New Compounding Regulations
(or how I spent my summer vacation)

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Learning Objectives for Pharmacists & Technicians

• Describe three sources of contaminants to compounded sterile preparations.
• Identify organizations that have enforcement authority with respect to USP <797>.
• List three proposed changes to USP <797>: Separation of Hazardous Drug standards, new product categories, new beyond use date.
• Identify important remaining dates in the USP <797> timeline to enforcement

What is USP?
The U.S. Pharmacopeial Convention (USP) is a scientific nonprofit organization that sets standards for the
• identity,
• strength,
• quality, and
• purity of medicines, food ingredients, and dietary supplements manufactured, distributed and consumed worldwide.
United States Pharmacopeia (USP)

- Chapters below <1000>
  - Compliance is mandatory
- Chapters above <1000>
  - Informational and advisory
- USP <797> Pharmaceutical Compounding – Sterile Preparations
  - First released in 2004
  - revision in 2008
  - another revision pending
  - anticipated to become official December 1, 2019

Quick Quiz
Test your memory from elementary school

What is a NOUN?
A. word that provides a description
B. an action word
C. a word that names a person, place or thing

USP <797> Pharmaceutical Compounding—Sterile Preparations
Chapter Objective

Chapter <797> should be followed to minimize harm, including death, to patients in the use of Compounded Sterile Preparations (CSP) due to:

- Microbial contamination (nonsterility)
- Excessive bacterial endotoxins
- Variability from intended strength of correct ingredients
- Physical and chemical incompatibilities
- Chemical and physical contaminants
- Ingredients of inappropriate quality

Factors affecting risk of contaminants

Factors affecting risk are NOUNs
- Persons
- Places
- Things
USP <797> Pharmaceutical Compounding—Sterile Preparations
Factors affecting risk of contaminants

- Persons
  - Personnel must be trained and properly garbed
- Places
  - Facilities must be designed appropriately
  - Equipment must be selected and maintained
- Things
  - Components must be sterile
  - Gowning & gloving with appropriate materials

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Factors affecting risk of contaminants - Personnel

**Personnel must be trained**
- Aseptic technique
- Hand hygiene and garbing
- Cleaning and disinfection
- Use of equipment
- Documentation

**Personnel must be tested**
- Written testing to include
  - Methods of preparation
  - Calculations
  - Policies on hand hygiene and garbing
  - Policies on cleaning and disinfection
- Every 12 months

***this is a change***
formerly only annually unless preparing high risk CSPs
Quick Quiz
Factors affecting risk - Personnel

Hand hygiene & garbing observation as well as media fill & glove sampling must occur
A. Every month
B. Every 3 months
C. Every 6 months
D. Every 12 months

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Factors affecting risk – facilities & equipment

• Places
  • Facilities must be designed appropriately
  • Equipment must be selected and maintained

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Factors affecting risk – Facilities & equipment

Facility design - Cleanroom suite
• Anteroom
  • ISO class 8 or better
• Buffer area
  • ISO class 7 or better
• Primary engineering control
  • ISO class 5 or better
• Provides clean environment for compounding

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Factors affecting risk – Facilities & equipment

Equipment selection
• Primary engineering control
  • ISO class 5 or better
  • Biological safety cabinet
• Laminar airflow workbench – horizontal or vertical
• Integrated vertical laminar airflow zone
• Restricted access barrier system = isolator
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Factors affecting risk – Facilities & equipment

*** no change under revised USP <797> for
• Facility design
• Equipment selection for primary engineering control

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Factors affecting risk - components

Components must be sterile
• Include only sterile components or
• Include nonsterile components and undergo sterilization
  • Filtration
  • Terminal sterilization: steam, dry heat, radiation

USP <797> Pharmaceutical Compounding—Sterile Preparations
Factors affecting risk – components and garb

Gowning & gloving with appropriate materials
• Low shedding materials
• Fit to prevent skin exposure
  • People shed 1 million skin cells each day
• Sterile gloves
  • Sterile isopropyl alcohol

*** no change under revised USP <797> for
• Gowning and garb selection of materials
• Component sterility
Quick Quiz
Risk of contaminants when compounding

Name 3 risk factors that impact compounded sterile preparations (CSP)

A. Distribution methods, personnel, equipment
B. Personnel, facilities, labeling
C. Personnel, equipment, facility

PRE Quiz
Enforcement of USP standards

Enforcement of USP standards is carried out by

A. FDA and DEA
B. USP during surprise visits
C. FDA and TJC as well as other organizations
D. There is no enforcement organization

Who enforces USP Standards?

USP’s drug standards are enforceable in the United States by

- The Food and Drug Administration (FDA)
- State regulators – Boards of Pharmacy
  - Illinois Board of Pharmacy
  - The Joint Commission (TJC)
  - Center for Medicare and Medicaid Services (CMS)

Who enforces USP Standards?

USP’s drug standards are enforceable in the United States by

- The Food and Drug Administration (FDA)
  - outsourcing facilities under section 503B are primarily overseen by FDA
  - inspected by FDA according to a risk-based schedule
- State boards of pharmacy
  - Not all states explicitly require compliance with USP
  - Illinois does NOT reference USP <797> in the Pharmacy Practice Act, Section 1330.670 Compounded Sterile Preparation Standards
**Who enforces USP Standards?**

USP’s drug standards are enforceable in the United States by:

- The Joint Commission (TJC) assesses sterile compounding activities during surveys
  - Expect increased attention on sterile compounding
  - Noted in TJC newsletter October 2017
- Center for Medicare and Medicaid Services (CMS)
  - Pharmaceutical services Condition of Participation (CoP)
  - Current accepted standards of practice including United States Pharmacopeia (USP) standards

**Quick Quiz**

Enforcement of USP standards is carried out by:

A. FDA and DEA
B. USP during surprise visits
C. FDA and TJC as well as other organizations
D. There is no enforcement organization

**USP <797> Pharmaceutical Compounding—Sterile Preparations**

What’s New

- Hazardous drug standards removed
  - See USP <800>
- Risk levels renamed to CSP categories
  - Low, medium, high revised to
  - Category 1 and Category 2
- New beyond use dating (BUD)
- Increased personnel testing
  - Previously noted

**USP <797> Pharmaceutical Compounding—Sterile Preparations**

What’s New

Risk levels renamed to CSP categories

- Low, medium, high revised to
- Category 1
  - Does not require classified area for PEC
  - Shorter BUD than category 2
- Category 2
  - Must be prepared in classified room
  - BUD can vary
Quick Quiz  
Changes to USP <797>

USP <797> changes that impact hospital compounding of sterile preparations include

A. Risk levels A through E with shorter BUD
B. Additional sections on hazardous drug compounding
C. Hazardous drugs segregated in <800> and only 2 CSP categories

Category 1
- Does not require classified area for PEC
- Segregated compounding area
- Shorter BUD than category 2
  - Room temp 12 hours
  - Refrigerated 24 hours

Category 2
- PEC must be in a class 7 buffer area
- Anteroom must be class 8 or better
- Longer BUDs than category 1
- BUD based on
  - Starting components
  - Sterility tests if applicable
  - Storage conditions

Category 2 BUD based on
- Starting components
  - 100% sterile vs. some non-sterile
- Terminal sterilization, if performed
- Sterility tests, if performed and passed
- Storage conditions
  - Room temperature, refrigerated, frozen
### Table 12. BUDs for Category 2 CSPs

<table>
<thead>
<tr>
<th>Preparation Characteristics</th>
<th>Storage Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sterilization Method</td>
<td></td>
</tr>
<tr>
<td>Sterility Testing</td>
<td>Sterility Testing Performed and Passed</td>
</tr>
<tr>
<td>Controlled Room Temp</td>
<td>Refrigerator</td>
</tr>
<tr>
<td>Refrigerator</td>
<td>Freezer</td>
</tr>
</tbody>
</table>

#### Aseptically prepared CSPs
- **No**
  - One or more nonsterile starting components 1 days
  - Only sterile starting components 4 days
  - Only sterile starting components 9 days
  - Only sterile starting components 45 days
  - Yes: 30 days, 45 days, 60 days

- **Yes**
  - 45 days, 60 days, 90 days

#### Terminally Sterilized CSPs
- **No**
  - 14 days, 28 days, 45 days

- **Yes**
  - 45 days, 60 days, 90 days

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**USP <797> Pharmaceutical Compounding—Sterile Preparations**

**What’s New**

**Table 12. BUDs for Category 2 CSPs**

- Terminal sterilization with sterility testing provides the longest BUDs
- Room temperature BUDs are extended

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**COMMON hospital compounding:**

- Sterile components with aseptic technique
  - Common doses of antibiotics from bulk vials
    - ex: Vancomycin, cefazolin
- No terminal sterilization and no sterility testing
- Room temperature 4 days *** change ***
  - Refrigerator 9 days
  - Freezer 45 days
USP <797> Pharmaceutical Compounding—Sterile Preparations
What’s New - Recap
• Hazardous drug compounding and handling moved to <800>
• Risk levels replaced by CSP categories
  • Category 1 – segregated compounding area
  • Category 2 – prepared in IV suite
• BUD depends on components and storage temperature
  • Category 1 – short BUD
  • Category 2 – some extended BUD
    • 4 days room temp for commonly prepared CSPs
    • All components are sterile, Aseptic technique, No sterility testing

Timeline for ICHP Annual Meeting presenters
• July 26, 2018 – submit learning objectives and methods to ICHP
• July 27, 2018 – proposed <797> Pre-Posted on USP website
• August 9-13, 2018 – Janet on vacation in the Northwoods
• August 16, 2018 – submit final slides to ICHP
  • September 4, 2018 - <797> to be formally published in Pharmacopeial Forum
  • September 5, 2018 – Open Microphone Session
• September 13-15, 2018 – ICHP Annual Meeting

Timeline for USP <797> update
• July 27, 2018 – proposed <797> Pre-Posted on USP website
• September 4, 2018 - <797> to be formally published in Pharmacopeial Forum
• September 5, 2018 – Open Microphone Session
• November 30, 2018 – Public Comment Period for <797> will close
• June 1, 2019 – Intended date of publication of <797> in USP-NF
• December 1, 2019 – Anticipated Official Date for <797>

Quick Quiz
Dates to watch for USP <797>
USP <797> is expected to become official on
A. January 1, 2019
B. June 1, 2019
C. December 1, 2019
D. As soon as this presentation ends 😊
## Changes to Pharmacy Practice

When USP <797> is becomes official on December 1, 2019*

- More frequent testing of personnel
  - Every 6 months for media fill and glove sampling
- Longer BUD for some compounded sterile preparations (CSP)
  - 4 days at room temperature for Category 2 CSPs
  - All sterile additives
  - Class 5 PEC within Class 7 buffer area (cleanroom suite)
  - Aseptic technique – no sterility testing

*Version is still not final*

Questions remain about the final version of USP <797>

Open for comments until November 30, 2018

Any questions?

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## Reference sources


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Reference sources