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

2

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

3

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[6,7]

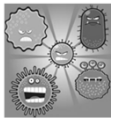
RISK LEVEL*	TEMPERATURE CONDITION		
	Room temperature	*Cold temperature*	*Frozen*
Low	< 48 hours	< 14 days	< 45 days
Medium	<30 hours	< 9 days	< 45 days
High	< 24 hours	< 3 days	< 45 days

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

4

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



5

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

6

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)**
Parenteral preparations	
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

7

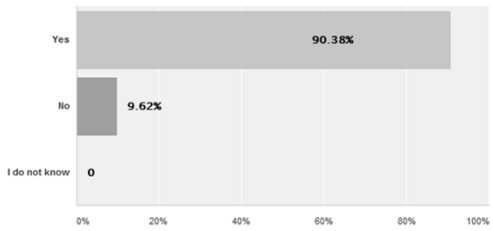
Sterile Products (CSPs): Extended Beyond Use Date Sterility Testing

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

8

Does your institution BATCH prepare Compounded Sterile Products (CSPs)?

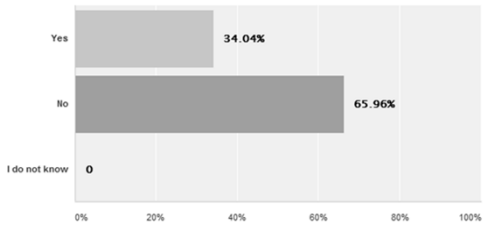
Answered: 52 Skipped: 0



9

Are ANY of your batched CSPs assigned Beyond Use Date expirations that exceed USP <797> allowance?

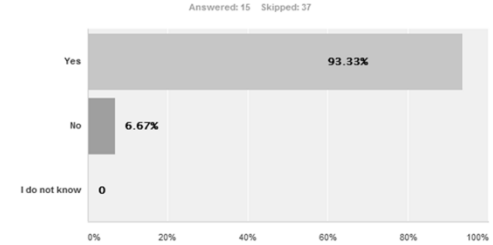
Answered: 47 Skipped: 5



10

For the product(s) that you assign extended Beyond Use Dating do you submit samples for sterility testing?

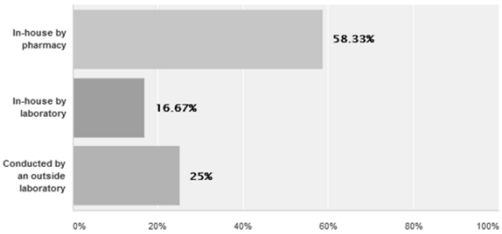
Answered: 15 Skipped: 37



11

Who conducts the sterility tests on batched CSPs?

Answered: 12 Skipped: 40



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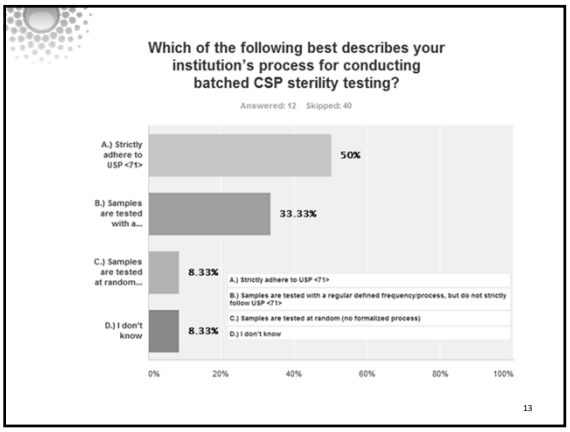
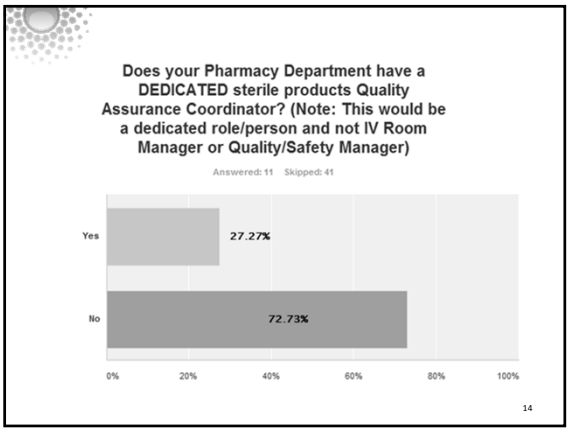




Evolution of a CSPs QA program

http://marccortez.com/wp-content/uploads/2012/04/evolution.jpg

15

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

16

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

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

ACYCLOVIR 200MG/100ML D5W 311380700P W-1-6659 RT BWH1 09/04/13 In Process

Test	TS Dur	Date	Specification	Result	Comment	QA	Select
Standard Sterility Test		09/05/13	Negative at 14 days	Negative at 5 days		○	☐

from: [redacted]
to:
Cc:
Subject: Results Notification as of 09/06/2013 03:00 PM

The following results are available online at [redacted]

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

17

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 2G IN 100ML NS		
Lot Number:	2104000897573		
Sample #:	W-1-6561		

RESULTS

Test	Specification	Result	Comment
Sterility (Bacteria/Fungi)[1]	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)

18

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"

19

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

20

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

21

The Next Horizon?

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

22

- While others may envision…

23

What do you need?

Time **Resources** **Space**

http://englishvocabulary2012.wikispaces.com/Cramped
http://en.wikipedia.org/wiki/Dry_well
http://powerofthought1.org/2012/02/i-dont-have-time/

24

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

25

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

26

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

27

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

28

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

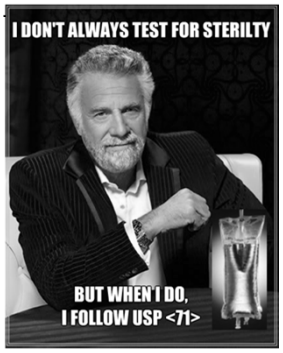
- Internal CSP tracking database
  - Batch preparation records
    - Date/time prepared
    - Prepared by
    - Drug Name/Concentration
    - Batch size & PAR level
    - Lot number & BUD expiration
    - Lab send out date
    - Sterility clearance (Y/N)
    - Release date into online inventory
    -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

29

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

30



31

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

A Pharmacy Technician

B Microbiologist

C Pharmacist

D Industrial Engineer

32

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%

33

True or False:

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

A True

B False

34