Implementation Strategies for Revised USP <797> Standards

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Presenter

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Disclaimer: I am a member of the USP Compounding Expert Committee, however this presentation is not affiliated or endorsed by USP.

Objectives

1. Summarize key changes to USP <797>
2. Differentiate between ‘must’ requirements and ‘should’ recommendations throughout revised USP <797>
3. Discuss a strategic approach to performing enterprise gap analysis
4. Outline a methodology for shared responsibilities for the designated persons in a multi-hospital health-system
5. Describe facility design and practices utilizing multiple anterooms

Abbreviations

- **BUD**: beyond-use date
- **CAPA**: corrective action and preventive action
- **CSP**: compounded sterile preparation
- **DP**: designated person
- **HD**: hazardous drug
- **SOP**: standard operating procedure
- **USP**: United States Pharmacopeia

Audience Polling Question #1

When does the revised USP <797> become official?

A. November 1, 2022
B. November 1, 2023
C. Immediately
D. USP <797> was revised?

Audience Polling Question #2

Category 1, 2, and 3 CSPs are determined primarily based on what factor?

A. Staff competency level
B. Number of products and packages
C. If using nonsterile starting ingredients
D. Environmental conditions

Audience Polling Question #3

The revised USP <797> requires creating 3 distinct programs, including: (1) training, (2) microbiological air and surface monitoring and (3) _____.

A. facility and engineering controls
B. establishing and maintaining pressure differentials
C. quality assurance and quality control
D. certification and recertification

Key Changes to USP <797>

Compounding Standards Revised

- **Major revisions** published on: Nov 1, 2022
  - USP <797> Pharmaceutical Compounding – Sterile Preparations
  - USP <795> Pharmaceutical Compounding – Nonsterile Preparations
- **Official date:** **Nov 1, 2023** (*1-year to prepare*)
- Also to **become official** on same date…
  - USP <800> Hazardous Drugs – Handling in Healthcare Settings
  - USP <825> Radiopharmaceuticals – Preparation, Compounding, Dispensing, and Repackaging

USP. Updates to USP General Chapters <795> and <797>. Available at: https://go.usp.org/2022_Revisions_795_797

USP <797> Timeline Journey

3 drafts

13,000 comments

2 appeals

3 cycles

13 years

3 standards

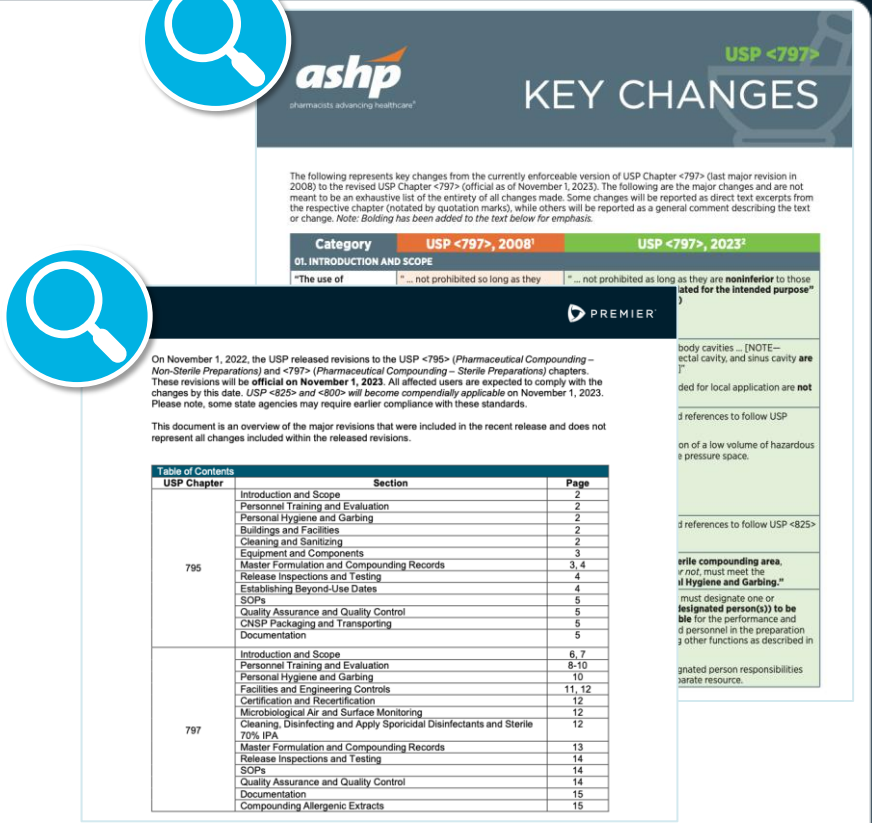
USP. Updates to USP General Chapters <795> and <797>. Available at: https://go.usp.org/2022_Revisions_795_797

Are you prepared?

USP. Updates to USP General Chapters <795> and <797>. Available at: https://go.usp.org/2022_Revisions_795_797

Key Changes to USP <797>

- Immediate-Use CSPs
- Preparation per approved labeling
- Personnel training & evaluation
- Microbiological air and surface monitoring
- CSP categories
- Establishing beyond-use dates



Immediate-Use CSPs

- Some changes that are:
  - **LESS** strict than current standard
  - **MORE** strict than current standard
- Few elements with no changes
- Early implementation: *'all or nothing'*
- Cannot only implement the desired or 'less' strict elements; these are supported by the 'more' strict changes

USP <797> 2008	USP <797> 2023
• Maximum BUD: **1-hour** • No more than 3 **packages** of sterile packages • Only for **emergency conditions**	• Maximum BUD: **4-hours** • No more than 3 **different sterile products** • Does not require emergency condition

Hansen, KN, et al. PPPmag. Feb 2023. 20(2): 10-17

USP <797> pharmaceutical compounding—sterile preparations (November 1, 2023)
USP <797> pharmaceutical compounding—sterile preparations (2008)

Preparation per Approved Labeling

- Only out of scope of this chapter **only if…**
  1. The product is prepared as a **single dose for an individual patient; and**
  2. The approved labeling includes information for the **diluent**, the **resultant strength**, the **container closure system**, and **storage time**.

USP <797> 2008	USP <797> 2023
Following manufacturers approved labeling/package insert is considered compounding and the requirements of chapter apply	Following manufactures approved labeling is not considered compounding (*must meet certain conditions*)

- *See <800> for additional recommendations for the preparation of hazardous drugs.*

USP <797> pharmaceutical compounding—sterile preparations (November 1, 2023)
USP <797> pharmaceutical compounding—sterile preparations (2008)

CSP Categories

USP <797> 2008	USP <797> 2023
• Low risk • Low risk w/ 12-hour BUD • Medium risk • High risk	• Category 1 • Category 2 • Category 3
Factors: 1. Type of manipulation 2. Complexity and length of preparation 3. If any nonsterile ingredient, component, or equipment is used 4. Number of sterile products and packages 5. Number of transfers into any single container 6. Number of doses being prepared 7. Following proper garb 8. Exposure to lower than ISO Class 5 air and duration	Factors: **1. Primarily based on environment/conditions of where the CSP is being compounded** 2. Level of garbing 3. Environmental testing and monitoring 4. Frequency of application of a sporicidal 5. Based on BUD assignment

USP <797> pharmaceutical compounding—sterile preparations (November 1, 2023)
USP <797> pharmaceutical compounding—sterile preparations (2008)

CSP Category Main Factors

Environment	Compounding Method	Sterility Test	Ingredients	Storage Conditions
SCA	Aseptic	Not Performed	Sterile	Controlled Room Temperature (20°to 25°C)
Cleanroom Suite	Terminal	USP <71>	Sterile OR Non-Sterile	Cold temperature (2°to 8°C)
				Frozen (-25° to -10°C)

USP <797> pharmaceutical compounding—sterile preparations (November 1, 2023)

Personnel Training & Evaluation

USP <797> 2008

- Required compounding personnel to perform/pass gloved fingertip and thumb sampling and media fill testing initially and then annually

USP <797> 2023

- Required based on specific job assignment and CSP category to perform/pass '**hand hygiene & garbing competency**' and '**aseptic manipulation competency**' initially and every 3-, 6-, or 12- months based on job assignment

Updated: 06.28.2018

Subject	Type	Training Documents	Training: Read	Training: See	Training: Do	Training: Good	Assessment	Competency: 0	1	2	3	4	5
Sterile Compounding (USP 797)													
Review: USP <797> Pharmaceutical Compounding - Sterile Preparations	Knowledge	USP <797>					Comprehensive sterile compounding assessment exam						

NIH Proficiency Scale

0 – N/A
1 - Fundamental Awareness
2 – Novice
3 – Intermediate
4 – Advanced
5 - Expert

USP <797> pharmaceutical compounding—sterile preparations (November 1, 2023)
USP <797> pharmaceutical compounding—sterile preparations (2008)

Competencies requiring visual observation & testing

Garbing & Hand Hygiene Competency

- Visual observation
- Hand hygiene
- Garbing
- **Gloved fingertip and thumb (GFT) sampling**

Required to pass 3 in succession (*initially only*)

Aseptic Manipulation Competency

- Visual observation
- **Media-fill testing**
- **Gloved fingertip and thumb (GFT) sampling**
- **Surface sample of direct compounding area**

USP <797> pharmaceutical compounding—sterile preparations (November 1, 2023)

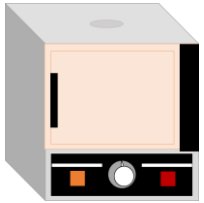
Implementation Approach

1. Start by **defining various personnel types** in an SOP for your organization:
    1. **Compounding personnel**
    2. **Designated person**
    3. **Personnel with direct oversight of compounding personnel**
    4. **Personnel who restock or clean the sterile compounding area**
    5. **Personnel who perform in-process checks or final verification of CSPs**
    6. **Personnel who only compound immediate-use CSPs**
    7. **Others who may need to enter the cleanroom suite (e.g., facilities management, certifiers, inspectors, surveyors, etc.)**
2. Map out chapter requirements based on USP <797> to the specific individuals defined in your SOP

USP <797> pharmaceutical compounding—sterile preparations (November 1, 2023)

Microbiological Air and Surface Monitoring

USP <797> 2008	USP <797> 2023
• Surface sampling shall be performed in all ISO classified areas on a ‘periodic’ basis	• Surface sampling shall be performed at least monthly (Category 1 & 2), or weekly (Category 3)



Sampling:

Performed by monthly outsourced cleanroom cleaning vendor (*single trained/qualified person for all locations*) [*outsourced*]

Incubation/Documentation/CAPA:

Performed by Pharmacy Technician Compounding Regulatory Coordinator [*insourced*]

Growth Speciation:

Current: offsite testing lab [*outsourced*]

Target: internal hospital microbiology lab [*insourced*]

Images used with permission

USP <797> pharmaceutical compounding—sterile preparations (November 1, 2023)
USP <797> pharmaceutical compounding—sterile preparations (2008)

Surface Sampling Map with Cleanroom Suite

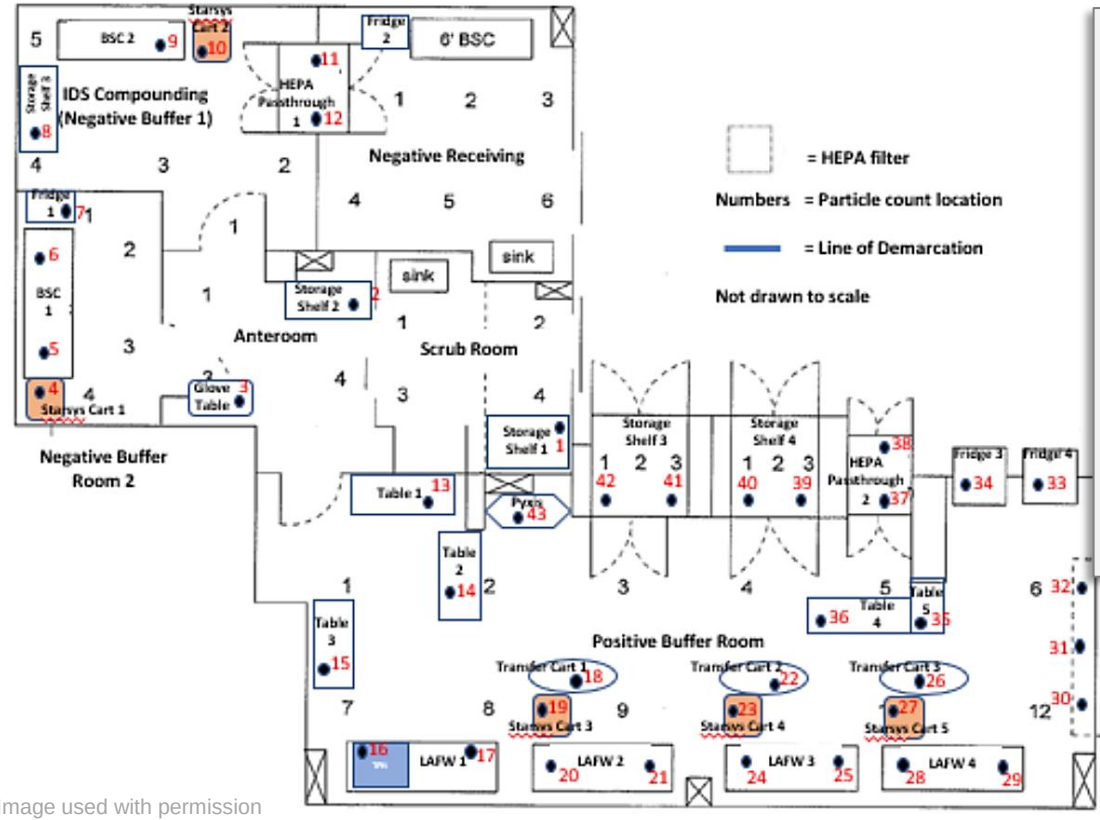


Image used with permission

43+ Samples for Large Cleanroom Suite

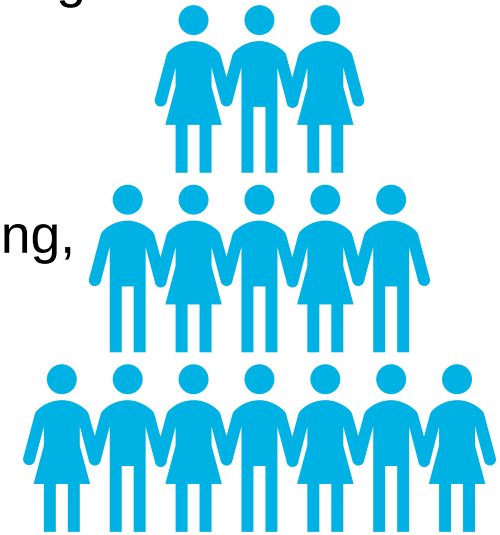
- Each classified area (room, and interior of PEC)
- Pass-through chambers connecting to classified areas
- Equipment contained within PEC
- Staging or work areas near PEC
- Frequently touched surfaces

USP <797> pharmaceutical compounding—sterile preparations (November 1, 2023)

Collaboration Opportunities

Develop relationships and partner with:

- **Outsourced Cleanroom Cleaning Vendor:** sampling
- **Microbiology Lab:** growth speciation, program writing/SOP, incubators, biohazardous waste management, plate selection
- **Industrial Hygiene:** auditing, CAPA, program writing,
- **Infection Prevention:** auditing, CAPA, program writing



Opportunities for:

- Centralized incubation (hub & spoke)
- Traveling/shared air sampler with industrial hygiene

Establishing BUD's

USP <797> 2008	USP <797> 2023
• Use BUDs up to those outlined in the corresponding risk level, in the absence of sterility testing, does not define maximum BUD if using sterility testing	• BUDs outlined based on Category 1, 2, or 3 and include information if performing/passing a sterility test (i.e. BUDs are maximums)

	Category 1	Category 2	Category 3
Maximum BUDs	• ≤ 12-hours RT • ≤ 24-hours REF	• > 12-hours RT • > 24-hours REF	Longer than Category 2 CSPs, up to 180 days
Sterility Testing	N/A	Based on BUD	Required

USP <797> pharmaceutical compounding—sterile preparations (November 1, 2023)
USP <797> pharmaceutical compounding—sterile preparations (2008)

BUDs for Category 2 CSPs

BUD Assignment: Shorter ⟷ Longer

Sterility Test	Compounding Method	Starting Ingredients	Room Temperature	Refrigerator	Freezer
No	Aseptically prepared	Some nonsterile	1 day	4 days	45 days
No	Aseptically prepared	All Sterile	4 days	10 days	45 days
No	Terminally Sterilized	Sterile/Nonsterile	14 days	28 days	45 days
Yes	Aseptically Prepared	Sterile/Nonsterile	30 days	45 days	60 days
Yes	Terminally Sterilized	Sterile/Nonsterile	45 days	60 days	90 days

BUD Assignment: Shorter ⟷ Longer

USP <797> pharmaceutical compounding—sterile preparations (November 1, 2023)
USP <797> pharmaceutical compounding—sterile preparations (2008)

Navigating USP <797>

Must vs. Should

“Must” = Requirement

~90%

“Should” = Recommendation

~10%

USP <797> pharmaceutical compounding—sterile preparations (November 1, 2023)

Standard Operating Procedures

Total of 46 required SOPs throughout chapter

Top 5 sections based on number of required SOPs:

1. Personnel training and evaluation: **x6**
2. Personal hygiene and garbing: **x5**
3. QA & QC: **x5**
4. Cleaning and disinfecting: **x4**
5. Sterilization and depyrogenation: **x4**

USP <797> offers flexibility for organizations to develop their SOPs in a manner that works for their operation.

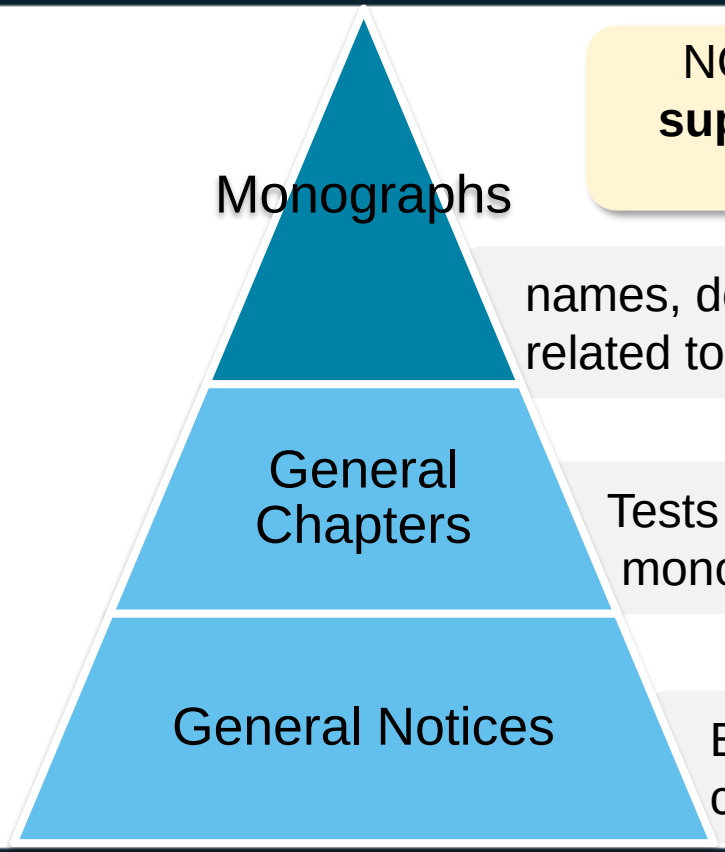
Required ‘Programs’

- In addition to SOPs, USP <797> names **3 programs** that are required
- An SOP and Program have different purposes and scope
- USP <797> required programs:
  - **Training program**
  - **Microbiological air and surface monitoring program**
  - **Quality assurance and quality control program**

SOP	Program
• Detailed instructions (step-by-step) • Can be used for training or reference • Ensures compliance with regulatory requirements	• Broad, comprehensive • Outlines overall policies, procedures, guidelines • Foundation of compliance efforts • Framework for developing SOPs • May include objectives, responsibilities, performance criteria, monitoring or evaluation methods

WHO. (20067 Quality assurance of pharmaceuticals: a compendium of guidelines and related materials. Good manufacturing practices and inspection. 2nd edition. Retrieved from: https://apps.who.int/iris/handle/10665/43532

USP Hierarchy



NOTE: Information in a monograph **supersedes** information in GC or GN *(when requirements differ)*

names, definitions, specifications, and requirements related to packaging, storage, and labeling

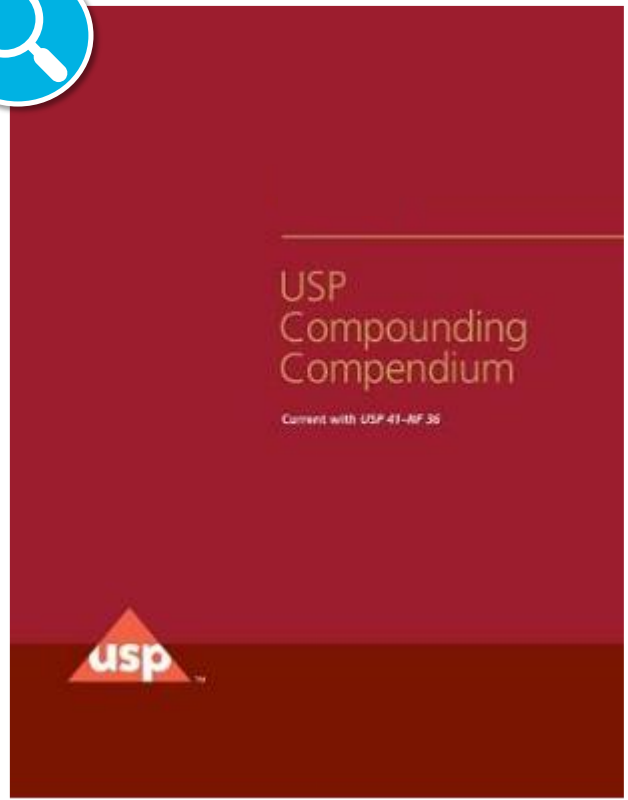
Tests and procedures related to multiple monographs

Basic assumptions, definitions, and default conditions for applying USP standards

USP-NF Online. 2023.

USP <800>

- USP <800> was created as a '**reference' chapter** from USP <795> and <797>
- Compendially applicable (on 11/1/2023) as it is numbered below <1000> and referenced in another applicable chapter below <1000>
- USP <800> ***only applies*** for activities that are within scope of <795>/<797>
  - Administration → **OUT OF SCOPE**
  - Compounding → **IN SCOPE**



USP-NF Online. 2023.

Standards vs. Guidelines vs. Regulations

- USP is an independent, scientific, nonprofit, nongovernmental organization that creates **standards**
- USP has no involvement in enforcement
- Regulatory agencies enforce USP standards
- Must also check requirements from:
  - **State board of pharmacy**
  - **Accreditation organizations**
  - **Federal regulatory authority**
  - **Other local requirements**

United States Pharmacopeia (USP). About the U.S. Pharmacopeia (USP). Available at: https://www.usp.org/about

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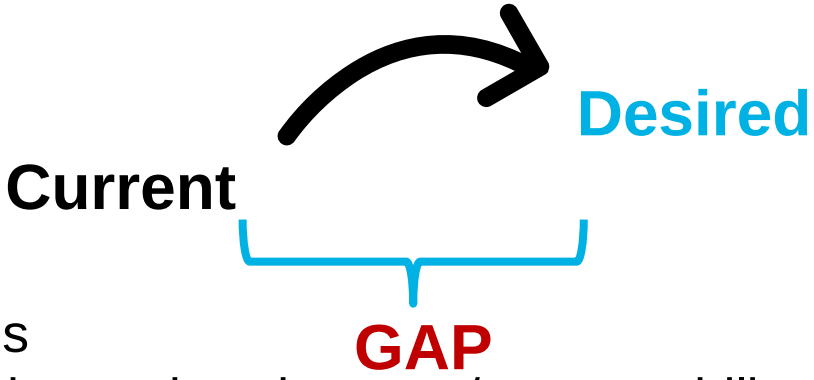
Gap Analysis

Gap Analysis

- Systematic process used to identify differences (i.e. gaps) between CURRENT state and DESIRED state
- When performing, take note of:
  - Existing resources
  - Capabilities
  - Processes and systems
  - Requirements vs. best practices



- System should allow for prioritization and assignment/accountability
- **Outcome: develop roadmap and action plan for steps to close gaps**

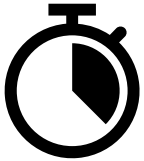
Barney JB, et al. Strategic Management and Competitive Advantage. Pearson Prentice Hall. 2006. 1(1).

Planning for Impact to Resources

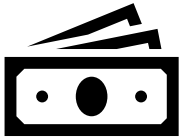
Resource Impact Key

Impact	Personnel	Financial
Low	Work can be absorbed, no additional personnel needed	No (or insignificant) financial impact
Medium	Additional new tasks requiring modifications to staffing	Only operational costs are impacted
High	Additional dedicated personnel required	Capital investment or significant operation costs are necessary

Personnel



Time & Priorities



Finances (operational/ capital)

Expertise

Facilities & Equipment

Price AS, et al. PPPmag. Jan 2022. 19(1): 8-12

Category 1 & 2 vs. Category 3 Gap Analysis

Category 1 & 2 Resource Impact

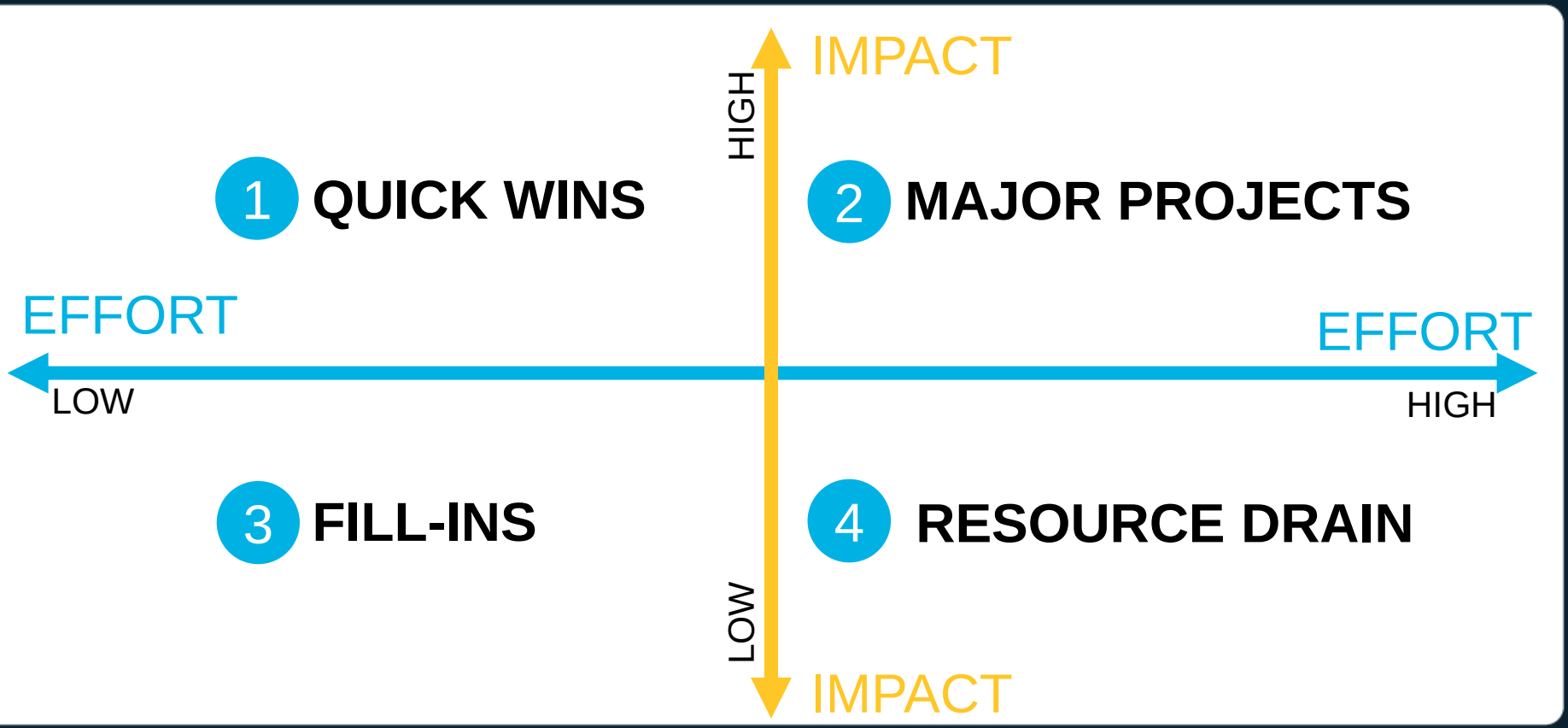
Compliance Item	Impact Multiplier	Personnel Impact	Financial Impact
Visual observation (garbing, aseptic manipulation, etc)	2x	Medium	Low
Gloved fingertip and thumb sampling	2x	Medium	Medium
Media-fill testing	2x	Medium	High
Post media-fill surface sampling	New Work (variable)	Low	Medium
Surface sampling	≥6x	High	High

Category 3 Resource Impact

Compliance Item	Impact Multiplier	Personnel Impact	Financial Impact
Visual observation (garbing, aseptic manipulation, etc)	≥4x	Medium	Low
Gloved fingertip and thumb sampling	≥4x	Medium	Medium
Media-fill testing	≥4	Medium	High
Post-media fill surface sampling	New work (variable)	Low	Medium
Viable air sampling	6x	Medium	High
Surface sampling	≥13x	High	High
Post batch surface sampling	New work (variable)	High	High
Sterility testing	>1x	Low	Low
Applying sporicidal disinfectant	4x	Medium	Medium
Stability data	Variable	Medium	High

Price AS, et al. PPPmag. Jan 2022. 19(1): 8-12

2x2 Effort/Impact Grid



Covey S. The 7 Habits of Highly Effective People: Powerful Lessons in Personal Change. Simon and Schuster, 2013.

Designated Person(s)

The Designated Person(s) Role

- Each compounding chapter lists a requirement to have a designated person or persons.
  - <797> sterile compounding
  - <795> nonsterile compounding
  - <800> hazardous drug handling
  - <825> radiopharmaceutical handling
- The person(s) must be responsible and accountable for specific defined elements
- Chapters give organizations flexibility in deciding who to assign, qualifications, etc.
- Consider short term (e.g., implementation) and ongoing maintenance of requirements

Sullivan E, et al. PPPmag. Apr 2021. 18(4): 6-9

Designated Persons Responsibility Mapping

- Across all 4 chapters:
  53 specific requirements
- Outline current roles with *‘accountability & responsibility’*
- Make assignments clear with source of truth (grid)
- *Primary* and *supporting* roles
- Consider adopting new model(s) where synergies or efficiencies can be created *(e.g., centralized training program)*

Designated Person(s) Responsibility Assignment

Key Definitions:
Designated Person(s): One or more individuals assigned to be responsible and accountable for the performance and operation of the facility and personnel as related to the preparation of the CSPs and CNSPs.

Assigned Trainer(s): one or more individuals assigned by the designated person(s) to be responsible and accountable for directly providing the training, observation, and/or evaluation of personnel for the preparation of CSPs or CNSPs.

Key: P = Primary | S = Supporting

Responsibility	Applies To	Personnel: Director of Compounding	Regulatory Coordinator	Site Compounding Leader	Director of Medication Safety	Industrial Hygienist	Specialist Tech	Pharmacists	Other? (define)
Personnel Training and Evaluation									
Creating and implementing a training program	795/797	P	S						
Training and observation (DP or assigned trainer)	795/797/825		P	S			P		
Documentation/sign-off of competency (DP or assigned trainer)	795/797/825		P	S			P		

Survey on Designated Person

In 2021, a survey was conducted to assess approaches to designated person for USP <800>. (n = 37)

- **Does your health system have, or plan to have, a single identified DP for the entire health system or a DP for each individual site?**
  - DP at each individual site: 56.7%
  - Single DP for health-system: 40%
  - Undecided: 3.3%
- **Is the DP a dedicated role or is it an added job responsibility?**
  - Dedicated role: 13.3%
  - Added job responsibility: 86.7%
- **Does your state require the DP to be a pharmacist?**
  - Yes: 0%
  - No: 73.3%
  - Unsure: 26.7%
- **Is the DP a pharmacist, pharmacy technician, or other individual?**
  - Pharmacist: 80%
  - Pharmacy technician: 6.8%
  - Safety officer: 3.3%
  - Quality and safety: 3.3%
  - Facilities manager: 3.3%
  - Undecided: 3.3%

Sullivan E, et al. PPPmag. Apr 2021. 18(4): 6-9

Approaching Multiple Anterooms

Sink Location

USP <797> excerpts regarding placement of sink:

- …the **order** of hand washing & garbing depends on the placement of the sink.
- …gowns and garb must be stored in a manner that **minimizes contamination** (e.g., away from sinks to avoid splashing).
- …the sink used for hand hygiene may be placed either **inside** or **outside** of the anteroom.

Image used with permission

Example of Sink Placement

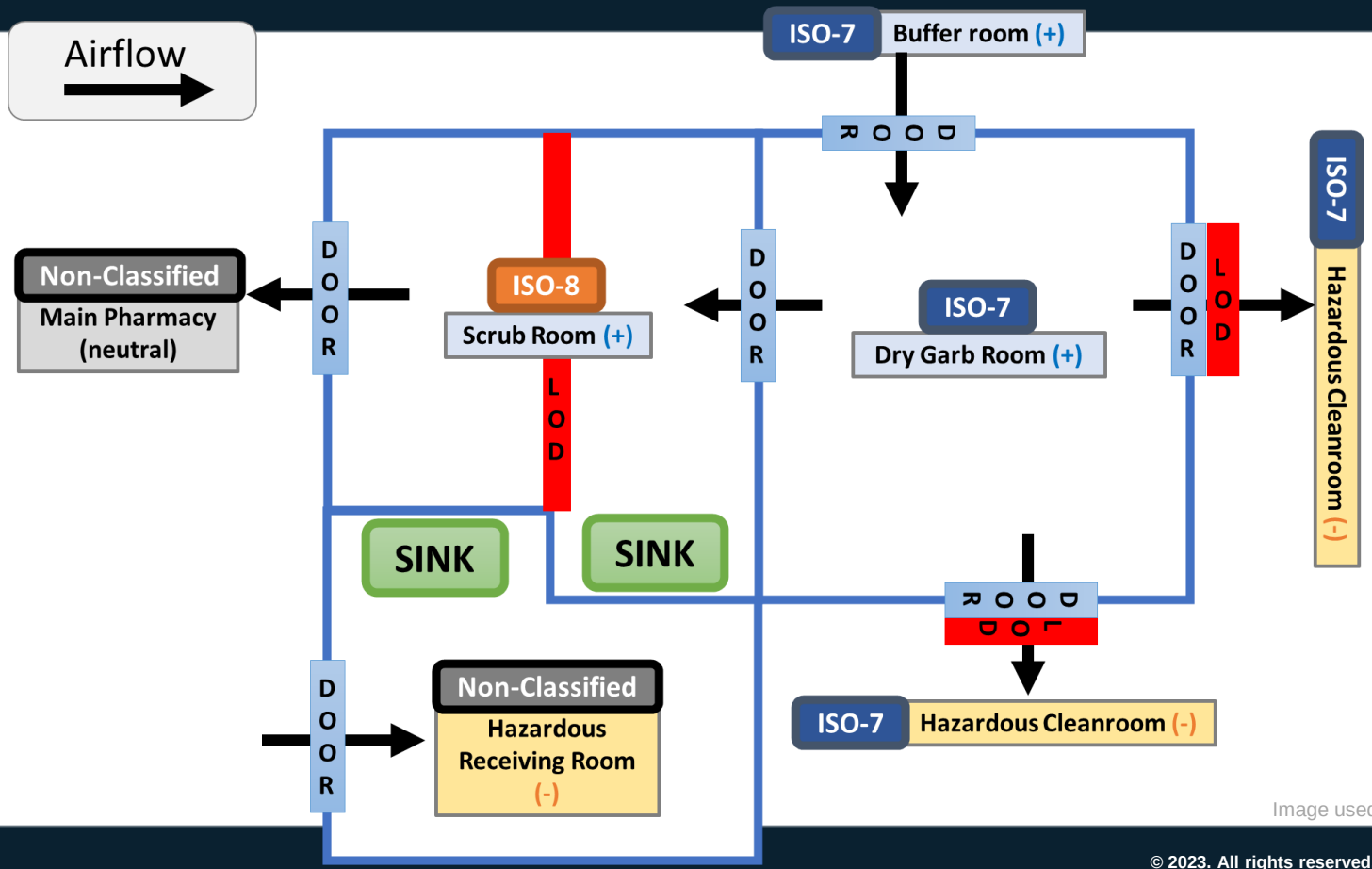


Image used with permission

Example of Hand Hygiene & Garbing

ISO-8 Scrub Room

ISO-7 Dry Garb Room

Before entering the scrub room, the following should be **removed:** outer garments, cosmetics, exposed jewelry, personal electronics, artificial nails or polish, and food/drink

1 Hair Cover & Face Mask

Location: Scrub Room

Put on **hair cover**, **facial hair cover**, and **face mask**.

2 Shoe Covers

Location: Scrub Room

Put on **shoe covers**, while stepping over line of demarcation, one foot at a time.

3 Hand Hygiene

Location: Scrub Room

1. Clean under fingernails with **pick**

2. Wash hands and forearms to elbows for *at least* 30 seconds with soap and warm water.

3. Dry hands and forearms completely with lint-free disposable towel.

4 Hand Antisepsis

Location: Anteroom

Apply product to hands and spread evenly until fully dried.

5 Gown

Location: Anteroom

Put on gown. Place thumbs in loops to cover wrists when arms are fully extended.

6 Sterile Gloves

Location: Anteroom

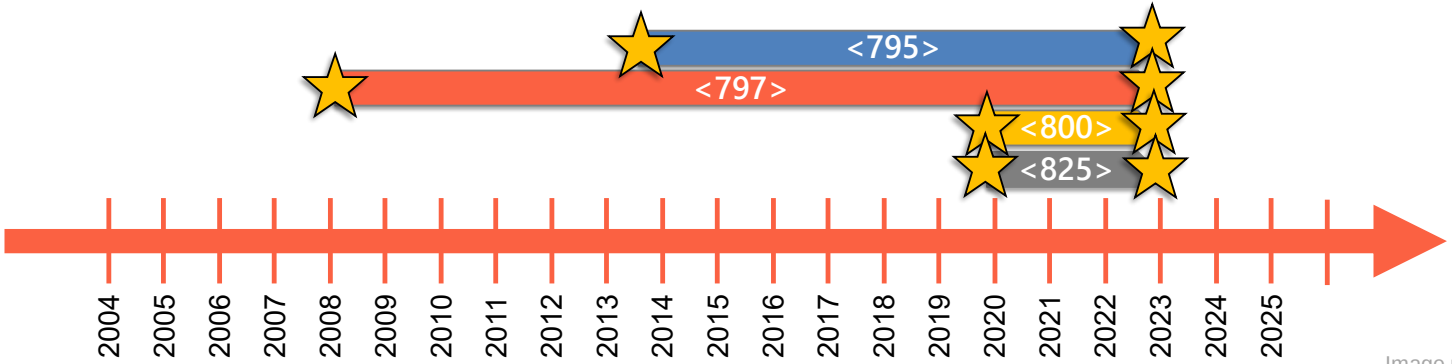
Aseptically put on **sterile gloves** and pull cuffs over gown sleeves.

Image used with permission

Key Take Aways

Key Take Aways

- Compliance is a journey, approach should be strategic
- Leverage partnerships and expertise within your organization outside of pharmacy
- Perform a gap analysis that results in a road map and an action plan for compliance
- Consider implementation of best practices along the journey



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Question & Answer