



## CSP Quality Assurance Testing and Advancing Pharmacy Roles for QA Monitoring Programs

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## Objective

- Describe components of compounded sterile preparation (CSP) quality assurance (QA) testing and the implementation of a quarantine program for extended beyond use date expirations

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## Preview

- USP <797> & extended beyond use dates (BUDs)
- USP <71> & sterility testing batched compounded sterile preparations (CSPs) with extended BUDs
- Evolution of a CSPs QA program
- Dedicated sterile products QA Coordinator
- How can IT help with QA to avoid a SOS!?
- The next horizon: end product quarantine

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## USP <797> & extended BUDs

- Governs compounded sterile preparations (CSPs) and environmental requirements
- Dictates maximum expiration date of CSPs based on risk level and storage conditions
- The Joint Commission and State Boards of Pharmacy may also use USP <797> guidelines during pharmacy inspection
- Product expiration is limited without evidenced based literature or Beyond Use Date Certification

Table 4  
USP <797>, Sterility-based beyond-use limitations<sup>1,2</sup>

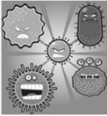
RISK LEVEL*	TEMPERATURE CONDITION		
	Room temperature	Cold temperature	Frozen
Low	< 48 hours	< 14 days	< 45 days
Medium	< 30 hours	< 9 days	< 45 days
High	< 24 hours	< 3 days	< 45 days

\* For complete list, refer to USP <797> or references. <http://www.cedrgstorenews.com>

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## Beyond Use Date Certification

- Increase expiration dating to decrease cost of waste and increase operational efficiency of high use CSPs
- End product testing for extended BUD
  - Stability - potency/purity via HPLC
  - **Sterility <USP 71>: aerobic/anaerobic/fungal**
  - Endotoxin <USP 85>
  - Particulate matter <USP 788>
  - pH testing



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## USP <71> Sterility Testing Batched CSPs with Extended BUDs

- Incubate portions of the media for 14 days
- Method suitability test
  - **Membrane filtration**
  - Direct inoculation of culture medium
- Growth promotion of positive controls
  - Can the media and drug in question even grow microbes?
  - Conducted as a one-time validation
- Test for sterility of product to be examined including negative controls
  - Limit false positives due to poor lab testing technique
  - Conducted each sterility testing session

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### USP <71> Sterility Testing batched CSPs with extended BUDs

- Number of articles to be tested

Minimum Number of Articles to be Tested in Relation to the Number of Articles in the Batch

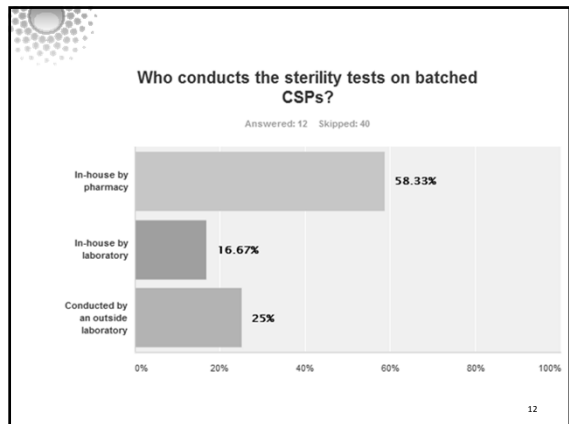
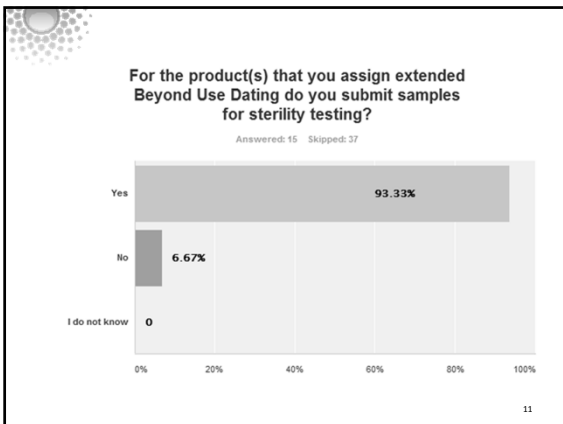
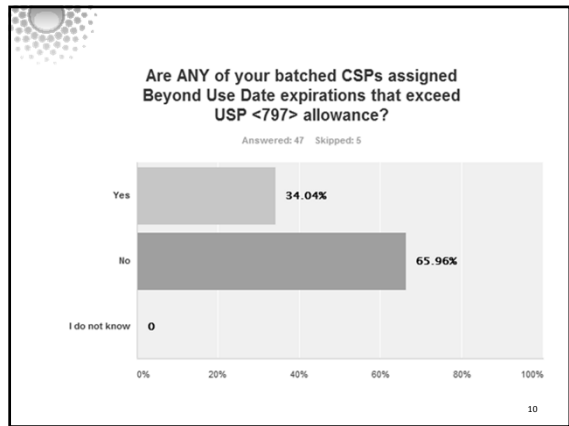
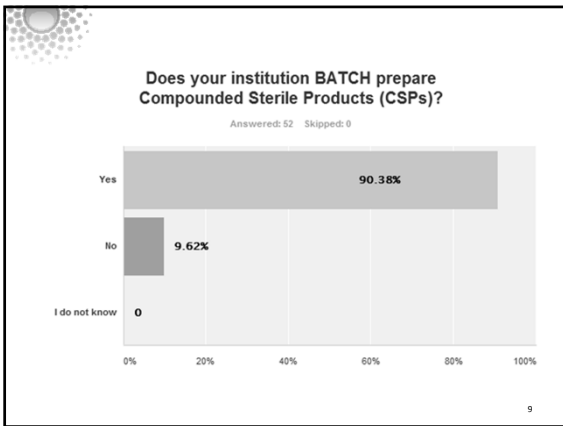
Number of Items in the Batch*	Minimum Number of Items to be Tested for Each Medium (unless otherwise justified and authorized)**
<i>Parenteral preparations</i>	
Not more than 100 containers	10% or 4 containers, whichever is the greater
More than 100 but not more than 500 containers	10 containers
More than 500 containers	2% or 20 containers, whichever is less
*For large-volume parenterals	2% or 10 containers, whichever is less

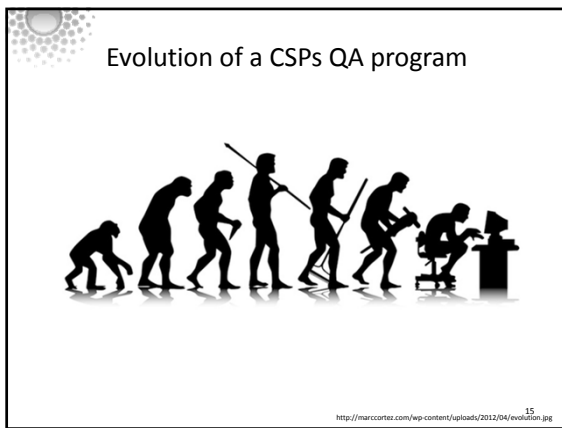
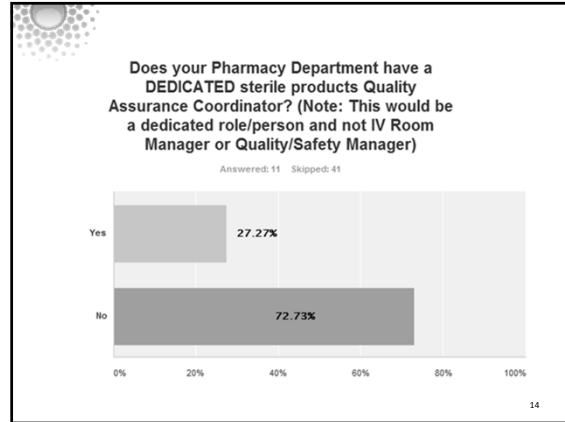
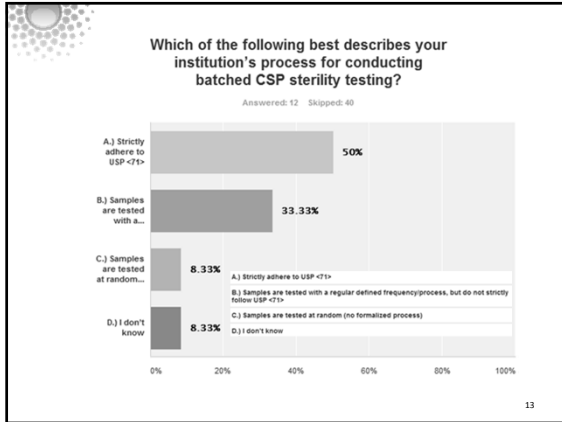
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### Sterile Products (CSPs): Extended Beyond Use Date Sterility Testing

University HealthSystem Consortium (UHC) Survey  
 August 2013 (n= 52 responding institutions)

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- ### Goldie Locks & The 3 Bears
- This porridge is too cold!
    - Under-testing
      - Initially, send end product samples for extended stability & sterility certification for each drug seeking extended BUD.
      - Then, randomly selected samples were sent twice weekly from each shift of extended BUD products
  - NECC tragedy - October 2012
  - This porridge is too hot!
    - Over-testing
      - 2% or greater of every batch was sent for sterility testing even if dating was within USP <797> dating standards
  - This porridge is juuuust right!
    - Sample testing only if BUD surpasses USP <797> allowance
    - USP <71> sample volume & quantity based on product & batch size

### How can IT help with QA to avoid a SOS!? – Part 1

- Outside laboratory: web based submission, real-time tracking, results notification

ACYCLOVR 200MG/100ML DSW 31138070P W-1-6559 RT BWH1 09/04/13 In Process

Test	ITS Dur	Date	Specification	Result	Comment	QA	Select
Standard Sterility Test		09/05/13	Negative at 14 days	Negative at 5 days		<input type="radio"/>	<input type="checkbox"/>

From: [Redacted]  
 To: [Redacted]  
 Cc: [Redacted]  
 Subject: Results Notification as of 09/05/2013 03:00 PM

The following results are available online at [Redacted]

Compound: HYDROMORPHONE HCL 1MG/5ML (PF) IN NS (0.2MG/ML) Lot Code: 201308213436 Sample #: W-1-6520 8/21/2013 12:02:58 PM

### How can IT help with QA to avoid a SOS!? – Part 1

- Outside laboratory: USP <71> Sterility certification

#### CERTIFICATE OF ANALYSIS

**SAMPLE INFORMATION**

Customer: Brigham and Women's Hospital Storage: Room Temperature  
 Received: August 26, 2013 Amount / Device: bag(s) 100 ml  
 Description: CALCIUM GLUCONATE 20 IN 100ML NS  
 Lot Number: 2104000897573  
 Sample #: W-1-6561

**RESULTS**

Test	Specification	Result	Comment
Sterility (Bacteria/Fungi)	Negative at 14 days	Negative at 14 days	

**AUTHORIZATION AND WARRANTY**

Authorizing Signature: \_\_\_\_\_ Date: 09/09/2013

1. Sterility Test. Includes tests for Aerobic and Anaerobic Bacteria, and Fungi (Mold and Yeasts)

### How can IT help with QA to avoid a SOS!? – Part 1

- What was lacking?
  - Program was a “one-way ticket” unless we were notified of a problem
  - Robust closed loop tracking
  - Assurance that appropriate sample quantities are sent for sterility testing based on USP <71> requirements
  - An internal electronic database all batches prepared, quarantined, and released
  - A dedicated, independent, non-pharmacist professional
    - An “outsider on the inside”

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### Dedicated Sterile Products QA Coordinator

- Business Plan
  - Based on influx of in-sourced products and increase in QA testing resulting from NECC tragedy
- Reports directly to the Chief of Pharmacy
  - Prevents conflict of interest/mediocrity if reporting to IV Room Manager
- Microbiologist by trait
  - Previous experience conducting USP environmental monitoring at a pharmaceutical manufacturer
- Learning curve
  - Health System Pharmacy, Pharmacy Specific USP Chapters, No predecessor
- On boarding process and training plan

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### Dedicated Sterile Products QA Coordinator

- Primary Role & Responsibilities
  - Environmental Monitoring: air sampling, surface sampling, staff media & finger tip testing, etc.
  - Staff education, training, & competencies
  - Authoring and enforcement of Sterile Products Room policies, cleaning agents, cleaning procedures
  - Knowledge and understanding of USP regulation
  - Coordination and follow-thru in daily collection, submission, tracking, and analysis of end product QA testing program
  - Monthly reports
  - Recall coordination
  - Quarantine program

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### The Next Horizon?

- Depending on your role, some of you may envision...



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- While others may envision...



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### What do you need?

**Time**



**Resources**



**Space**



<http://englishvocabulary2012.wikispaces.com/Comped>  
[http://en.wikipedia.org/wiki/Dr.\\_weil](http://en.wikipedia.org/wiki/Dr._weil)  
<http://powerthought.org/2012/02/14-04nt-Avian-Flu/>

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### Quarantine Program Overview

- BUD for batched refrigerated meds scaled back to USP 797 dating
  - Decrease cost of testing and storage space
- Room temp batched medications with extended BUD exceeding USP 797 continue to undergo USP 71 sterility testing
  - CSPs quarantined 14 days until USP 71 sterility test is resulted
  - Designated quarantine area, optimal batch size forecasting, tighter PAR level monitoring
  - Enough product must available until next batch release
  - If online inventory exhausted, immediate-use products will be made & USP 797 dating applied until quarantined batch is cleared

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### Quarantine Time & Resources

- Optimum batch sizes & supplies calculations for 3 week lead time implementation
- Increased CSP production to cover initial 14 day quarantine holding period
- Segregated storage space reallocation & construction planning
- Quarantine-release process of batches via sterility certificates
- Quarantine progress tracking database
- Update of Quality Assurance testing policy
- CSP Recall Policy
- All hands on deck
  - Sterile Products Manager, Central Pharmacy Manager, QA Coordinator, Medication Safety & Technology Manager, Director of Pharmacy, Sterile Products Room Technicians & Pharmacists



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### Quarantine Storage

- Current piecemeal conversion of small spaces:
  - ADC spare parts closet
  - Employee coat closet
  - Reconstruction of a workbench alcove area into a new walled storage area
  - Restructuring robot room for storage space
  - Pharmacy conference room (emergency contingency?)
- Long Term Plan
  - Continued pursuit to acquire new storage space
  - Acquisition of additional medication carousel
  - Assess total cost-benefit of batch continuation and/or re-outsourcing of certain products

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### Quarantine Inventory Management

- Inventory and Preparation Forecasting
  - Based on rolling 12 month analysis of actual quantity and number of batches produced per drug
  - Initial increase of 3 weeks supply of drugs vials, end disposable goods, and end product CSPs
- If Pharmacy runs OUT of a quarantined CSP
  - Staff to alert QA Coordinator and Pharmacy Manager
  - Manager(s) to assess next steps on a case by case basis
- If quarantine-released outage happens on an off shift
  - Small batch preparation(s) to get thru next release date
  - Expiration date of 48 hours room temp (low risk) assigned for temporary non-quarantined CSP batches

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### How can IT help with QA to avoid a SOS!? – Part 2

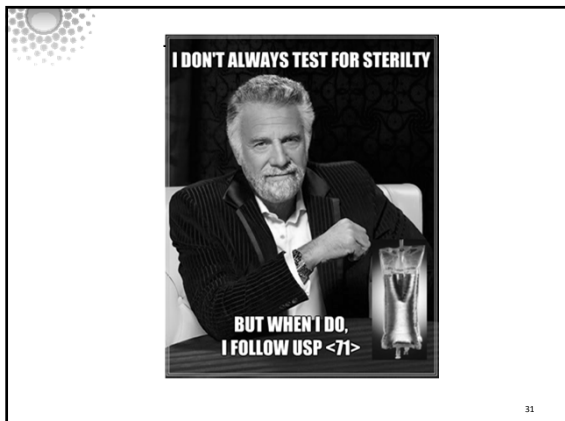
- Internal CSP tracking database
  - Batch preparation records
    - Date/time prepared
    - Prepared by
    - Drug Name/Concentration
    - Batch size & PAR level
    - Lot number & BUD expiration
    - Lab send out date
    - Sterility clearance (Y/N)
    - Release date into online inventory
    - Total quantity quarantined & released
  - Final quarantine-release based on USP <71> Sterility Certificate

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### Conclusion

- The Takeaways
  - USP 797 BUD and extended BUD requirements
  - USP 71 requirements
  - CSP QA Program and QA Coordinator
  - The next horizon: quarantining CSPs
  - Tracking mechanism for CSP preparation and quarantine-release process

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What is the professional background of the Brigham & Women's Hospital dedicated QA Coordinator? 


- A Pharmacy Technician
- B Microbiologist
- C Pharmacist
- D Industrial Engineer

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What percentage of UHC survey responders indicated that they **strictly adhere to USP <71>** when conducting extended BUD sterility testing? 

- A 25%
- B 50%
- C 75%
- D 100%

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True or False:  
Per USP <71>: 2% of all batched CSPs require sterility testing? 

- A True
- B False

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