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

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

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

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

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

<table>
<thead>
<tr>
<th>Minimum Number of Articles to be Tested in Relation to the Number of Articles in the Batch</th>
<th>Number of Items in the Batch</th>
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<tbody>
<tr>
<td>- Potential preparation:</td>
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<td>- Not more than 100 containers: 10% or 4 containers, whichever is the greater.</td>
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<tr>
<td>- More than 100 but not more than 500 containers: 10 containers</td>
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<tr>
<td>- More than 500 containers: 2% or 20 containers, whichever is the greater.</td>
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<tr>
<td>- *For large-volume parenteral: 2% or 10 containers, whichever is the greater.</td>
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Sterile Products (CSPs): Extended Beyond Use Date Sterility Testing

University HealthSystem Consortium (UHC) Survey
August 2013 (n= 52 responding institutions)
Evolution of a CSPs QA program

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Goldie Locks & The 3 Bears

- This porridge is too cold!
  - Under-testing
    - Initially, sent 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

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

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

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

- Outside laboratory: USP <71> Sterility certification
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”

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

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

The Next Horizon?

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

What do you need?

- Time
- Resources
- Space

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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

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

Quarantine Storage

- Current piecemeal conversion of small spaces:
  - ADC spare parts closet
  - Employee coat closet
  - Reconstruction of a workbench alcove 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-outourcing of certain products

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

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

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

A Pharmacy Technician
B Microbiologist
C Pharmacist
D Industrial Engineer

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%

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

A True
B False