



UTAH SOCIETY OF
HEALTH-SYSTEM PHARMACISTS

USP <797>: Updates and Revisions

Nathan Bartley
PGY1 HSPAL Resident
University of Utah Health
nathan.bartley@hsc.utah.edu
March 23, 2023

Disclosure

- **Relevant Financial Conflicts of Interest**
 - **CE presenter, Nathan Bartley:**
 - None
 - **CE mentor, Amanda Woods:**
 - None
 - **CE mentor, Ashley Bowden:**
 - None
 - **CE mentor, Christian Tulio:**
 - None
- **Off-Label Uses of Medications**
 - None



3

Learning Objectives

Pharmacists

1. Compare and contrast USP <797> updates with the previous version
2. Recognize potential barriers to USP <797> implementation
3. Recommend potential solutions to implementation barriers

Learning Objectives

Technicians

1. Discuss proposed updates to USP <797>
2. Differentiate different categories of CSPs and associated BUDs
3. Outline possible new roles and responsibilities to assist with compliance of USP <797> standards



4



5

Abbreviations

- USP – US Pharmacopeia
- CSPs – Compounded Sterile Products
- BUD – beyond use dating
- PNSU – Probability of a non-sterilized unit
- SCA – segregated compounding area
- GFTs – glove and fingertip sampling
- EM – environmental monitoring



6

The image shows a screenshot of an NBC News article. The main headline is "Hepatitis C cluster near...". Below it, there are several sub-headlines: "A Multistate Outbreak of Serratia marcescens Bloodstream Infection Associated with Contaminated Intravenous Magnesium Sulfate from [redacted] Pharmacy", "Compounding pharmacy initiates voluntary recall", "Pharmacy Charged With [redacted] Missouri, New York, Texas, and [redacted]", and "Pseudomonas Bloodstream Infections Associated with a Heparin/Saline Flush ... in blue". The article is dated Oct 1, 2005. There are social media sharing icons for Facebook, Twitter, LinkedIn, and Pinterest. At the bottom of the article, it says "Richfield, MN—A small compounding pharmacy patients who used it had symptoms" and "...alling some lots of its trypan blue 0.06% ophthalmic solution after a customer said two".



The Largest Health Care Associated Fungal Outbreak in the U.S.

Tricia Meyer, PharmD; Emory Martin, PharmD; Richard Priellipp, MD

During this presentation think about...

Have you heard of similar issues?

Have you experienced a situation like this?

Background



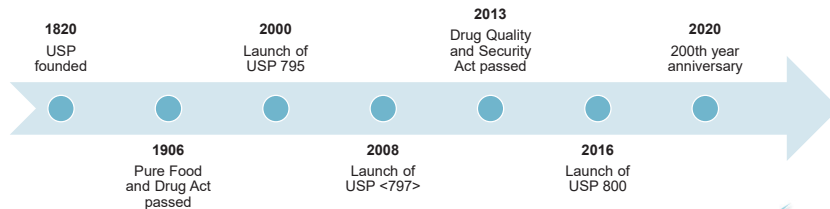
8



9

Timeline

- US Pharmacopeia (USP) was founded in 1820 by a group of physicians
 - Purpose: Needed more consistency when administering medications



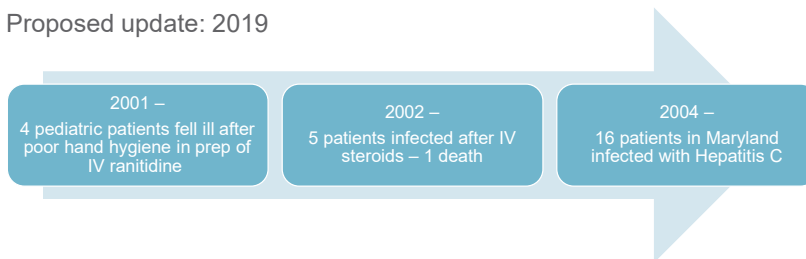
Purpose of USP <797>

- **Purpose:** To maximize safety and quality of sterile compounded medication by creating and maintaining minimum standards for safe compounding practices
- Mid 1990s – early 2000s
 - Many infections due to poor hand hygiene
 - Most pharmacy graduates did not have adequate training



USP <797> Updates

- Originally created: 2008
- Proposed update: 2019



USP <797>

- Who do these changes apply to?
 - Any person or institution who prepares compounded sterile products (CSPs) for animal or human use
- When do revisions go into effect?
 - November 1, 2023 – USP has no enforcement



Updates to USP <797>

1. Beyond use dating (BUD)
2. Personnel Training and Evaluation
3. Endotoxin testing
4. Garbing practices
5. Environmental monitoring (EM)
6. Cleaning and Sanitizing



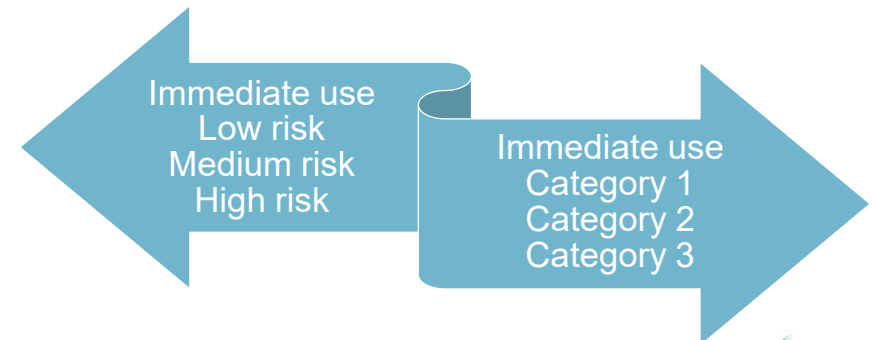
1. Beyond Use Dating



Current BUDs

Risk Level	BUD – Room Temperature (20 – 25°C)	BUD – Refrigerator (2 – 8°C)	BUD – Freezer (-25 – -10°C)
Immediate Use	1 hour	--	--
Low risk	48 hours	14 days	45 days
Medium risk	30 hours	9 days	45 days
High risk	24 hours	3 days	45 days

BUD



Immediate Use

- Four (4) conditions for preparation:
 1. Aseptic technique and minimal contact with nonsterile surfaces
 2. Appropriately trained personnel
 3. Physical and chemical stability has been established
 4. No more than three (3) components
- Examples: Norepinephrine infusion



18

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Immediate Use

Category	BUD – Room Temperature (20 – 25°C)	BUD – Refrigerator (2 – 8°C)	BUD – Freezer (-25 – -10°C)
Immediate Use	4 hours	--	--



19

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Category 1

- Compounded under least controlled environment
 - May be compounded in an unclassified SCA (eg., medication room) without a buffer or ante-room
- Examples: reconstituted antibiotics in emergency department



20

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Category 1

Category	BUD – Room Temperature (20 – 25°C)	BUD – Refrigerator (2 – 8°C)	BUD – Freezer (-25 – -10°C)
Category 1	≤ 12 hours	≤ 24 hours	--



21

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Category 2

- Compounded in more controlled environment than Category 1
 - Must be compounded in ISO Class 7 area with ISO Class 8 ante-room
- Examples: patient specific weight-based doses



Category 2

Category	Compounding Method	Sterility Testing Passed?	BUD – Room Temperature (20 – 25°C)	BUD – Refrigerator (2 – 8°C)	BUD – Freezer (-25 – -10°C)
Category 2	Aseptically processed	No	1+ nonsterile starting components: 24 hours	4 days	45 days
		No	Only sterile products: 4 days	10 days	45 days
	Yes		30 days	45 days	45 days
	Terminally sterilized	No		14 days	28 days
Yes			45 days	60 days	90 days



Category 3

- Compounded under most controlled conditions
 - Must be compounded in ISO Class 7 area with ISO Class 8 ante-room
- Examples: batched compounds where longer BUD dating is desired



Category 3

Category	Compounding Method	BUD – Room Temperature (20 – 25°C)	BUD – Refrigerator (2 – 8°C)	BUD – Freezer (-25 – -10°C)
Category 3	Aseptically processed + sterility testing + all other testing	60 days	90 days	120 days
	Terminally sterilized + sterility testing + all other testing	90 days	120 days	180 days



Other BUD Considerations

- Stability of the product
- Manufacturer expiration date
- Environmental monitoring



Sterility Testing and Other Tests

- Sterility Testing – USP <71>
- Endotoxin testing – USP <1085>
- Terminal Sterilization – application of lethal process to sealed containers to achieve PNSU of more than 10^{-6}
 - Process of applying heat, gas, vapor, or chemicals for a period of time to drastically reduce the probability that microbes will cause infection
- Aseptically processed



2. Personnel Training and Evaluation

Initial Training – Current Practices

- Aseptic technique – media fill test
- GFTs
 - Zero (0) CFUs – triplicate



Initial Training – Updates

Personnel Function	Defined by SOPs	Required USP <797> Training and Competency in:			
		Maintaining the quality and of the sterile environment	Sterile compounding principles and practices	Garbing competency (including GFT)	Media fill with post-GFT and surface sampling
Compounder		X	X	X	X
Designated Person and anyone with direct oversight		X	X	X	X
Cleaning and restocking staff	X				
Immediate use only CSP compounders	X				
All other personnel	X				



Ongoing Training – Current Practices

Risk level	Aseptic Technique*	GFTs*
Low-risk	Every 12 months	Every 12 months
Medium-risk	Every 12 months	Every 12 months
High-risk	Every 6 months	Every 6 months

* ≤ 3 CFUs is acceptable



Ongoing Training – Updates

Personnel Function	Defined by SOPs	Required USP <797> Training and Competency in:		
		Sterile compounding principles and practices	Garbing competency (including GFT)	Media fill with post-GFT and surface sampling
Compounder		Every 12 months	Category 1 and 2: every 6 months Category 3: every 3 months	Category 1 and 2: every 6 months Category 3: every 3 months
Designated Person and anyone with direct oversight		Every 12 months	Every 12 months unless compounding	Every 12 months unless compounding
Cleaning and restocking staff	X			
Immediate use only CSP compounders	X			
All other personnel	X			



3. Bacterial Endotoxin Testing



Bacterial Endotoxin Testing

Recommended

Required

Category	Compounding Method	Sterility Testing Passed?	BUD – Room Temperature (20 – 25°C)	BUD – Refrigerator (2 – 8°C)	BUD – Freezer (-25 – -10°C)
Category 2	Aseptically processed	No	1+ nonsterile starting components: 24 hours	4 days	45 days
		No	Only sterile products: 4 days	10 days	45 days
		Yes	30 days	45 days	45 days
	Terminally sterilized	No	14 days	28 days	45 days
		Yes	45 days	60 days	90 days



Bacterial Endotoxin Testing

Required

Category	Compounding Method	BUD – Room Temperature (20 – 25°C)	BUD – Refrigerator (2 – 8°C)	BUD – Freezer (-25 – -10°C)
Category 3	Aseptically processed + sterility testing + all other testing	60 days	90 days	120 days
	Terminally sterilized + sterility testing + all other testing	90 days	120 days	180 days



Bacterial Endotoxin Testing

- Category 1:
 - Not required
- Category 2:
 - MUST be tested for endotoxins when assigning extended BUDs
 - SHOULD be tested for endotoxins when using a nonsterile ingredients
- Category 3:
 - MUST be tested for endotoxins when assigning extended BUDs

4. Garbing Practices



Garbing - Current Practices

Don PPE in the following order:

1. Shoe covers
2. Hair cover
3. Face mask
4. Wash hands
5. Gown
6. Sterile gloves



42

USP <797>. 2020.

Garbing - Updates

- No changes for Category 1 and 2 from previous versions
- Only Category 3 has changed
 - Compounder must have NO exposed skin – including face and neck
 - All garb must be sterile and low-lint
 - After leaving classified area
 - Disposable garb – must be discarded
 - Laundered garb – must be laundered and re-sterilized



43

USP <797>. 2023.
pharmacypracticenews.com/Covid-19/Article/06-20/Sterile-Compounding-In-the-Time-of-COVID-19/58408

5. Environmental Monitoring

EM – Current Practices

Category	Air Monitoring	Surface Monitoring
Low risk	Every 6 months	Every 6 months
Medium risk	Every 6 months	Every 6 months
High risk	Every 6 months	Every 6 months



44



45

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EM – Updates

Category	Air Monitoring	Surface Monitoring
Category 1	Every 6 months	Every month
Category 2	Every 6 months	Every month
Category 3	Every month	Before and after every batch, and weekly If self-enclosed robot – daily after operations are complete

6. Cleaning and Sanitation



Cleaning and Sanitation – Current Practices

Site	Frequency
Sterile hood	Each shift, before each batch, every 30 minutes, after contamination
Counters and workspaces	Daily
Floors	Daily
Walls	Monthly
Ceilings	Monthly
Storage shelves	Monthly

Cleaning and Sanitation – Updates

Type of Agent	Purpose	Example
Cleaning	Removal of substances like drug residue, dirt, debris	70% isopropyl alcohol
Disinfectant	Agent that destroys bacteria, fungi, and viruses	70% isopropyl alcohol
Sporicidal	Destroys bacterial and fungal spores and other vegetative microbes	Hydrogen peroxide



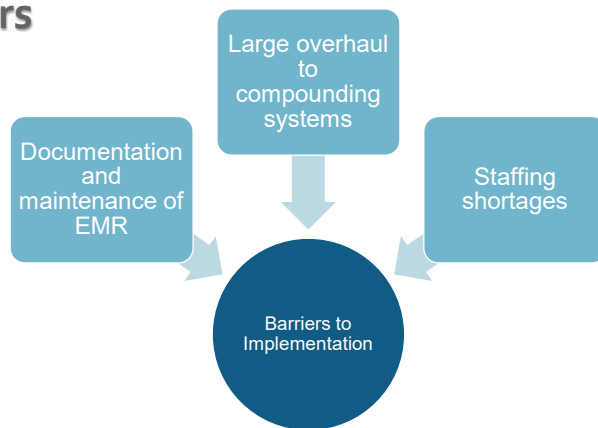
Cleaning and Sanitation – Updates

Site	Cleaning	Disinfecting	Sporicidal
PECs	Daily and after contamination	Daily and after contamination	Category 1 & 2: monthly Category 3: Weekly
Pass-throughs, floors, working surfaces	Daily	Daily	Category 1 & 2: monthly Category 3: Weekly
Walls, doors, ceilings, storage shelves	Monthly	Monthly	Monthly

Barriers to Implementation



Barriers



Possible Solutions



Solutions

Barrier	Proposed Solution
Large overhaul to compounding systems	<ul style="list-style-type: none"> Designate a work group to divide tasks to make changes more manageable Utilize learners Meet regularly to talk about progress
Documentation and maintenance of EMR	<ul style="list-style-type: none"> Utilize learners Automate EMR updates Reach out to peer institutions for stability data
Staffing shortages	<ul style="list-style-type: none"> Cross train staff to help with compounding and increased EM Utilize learners



54

Summary

- Major updates:
 - BUD
 - Personnel Training and Evaluation
 - Endotoxin testing
 - Garbing practices
 - EM
 - Cleaning and Sanitizing
- Barriers and solutions



57

Summary – BUD

Current Practices

- Immediate Use
 - 1 hour
- Low Risk
 - 48 hours – 45 days
- Medium Risk
 - 30 hours – 45 days
- High Risk
 - 24 hours – 45 days



Updates

- Immediate Use
 - 4 hours
- Category 1
 - 12 – 24 hours
- Category 2
 - 24 hours – 90 days
- Category 3
 - 60 – 180 days



58

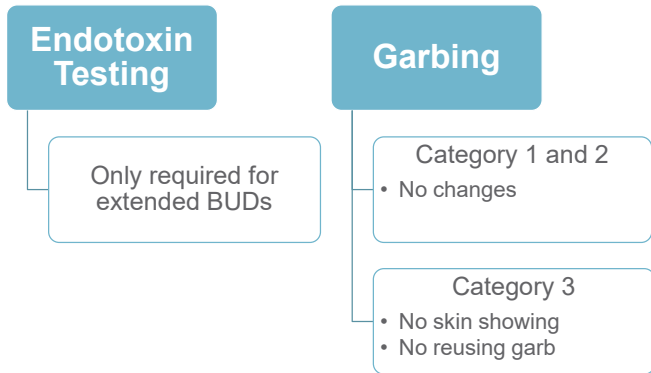
Summary – Personnel Training

	Current Practices	Updates
Initial Training	Media fill tests GFTs	More in-depth and more frequent Who and how to train new personnel
Ongoing Training	Every 6-12 months	Every 3-6 months

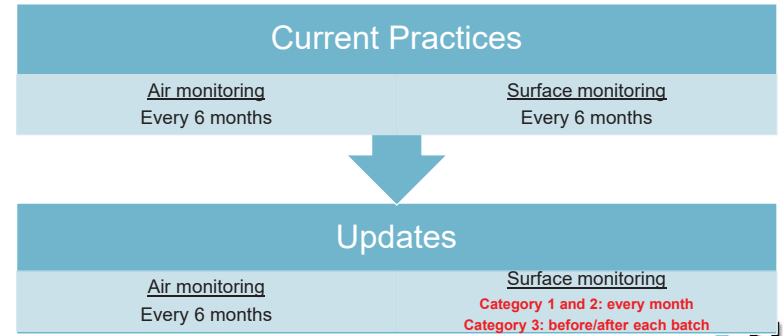


59

Summary – Endotoxin Testing and Garbing



Summary – EM



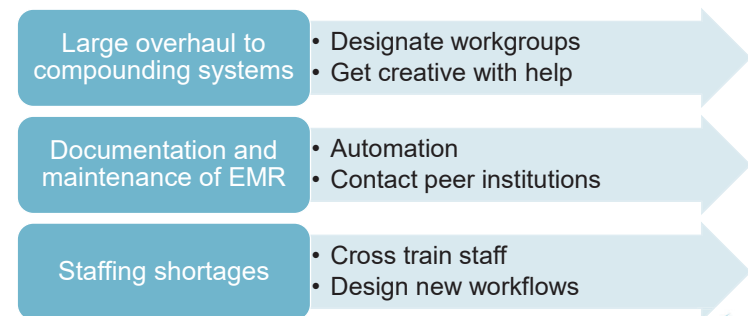
Summary – Cleaning and Sanitation

Updates

- More frequent sporicidal use
- Category 1 and 2: every month
- Category 3: every week



Summary – Barriers and Solutions



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