United States Pharmacopeia (USP)

History and Update of Chapters 797 and 800

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Disclaimer

The views and opinions expressed are those of the speaker and are not endorsed by or affiliated with USP.

Conflict of Interest

The speaker has no conflicts to disclose.

Objectives

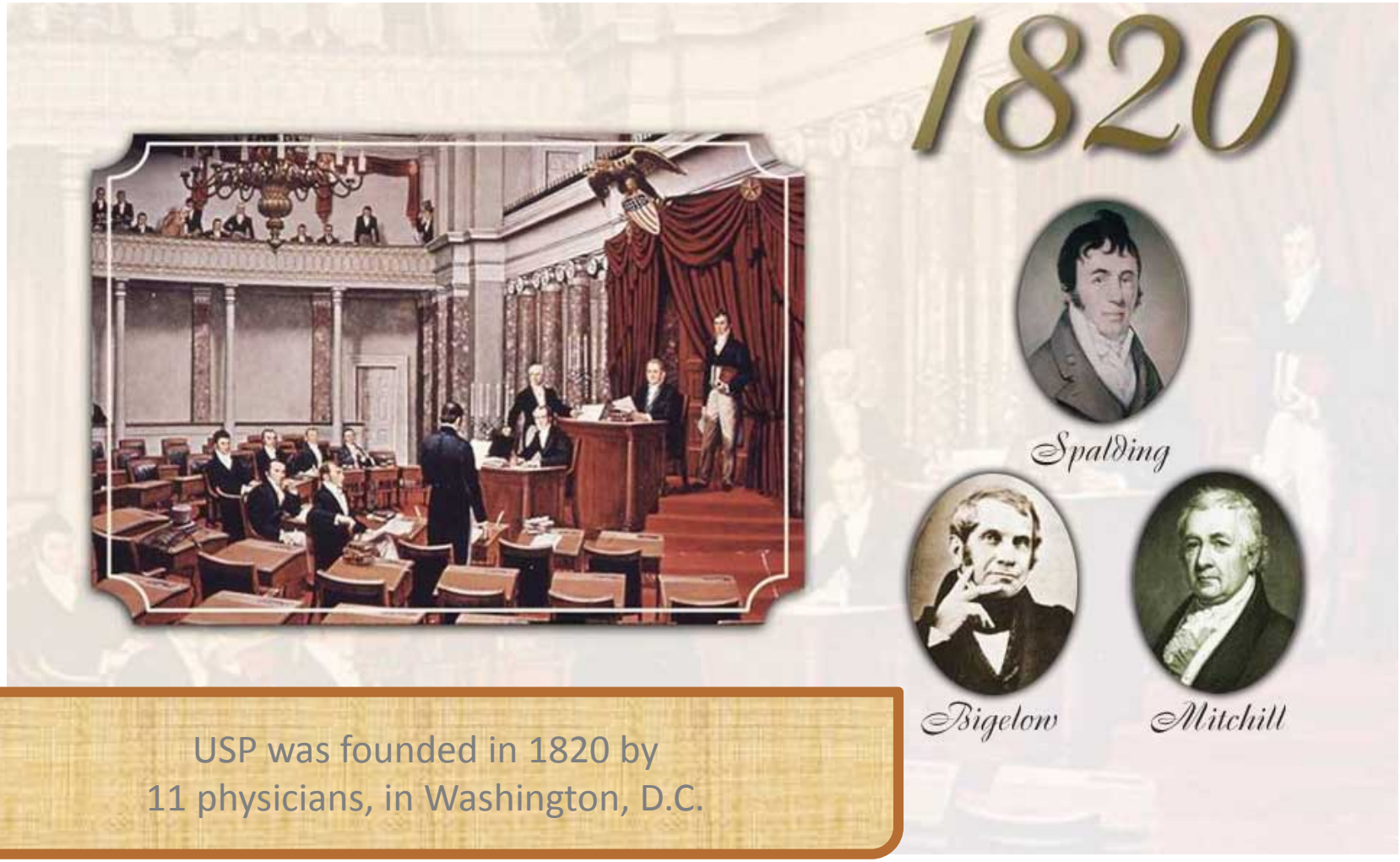
At the conclusion of this activity, the pharmacist participant will be able to:

- ✓ Understand the history of USP as a standard setting organization.
- ✓ Discuss the history and importance of USP 797 as the standard for compounding sterile preparations.
- ✓ Discuss the history and importance of USP 800 for handling hazardous medications in healthcare settings.
- ✓ Knowledge of differences between USP 797 and TSBP regulations.

At the conclusion of this activity, the technician participant will be able to:

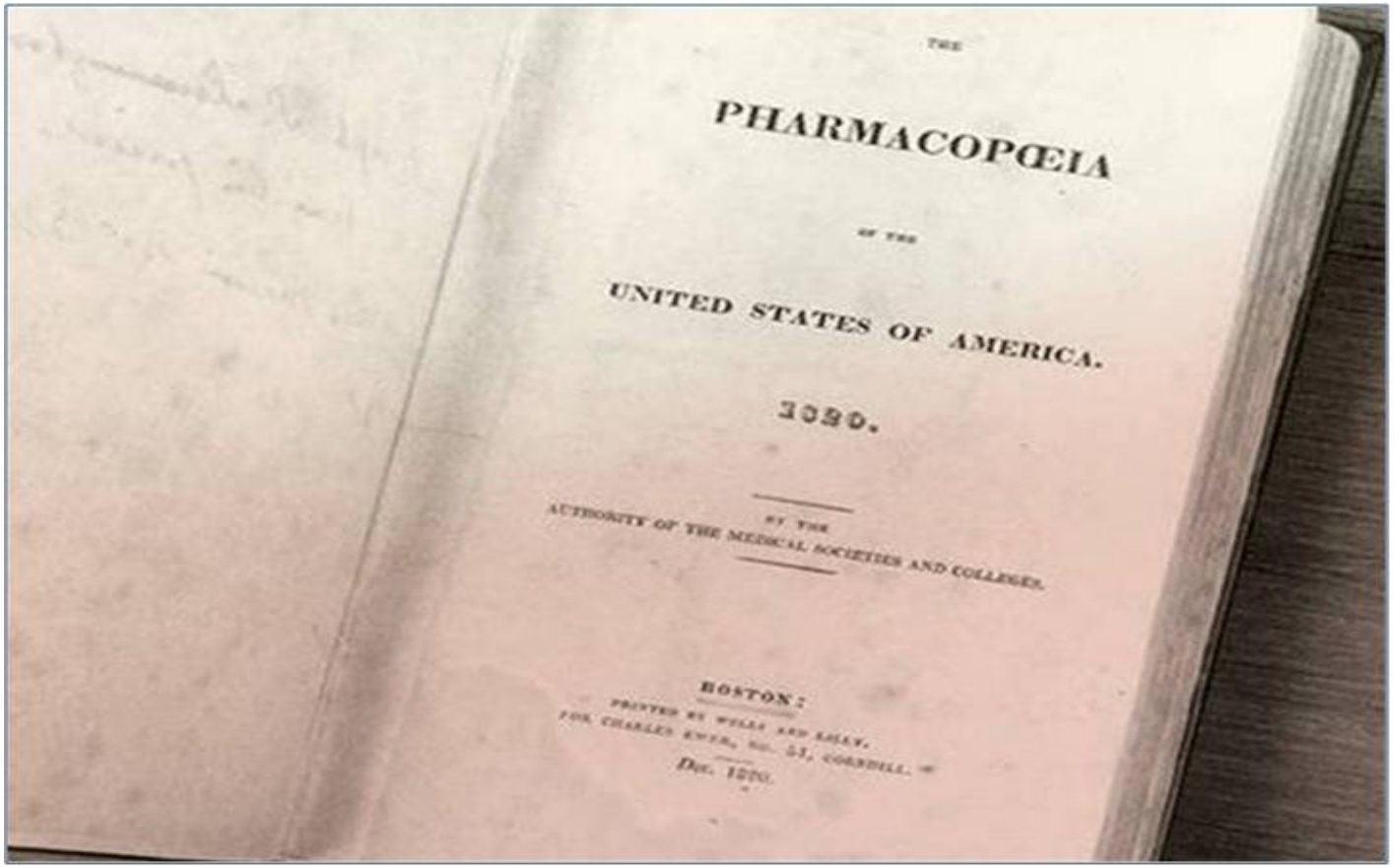
- ✓ Know the history of USP as a standard setting organization.
- ✓ Recognize the importance of USP 797 ands the standard for compounding sterile preparations.
- ✓ Recognize the importance of USP 800 as the standard for handling hazardous medications in healthcare settings.

USP's Beginning



USP was founded in 1820 by
11 physicians, in Washington, D.C.

The first Pharmacopeia (1820)



THE

PHARMACOPŒIA

OF THE

UNITED STATES OF AMERICA.

1820.

BY THE

AUTHORITY OF THE MEDICAL SOCIETIES AND COLLEGES.

BOSTON:

PRINTED BY WELLS AND LILLY,

FOR CHARLES EWER, No. 51, CORNHILL.

Dec. 1820.

The first Pharmacopoeia of the United States contained 217 of the “most fully established and best understood” medicines in the U.S. It was published “by the authority of the medical societies and colleges.”

Legal Recognition in the US

- **1848 Drug Import Act** recognized USP standards to stop the dumping of drugs by Europeans

- **1906 Pure Food and Drugs Act** enforced USP and NF standards for strength, quality, and purity

- **1938 Food, Drug and Cosmetic Act** recognized USP & NF standards for strength, quality, purity, packaging, and labeling

- **1994 Dietary Supplement Health Education Act** recognize USP standards for dietary

Legal Recognition in the US

The requirements of the Federal Food Drug and Cosmetic Act (FD&C Act) apply equally to drugs that are compounded and those that are manufactured….

- **1997 FDA Modernization Act** Sec. 503A stated that compounding must comply with USP-NF standards and chapter on pharmacy compounding

- **2003 Medicare Modernization Act** requested USP to develop and revise the Model Guidelines for Medicare Formularies

- **2010 Affordable Care Act** recognizes USP Model Guidelines to assess coverage of *Essential Health Benefits*

- **2013 Drug Quality and Security Act** recognize USP monographs for bulk drug substances and USP chapters on pharmacy compounding

Legal Recognition in the US

2013 Drug Quality and Security Act recognized USP monographs for bulk drug substances and USP chapters on pharmacy compounding

- As a result of the October **2012** compounding disaster
- Described **503A** pharmacies
- Described **503B** pharmacies
- Reinforced or continued things commissioned in **FDAMA 1997**
  - **Pharmacy Compounding Advisory Committee (PCAC)**
  - **Do Not Compound or Negative List**
  - **Positive List**
  - **Demonstrably Difficult to Compound List**
- Does not apply to **Animal Compounding**

- **Questions**
  - **Dietary Supplements and Herbals** used in compounding **that have a USP monograph**

USP Today

- Scientific non-profit organization that sets standards for the identity, strength, quality, and purity of medicines, food ingredients, and dietary supplements

USP Headquarters
Rockville, MD

USP's Mission:

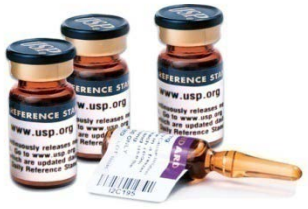
To improve global health through public standards and related programs that help ensure the **quality**, **safety**, and **benefit of medicines and foods**.

USP The Organization

- **What We Do Today**
  - Establish and disseminate public written standards for the quality, purity, identity, strength, and labeling of medicines
  - Provide recommendations to practitioners on the safe use of medicines
  - Work with international health agencies to improve the quality of medicines worldwide
  - Educate practitioners, producers and others seeking information on quality and USP standards

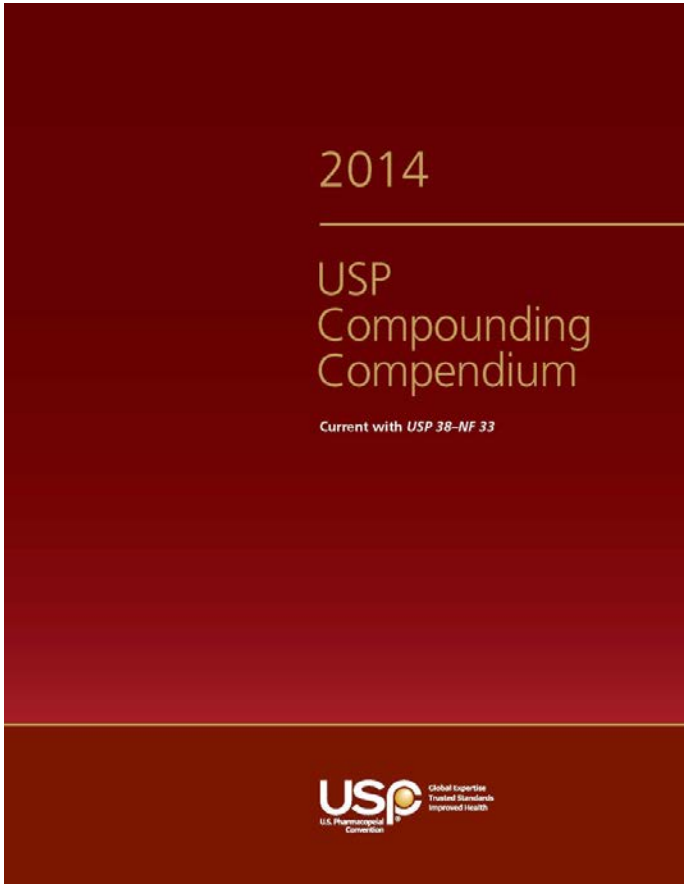
USP Standards

- The United States Pharmacopeia National Formulary (USP–NF)
- Food Chemicals Codex (FCC)
- USP Dietary Supplements Compendium (DSC)
- USP Compounding Compendium (CC)
- USP Medicines Compendium (MC)
- Herbal Medicines Compendium (HMC)
- Reference Standards
- Other Resources
  - Pharmacopeial Forum (PF)
  - FCC Forum (FCCF)
  - USP Dictionary
  - Chromatographic Columns



USP Compounding

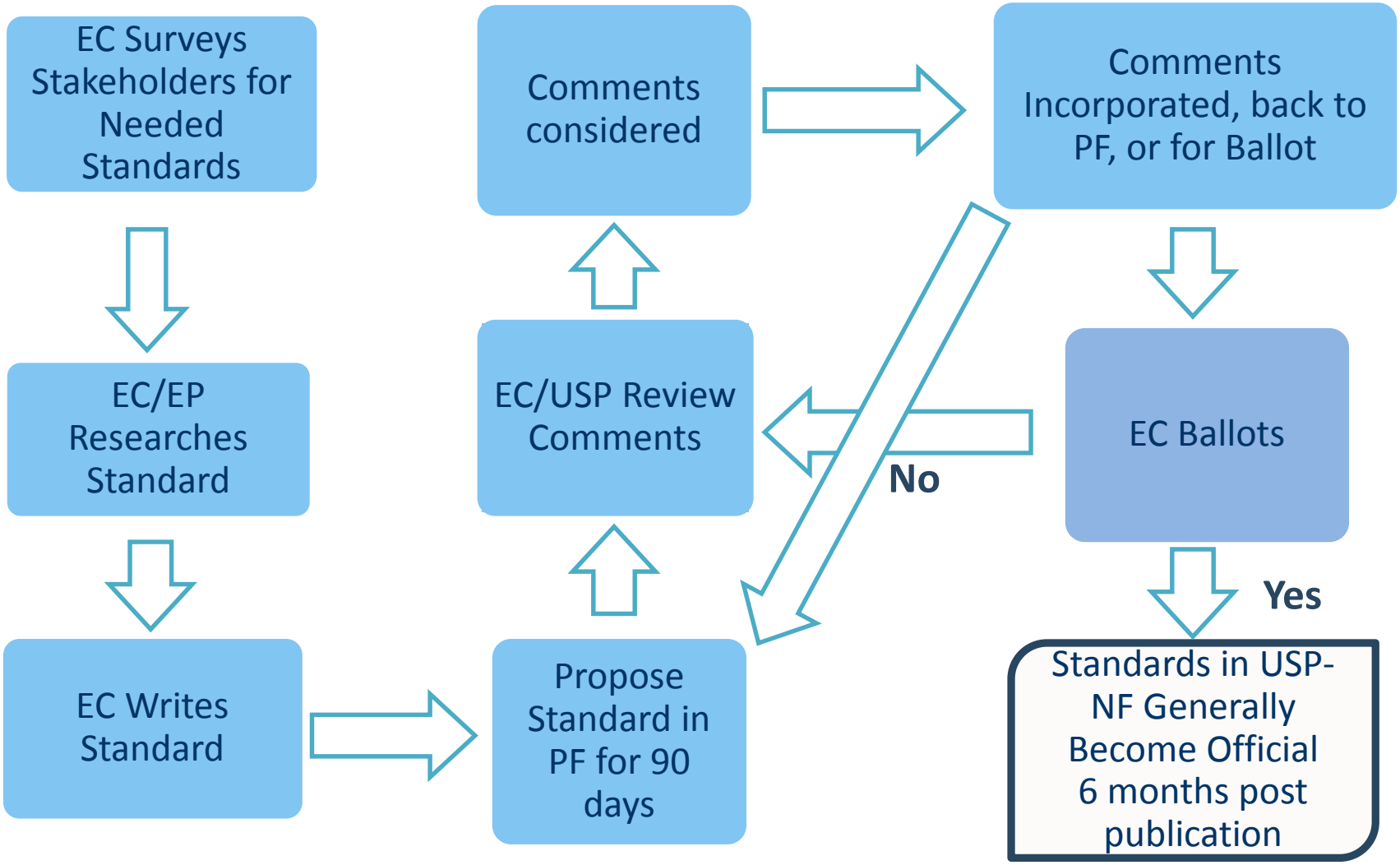
USP Compounding Compendium



Downloadable pdf
Annual Subscription

- **Launched November 3, 2014**
- **Electronic Download includes:**
  - **Mission & Preface**
  - **General Notices & Requirements**
  - **Compounding Related Chapters**
    - 6 essential compounding chapters
  - **Supporting General Chapters**
    - Over 40 referenced Chapters
  - **Compounded Preparation Monographs**
    - 175 formulations

USP Standards - Setting Process



General Chapters Overview

General Chapters can be:

Enforceable

–Numbered below <1000>

Informational

–Numbered above <1000>

Specific for dietary supplements

–Numbered above <2000>

Terminology

"Shall" requirements – "Must"

"Should" recommendations

How often are USP Compounding Chapters revised?

A. Ideally every 5 years
B. USP Chapters are living standards constantly in revision
C. Every 10 years
D. All of the above

Compounding General Chapters

Official

- <795> Pharmaceutical Compounding – Nonsterile Preparations
- <797> Pharmaceutical Compounding-Sterile Preparations
- <800> Hazardous Drugs – Handling in Healthcare Settings
- <1163> Quality Assurance in Pharmaceutical Compounding
- <1160> Pharmaceutical Calculations in Prescription Compounding
- <1176>Prescription Balances & Volumetric Apparatus

Unofficial

- <1168> Compounding for Investigational Studies

Pharmaceutical Compounding – Sterile Preparations

General Chapter <797>

USP <797>: Revision History

- **Sterile Compounding Standards**
  - 1992 **First Standard** proposed in PF18(2) Mar-April 1992
    - <1074> Dispensing Practices for Sterile Drug Products Intended for Home Use
  - 1996 **Revised** in USP23-NF18 5th supplement
    - <1206> Sterile Drug Products for Home Use

- **General Chapter <797> History**
  - 2004 **First Published** in USP27-NF22
    - Revision from <1206> Sterile Drug Products for Home Use
  - 2008 **First Revised** in USP 31-NF26 2S
    - Official on June 1, 2008
  - 2015 **Proposed Revision issued for comment September**
    - Intent to Revise http://www.usp.org/usp-nf/official-text/revision-bulletins/general-chapter-pharmaceutical-compounding-sterile-preparations
  - 2016 **Comments Due by January 31, 2016**
  - 2016 to current EC begins review of ALL of the almost 9,000 comments received
  - 2017 **November 1,** USP announced the chapter is anticipated to be published in the PF 44(5) September-October 2018 for a second round of public comment

U.S. Pharmacopeia
The Standard of Quality℠

USP <797>: Introduction

- **Purpose:** Provide minimum practice and quality standards for compounded sterile preparations (CSPs) based on current scientific information and best sterile compounding practices

- **Objective**: To describe conditions and practices to prevent harm, including death, to patients that could result from

  (1) microbial contamina

  (2) excessive bacterial

  (3) variability in the int exceeds either monograph limits articles

  (4) unintended c

  (5) ingredients of ina eparations (CSPs)

Contaminants of concern include:

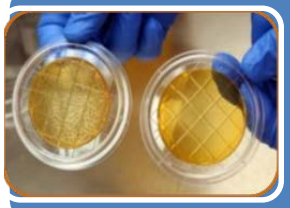
- Bacteria
- Fungus
- Pyrogens
- Particulate matter
- Allergens
- Drug residues

USP <797>: Major Elements

Key Definitions

CSP Risk Levels

Facilities



Monitoring

USP <797>: Key Definitions

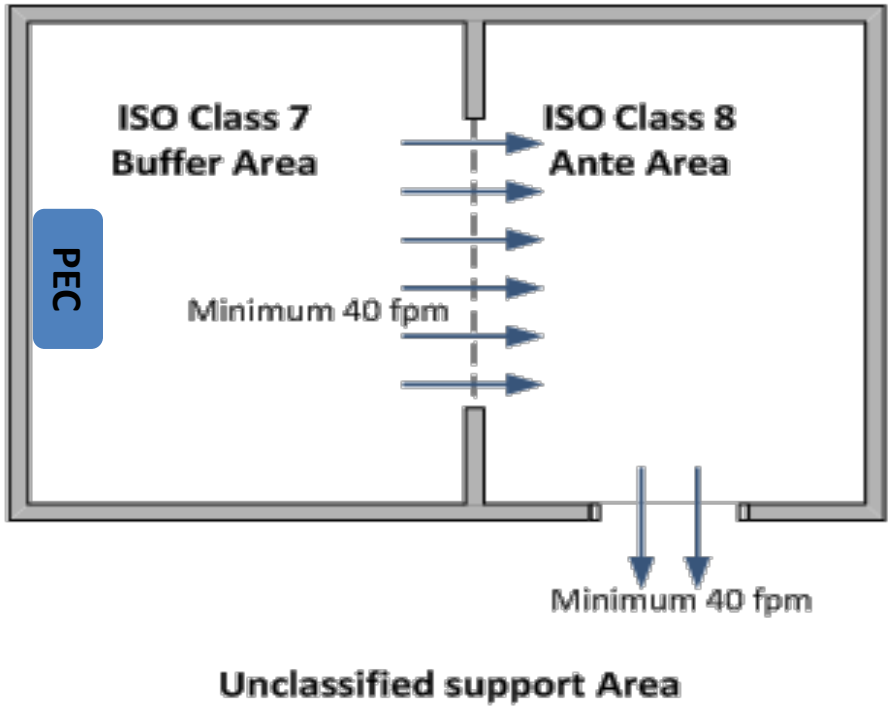
- **ISO Classification** – defines performance of environment with respect to total particulates per volume

Class Name	Particle Count
ISO Class	ISO, m3
3	35.2
4	352
5	3,520
6	35,200
7	352,000
8	3,520,000

Primary Engineering Control (PEC) – Source of ISO Class 5 environment where compounding occurs.

USP <797>: Key Definitions

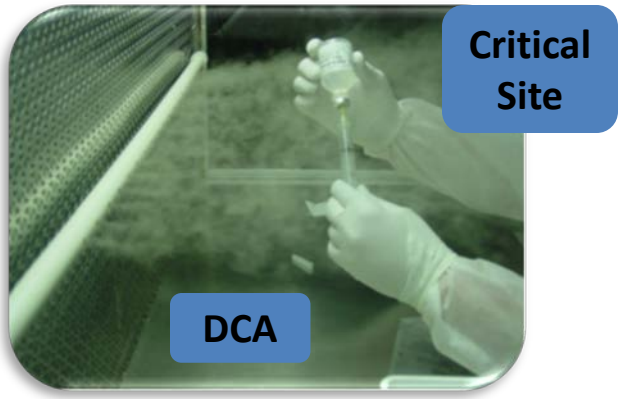
- **Buffer Area** (or Cleanroom) – ISO Class 7 area where the PEC is physical located. Used for preparation and staging of components and supplies to be used when compounding
- **Ante-Area** – ISO Class 8 where personnel hand hygiene and garbing occurs. Serves as a transition area to maintain pressure relationships for air to flow from clean to dirty areas



USP <797>: Key Definitions

- **Critical Site –** Any component of fluid pathway surface or opening exposed to air, moisture, or touch

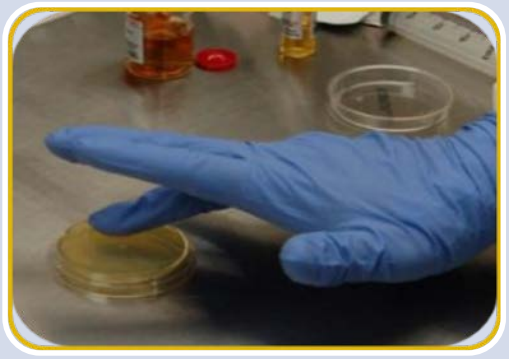
- **Direct Compounding Area (DCA)** – Critical area within an ISO Class 5 PEC where critical sites are exposed to unidirectional “first air”



USP <797>: CSP Microbial Contamination Risk Levels

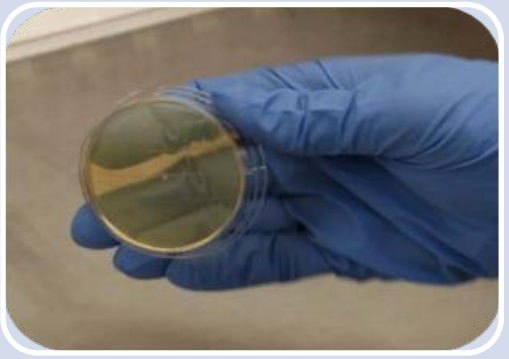
	Low-Risk with 12 hour	Low-Risk Level CSPs	Medium-Risk Level CSPs	High-Risk Level CSPs
Controlled Room Temperature (20° to 25° C)	• 12 hours	• 48 hours	• 30 hours	• 24 hours
Cold Temperature (2° to 8° C)	• 12 hours	• 14 days	• 9 days	• 3 days
Solid Frozen State (-25° to -10° C)	• N/A	• 45 days	• 45 days	• 45 days

USP <797>: Monitoring - Personnel



Gloved Fingertip Testing

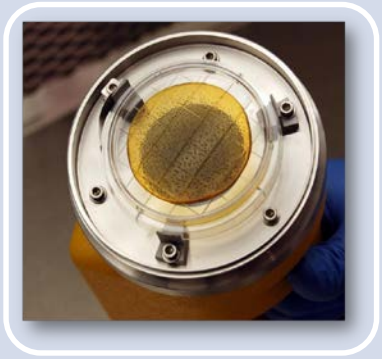
Aseptic Media Fill Testing



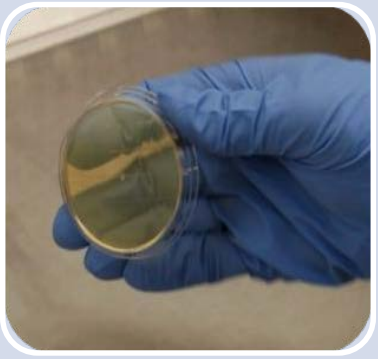
Surface Sampling

USP <797>: Monitoring – Facilities

Nonviable Particle Testing



Air Viable Sampling



Surface Sampling

Pressure Differential

TSBP and USP 797 Differences

TSBP states more specifics about training of Personnel in Sections (2) Pharmacists (3) Pharmacy technicians and pharmacy technician trainees

Subsection B under both(2) & (3) states the completion of a single course and the # of hours of instruction

(6) Environment

(A) Low and Medium Risk Preparations

The clean room

(iv) shall be designed such that hand sanitizing and gowning occurs outside the buffer area but allows hands-free access by compounding personnel to the buffer area;

(xi) contain an ante-area that provides at least an ISO class 8 air quality and contains a sink with hot and cold running water that enables hands-free use with a closed system of soap dispensing to minimize the risk of extrinsic contamination. A Class B pharmacy may have a sink with hot and cold running water that enables hands-free use of a closed system of soap dispensing immediately outside the ante-area if antiseptic hand cleansing is performed using a waterless alcohol-based surgical hand scrub with persistent activity following manufacturers' recommendations once inside the ante-area;

Hazardous Drugs – Handling in Healthcare Settings

General Chapter <800>

USP <800>: Timeline History

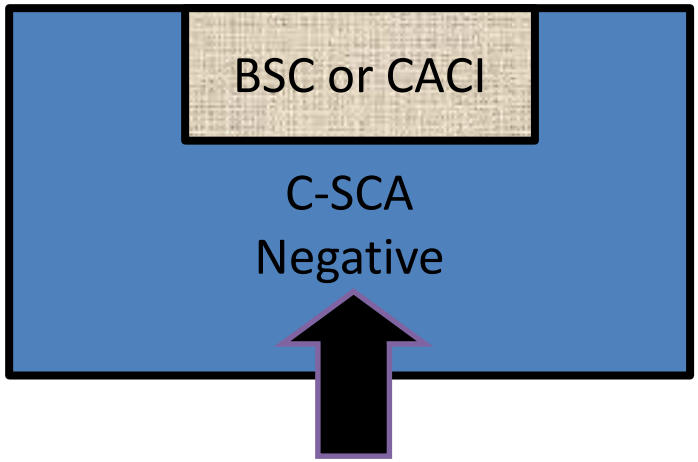
Date	Activity
March 28, 2014	General Chapter <800> **Posted Online for Public Comment** (Published in PF 40(3) May/June 2014)
June 12th, 2014	Open Microphone Web Meeting
July 31, 2014	Deadline for Submitting Public Comments
Early August through October 2014	Hazardous Drug Expert Panel and Subcommittee Reviews ALL comments submitted
October 13, 2014	Notice of Intent to Revise after review of comments submitted
December 1, 2014	**Revised GC <800> Posted Online for Public Comment** (Published in PF 41(2) March/April 2015)
February 20, 2015	Open Microphone Web Meeting
May 31, 2015	Deadline for Submitting Public Comments
February 1, 2016	<800> published in the First Supplement to USP 39-NF 34 with a delayed official implementation date of July 1, 2018
May 26, 2016	Notice of Intent to Revise Errata to correct Section 5.3 revised to indicate that the C-SEC used for sterile and nonsterile compounding must be externally vented. The C-SEC does not need to be vented through HEPA filtration.
November 1, 2017	Notice of Intent to Revise – Postponement of official implementation date of USP <800> to December 1, 2019, to align with the anticipated official date of USP <797>

FAQs http://www.usp.org/frequently-asked-questions/hazardous-drugs-handling-healthcare-settings

USP <800>: Major Differences from <797>

- Elimination of the exemption for facilities that prepare a low-volume of HDs that permits placement of a BSC or CACI in a non-negative room
- Allowance of a Containment Segregated Compounding Area (C-SCA), a separate negative pressure room with at least 12 air changes per hour

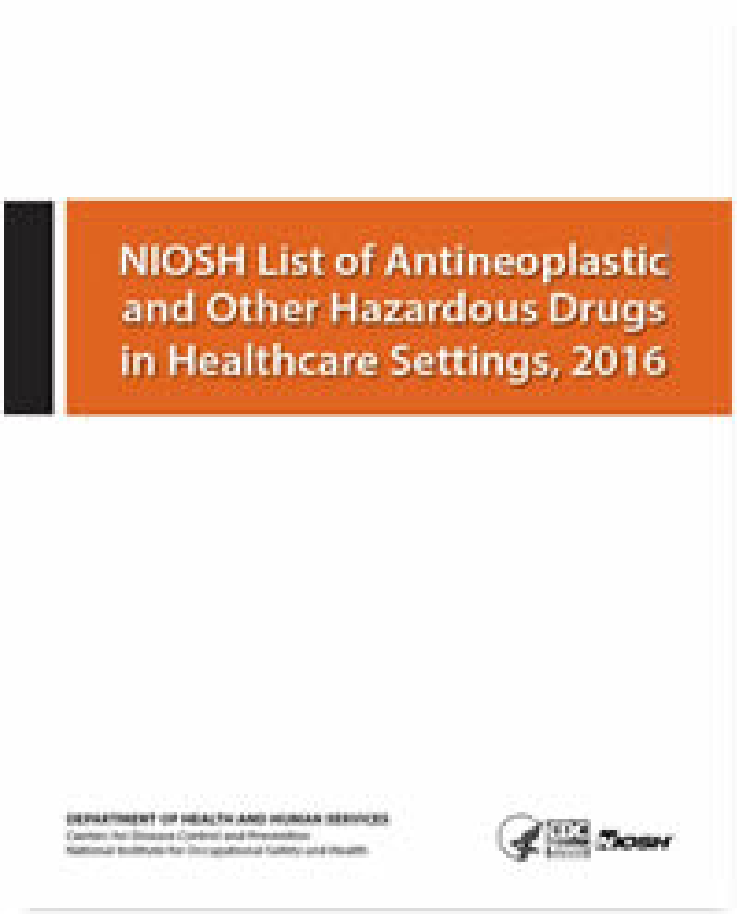
General Chapter <797> will be harmonized with the new proposed chapter



USP <800>: Why and Existing References

- Chapter builds on the standards existing in compounding chapters 795 and 797
  - Adds in the elements of containment of hazardous drugs (HDs)
  - Incorporates principles of medication safety and worker protection from existing references

- Existing references
  - NIOSH Alert
  - ASHP Guidelines on Handling Hazardous Drugs



NIOSH Hazardous Drugs History

National Institute for Occupational Safety & Health (NIOSH) 2016

- Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings Published 2004
  - Included sample list of major hazardous drugs
- Renamed: NIOSH List of Antineoplastic and Other Hazardous Drugs in Healthcare Settings 2010
- Updates to the list of antineoplastic and other hazardous drugs
  - published 2012, 2014, **2016 (current)**

HD includes any drug identified by at least one of the following six criteria:

Carcinogenicity
Teratogenicity or developmental toxicity
Reproductive toxicity in humans
Organ toxicity at low doses in humans or animals
Genotoxicity
New drugs that mimic existing HDs in structure or toxicity

USP <800> Chapter Outline

1. Introduction and Scope
2. List of Hazardous Drugs
3. Types of Exposure
4. Responsibilities of Personnel Handling Hazardous Drugs
5. Facilities and Engineering controls
    - 5.1 Receipt
    - 5.2 Storage
    - 5.3 Compounding
        - 5.3.1 Nonsterile Compounding
        - 5.3.2 Sterile Compounding
    - 5.4 Containment Supplemental Engineering Controls
6. Environmental Quality and Control
7. Personal Protective Equipment
    - 7.1 Gloves
    - 7.2 Gowns
    - 7.3 Head, Hair, Shoe, and Sleeve Covers
    - 7.4 Eye and Face Protection
    - 7.5 Respiratory Protection
    - 7.6 Disposal of Used Personal Protective Equipment
8. Hazard Communication Program
9. Personnel Training
10. Receiving
11. Labeling, Packaging, Transport and Disposal
    - 11.1 Labeling
    - 11.2 Packaging
    - 11.3 Transport
    - 11.4 Disposal
12. Dispensing Final Dosage Forms
13. Compounding
14. Administering
15. Deactivating, Decontaminating, Cleaning, and Disinfecting
    - 15.1 Deactivation
    - 15.2 Decontamination
    - 15.3 Cleaning
    - 15.4 Disinfection
16. Spill Control
17. Documentation and Standard Operating Procedures
18. Medical Surveillance
    - 18.1 Follow-Up Plan

Glossary

Appendices

Appendix 1: Acronyms

Appendix 2: Examples off Designs for Hazardous Drug Compounding Areas

Appendix 3: Types of Biological Safety Cabinets

References

1. Introduction and Scope

- Entities that handle HDs must incorporate the standards in this chapter into their occupational safety plan.
- Explain how hazardous drugs are defined by USP <800> and NIOSH
- Understand the three Groups of drugs on the NIOSH Hazardous List
- Understand how these 3 Groups are categorized
  - Chemotherapy, sterile and non-sterile
  - Hazardous, sterile and non-sterile
- The entity's health and safety management system must, at a minimum, include:
  - A list of HDs
  - Facility and engineering controls
  - Competent personnel
  - Safe work practices
  - Proper use of appropriate Personal Protective Equipment (PPE)
  - Policies
  - Documentation

2. List of Hazardous Drugs

- An entity must maintain a list of HDs, which must include any items on the current NIOSH list that it handles.
- The list must be reviewed at least every 12 months.
- The NIOSH list of antineoplastic and other HDs provides the criteria used to identify HDs. These criteria must be used to identify HDs that enter the market after the most recent version of the NIOSH list, or that the entity handles as an investigational drug.
  - If the information available on a drug is deemed insufficient to make an informed decision, consider the drug hazardous until more information is available.

2. List of Hazardous Drugs

- Drugs on the NIOSH list that must follow the requirements in this chapter:
  - Any HD API
  - Any antineoplastic requiring HD manipulation
- Drugs on the NIOSH list that do not have to follow all the containment requirements of this chapter *if an assessment of risk is performed* and implemented:
  - Final dosage forms of compounded HD preparations and conventionally manufactured HD products that do not require any further manipulation other than counting or repackaging (unless required by the manufacturer e.g. Methotrexate IM Inj.) and dosage forms of other HDs on the NIOSH list.

3. Types of Exposure

- Routes of unintentional entry of HDs into the body include
  - dermal and mucosal absorption
  - inhalation
  - injection
  - ingestion

This section also lists examples of potential routes of exposure based on activity.

(See Table 1 in USP <800>)

HAZARDOUS DRUGS

4. Responsibilities of Personnel Handling Hazardous Drugs

Each entity must have a designated person who is qualified and trained to be responsible for:

- developing and implementing procedures
- overseeing compliance
- ensuring competency of personnel and
- ensuring environmental control of the storage and compounding areas.

He or she must understand the rationale for risk-prevention policies, risks to themselves and others, risks of noncompliance, and the responsibility to report potentially hazardous situations to management.

He or she must also be responsible for the oversight of monitoring the facility and maintaining reports of testing and sampling performed and acting on the results.

Claiming Your CE Credit

- https://tshp.wcea.education/homepage
- Pharmacist: bcyy
- Pharmacy Technician: WHhW

Thank You

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Questions