USP 797 & 800 Compliance: Pathways to Competency and Accreditation Essentials

Dr. Marisol López Nieves
PharmD. MPH. BSPharm. RPh. FACA.
Assistant Professor
School of Pharmacy
Medical Sciences Campus
University of Puerto Rico

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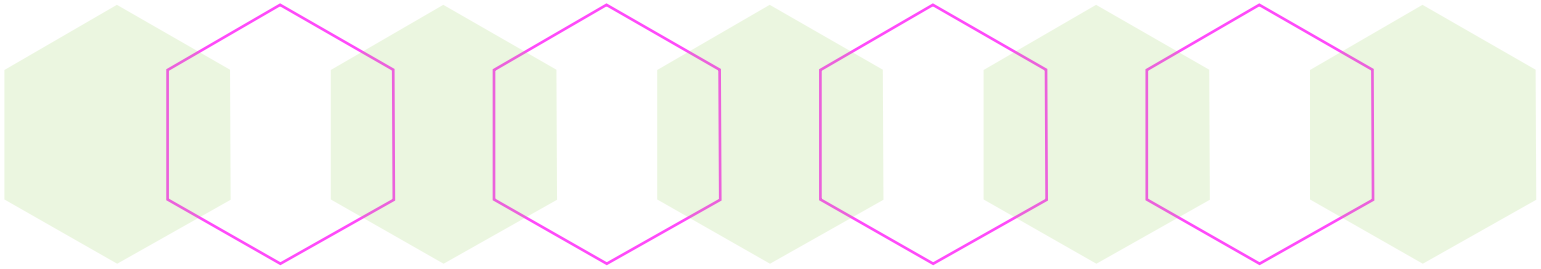

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Objectives - USP 797

- Explain the 2023 USP 797 updates and their application to sterile preparation practices.
- Explain the difference between risk levels and the new categories in USP 797.
- Discuss the competencies of personnel involved in sterile preparations as per USP 797.
- List the development and implementation steps of environmental, surface, and personnel monitoring programs, including Media-Fill and Finger-Tips tests.
- Describe key aspects of cleanroom engineering, design, and environmental controls required by accrediting agencies.
- Discuss the process of creating Standard Operating Procedures (SOPs) and Master Formulation documents with examples as required by USP 797.

Objectives -USP 800

- Identify Hazardous Drugs (HD), according to USP 800 and NIOSH criteria.
- List potential exposure routes and risks for handling Hazardous Drugs (HD) as per USP 800.
- Describe facility design for receiving, storing, and compounding hazardous drugs.
- Explain the use of personal protective equipment (PPE), and closed system drug transfer devices (CSTDs), following NIOSH and USP 800 guidelines, including the process for deactivation, cleaning, and disinfection after handling Hazardous Drugs (HD)

USP 797 Key Updates & How to Ensure Compliance with Audits

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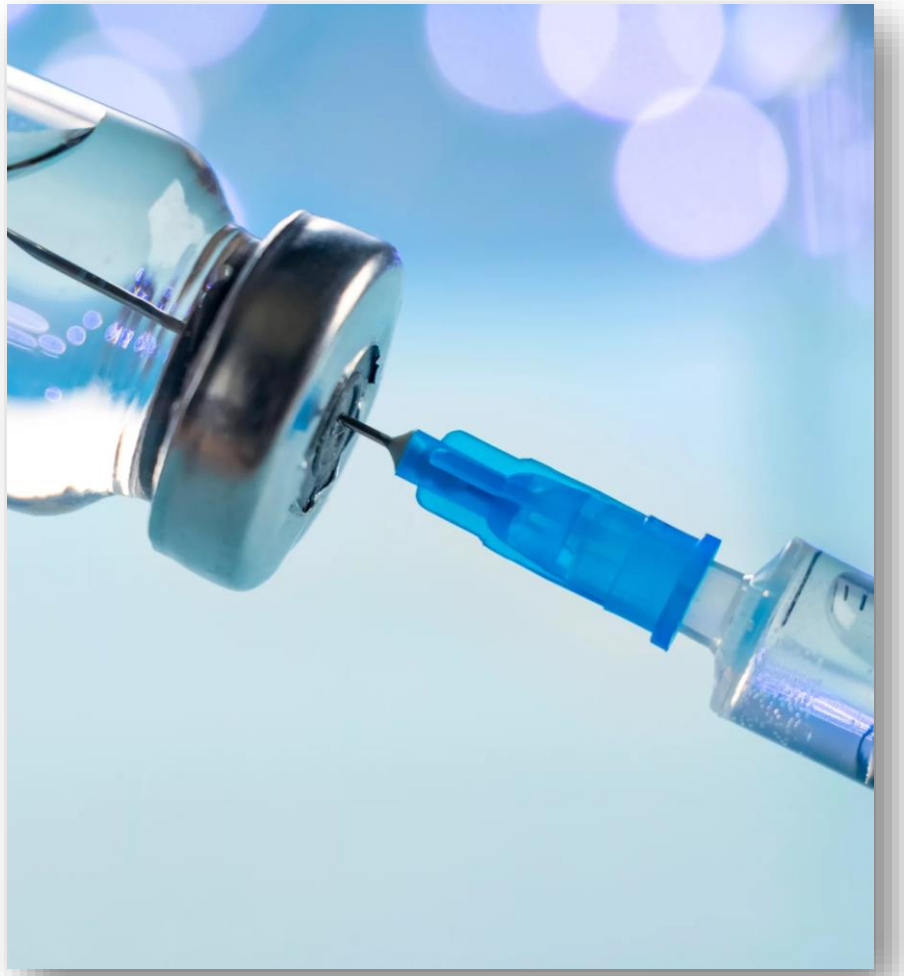


Image: https://emmainternational.com/aseptic-technique-in-sterile-drug-manufacturing/

USP Chapter Revision Dates

2008 Official → First Revision: 2019 → Second Revision: Sept 2021 → Third: Nov 1, 2022; Official Nov. 1, 2023

USP General Chapter <795>

USP General Chapter <797>

USP General Chapter <800>

https://www.usp.org/compounding

Top Areas of USP <797> Noncompliance

Standard	Requirement	Percent of Surveys Scored Noncompliant
HR.01.06.01	Competency Assessment	42.3%
IC.02.01.01	Infection Control Practices	31.2%
EC.02.06.01	Appropriate and Safe Environment	31.1%
EC.02.05.01	Maintaining Air Pressure	6.2%
LD.01.02.01	Taking Action for Testing Certification Reports	4.9%

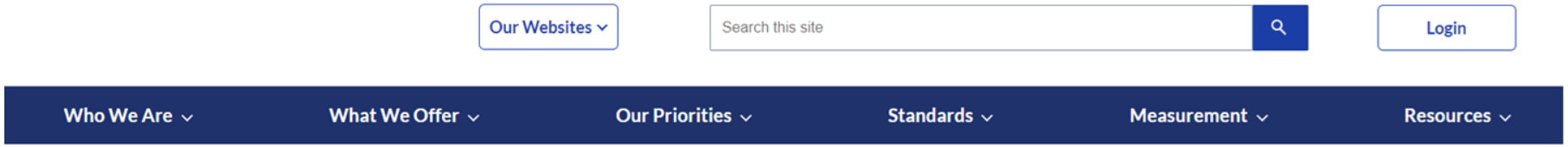
This table summarizes the top areas of noncompliance with USP <797> standards based on The Joint Commission 2018 survey data, Reference :https://www.pppmag.com/article/2514

Tops Areas of USP <797> Noncompliance

Standard	Requirement	Noncompliance Rate	Issues	Actions Required
HR.01.06.01	Staff Competency Assessment	Over 40%	Incomplete, insufficient, or infrequent assessments; observational and didactics with passing a test.	Perform observational and didactic assessments followed by a graded exam; regular testing
IC.02.01.01	Infection Control Practices	Over 30%	Improper use of PPE, incorrect aseptic practices, poor hand hygiene, HEPA filter performance	Ensure correct infection control practices and maintain HEPA filter performance
EC.02.06.01	Appropriate and Safe Environment	Over 30%	Failure to assure appropriate and safe environment in cleanroom design and function	Maintain cleanroom standards as per Environment of Care standards
LD.01.02.01	Correcting Certification Report Deficiencies	Almost 5%	Failure to correct deficiencies identified in certification reports	Address and document corrective actions for all identified deficiencies

The Joint Commission 2018 survey data, Reference :https://www.pppmag.com/article/2514

The Joint Commission Requirements



Home > Resources > News & Multimedia > Newsletters > Joint Commission Online > July 19 2023 > Updated reqs MC USP

Updated requirements for Medication Compounding align with USP revisions

To align with the U.S. Pharmacopeia (USP) revisions for medication compounding released in November 2022, The Joint Commission has revised its Medication Compounding (MC) chapter for home care organizations and the Medication Compounding Certification (MDC) program, which is available to Joint Commission-accredited hospitals, critical access hospitals, and home care pharmacy organizations. The revisions go into effect on Jan. 1, 2024.

The Joint Commission undertook a thorough analysis of the USP revisions and rewrote the MC and MDC requirements, resulting in the following:

- Revisions to the requirements to align with the updated USP requirements.
- Reorganization of the requirements.
- Renumbering of the standards.
- Reducing the number of elements of performance (EPs) in MC by 58% and MDC by 72%.

The revisions relate to general responsibilities, staff competency, the compounding environment, compounding operations, sterile and nonsterile compounding, and nuclear pharmacy.

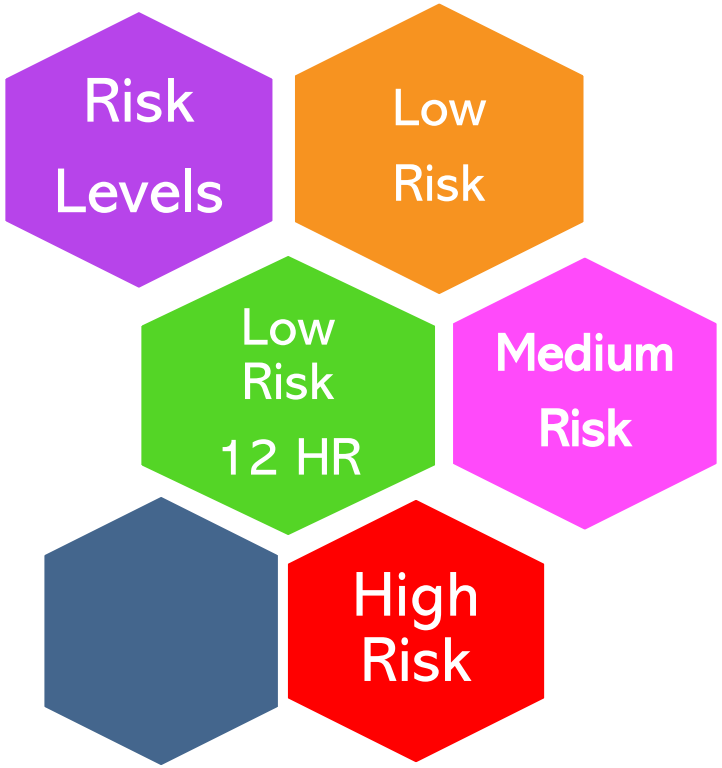
https://www.jointcommission.org/resources/news-and-multimedia/newsletters/newsletters/joint-commission-online/july-19-2023/updated-reqs-mc-usp/

Major Changes with USP Chapter <797>

- Official Date: November 1, 2023
  - Resulted from extensive public comments and practitioner feedback.

- **Key Changes Include:**
  1. **Facility Standards**: Enhanced requirements for cleanrooms and compounding areas.
  2. **Personnel Requirements**: Updated training and competency assessment protocols.
  3. **Monitoring Procedures**: Improved guidelines for environmental and quality control.
  4. **Work Practices**: Revised protocols to ensure safety and compliance.

From Risk Levels to Compounding Categories



Category 1

Category 2

Category 3

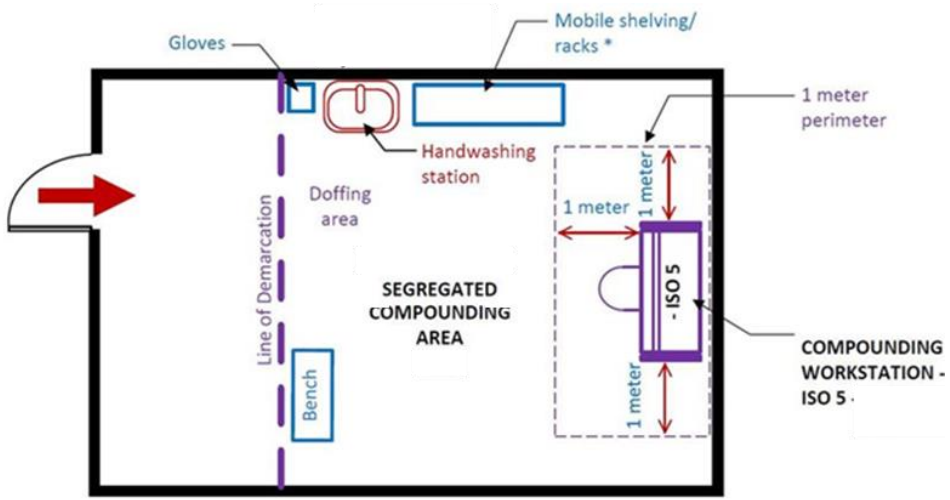
Compounding Categories

Category	Description	Requirements
Category 1	Compounded under **the least controlled environmental conditions**. BUD: 12 hours or less at room temperature; 24 hours or less when refrigerated.	- Compounded by applicable requirements for Category 1 CSPs. **- BUD: ≤12 hours at controlled room temperature or ≤24 hours when refrigerated.**
Category 2	**Require more environmental controls and testing** than Category 1 CSPs. May be assigned a BUD of greater than 12 hours at room temperature or more than 24 hours if refrigerated, but not exceeding established limits.	**- More stringent environmental controls and testing.** - BUD: >12 hours at controlled room temperature or >24 hours when refrigerated, but within established limits.
Category 3	**Undergo sterility testing, supplemented by endotoxin testing when applicable**. **More requirements than Category 2** CSPs for personnel qualification, use of sterile garb, use of sporicidal disinfectants, frequency of environmental monitoring, and stability determination. Assigned longer BUDs.	**- Sterility testing and endotoxin testing when applicable.** **- Additional requirements for personnel qualification, sterile garb, sporicidal disinfectants, environmental monitoring, and stability determination**. - **BUD: Longer than Category 2 CSPs** but within established limits.

Compounding Categories

Category 1

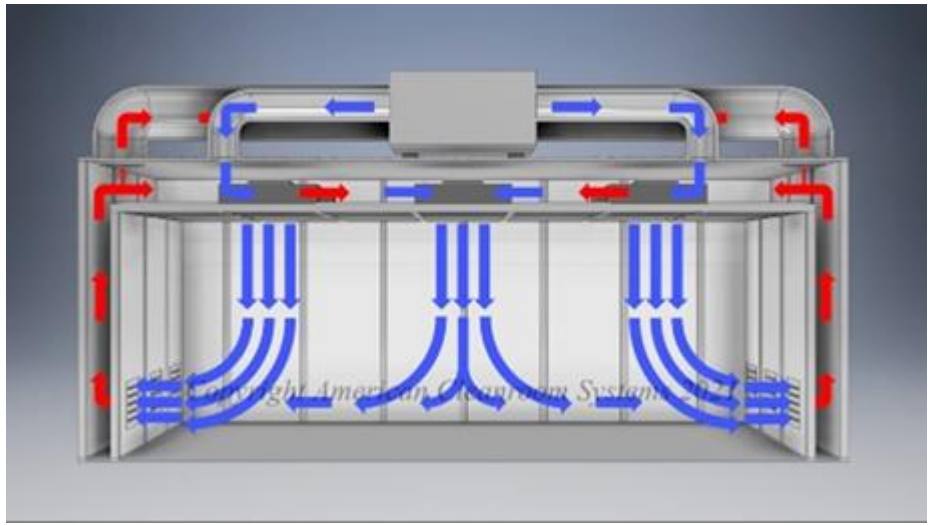
- Segregated Compounding Area (SCA)



BUD:
- ≤12 hours at controlled room temperature
- ≤24 hours when refrigerated.

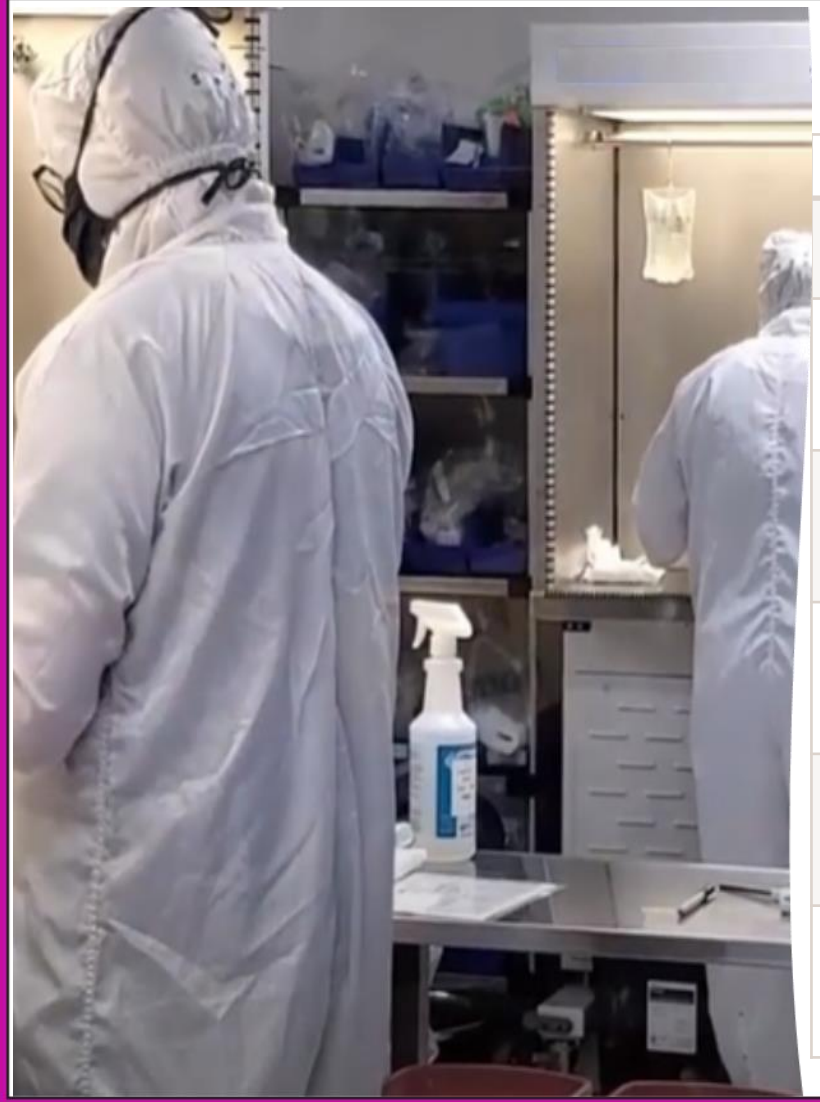
Image: https://www.readkong.com/page/sterile-compounding-pharmacies-for-hospital-facilities-1492087

Category 2



BUD:
>12 hours at controlled room temperature
>24 hours when refrigerated, but within established limits

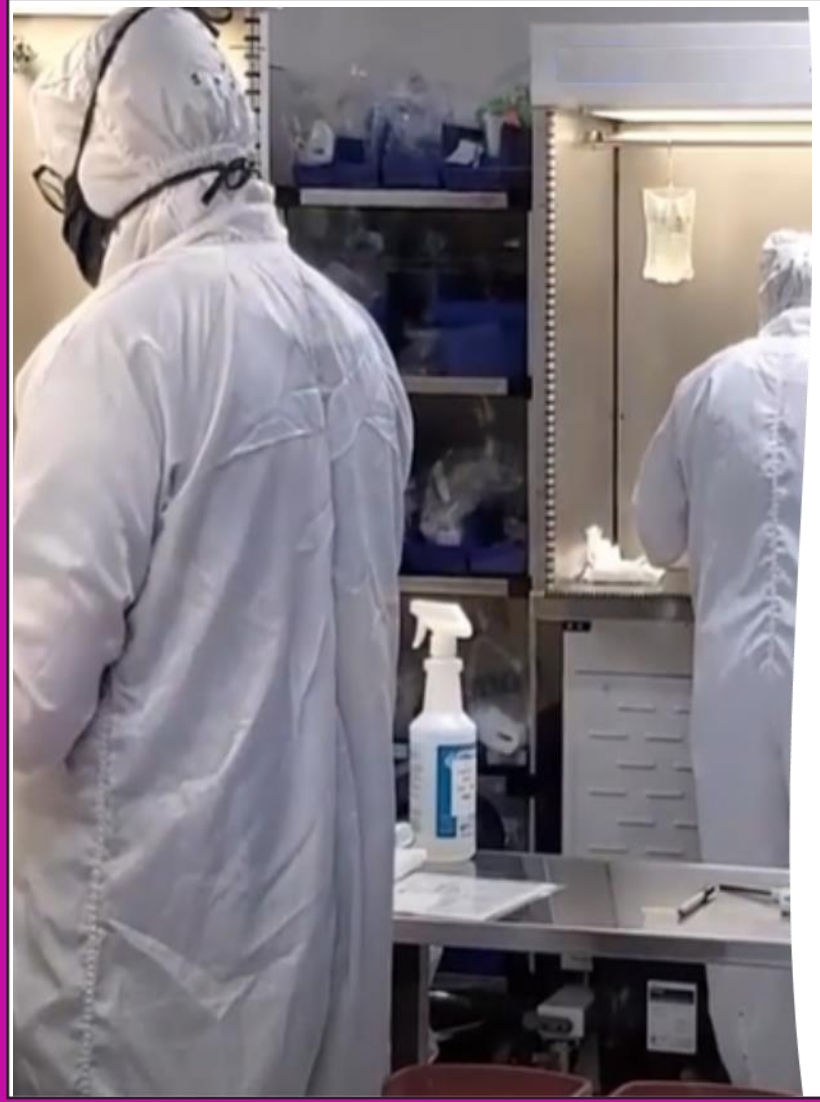
Image: https://www.americancleanrooms.com/all-about-cleanroom-hepa-fan-filter-units/



Demonstrating Knowledge and Competency of Core Skills

Competency Area	Description
Hand hygiene	Proper handwashing techniques to reduce contamination risk.
Garbing	Correct use of personal protective equipment (PPE), including gowns, gloves, masks, and other garbing procedures.
Cleaning and disinfection	Knowledge of protocols for cleaning and disinfecting compounding areas and equipment to prevent contamination.
Calculations, measuring, and mixing	Ability to accurately perform pharmaceutical calculations, measure ingredients, and mix compounds.
Aseptic technique	Mastery of techniques to maintain sterility during the compounding process, preventing contamination of CSPs.
Achieving and/or maintaining sterility (and apyrogenicity)	Ensuring the sterility of compounded products and preventing pyrogenic contamination, especially with nonsterile components.

Images: Best Practices for Compounding Garbing https://www.pppmag.com/article/1988



Demonstrating Knowledge and Competency of Core Skills

Competency Area	Description
Use of equipment	Competency in operating and maintaining all equipment used in the compounding process.
Documentation	Proper documentation of the compounding process (e.g., master formulation and compounding records).
HEPA-filtered airflow	Understanding principles of high-efficiency particulate air (HEPA)-filtered unidirectional airflow within the ISO Class 5 area.
Proper use of Primary Engineering Controls PECs	Proficient (skilled and competent) use of primary engineering controls (PECs) in the compounding process.
Movement principles	Understanding principles of movement of materials and personnel within the compounding area to minimize contamination.

Images: Best Practices for Compounding Garbing https://www.pppmag.com/article/1988

Reference: https://ashpadvantage.com/expert-insight/dos-and-donts-of-usp-chapter-797-personnel-training/

Personnel Training and Evaluation

Aspect	Details
Initial Training and Qualification	Personnel must demonstrate knowledge and competency in compounding CSPs before starting their job independently.
Designated Person(s) Responsibility	Responsible for creating and implementing the training program and ensuring all relevant personnel are trained and qualified.
Trainer	Training and observation can be performed by the designated person(s) or an assigned trainer.
Training Frequency	- **Compounding personnel**: **Initially and every 12 months.;** **Restocking/cleaning personnel**: As per facility SOPs.; **Immediate-use CSPs personnel**: As per facility SOPs.
Written Training Program	Must **detail required training, frequency, and evaluation processes**.
Skills and Knowledge Demonstration	Must demonstrate competency in sterile manipulations and maintaining environmental conditions **initially and every 12 months.**
Documentation	Training and evaluation must be documented.

Image: https://www.pharmaceutical-technology.com/features/pharma-inspections/

Competencies and frequency requirements for USP 797

Competency	2008	Official Nov 1, 2023
Visual Observation of Hand Hygiene and Garbing	Annually	**- Category 1 & 2: Every 6 months** - Category 3: Every 3 months for personnel who compound Category 3 CSPs
Gloved Fingertip and Thumb Sampling	- Low/Medium-Risk CSPs: Annually - High-Risk CSPs: Semi-annually	**- Category 1 & 2: Every 6 months** - Category 3: Every 3 months for personnel who compound Category 3 CSPs as part of garbing competency and aseptic competency
Media-Fill Test	- Low/Medium-Risk CSPs: Annually - High-Risk CSPs: Semi-annually	**- Category 1 & 2: Every 6 months** - Category 3: Every 3 months for personnel who compound Category 3 CSPs

Garbing & Hand Hygiene

Action	Description
Remove Outer Garments	Remove personal outer garments (e.g., bandanas, coats, hats, jackets, sweaters, vests).
Remove Cosmetics	Remove all cosmetics to prevent shedding flakes and particles.
Remove Jewelry	Remove all hand, wrist, and other exposed jewelry, including piercings, that could interfere with garbing or increase contamination risk. Cover if necessary.
No Earbuds or Headphones	Do not wear earbuds or headphones.
No Unnecessary Electronic Devices	Do not bring unnecessary electronic devices into the compounding area.
Maintain Nail Hygiene	Keep nails clean and trimmed. Do not wear nail products (e.g., polish, artificial nails, extenders).
Wipe Eyeglasses	Wipe eyeglasses if worn.

Images: Best Practices for Compounding Garbing https://www.pppmag.com/article/1988
https://chaddertonopticians.co.uk/how-to-clean-your-glasses-properly/w-to-clean-your-glasses-properly/

Hand Hygiene

Hand Washing Procedures

Nail Cleaning: Clean underneath fingernails under warm running water using a disposable nail cleaner.

Washing: Wash hands and forearms up to the elbows with soap and water for at least 30 seconds.

Drying: Dry hands and forearms completely with low-lint disposable towels or wipers.

Images: Best Practices for Compounding Garbing https://www.pppmag.com/article/1988

Garbing and Gloving Requirements for Category 1 and Category 2

Low-lint Garments:

- Snug-fitting sleeves and enclosed neck (e.g., gown or coverall).
- Shoe covers, head cover, face mask, and facial hair cover if needed.

Sterile Powder-free Gloves:

- Must be sterile and powder-free.
- Apply sterile 70% IPA before and during compounding.
- Inspect and replace if damaged.

Additional Requirements

- **Replace Garb**: If soiled or compromised.
- **Store Garb**: Away from contamination sources like sinks.
- **Reuse Gowns:** Within the same shift, if kept in a clean area.
- **Discard Garb:** Except gowns, when exiting the compounding area.

Images: Best Practices for Compounding Garbing https://www.pppmag.com/article/1988

Competency Testing in Aseptic Manipulation

Gloved Fingertip and Thumb sampling; **Frequency: Minimum every 6 months**

Procedure Step	Description
Sampling Media Device	Use one media device (e.g., plates) per hand with TSA agar and neutralizing additives (lecithin, polysorbate 80).
Labeling	Label device with personnel identifier, hand (right/left), and date/time of sampling.
Avoiding False-Negatives	**Do NOT apply sterile 70% IPA to gloves before sampling.**
Sampling Procedure	Roll fingertip and thumb pads over the agar surface on separate devices for each hand.
Incubation	Incubate **at 30°–35°C for ≥48 hours, then at 20°–25°C for ≥5 days.**
Handling and Storage	Prevent contamination and condensate on agar by inverting plates during incubation.
Recording Results	Record colony-forming units (cfu) per hand.
CFU Count and Action Level	Count total cfu from both hands to determine if action levels are exceeded.

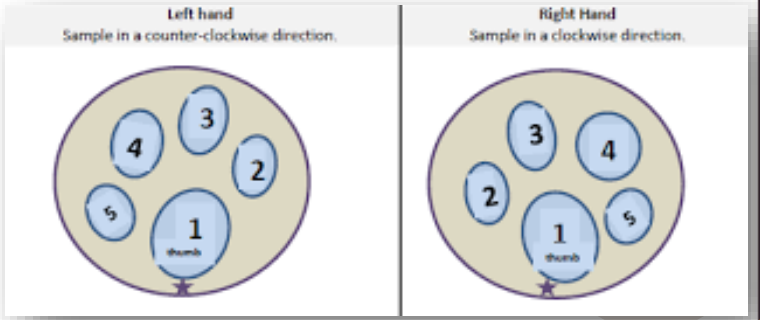


Image: http://www.bccancer.bc.ca/pharmacy-site/Documents/

Action levels for gloved fingertip and thumb sampling from USP <797>

Action Levels for Gloved Fingertip and Thumb Sampling	Action Levels (cfu, total from both hands)
After garbing	>0
After media-fill testing	>3

Successful completion of the gloved fingertip and thumb sampling after media-fill testing is defined as ≤3 cfu as a total from both hands

Competency Testing in Aseptic Manipulation: Media-Fill Testing Procedure

Frequency: Minimum every 6 months

Media-Fill Test Procedures

- **Simulation**:
  - Use soybean–casein digest media to simulate challenging aseptic compounding procedures.
- **Capture Factors**:
  - **Process length (operator fatigue, equipment quality)**.
  - Number of aseptic additions or transfers.
  - **Type and complexity of manipulations**.
  - Number of personnel in the buffer room or Segregated Compounding Area (SCA).
- **Commercial Media**:
  - Obtain a Certificate of Analysis (COA).
  - Store as per manufacturer instructions.
  - Use before the expiration date.

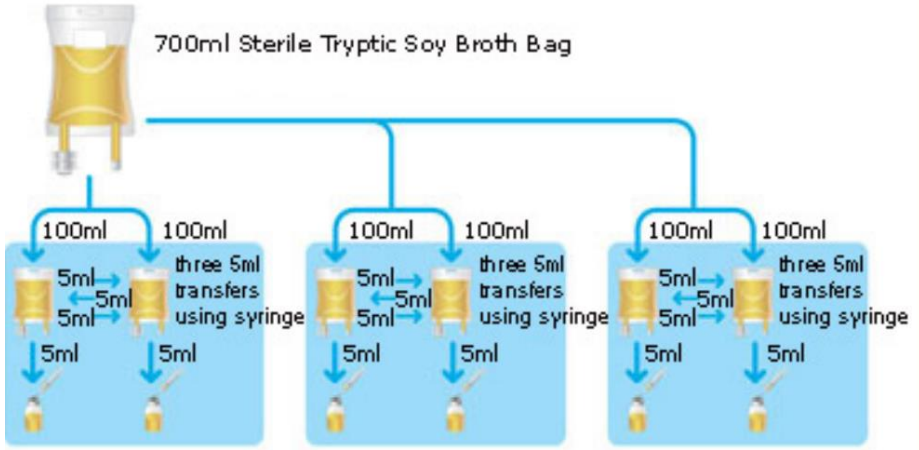


Image: https://hardydiagnostics.com/media/assets/product/documents/HardyValMedium-RiskLevelKit.pdf

Competency Testing in Aseptic Manipulation: Media-Fill Testing Procedure

Procedure Step	Description
Sterile Components Simulation	Simulate sterile-to-sterile compounding using sterile soybean–casein digest media in facility containers. No further dilution unless specified.
Nonsterile Components Simulation	Make a 3% solution with nonsterile soybean–casein digest powder and nonbacteriostatic water. Simulate nonsterile-to-sterile compounding. Prepare a positive control to show growth (turbidity upon incubation).
Sampling After Compounding	**Perform gloved fingertip and thumb sampling, and surface sampling inside the PEC before disinfecting gloves and PEC.** Store samples inverted to prevent contamination.
Incubation	**Incubate at 20°–25°C and 30°–35°C for at least 7 days each. Follow SOPs for incubation order. Use an incubator.**
Failure Indicators	**Visible turbidity or growth in any container closure unit within 14 days indicates failure.**

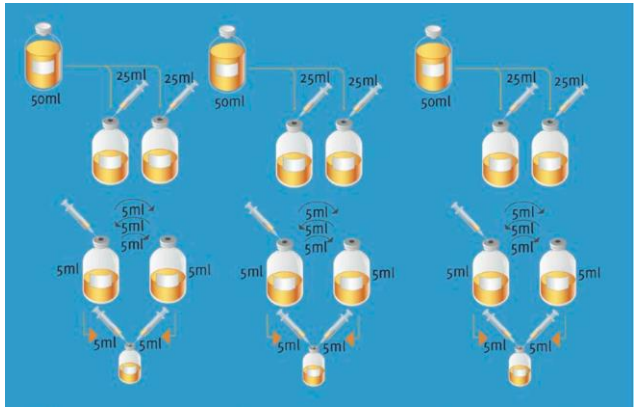


Image: https://hardydiagnostics.com/media/assets/product/documents/HardyValMedium-RiskLevelKit.pdf

Cleanroom Engineering

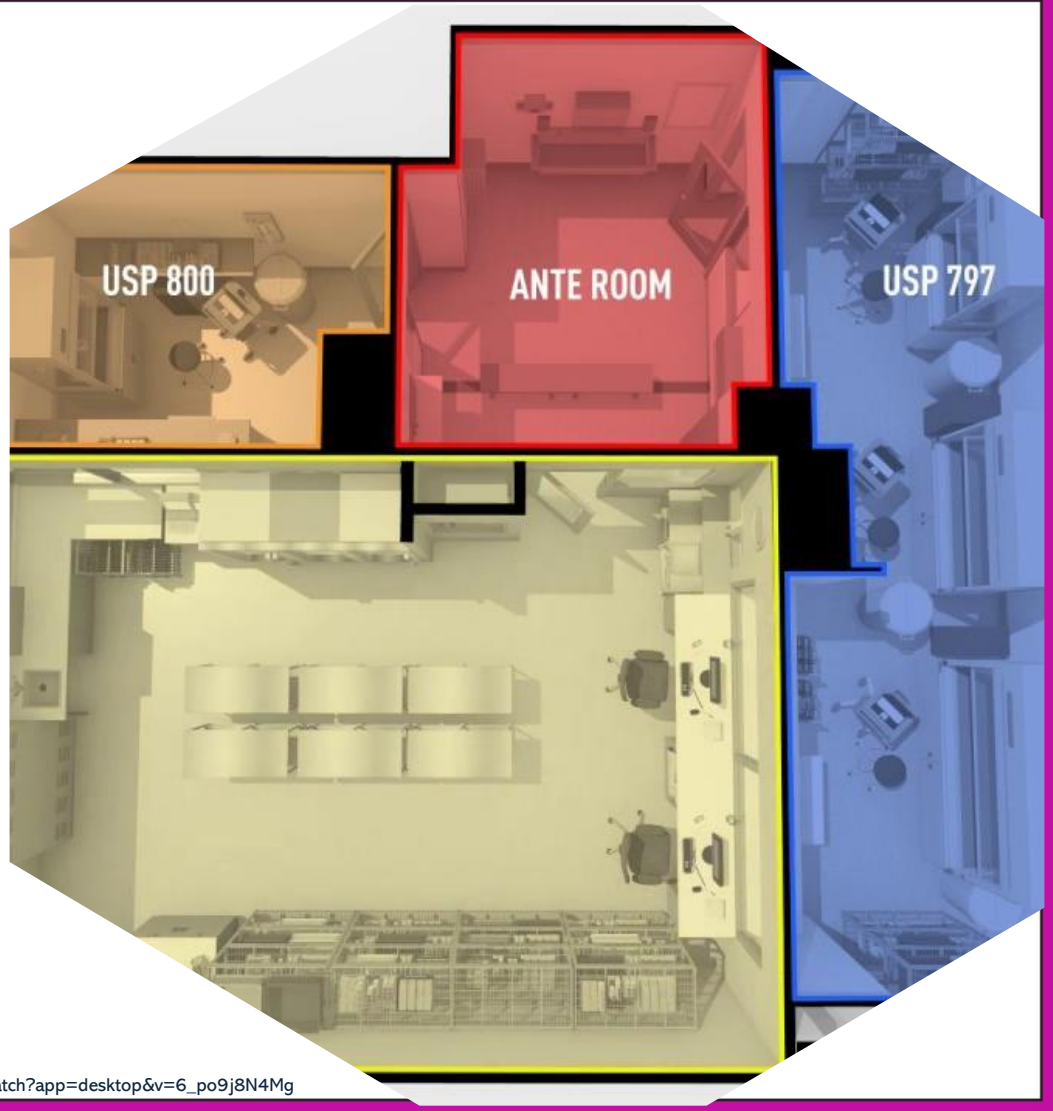


Image: Clean Room Design: Pharmacy Flow with USP 797 and USP 800 Standards: https://www.youtube.com/watch?app=desktop&v=6_po9j8N4Mg

Design Requirements to Maintain Air Quality

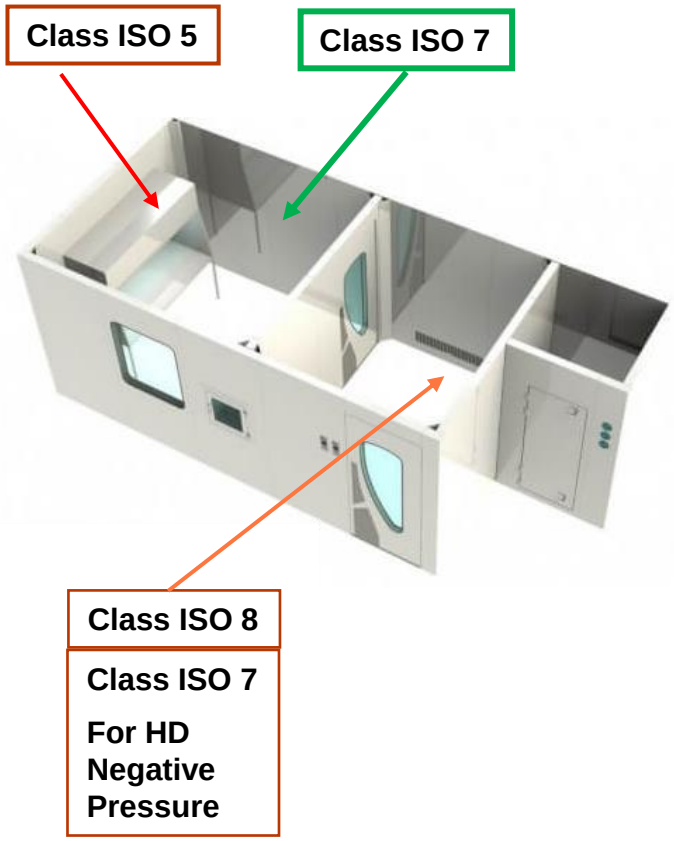
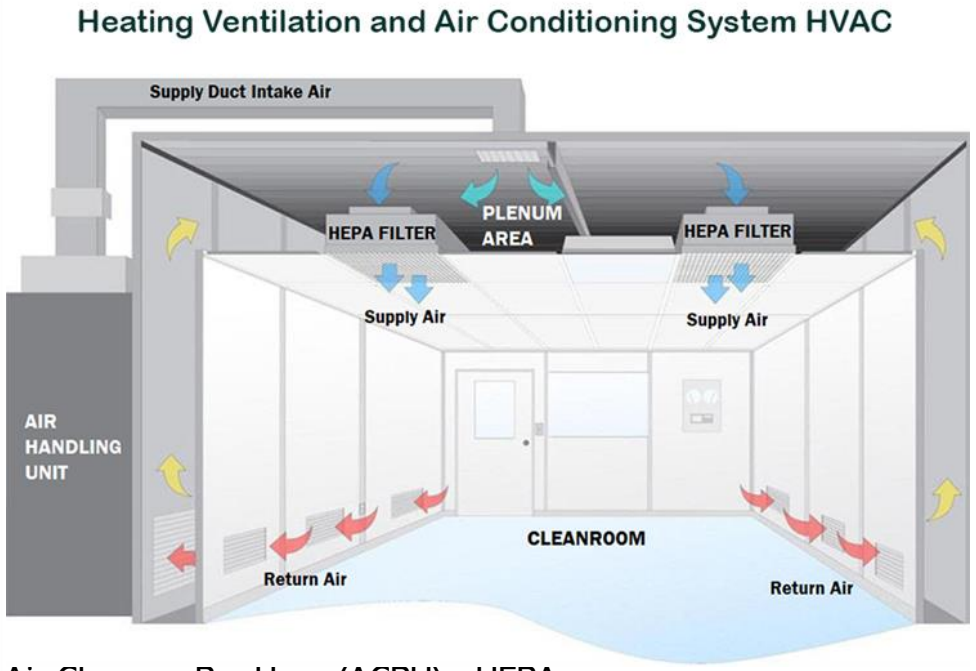


Image: https://www.mecart-cleanrooms.com

ISO Class	Particle Count per Cubic Meter
5	3,520
7	352,000
8	3,520,000

	ISO Class	Requirements
Cleanroom Suite		**Temperature ≤ 20°C, humidity ≤ 60%; monitored and documented daily**; controlled by HVAC system.
Anteroom (positive-pressure buffer room access)	ISO Class 8	For hand hygiene, garbing, and staging components; maintains air classification and pressure relationships.
Anteroom (HD negative-pressure buffer room access)	ISO Class 7	For hand hygiene, garbing, and staging components; maintains air classification and pressure relationships.
Buffer Room	ISO Class 7	Minimize activities affecting air quality where CSPs are prepared.
PEC (Category 1, 2, 3 CSPs)	ISO Class 5	For compounding CSPs. Category 1 CSPs can be compounded in an unclassified SCA.

Design Requirements to Maintain Air Quality



Air Changes Per Hour (ACPH) - HEPA
HVAC- Heating, ventilation, and Air conditioning
Pressure Requirements: inches of water column

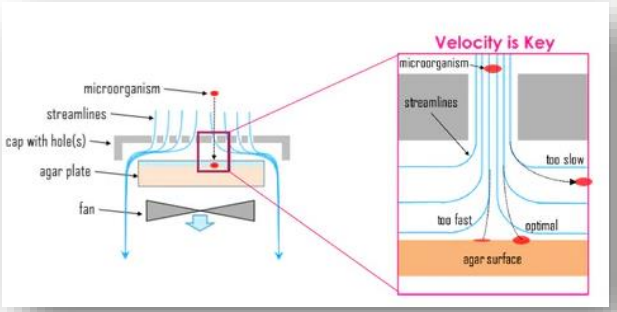
Image: https://ciqa.net/what-is-a-cleanroom/

Compounding Area	ACPH Requirement	Pressure Requirement
Unclassified SCA	No requirement	No differential required between SCA and surrounding area.
ISO Class 7 room(s)	≥30 ACPH	Minimum **0.020 -** inch water column between buffer room and anteroom.
ISO Class 7 room(s) HD Drugs WITH Ante-room ISO 7	≥30 ACPH	**Minimum 0.01- 0.03- inch water column** between buffer room and anteroom.
ISO Class 8 room(s)	≥20 ACPH	Minimum **0.020** - inch water column between anteroom and unclassified area.

Temperature and humidity monitoring **devices must be verified for accuracy at least every 12 months** or as required by the manufacturer.

Microbiological air and surface monitoring program

Monitoring Air for Viable Particles	Monitoring Surfaces for Viable Particles
Purpose: Assess microbiological air quality in all classified areas.	**Purpose**: Maintain a controlled environment for compounding CSPs.
Sampling Method: Volumetric active air sampling using an impaction air sampler.	**Sampling Method**: Surface sampling to evaluate cleaning, material handling, and personnel competency.
Frequency: Every 6 months.	**Frequency: Monthly, Verify with PR Dept. of Health** **Locations**: Each classified area, including rooms, interior of ISO Class 5 PEC, and pass-through chambers.
Viable Air Sampling Procedures - Avoid disturbing unidirectional airflow during sampling. - Incubate samples at specified temperatures. - Monitor and document incubator temperature. - Evaluate cfu counts against action levels and previous data to identify trends.	**Specific Sites**: Equipment in the PEC, staging/work areas near the PEC, and frequently touched surfaces. **Surface Sampling with Media-Fill Testing**: Conducted in the DCA to assess aseptic manipulation competency. **Timing**: At the end of a compounding activity or shift, but before cleaning and disinfecting the area. **Surface Sampling Procedures**: - Use media devices (e.g., plates, paddles, slides) containing microbial growth media for sampling flat surfaces; Verify sampling media devices meet growth promotion, pH, and sterilization requirements with COAs from the manufacturer. - Incubate samples at specified temperatures and monitor/document incubator temperature.
Goals: Determine contamination levels, assess personnel practices, and ensure cleaning/disinfecting agents are effective.	



Images:
https://pmtgbshop.com/blogs/news/active-air-sampling;
https://eagleanalytical.com/product-category/eagleshield/

Microbiological air and surface monitoring program

Action Levels for Viable Airborne Particle Air Sampling and Surface Sampling: These are set at levels where product quality, safety, or environmental control are potentially compromised

ISO Class	Air Sampling Action Levels (cfu/m³ or 1000 L of air/media device) Note: FDA indicates insanitary conditions if CUFs are present in ISO 5 *	Surface Sampling Action Levels (cfu/media device)
5	>1	>3
7	>10	>5
8	>100	>50

*FDA: https://www.fda.gov/media/124948/download

Image: https://www.oculyze.net/how-to-count-bacterial-colonies-on-agar-plate/

Corrective Actions for Exceeding Detection Frequencies

Aspect	Details
Detection Frequency	Should be based on actual monitoring data and tabulated monthly.
Action Levels	Should be based on empirical process capability. Corrective actions are needed if detection frequencies exceed recommendations or established process capability.
Corrective Actions	- Revision of the sanitization program (selection of antimicrobial agents, application methods, and frequencies) - Increased surveillance of personnel practices (including written critiques of aseptic methods and techniques) - Review of microbiological sampling methods and techniques - Additional training for gowning practices (if higher-than-typical recovery levels for glove and garment contamination are observed)

USP Chapter 1116: MICROBIOLOGICAL CONTROL AND MONITORING OF ASEPTIC PROCESSING ENVIRONMENTS, https://online.uspnf.com/uspnf/document/

CLEANING, DISINFECTING, AND APPLYING SPORICIDAL DISINFECTANTS AND STERILE 70% IPA

Activity	Description
Cleaning	Removing organic and inorganic materials from surfaces with a cleaning agent, using manual or mechanical processes.
Disinfecting	Destroying microorganisms using a chemical agent.
Applying Sporicidal Disinfectant	Destroying bacterial and fungal spores using a sporicidal agent.
Applying Sterile 70% IPA	- **After cleaning and disinfecting, or after using a one-step disinfectant cleaner or sporicidal disinfectant, to remove residue.** - Immediately before compounding. - During compounding on horizontal work surfaces of PEC **at least every 30 minutes** if the process takes 30 minutes or less; - **if more than 30 minutes, disinfect immediately after compounding.**

Image: https://www.pharmacypracticenews.com/Review-Articles/Article/06-23/Environmental-Monitoring-for-Sterile-Hazardous-Drug-Compounding/70371?ses=ogst

Cleaning and Disinfecting Frequency for Classified Areas and SCA

Site	Cleaning	Disinfecting	Applying Sporicidal Disinfectant
PEC(s) and Equipment Inside PEC	Daily on compounding days; when contamination is suspected	Daily on compounding days; when contamination is suspected	**Monthly (Category 1 & 2 CSPs)** Weekly (Category 3 CSPs)
Removable Work Tray of PEC	Daily work surface; monthly all surfaces and underneath	Daily work surface; monthly all surfaces and underneath	Monthly work surfaces Monthly all surfaces and underneath
Pass-through Chambers	Daily on compounding days	Daily on compounding days	**Monthly Category 1 & 2 CSPs)** Weekly (Category 3 CSPs)
Work Surface(s) Outside PEC	Daily on compounding days	Daily on compounding days	
Floor(s)	Daily on compounding days	Daily on compounding days	
Wall(s), Door(s), Door Frame(s)	Monthly	Monthly	Monthly
Ceiling(s)			
Storage Shelving and Bin(s)			
Equipment Outside PEC(s)			

Image: https://healthcare.contecinc.com/pharmacy-cleanroom-cleaning

DOCUMENTATION

Image: https://helpjuice.com/blog/software-documentation

Documentation Requirements

Category	Details
Personnel Training	Competency assessments and qualification records, including corrective actions for failures.
Certification Reports	Including corrective actions for failures.
Environmental Monitoring	Air and surface monitoring procedures and results.
Equipment Records	Calibration, verification, and maintenance reports.
Receipt of Components	Documentation of component receipt.
SOPs, MFRs, and CRs	Standard Operating Procedures (SOPs), Master Formulation Records (MFRs), and Compounding Records (CRs).
Release Inspection and Testing	Inspection and testing records upon release.
Complaints and Adverse Events	Information related to complaints and adverse events, including corrective actions taken.
Investigation Results	Results of investigations and corrective actions.

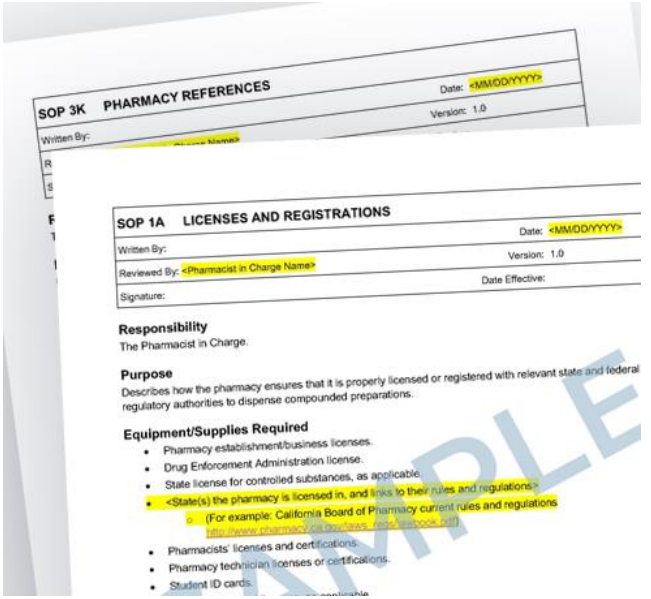
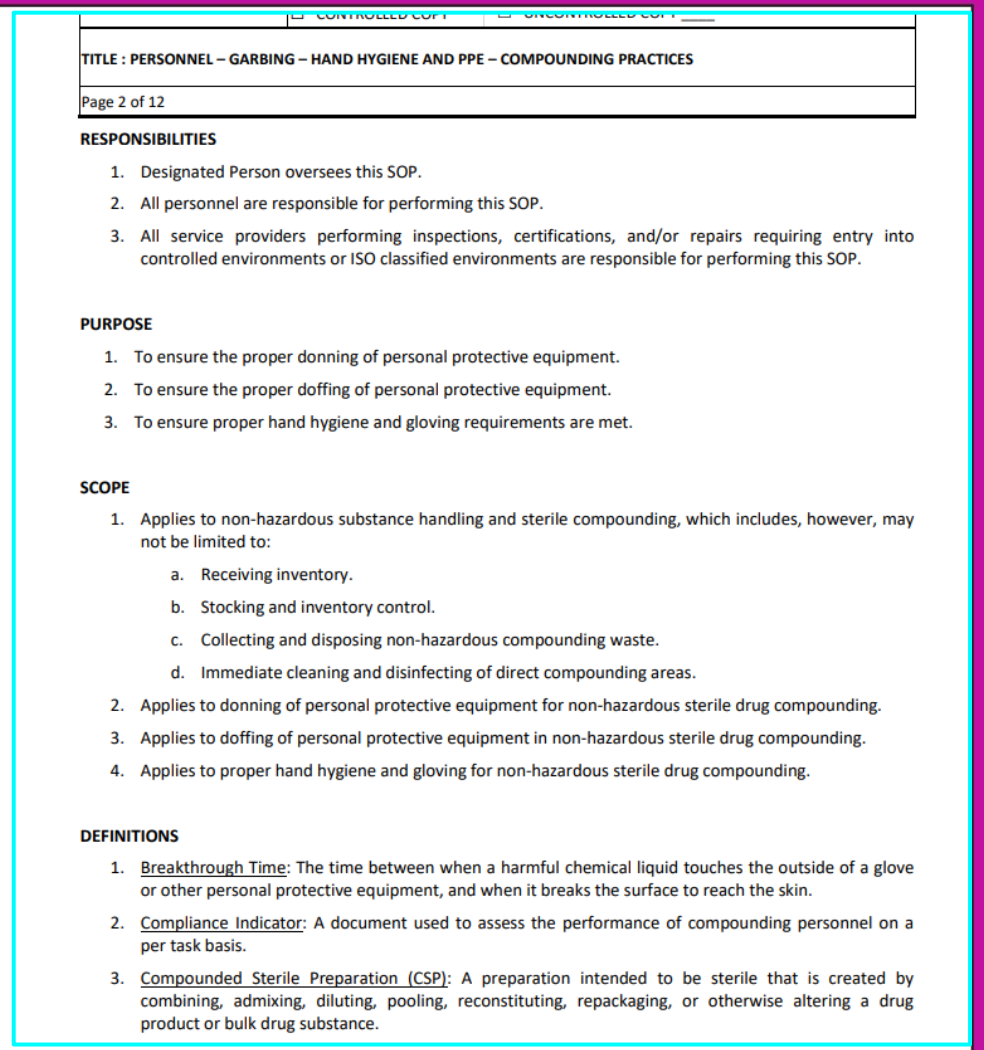


Image: https://www.accreditationuniversity.com/compounding-pharmacy-manua

SOP Sample

Section	Description
Purpose	Clearly state the reason for the SOP, including specific goals and objectives.
Scope	Define the boundaries and applicability of the SOP, specifying processes, departments, and personnel covered.
Responsibilities	Detail the roles and duties of individuals involved, specifying who performs, oversees, and ensures compliance.
Definitions	Provide clear explanations of terms and acronyms used within the SOP.
Frequency	Specify how often the procedures should be performed (daily, weekly, monthly, etc.).
Special Circumstances	Detail specific conditions requiring deviations from the standard procedure.
Procedure	Provide a step-by-step guide to completing the task, including instructions, necessary equipment, and safety precautions.



TITLE : PERSONNEL – GARBING – HAND HYGIENE AND PPE – COMPOUNDING PRACTICES

Page 2 of 12

RESPONSIBILITIES

1. Designated Person oversees this SOP.
2. All personnel are responsible for performing this SOP.
3. All service providers performing inspections, certifications, and/or repairs requiring entry into controlled environments or ISO classified environments are responsible for performing this SOP.

PURPOSE

1. To ensure the proper donning of personal protective equipment.
2. To ensure the proper doffing of personal protective equipment.
3. To ensure proper hand hygiene and gloving requirements are met.

SCOPE

1. Applies to non-hazardous substance handling and sterile compounding, which includes, however, may not be limited to:
   a. Receiving inventory.
   b. Stocking and inventory control.
   c. Collecting and disposing non-hazardous compounding waste.
   d. Immediate cleaning and disinfecting of direct compounding areas.
2. Applies to donning of personal protective equipment for non-hazardous sterile drug compounding.
3. Applies to doffing of personal protective equipment in non-hazardous sterile drug compounding.
4. Applies to proper hand hygiene and gloving for non-hazardous sterile drug compounding.

DEFINITIONS

1. Breakthrough Time: The time between when a harmful chemical liquid touches the outside of a glove or other personal protective equipment, and when it breaks the surface to reach the skin.
2. Compliance Indicator: A document used to assess the performance of compounding personnel on a per task basis.
3. Compounded Sterile Preparation (CSP): A preparation intended to be sterile that is created by combining, admixing, diluting, pooling, reconstituting, repackaging, or otherwise altering a drug product or bulk drug substance.

Reference: https://www.medisca.net/technical-services/standard-operating-procedures/package-options

Master Formulation Records (MFR)

Information	Details
Name, Strength or Activity, and Dosage Form	Include the name, strength, or activity, and dosage form of the CSP.
Ingredients	List identities and amounts of all ingredients. Include relevant characteristics (e.g., particle size, salt form, purity grade, solubility) if applicable.
Container Closure System	Specify the type and size of container closure system(s).
Preparation Instructions	Provide complete instructions for preparing the CSP. Include equipment, supplies, a description of the compounding steps, and any special precautions.
Physical Description	Describe the final CSP physically.
Beyond Use Date (BUD) and Storage Requirements	Specify BUD and storage requirements.
Stability Reference	Reference source to support the stability of the CSP.
Quality Control (QC) Procedures	Include QC procedures (e.g., pH testing, filter integrity testing).
Additional Information	Add other information as needed to describe the compounding process and ensure repeatability. Examples: adjusting pH and tonicity, sterilization method (steam, dry heat, irradiation, or filter).

Compounding Records (CR)

Information	Details
Name, Strength or Activity, and Dosage Form	Include the name, strength, or activity, and dosage form of the CSP.
Date and Time of Preparation	Record the date and time of preparation of the CSP.
Internal Identification Number	Assigned internal identification number (e.g., prescription, order, or lot number).
Identification of Individuals	Method to identify individuals involved in the compounding process and those verifying the final CSP.
Name of Each Component	List the name of each component used in the CSP.
Component Details	Include vendor, lot number, and expiration date for each component for CSPs prepared for more than one patient and for CSPs prepared from nonsterile ingredient(s).
Weight or Volume of Each Component	Record the weight or volume of each component used.
Strength or Activity of Each Component	Document the strength or activity of each component.
Total Quantity Compounded	Specify the total quantity compounded.
Final Yield	Record the final yield (e.g., quantity, containers, number of units).
BUD and Storage Requirements	Assigned BUD and storage requirements.
Results of QC Procedures	Document the results of QC procedures (e.g., visual inspection, filter integrity testing, pH testing).
Additional Information (if applicable)	
MFR Reference	Reference the MFR for the CSP.
Calculations	Document calculations made to determine and verify quantities and/or concentrations of components.

USP 800

https://www.usp.org/compounding/general-chapter-hazardous-drugs-handling-healthcare

USP 800: Handling Hazardous Drugs

Purpose:

- Establish standards for handling hazardous drugs (HDs) to ensure safety and environmental protection.

Scope:

- Applies to all healthcare personnel and entities involved in the receipt, storage, compounding, dispensing, administration, and disposal of HDs.

Applicable Personnel:

- Includes pharmacists, pharmacy technicians, nurses, physicians, physician assistants, home healthcare workers, veterinarians, and veterinary technicians.

Exposure to Hazardous Drugs

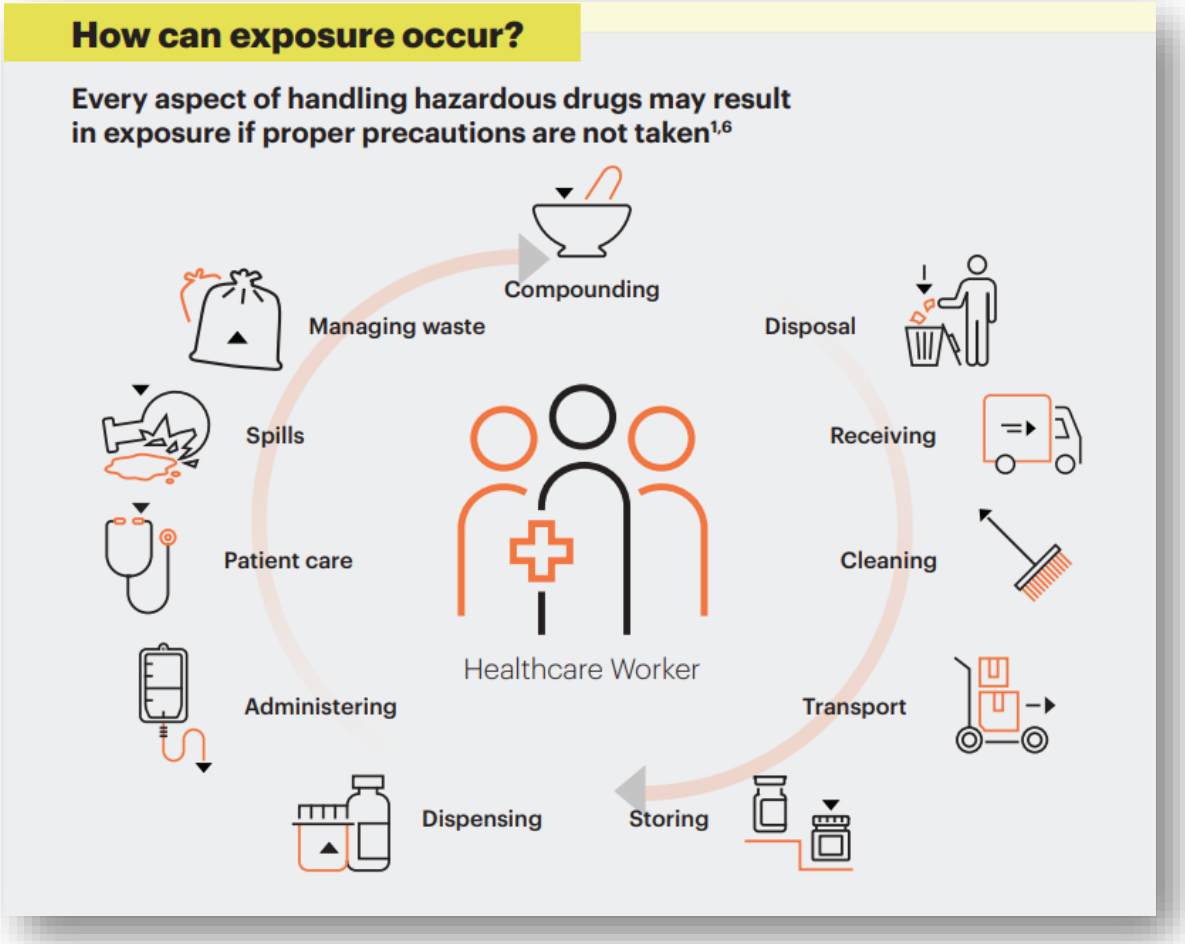


Image: https://go.usp.org/l/323321/2024-06-21/933zjb/323321/1719262147J1QzHs8e/USP_GC_800_know_your_exposure_to_hazardous_drugs

Activity	Potential Opportunity of Exposure
Receipt	- Contacting HD residues on drug containers, individual dosage units, outer containers, work surfaces, or floors.
Dispensing	- Counting or repackaging tablets and capsules.
Compounding and Other Manipulations	- Crushing or splitting tablets or opening capsules. -Pouring oral or topical liquids from one container to another. - Weighing or mixing components. - Constituting or reconstituting powdered or lyophilized HDs. - Withdrawing or diluting injectable HDs from parenteral containers. - Expelling air or HDs from syringes. - Contacting HD residue on PPE or other garments. - Deactivating, decontaminating, cleaning, and disinfecting contaminated areas. - Maintenance of potentially contaminated equipment and devices.
Administration	- Generating aerosols during HD administration (e.g., injection, irrigation, oral, inhalation, or topical application). - Performing specialized procedures (e.g., intraoperative intraperitoneal injection or bladder instillation). - Priming an IV administration set.
Patient-Care Activities	- Handling body fluids (e.g., urine, feces, sweat, or vomit) or body-fluid-contaminated clothing, dressings, linens, and other materials.
Spills	- Spill generation, management, and disposal.
Transport	- Moving HDs within a healthcare setting.
Waste	- Collection and disposal of hazardous waste and trace contaminated waste.

Comparison of NIOSH and ASHP Definitions of Hazardous Drugs

Comparison of NIOSH and ASHP Definitions of Hazardous Drugs

NIOSH[6]	ASHP[4]
Carcinogenicity	Carcinogenicity in animal models, in the patient population, or in both as reported by the International Agency for Research on Cancer
Teratogenicity or developmental toxicity[a]	Teratogenicity in animal studies or in treated patients
Reproductive toxicity[a]	Fertility impairment in animal studies or in treated patients
Organ toxicity at low doses[a]	Evidence of serious organ or other toxicity at low doses in animal models or in treated patients
Genotoxicity[b]	Genotoxicity (i.e., mutagenicity and clastogenicity in short-term test systems)
Structure and toxicity profile of new drugs that mimic existing drugs determined hazardous by the above criteria	. . .

[a]The National Institute for Occupational Safety and Health (NIOSH) definition contains the following explanation: "All drugs have toxic side effects, but some exhibit toxicity at low doses. The level of toxicity reflects a continuum from relatively nontoxic to production of toxic effects in patients at low doses (for example, a few milligrams or less). For example, a daily therapeutic dose of 10 mg/day or a dose of 1 mg/kg/day in laboratory animals that produces serious organ toxicity, developmental toxicity, or reproductive toxicity has been used by the pharmaceutical industry to develop occupational exposure limits (OELs) of less than 10 micrograms/meter^3 after applying appropriate uncertainty factors [Sargent and Kirk 1988; Nauman and Sargent 1997; Sargent et al. 2002]. OELs in this range are typically established for potent or toxic drugs in the pharmaceutical industry. Under all circumstances, an evaluation of all available data should be conducted to protect health care workers."[6]

[b]The NIOSH definition contains the following explanation: "In evaluating mutagenicity for potentially hazardous drugs, responses from multiple test systems are needed before precautions can be required for handling such agents. The EPA evaluations include the type of cells affected and in vitro versus in vivo testing [51 Fed. Reg. 34006-34012 (1986)]."[6]

Reference: https://www.ashp.org/-/media/assets/policy-guidelines/docs/guidelines/handling-hazardous-drugs.ashx

NIOSH Procedures for Developing Hazardous Drug List

NIOSH Finalized Documents:

- Managing Hazardous Drug Exposures: Information for Healthcare Settings.
- Procedures for Developing the NIOSH List of Hazardous Drugs in Healthcare Settings.

New Two-Table Format:

- Developed from 2020 draft guidance.
- Allows more flexibility for certain drugs under USP General Chapter <800>.

ASHP Support:

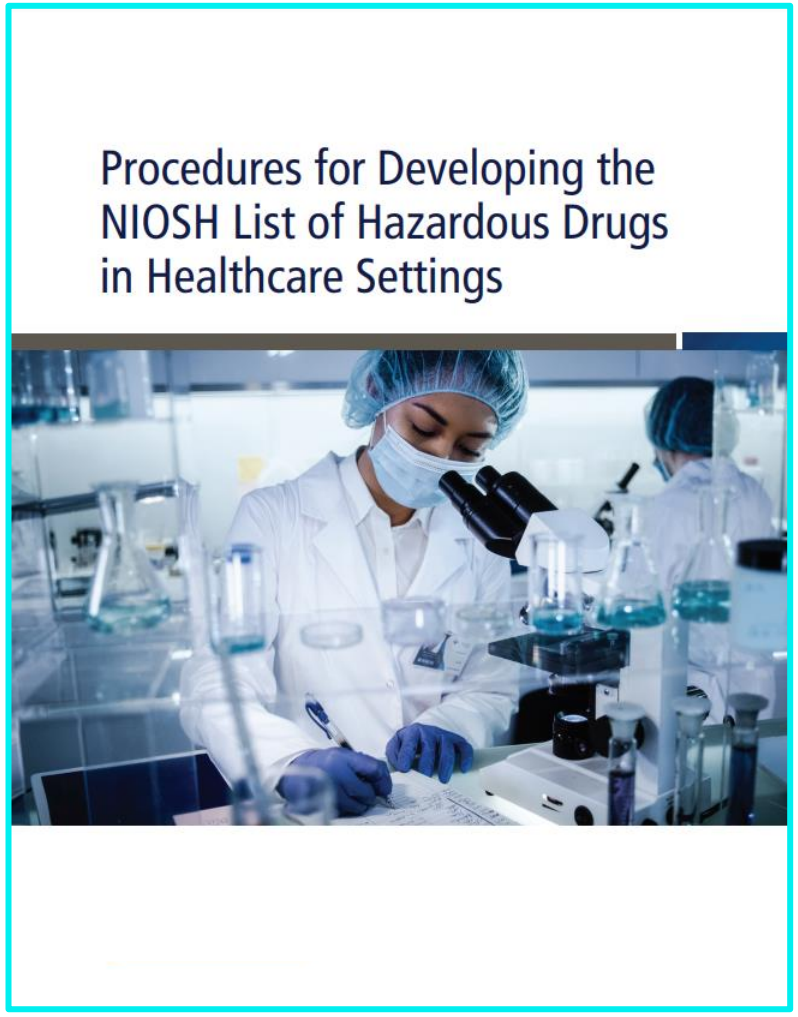
- ASHP submitted comments supporting the new format in 2020.

Current NIOSH List:

- **2016 list is the most recent final document** until the 2023 list is published in the Federal Register.

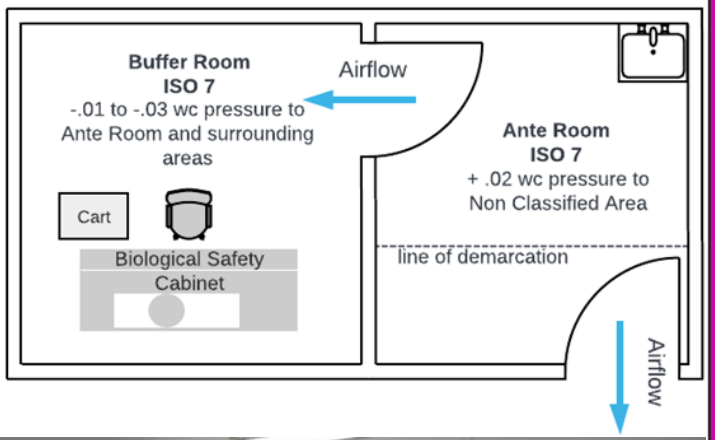
https://news.ashp.org/news/ashp-news/2023/04/27/niosh-finalizes-procedures-for-developing-hazardous-drug-list

https://www.cdc.gov/niosh/docs/2023-130/



https://www.cdc.gov/niosh/docs/2023-129/

Aspect	Details of Engineering Controls for Handling HDs
Receipt	- Antineoplastic HDs and HD APIs **must be unpacked in neutral/negative pressure areas.** - Not in sterile compounding or positive pressure areas.
Storage	- **Prevent spillage or breakage**. - Not stored on the floor. - **Antineoplastic HDs requiring manipulation and HD APIs stored separately in a negative pressure room with at least 12 ACPH.** - **Refrigerated antineoplastic HDs stored in a dedicated fridge in a negative pressure area with at least 12 ACPH.**
Compounding	**Containment Secondary Engineering Control (C-SEC):** -The room where the C-PEC is placed, is designed to contain HD contamination. - **Must be externally vented**. - Physically separated from other preparation areas. Appropriate air exchange (e.g., ACPH). - **Negative pressure (0.01 to 0.03 inches of water column)** relative to adjacent areas. **Additional controls (e.g., closed-system drug-transfer devices [CSTDs]) to provide extra protection**.



Images: https://www.propharmacleanrooms.com/news/cascading-airflow-design
https://mcdmag.com/2019/05/is-your-hospital-ready-for-usp797-800/

Receipt of Hazardous Drugs

- **Unpacking Area**:
  - Must be neutral/normal or negative pressure relative to surrounding areas.
- **Prohibited Areas**:
  - Do not unpack antineoplastic HDs and HD APIs in sterile compounding areas.
  - Do not unpack in positive pressure areas.

Image: Ready for 800 Receiving and Storage: https://youtu.be/ZnOTQ9EBcTQ

Personal Protective Equipment (PPE) for Handling Hazardous Drugs

Type of PPE	Description
Gloves	- **Must meet ASTM standard D6978** (or its successor); Powder-free. - Inspected for defects before use; **Outer chemotherapy gloves must be sterile for sterile compounding**; - **Changed every 30 minutes or when torn, punctured, or contaminated**. - Hands washed after removal.
Gowns	- **Disposable and resistant to HD permeability**; Made of polyethylene-coated polypropylene or similar materials; Closed in the back, long-sleeved, with closed cuffs. - **Changed every 2–3 hours or after a spill/splash; Not worn to other areas**.
Head, Hair, Shoe, and Sleeve Covers	- Head and hair covers (including beard and mustache, if applicable), shoe covers, and sleeve covers protect from HD residue. - Second pair of shoe covers required when compounding HDs in C-SEC. - Disposable sleeve covers made of polyethylene-coated polypropylene offer better protection.
Eye and Face Protection	- Worn when there is a risk of spills or splashes. - Full-facepiece respirator or goggles with face shields are recommended. - Eyeglasses or safety glasses with side shields do not provide adequate protection.
Respiratory Protection	- Elastomeric half-mask with multi-gas cartridge and P100-filter for unpacking HDs. - N95 respirator for most activities but does not protect against gases and vapors. - Full-facepiece, chemical cartridge-type respirator or PAPR for high-risk situations (e.g., large spills, deactivating/cleaning C-PEC).

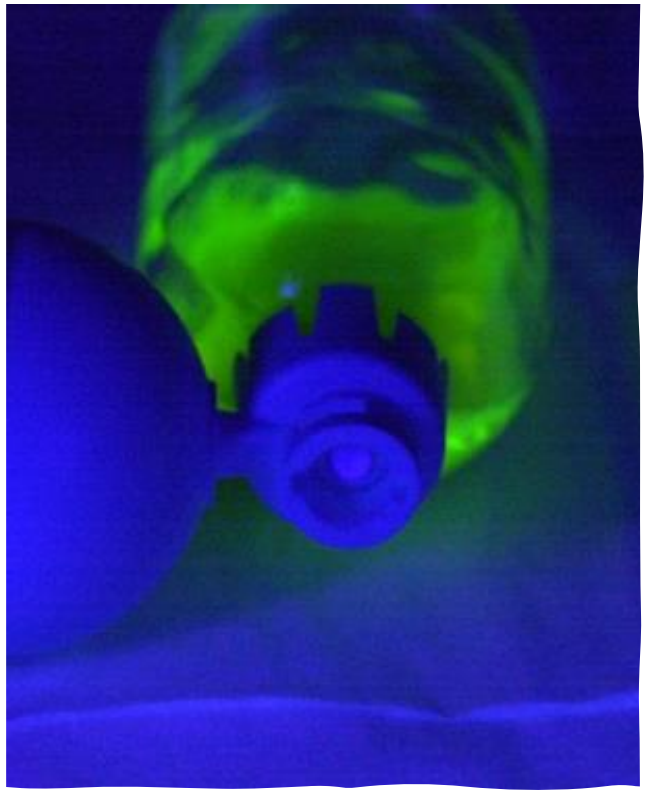
Personal Protective Equipment (PPE) for Handling Hazardous Drugs

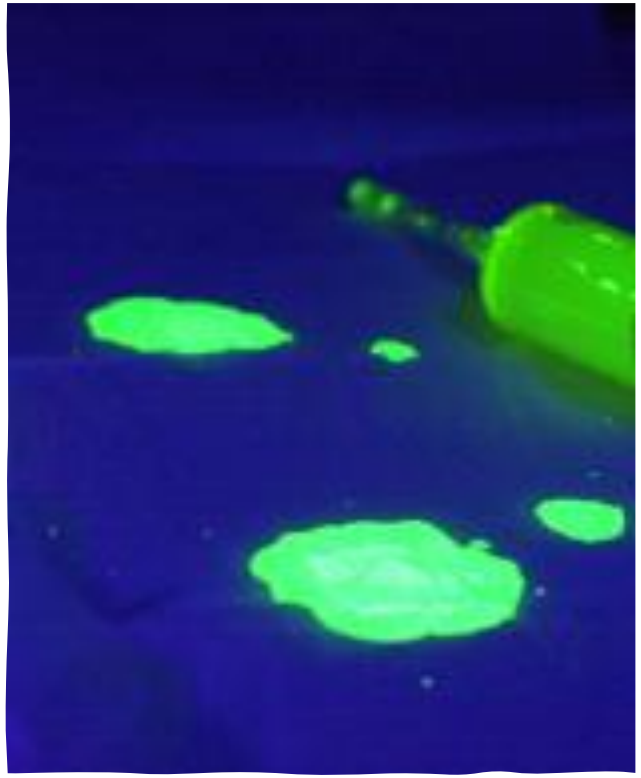





Images: Best Practices for Compounding Garbing https://www.pppmag.com/article/1988

Containment Supplemental Engineering Controls (CSTDs)





Containment Supplemental Engineering Controls (CSTDs)

- **Purpose:**
  - **Provide additional protection during compounding or administration**.
  - Some CSTDs limit aerosol generation during compounding.
- **Performance Evaluation:**
  - No universal performance standard for CSTD containment.
  - **Evaluate performance claims based on independent, peer-reviewed studies.**
- **Usage Guidelines:**
  - **Not a substitute for a C-PEC** when compounding.
  - Should be used when compounding HDs if the dosage form allows.
  - Must be used when administering antineoplastic HDs if the dosage form allows.
  - Do not use CSTDs that are physically or chemically incompatible with a specific HD.

Images: BD PhaSeal https://youtu.be/whKZWkCPbc8
https://www.equashield.com 800 Receiving and Storage

Cleaning Steps for Handling Hazardous Drugs (HDs)

Cleaning Step	Purpose	Example Agents
Deactivation 	Render compound inert or inactive	- As listed in the HD labeling. - EPA-registered oxidizers (e.g., peroxide formulations, sodium hypochlorite).
Decontamination 	Remove HD residue	- Materials validated for HD decontamination. - Effective materials (e.g., alcohol, sterile water, peroxide, sodium hypochlorite).
Cleaning 	Remove organic and inorganic material	- Germicidal detergent.

Key Take-Away Points

Topic	Summary
USP 797: 2023 Updates	Understand major 2023 updates impacting sterile preparation practices, facility design, and environmental controls.
USP 797: Risk Levels	Differentiate old risk levels from new categories (1, 2, 3) focusing on BUDs and environmental requirements.
USP 797: Personnel Competencies	Emphasize ongoing training and competency assessments in hand hygiene, garbing, and aseptic techniques.
USP 797: Monitoring Programs	Implement Media-Fill and Fingertip tests ensuring adherence to environmental and personnel monitoring protocols.
USP 800: Handling Hazardous Drugs	Identify HDs per USP 800 and NIOSH criteria, recognizing potential exposure routes and handling risks.
USP 800: Facility Design	Designate and ventilate areas for receiving, storing, and compounding HDs, separated to minimize contamination.
USP 800: Use of PPE and CSTDs	Use PPE and CSTDs as per guidelines, following rigorous deactivation, cleaning, and disinfection procedures after handling HDs.

Contact Information

Marisol López Nieves

PharmD. MPH BSPharm. RPh. FACA.

- Email:
  - marisol.lopez@upr.edu
  - marisol@compoundingcompliance.pro
- Tel. 787-309-6097

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Post-Test

According to USP 797, which of the following is a key competency that personnel must demonstrate before they can independently compound sterile preparations (CSPs) or oversee compounding personnel?

- A. Using Primary Engineering Controls (PECs) correctly.
- B. Operating general ventilation systems.
- C. Practicing hand hygiene.
- D. Keeping detailed compounding records.

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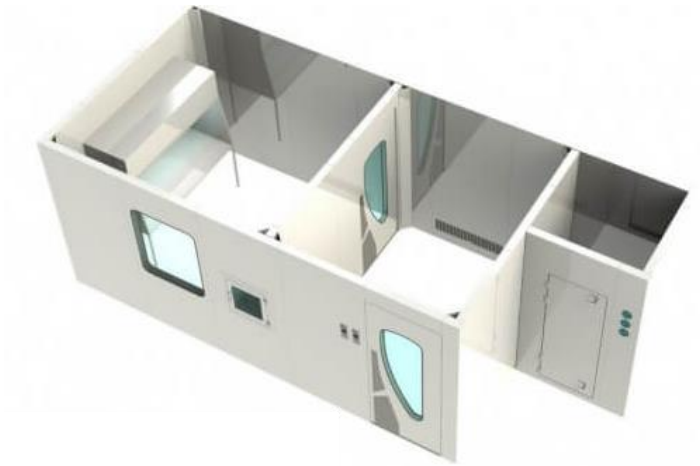
Post-Test

In facilities used for compounding sterile preparations (CSPs), what air quality classification must an anteroom meet when it provides access to a negative-pressure buffer room?

- A. ISO Class 5
- B. ISO Class 6
- C. ISO Class 7
- D. ISO Class 8
- E. ISO Class 9



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Post-Test

For gloved fingertip and thumb sampling procedures, it is recommended to apply sterile 70% isopropyl alcohol (IPA) to gloves immediately before touching the media device to ensure the accuracy of the results.

- A. True
- B. False

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Post-Test

Which of the following statements **accurately describes the requirements** for Compounding Records (CR) for compounding sterile preparations (CSP) according to USP 797 standard?

- A. A CR must list only the name and dosage form of the CSP.
- B. A CR should include the date and time of preparation, along with the assigned internal identification number such as a prescription or lot number.
- C. The CR needs only to document the final yield and does not need to include weights or volumes of components used.
- D. A CR should detail the individuals involved in the compounding and verification processes of the CSP.

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Post-Test

According to USP 800, potential opportunities for exposure to hazardous drugs (HDs) include activities such as withdrawing or diluting injectable HDs, expelling air or HDs from syringes, and contacting HD residue on personal protective equipment (PPE).

- A. True
- B. False

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Marisol López Nieves

PharmD. MPH BSPharm. RPh. FACA.

- Email:
  - marisol.lopez@upr.edu
  - marisol@compoundingcompliance.pro
- Tel. 787-309-6097

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