


New Compounding Regulations

(or how I spent my summer vacation)

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New Compounding Regulations

The author has no actual or potential conflict of interest in relation to this activity

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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

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

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

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Factors affecting risk of contaminants

Factors affecting risk are NOUNs

- Persons
- Places
- Things

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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

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Factors affecting risk of contaminants - Personnel

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

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Factors affecting risk of contaminants - Personnel

Personnel must be tested

- Hands-on demonstration of skills
  - Hand hygiene and garbing
  - Media fill
  - Glove sampling
- Every 6 months for **all** compounding personnel

*** 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

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Factors affecting risk - 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

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Factors affecting risk – components and garb

*** 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

Enforcement of USP standards is carried out by

A. FDA and DEA
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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

What's New

Category 1

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

What's New

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

What's New

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

Preparation Characteristics		Storage Conditions		
Sterilization Method	Sterility Testing Performed and Passed	Controlled Room Temp	Refrigerator	Freezer
Aseptically prepared CSPs	No	One or more nonsterile starting components 1 days	One or more nonsterile starting components 4 days	One or more nonsterile starting components 45 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
Terminally Sterilized CSPs	No	14 days	28 days	45 days
	Yes	45 days	60 days	90 days

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What's New

Table 12. BUDs for Category 2 CSPs

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

Table 12. BUDs for Category 2 CSPs

Preparation Characteristics		Storage Conditions		
Sterilization Method	Sterility Testing Performed and Passed	Controlled Room Temp	Refrigerator	Freezer
Aseptically prepared CSPs	**No**	One or more nonsterile starting components 1 days	One or more nonsterile starting components 4 days	One or more nonsterile starting components 45 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
Terminally Sterilized CSPs	No	14 days	28 days	45 days
	Yes	45 days	60 days	90 days

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What's New - BUDs for Category 2 CSPs

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

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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

<797> 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

- US Pharmacopeial Convention General Chapter <797> Pharmaceutical Compounding – Sterile Preparations. Download the Proposed Revision to GC <797>. Available at http://www.usp.org/compounding/general-chapter-797. Accessed August 6, 2018.
- Reducing Risk Associated with Sterile Medication Compounding. The Joint Commission Perspectives, the Official Newsletter of the Joint Commission. October 2017; Vol 37; Number 10: 12-13.

Reference sources

- US Food and Drug Administration. Compounding and the FDA: Questions and Answers. Available at https://www.fda.gov/drugs/guidancecomplianceregulatoryinformation/pharmacycompounding/ucm339764.htm. Accessed August 10, 2018.
- Pharmacy Practice Act. Title 68 of Illinois Administrative Code: §1330.670. Available at ftp://www.ilga.gov/jcar/admincode/068/06801330sections.html. Accessed August 10, 2018.

Reference sources

- Centers for Medicare & Medicaid Services, Center for Clinical Standards and Quality/Survey & Certification Group. Memo to State Survey Agency Directors dated October 30, 2015. Revised Hospital Guidance for Pharmaceutical Services and Expanded Guidance Related to Compounding of Medications. Available at https://www.cms.gov/Medicare/Provider-Enrollment-and-Certification/SurveyCertificationGenInfo/Downloads/Survey-and-Cert-Letter-16-01.pdf Accessed July 25, 2018.