Disinfectant:
  - Weekly if compounding Category 3 CSPs:
    - Equipment inside the PEC and all interior surfaces of the PEC, pass-through chambers, work surfaces outside the PEC, floors
  - Monthly if compounding Category 1 and/or Category 2 CSPs:
    - Equipment inside the PEC and all interior surfaces of the PEC, pass-through chambers, work surfaces outside the PEC, floors
  - Monthly:
    - Walls, doors, door frames, ceilings, storage shelving and bins, equipment outside the PEC, work surface and all surfaces and area underneath the removable work tray of the PEC

Cleaning/Disinfecting Supplies

- Cleaning and disinfecting supplies (e.g., wipers, sponges, pads, mop heads)
  - Must be low-lint
  - Should be disposable
  - Reusable cleaning tools must be dedicated for use and not be removed from classified areas or segregated compounding area and be made of cleanable materials (e.g., not wood or any other porous material)
- Cleaning, disinfecting and sporicidal agents used within the PEC must be sterile. Sterile water must be used when diluting concentrated agents for use in the PEC.

Master Formulation Records (MFR)

- Must be created for all CSPs prepared for more than one patient or when using non-sterile components
- Any changes or alterations must be approved and documented based on facility's SOPs
- Requirements for MFR are listed in section

Compounding Records (CR)

- Must be created for all Category 1, Category 2, and Category 3 CSPs and for immediate-use CSPs when prepared for more than one patient
- Requirements for CR are listed in section

Sterility Testing Requirements

- Category 1 – not required
- Category 2 – based on BUD
- Category 3 – required

BUD for Category 1 CSP

- ≤ 12 hours at controlled room temperature
- ≤ 24 hours in refrigerator

BUD for Category 2 CSP

- Aseptically processed, no sterility testing, one or more nonsterile starting components
  - 1 day at controlled room temperature
  - 4 days in refrigerator
  - 45 days in freezer
- Aseptically processed, no sterility testing, only sterile starting components
  - 4 days at controlled room temperature
  - 10 days in refrigerator
  - 45 days in freezer
- Aseptically processed, passed sterility testing
  - 30 days at controlled room temperature
  - 45 days in refrigerator
  - 60 days in freezer

BUD for Category 2 CSP

- Terminally sterilized, no sterility testing
  - 14 days at controlled room temperature
  - 28 days in refrigerator
  - 45 days in freezer

- Terminally sterilized, passed sterility testing
  - 45 days at controlled room temperature
  - 60 days in refrigerator
  - 90 days in freezer

BUD for Category 3 CSP

- Aseptically processed, sterility tested, and passed all applicable tests for Category 3 CSPs
  - 60 days at controlled room temperature
  - 90 days in refrigerator
  - 120 days in freezer

- Terminally sterilized, sterility tested, and passed all applicable tests for Category 3 CSPs
  - 90 days at controlled room temperature
  - 120 days in refrigerator
  - 180 days in freezer

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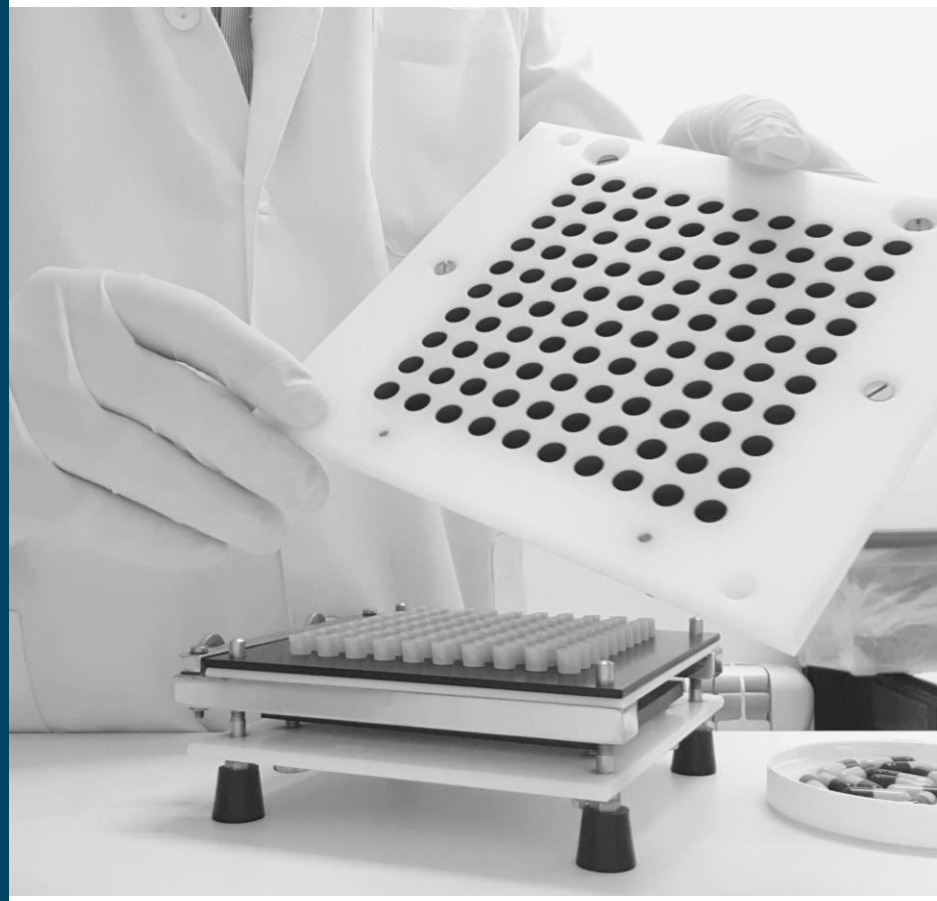
Standard Operating Procedures (SOPs)



Policies and Procedures versus SOPs

- Policies define the outcome, and procedures explain how things will be done. They tell personnel what to do and why but do **not** provide detailed step-by-step instructions on how to do it.
- SOPs provide clear-cut directions and detailed instructions needed to perform a specific task or operation consistently and efficiently.
- USP considers policies and procedures and SOPs as the same thing.
- They should not require any interpretation on behalf of personnel performing the specific task or operation.

SOP Requirements

- They can be written or electronic and must be readily retrievable.
- They need to be reviewed as new products are used, new compounds are made, new equipment is used, and new procedures and processes are instituted.
- The facility's SOPs must identify the designated person(s).
- The designated person must review the SOPs at least every 12 months to ensure they reflect current practices.

USP <795> SOPs Requiring Changes

- Personnel training and competency
- Garbing
- Cleaning and sanitizing
- Master formulation records
- Beyond-Use-Dates
- Release inspections and testing
- Quality assurance/quality control
- Recalls

USP <797> SOPs Requiring Changes

- Immediate-Use CSPs
- CSP categories
- Personnel training and competency
- Garbing
- Cleaning, disinfecting, and applying sporicidal disinfectant
- Microbiological air and surface sampling
- Master formulation records and compounding records
- Sterilization and depyrogenation
- Sterility Testing
- Recalls

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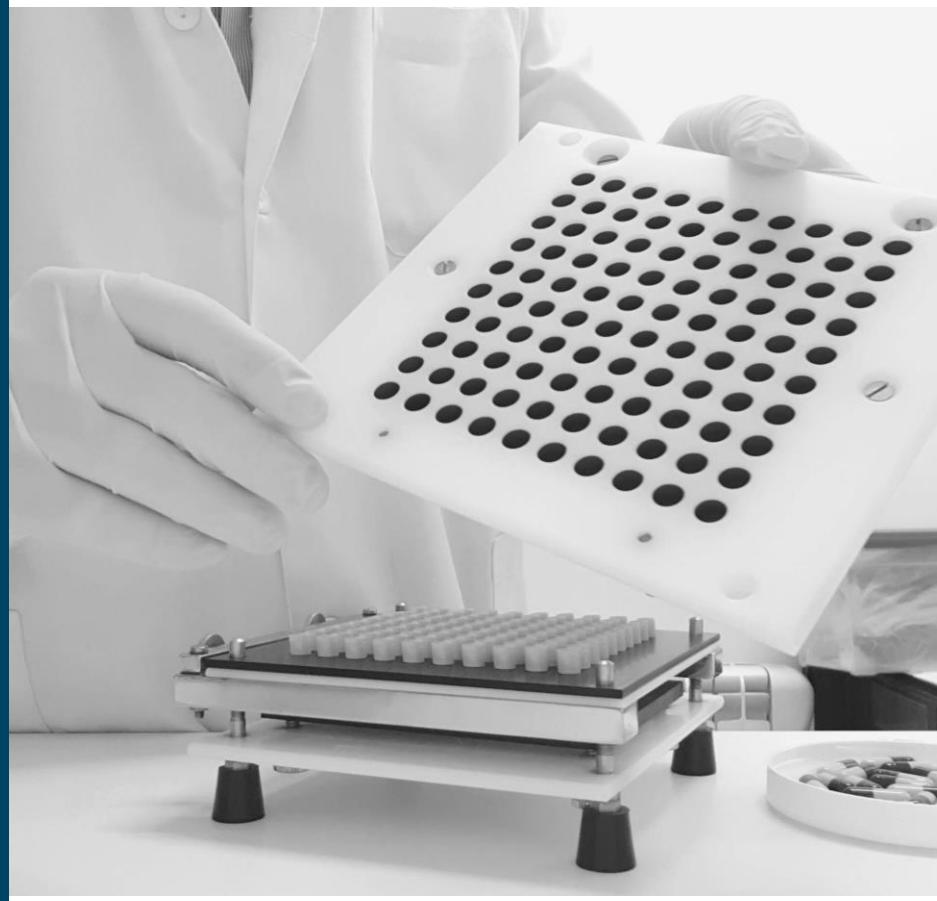
ACHCU Resources



ACHCU Resources

- Self-Assessment Tool
- Compounding Manuals

Questions?

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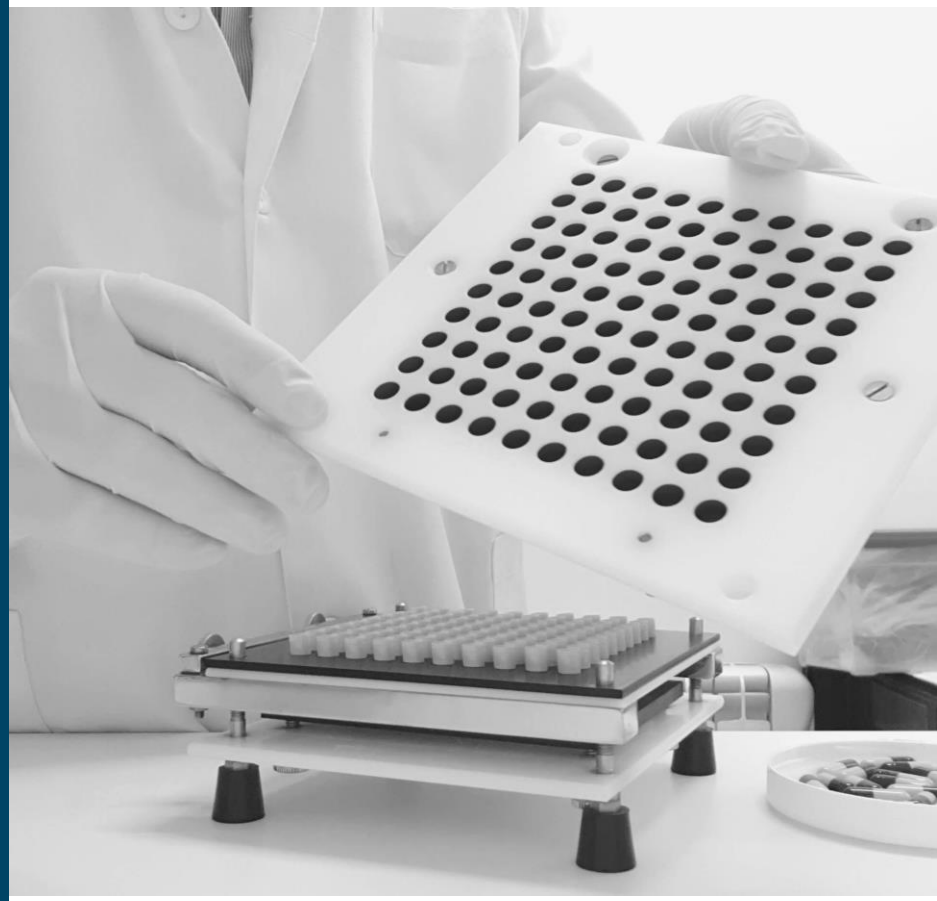

Thank you

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