Chapter Tales:
Practical USP Updates for 2018

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Disclosure

• **Patricia Kienle:** ASHP: Author; Cardinal Health: Employee; Critical Point: Consultant; USP: Advisory Committee/Board Member

• All other planners, presenters, and reviewers of this session report no financial relationships relevant to this activity.
Learning Objectives

• State the status of USP <797> and <800> and when revisions will be official
• Differentiate cleanrooms from segregated compounding areas
• List the training and physical tests required to independently compound sterile preparations
• Cite the document used to establish an entity’s list of hazardous drugs
• Describe the types of solutions used in the cleaning processes for sterile compounding areas
United States Pharmacopeia

- USP sets standards
- USP <795>, <797>, and <800> are minimum standards
  - Not guidelines
  - Not stretch goals
- Regulatory agencies and accreditation organizations enforce the standards

Photo courtesy of USP
FDA Compounding Guidance Documents

• Final
  – Pharmacy compounding
  – Repackaging
  – Using bulk drug substances

• Draft
  – Insanitary conditions
  – Hospital and health system compounding
  – Mixing biological products
  – Copies of available drug products

• Proposals

Selected documents for 503A pharmacies as of March 1, 2018
USP Compounding Chapters

• <795> Pharmaceutical Compounding – Nonsterile Preparations
• <797> Pharmaceutical Compounding – Sterile Preparations
• <800> Hazardous Drugs – Handling in Health Care Settings
USP <795> Nonsterile Compounding

Electronic Posting
March 30, 2018

Open Mic
April 20, 2018

Pharmacopeial Forum
May 1, 2018

Public Comments Due
July 31, 2018
USP <797> Sterile Compounding

Electronic Posting
July 27, 2018

Pharmacopeial Forum
September 4, 2018

Open Mic
September 5, 2018

Public Comments Due
November 30, 2018
USP <800> Hazardous Drugs

First Public Comment Version
March 2014

Second Public Comment Version
December 2014

Final Version
February 1, 2016
How This All Fits Together

Public Comment <795>

March 30, 2018
Web pre-posting *9/1 publication in Pharmacopeial Forum

April 20, 2018
Open Microphone Session

July 31, 2018
Close of public comment

June 1, 2019
<795>
Intended Publication USP-NF

Dec 1, 2019
<800><795><797>
Intended Official Date

Public Comment <797>

February 2016
<800>
Publication USP-NF

July 27, 2018
Web pre-posting *9/4 publication in Pharmacopeial Forum

Sept 5, 2018
Open Microphone Session

Nov 30, 2018
Close of public comment

June 1, 2019
<797>
Intended Publication USP-NF

Note: The current version of General Chapters <795> and <797> published in USP-NF are official.
Key Elements

• Personnel
• Documentation
• Facility
• Garb/Personal Protective Equipment
• Work Practices
• Cleaning
• Certification of devices and rooms
• Environmental Monitoring
Current <795>

- Personnel training
- Master Formulation Record
- Compounding Record
- Beyond-Use Dates

Philadelphia College of Pharmacy c 1930s
The BUD cannot exceed the expiration date of any component

<table>
<thead>
<tr>
<th>Type of Formulation</th>
<th>Maximum BUD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-aqueous formulation</td>
<td>6 months</td>
</tr>
<tr>
<td>Water-containing oral formulation</td>
<td>14 days under refrigeration</td>
</tr>
<tr>
<td>Water-containing topical/dermal and mucosal liquid and</td>
<td></td>
</tr>
<tr>
<td>semisolid formulations</td>
<td>30 days</td>
</tr>
</tbody>
</table>
Proposed Revised USP <795>

- Compounded Nonsterile Preparation (CNSP)
- Designated person
- Requirement for gloves
- Requirement to weigh powders in a Containment Ventilated Enclosure (CVE, powder hood)
- Use of Purified Water (USP <1231>)
- Date components when received and use within one year
- Beyond-use dates (BUDs)
## Proposed Revised <795> BUDs

<table>
<thead>
<tr>
<th>Type of Preparation</th>
<th>BUD</th>
<th>Storage Temperature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solid dosage forms</td>
<td>180 days</td>
<td>Controlled room temperature</td>
</tr>
<tr>
<td>Preserved aqueous dosage forms</td>
<td>30 days</td>
<td>Controlled room temperature</td>
</tr>
<tr>
<td>Non-preserved aqueous dosage forms</td>
<td>14 days</td>
<td>Refrigerator</td>
</tr>
<tr>
<td>Nonaqueous dosage forms</td>
<td>90 days</td>
<td>Controlled room temperature</td>
</tr>
</tbody>
</table>
USP <797> Sterile Preparations

- 2004 – Original chapter
- 2008 – Current chapter
- 2015 – First public comment version of proposed revised
- 2018 – Second public comment version of proposed revised
- 2019 – Planned new official revision
Philosophical Change

• Current: BUD based on components
• Proposed: BUD based on facility in which compounded
  – Category 1 = Segregated Compounding Area (SCA) with maximum of 12 hour room temperature or 24 hour refrigerated BUD
  – Category 2 = Cleanroom Suite with BUDs based on
    • Component type
    • Addition (or not) of preservative
    • Sterility testing
    • Endotoxin testing
Balance

Personnel Testing and Environmental Monitoring

State of Control

BUDs
Key Elements

• Personnel
• Documentation
• Facility
• Garb/Personal Protective Equipment
• Work Practices
• Cleaning
• Certification of devices and rooms
• Environmental Monitoring
<797> Personnel

- Initial training
- Requalification
  - Remediation
- Didactic
- Physical tests
  - Media fill
  - Gloved fingertip

Who has to do these tests?
POLLING QUESTION

• How many gloved fingertip samples of each hand must be taken to comply with current <797>?

• A. One initially, then one annually
• B. One initially, then three annually
• C. Three initially, then one annually
• D. Three initially, then three annually
<797> Documentation

- Policies and procedures
- Competency
  - <797> appendices
- Master Formulation Records
- Compounding Records
<797> Facilities

- Segregated Compounding Area
  - ISO 5 Primary Engineering Control (PEC) in defined area
  - Limited to 12 hour beyond-use date (BUD)
- Cleanroom suite
  - ISO classified anteroom
    - ISO 7 if opens into any negative space
    - ISO 8 if opens only into positive space
  - ISO 5 PEC in ISO 7 buffer room
POLLING QUESTION

• What ISO classification is required for a SCA?

• A. ISO 5
• B. ISO 7
• C. ISO 8
• D. No requirement
<table>
<thead>
<tr>
<th>Configuration</th>
<th>Current &lt;797&gt;</th>
<th>Proposed Revised &lt;797&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cleanroom suite</td>
<td>BUDs in &lt;797&gt;</td>
<td>BUDs in &lt;797&gt;</td>
</tr>
<tr>
<td>Combined ante/buffer room</td>
<td>Allowed</td>
<td>Not allowed</td>
</tr>
<tr>
<td>SCA with Laminar Air Flow Workbench (LAFW)</td>
<td>Maximum of 12 hours</td>
<td>Maximum of 12 hours room temperature; 24 hours refrigerated</td>
</tr>
<tr>
<td>SCA with Compounding Aseptic Isolator (CAI)</td>
<td>BUDs in &lt;797&gt;</td>
<td></td>
</tr>
</tbody>
</table>
POLLING QUESTION

• You reconstitute a 10 gm vancomycin vial and make ten 1 gm doses. The information on the vial indicates stability for 14 days. What is the maximum refrigerated BUD?

• A. 6 hours
• B. 48 hours
• C. 9 days
• D. 14 days
Garb

- Mask
- Hair covers
- Shoe covers
- Gowns
- Sterile gloves
Work Practices

- Allowance for immediate use preparations
- Order of garbing
- Hand hygiene
- Uses of equipment
  - Automated compounders
  - Repeater pumps
Cleaning

Clean with detergent

Disinfect with sterile alcohol
Certification

• Evaluation of non-viable conditions
• Every six months by independent qualified certifier
• Elements described in Controlled Environment Testing Association documents must be assessed
• Pass, fail, needs attention
• Joint Commission Sterile Compounding FAQs
Environmental Monitoring

- Evaluation of **viable** conditions
- Electronic air sampling
  - Current <797>: at least every six months
- Surface sampling
  - Current <797>: periodically

Photo courtesy of CriticalPoint
Handling Hazardous Drugs

- <795> and <797> will refer to <800> for hazardous drug (HD) issues
  - More than compounding
  - Handling throughout health care settings
- HDs are defined by NIOSH
  - Use 2016 list until 2018 list published

www.cdc.gov/niosh/docs/2016-161/pdfs/2016-161.pdf
NIOSH Approach to Mitigating Risk

Hierarchy of Controls

1. Elimination
   - Physically remove the hazard

2. Substitution
   - Replace the hazard

3. Engineering Controls
   - Isolate people from the hazard

4. Administrative Controls
   - Change the way people work

5. PPE
   - Protect the worker with Personal Protective Equipment

https://www.cdc.gov/niosh/topics/hierarchy/
Personnel

- Training
- Requalification
- Designated person to oversee
Documentation: Assessment of Risk

- All dosage forms of all HDs on the NIOSH list must be handled with all containment and work practices listed in <800> unless you perform an Assessment of Risk for eligible drugs and dosage forms
  - Table 1 = Antineoplastics
  - Table 2 = Non-antineoplastics
  - Table 3 = Reproductive only hazards
- Use NIOSH Table 5 (PPE) to develop your policies and procedures
<800> Minimum Facility Requirements

Room with fixed walls separate from HD storage and compounding

Vented outside the building

Negative pressure of 0.01 to 0.03” to adjacent space

At least 12 air changes per hour for storage & SCA; 30 for cleanroom suite

Contains hazard

Removes hazard
# Facilities for Hazardous Drugs

<table>
<thead>
<tr>
<th>Configuration</th>
<th>Allowed in &lt;797&gt;</th>
<th>Allowed in &lt;800&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cleanroom suite (ISO positive anteroom opening into ISO 7 negative buffer room)</td>
<td>Yes, with negative pressure of at least 0.01” negative to adjacent space</td>
<td>Yes, with pressure range of 0.01 to 0.03” negative to adjacent space</td>
</tr>
<tr>
<td>Low Use Exemption</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Containment Segregated Compounding Area</td>
<td>Not addressed in &lt;797&gt;</td>
<td>Yes, if externally vented and pressure range of 0.01 to 0.03” negative to adjacent space, but limited to 12 hour beyond use date (BUD)</td>
</tr>
<tr>
<td>CACI in negative room with 12 air changes per hour</td>
<td>Yes, optimally vented</td>
<td></td>
</tr>
<tr>
<td>BSC outside of cleanroom</td>
<td>No</td>
<td></td>
</tr>
</tbody>
</table>
<800> PPE

- Gloves that meet ASTM standard D6978
  - Sterile for sterile compounding
- Gowns that are impervious and intended for use with HDs
- Two pairs of shoe covers in negative rooms
- Respiratory and eye protection
  - Respirator (not surgical mask)
  - Goggles (not eye glasses or face shield)

Photo courtesy of Contec, Inc.
<800> Work Practices

• Handling HDs throughout the facility
  – Receiving
  – Transport
  – Storage
  – Finished preparations

• Containment
  – Closed system drug-transfer devices
  – Negative pressure compounding technique
POLLING QUESTION

• What type of solutions is used to decontaminate HD surfaces?

• A. Sterile water
• B. Detergent
• C. Oxidizer
• D. Alcohol (sterile for sterile compounding)
Cleaning

1. Deactivate/decontaminate with oxidizer
2. Clean with detergent
3. Disinfect with sterile alcohol
<800> Certification

- Containment Ventilated Enclosure (CVE) for non-sterile
- Room pressure must be 0.01 to 0.03” negative to adjacent areas

Photo courtesy of LabConco
<800> Recommendations

• CSTDs for compounding
• Wipe sampling
  – Baseline and every six months
• Medical surveillance
Resources

• USP
  – *Compounding Compendium*
  – FAQs at [www.usp.org](http://www.usp.org)
• State Board of Pharmacy regulations
• ASHP
  – Compounding Resource Center
  – Publications
• Joint Commission
  – Medication Management standards
  – Compounding Certification
  – Sterile Compounding FAQs
  – [www.hazmedsafety.com](http://www.hazmedsafety.com) (with BD)
Resources

• Oncology Nursing Society
  – *Handling Hazardous Drugs*

• Critical Point
  – Monthly Sterile Compounding Pearls
  – www.criticalpoint.info

• Pharmacy Purchasing and Products
  – www.pppmag.com

• bbraun
  – www.readyfor800.com
Key Takeaways

• <795> and <797> are under revision
  – Provide comments to USP
  – Watch for final version

• <800> is a final document
  – Complete your Assessment of Risk
  – Ensure facilities and work practices are compliant

• Review your certification documents

• Ensure personnel and environmental monitoring is complete