USP <797> Compliance
Common Challenges and Potential Solutions

Angela Yaniv, Pharm.D
Assistant Director - Sterile Products
May 2, 2017 - OSHP Annual Meeting
Speaker Disclosure

Angela Yaniv has no actual or potential conflict of interest with regard to this presentation.
Objectives

- Review USP <797> requirements for sterile compounding
- Discuss common challenges in maintaining USP <797> compliance
- Describe strategies to maintain and improve compliance with USP <797>
A Long Time in the Making

1971 - Deadly Nosocomial Infection Outbreak

1980’s-90’s - Infections from contaminated cardioplegia solutions and ophthalmics

2000’s - Multiple reports of infections, injury, and death linked to compounded sterile products

2011 - 9 deaths from contaminated parenteral nutrition in Alabama

2012 - NECC Tragedy - over 700 infections and 64 deaths

1970’s - Recommendations from NCCLVP

1990’s - FDA Compliance Guide; ASHP Technical Assistance Bulletin

2000’s - ASHP Guidelines; USP <797> and Revision

2013 - DQSA (503B);
2015 - Draft Revision of USP <797>
United States Pharmacopeia

Sets standards for:
- Identity
- Strength
- Quality
- Purity

For:
- Medicines
- Foods
- Dietary Supplements

- 2004 - USP <797>

Pharmaceutical Compounding - Sterile Preparations
- Previously USP <1206> - Sterile Drug Products for Home Use

Below:
- <1000> • Required
- <1XXX> • Informational
- <2XXX> • Specific for dietary supplements

Objectives

- Review USP <797> requirements for sterile compounding
- Discuss common challenges in maintaining USP <797> compliance
- Describe strategies to maintain and improve compliance with USP <797>
Purpose:
“...to prevent harm, including death, to patients that could result from (1) microbial contamination (nonsterility), (2) excessive bacterial endotoxins, (3) variability in the intended strength of correct ingredients, (4) unintended chemical or physical contaminants, and (5) ingredients of inappropriate quality...”

• Original version published in 2004
• Current version published in 2008
• Enforcement - through 2012 widely variable from state to state
• Focus has increased and expanded since NECC
  • States, FDA, CMS, JC
• Ohio BOP adopted USP <797> on 1/1/15
• Draft of next revision published for comment 9/28/15
USP <797> - Requirements
Pharmaceutical Compounding - Sterile Preparations

- **Environmental Quality and Control**
  - Clean environment for compounding

- **Personnel Training and Competency**
  - People know what they are doing

- **Standard Procedures**
  - People do what they are supposed to AND document it

- **Handling and Storage to Maintain Sterility**
  - Stable ≠ Sterile
Environmental Quality and Control
Make it Clean

Create and Maintain Appropriate Air Quality for Compounding

<table>
<thead>
<tr>
<th>ISO Class</th>
<th>Particles per m³</th>
<th>Particles per ft³</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>35.2</td>
<td>1</td>
</tr>
<tr>
<td>4</td>
<td>352</td>
<td>10</td>
</tr>
<tr>
<td>5</td>
<td>3,520</td>
<td>100</td>
</tr>
<tr>
<td>6</td>
<td>35,200</td>
<td>1,000</td>
</tr>
<tr>
<td>7</td>
<td>352,000</td>
<td>10,000</td>
</tr>
<tr>
<td>8</td>
<td>3,520,000</td>
<td>100,000</td>
</tr>
</tbody>
</table>

- Ante Room (SEC) ISO 7 or 8
- Buffer Room (SEC) ISO 7
- LAFS (PEC) ISO 5
Environmental Quality and Control
Make it Clean

- Access limited to qualified garbed personnel
- Surfaces are cleanable
  - No dust-collecting overhangs or windowsills
- Penetrations through walls and ceiling are sealed
  - Junctures between surfaces are sealed
  - Plumbing is covered
- Well lit
  - Fixtures sealed and flush mounted
  - Room side of lens is flat
- Temperature and humidity for comfort of fully garbed personnel
  - 20°C/68°F, humidity < 60%
Environmental Quality and Control
Keep it Clean

- Prevent particles from entering
  - ISO 7 – minimum of 30 air changes per hour
- Pressure gradients between spaces
- Limit particle generators
  - Control what comes in
- Limit quantity of supplies in SEC
- Prohibit unnecessary items in PEC
- Proper gown and garb to cover skin
- Frequently sanitize gloves
- Clean EVERYTHING coming in to the SEC
  - Wipe with Sterile IPA
- Clean it all again routinely

### Table 3. Minimum Frequency of Cleaning and Disinfecting Compounding Areas

<table>
<thead>
<tr>
<th>Site</th>
<th>Minimum Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>ISO Class 5 (see Table 1) Primary Engineering Control (e.g., LAFW, BSC, CAI, CACI)</td>
<td>At the beginning of each shift, before each batch, not longer than 30 minutes following the previous surface disinfection when ongoing compounding activities are occurring, after spills, and when surface contamination is known or suspected</td>
</tr>
<tr>
<td>Counters and easily cleanable work surfaces</td>
<td>Daily</td>
</tr>
<tr>
<td>Floors</td>
<td>Daily</td>
</tr>
<tr>
<td>Walls</td>
<td>Monthly</td>
</tr>
<tr>
<td>Ceilings</td>
<td>Monthly</td>
</tr>
<tr>
<td>Storage shelving</td>
<td>Monthly</td>
</tr>
</tbody>
</table>

From USP <797>
Environmental Quality and Control
Prove it’s Clean

- Environmental Sampling Plan
- Documentation
- Trending
- Set action limits
- Defined intervention plan

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Frequency of Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temperature</td>
<td>Daily</td>
</tr>
<tr>
<td>Pressure Differentials</td>
<td>Every work shift (minimum daily)</td>
</tr>
<tr>
<td>Air Changes Per Hour</td>
<td>Every 6 Months</td>
</tr>
<tr>
<td>Particle Counts</td>
<td>Every 6 Months</td>
</tr>
<tr>
<td>Viable Particle Sampling</td>
<td>Every 6 Months</td>
</tr>
<tr>
<td>Surface Sampling</td>
<td>Periodic</td>
</tr>
</tbody>
</table>

*Tables 2 and 4 from USP <797>*
Personnel Training and Competency Assessment Before Live Compounding

- Before compounding for patients
  - Gown and garb x 3
  - Fingertip samples x 3 with zero growth
  - Media-fill challenge test
- Didactic and practical teaching
  - Video modules
  - Reading materials
  - Observe expert compounding personnel
  - Practice aseptic manipulations
  - Cleaning and disinfecting surfaces
- Written tests
Personnel Training and Competency
Regular Reassessment

• Observed Competencies
  • Gown and garb
  • Fingertip samples
  • Media-fill challenge test
  • Surface cleaning and disinfection
• Written tests

• Remediation plan for failed competencies
  • Remove from compounding until retrained and reassessed
Standard Procedures

• Clean Room Behavior; Personnel Expectations
• Training
• Competency assessment and remediation
• Compounding
• Assignment of BUDs
• Cleaning
• Environmental monitoring
• Response to action limits
From the Audience

What is the highest compounding risk level at your facility?

a. Immediate Use Low Risk
b. Low risk
c. Medium Risk
d. High Risk
Handling and Storage to Maintain Sterility

Assessment of Compounding Risk Levels

- **Immediate Use**
  - Compounding outside of ISO 5 air in emergency situations
  - Simple transfers meeting Low-Risk criteria
  - Begin administration within 1 hour

- **Low Risk**
  - Simple volumetric transfers
  - All components are sterile
  - No more than 3 components; no more than 2 entries into any container

- **Low Risk with 12 hour Beyond Use Date**
  - Compounding in ISO 5 air but outside of a clean room

- **Medium Risk**
  - Transfer from multiple containers to a final container
  - Multiple or complex manipulations
  - All components are sterile

- **High Risk**
  - Use of non-sterile ingredients or devices
  - Components exposed to worse than ISO 5 air for more than 1 hour
Handling and Storage to Maintain Sterility
Assign Appropriate BUDs

- Limits for sterility
  - Product must also be stable
- Assure appropriate temperature is maintained during transport or delivery
- Assure product is stored appropriately in the patient-care area
- Products are labeled with BUD and storage condition

- Dating and management of single-dose and multi-dose vials and pharmacy bulk packages

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**USP <797> Beyond Use Date (BUD) Limitations for CSP’s compounded in a clean room**

<table>
<thead>
<tr>
<th>CSP Risk Level</th>
<th>BUD - Room Temperature Storage</th>
<th>BUD - Cold Storage</th>
<th>BUD - Frozen Storage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>48 hours</td>
<td>14 days</td>
<td>45 days</td>
</tr>
<tr>
<td>Medium</td>
<td>30 hours</td>
<td>9 days</td>
<td>45 days</td>
</tr>
<tr>
<td>High</td>
<td>24 hours</td>
<td>3 days</td>
<td>45 days</td>
</tr>
</tbody>
</table>
Handling and Storage to Maintain Sterility Requirements to Extend BUDs

- **Stability**
  - Published data for the same concentration, fluid, and container
  - Internal data

- **Sterility**
  - Sterility testing for each batch
    - Methods and sample sizes per USP <71>
  - Quarantine procedures
Objectives

Review USP <797> requirements for sterile compounding

Discuss common challenges in maintaining USP <797> compliance

Describe strategies to maintain and improve compliance with USP <797>
From the Audience

How would you rate your pharmacy for compliance with USP <797>?

a. Not compliant
b. Partially compliant
c. Fully compliant
Compliance Challenges

The 2016 USP <797> Compliance Study:
A National Study of Sterile Compounding Practices
Douglas K, Kastango E, Cantor P
*Pharmacy Purchasing and Products; Clean Rooms and Compounding.* October 2016; S1-20

**FIGURE 5**
**<797> Compliance Trends**

Hospitals have worked hard to catch up to the rest of the provider cohorts in terms of overall compliance with the elements of the chapter; however, there is still significant work to do to achieve full compliance.

<table>
<thead>
<tr>
<th>Year</th>
<th>All cohorts</th>
<th>Hospital only</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011</td>
<td>74%</td>
<td>72%</td>
</tr>
<tr>
<td>2015</td>
<td>82%</td>
<td>80%</td>
</tr>
<tr>
<td>2016</td>
<td>83%</td>
<td>83%</td>
</tr>
</tbody>
</table>
Compliance - Assessing Your Gap

Annual USP <797> Compliance Study
• Participants receive a report on their compliance

Ohio BOP Inspection Form
• http://www.pharmacy.ohio.gov and search on 797

Joint Commission
• Compounding Certification Requirements

Pharmacy Compounding Certification Board
• PCAB Certification Requirements
From the Audience

What is your top barrier to compliance?

a. Facilities
b. Training/Competency
c. Supplies/Equipment
USP <797> - Compliance Challenges

Environmental Quality and Control
Make it Clean
Create and Maintain Appropriate Air Quality for Compounding

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  - Plumbing is covered
- Well lit
  - Fixtures sealed and flush mounted
  - Room side of lens is flat
- Temperature and humidity for comfort of fully garbed personnel
  - 20°C/68°F, humidity < 60%
USP <797> - Compliance Challenges & Strategies

Keep it Clean

Environmental Quality and Control
Keep it Clean

Challenges
- Outer packaging materials
- Hoarding supplies
- Location of printers, refrigerators, computers, etc
- Pens
- Paper
- Personal items in controlled area
- Et cetera

Strategies
What do you need to do the work? How can you minimize it?
- Design workflow and storage space to limit storage in controlled space
- Assess whether equipment is truly needed in the controlled space and, if so, place it away from the primary engineering control - it can’t negatively impact air flow or particle control

The People Factor
- Define expectations in standard procedures and consistently enforce/reinforce expectations
USP <797> - Compliance Challenges & Strategies

Keep it Clean

What can you wear and how do you wear it?

**Challenges**
- Exposed jewelry
- Improperly fitting or improperly worn PPE

**Strategies**

**Supplies**
- Provide adequate and compliant PPE

**People**
- Define expectations in standard procedures and consistently enforce/reinforce expectations
USP <797> - Compliance Challenges & Strategies

Keep it Clean

Who’s going to do all that cleaning?

**Challenges**
- Inadequate space to wipe down
- Sloppy wipe down procedures
  - Don’t spray; wipe
- Time for daily/monthly cleaning
- Appropriate surface cleaning techniques
- Availability of cleaning supplies
  - Disposable vs reusable
- Rotation of cleaning agents
- Did it really get done?

**Strategies**

**Supplies and Space**
- Enough
- Easy to use/RTU
- Disposable
- Designate space for wipe-down

**Time**
- Schedule workflow to give time for daily cleaning
- Staff for/plan for monthly cleaning

**People**
- Define expectations
- Consistently enforce and reinforce expectations
- Make it part of the culture
Challenges

• Lack of written environmental sampling plan
• Inappropriate sampling locations
• Additional media for high risk compounding
• Surface sampling requirement is vague
• Lack of written plan for correction when action limits are triggered

Strategies

• Outsource sampling to Certifier
  • Third party documentation
  • Convenient with current requirements, but frequency of monitoring will likely increase
• Incorporate the activity onsite
  • Equipment needs
  • Identification of biological contaminants
  • Expertise for sample collection and interpretation
• Develop a formalized remediation plan
  • Include triggers to escalate investigation
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  - Remove from compounding until retrained and reassessed

Challenges

- How do you train someone without letting them compound?
- Planning and scheduling assessments before live compounding
  - Allow time for samples to be read negative
- What does “expert personnel” mean?
- Media fills have to reflect the site’s most complex compounding activities
- Train and assess cleaning techniques
- Timing of reassessment - medium risk/high risk
- Observation of technique
- Documentation of assessments, feedback provided, corrections
- Ability to retrieve documentation of training and competency assessments
- Need a written training plan that includes remediation
Didactic Training Strategies and Options

- Purchased materials
  - Review for relevance and consistency with language typically used at your facility
- Home-grown
  - Make sure that all required elements are covered
- Training programs
  - In person
  - On-line
- Regular updating as regulations change
- Ongoing education
- Who is best to do this teaching?
USP <797> - Compliance Challenges & Strategies
Personnel Training and Competency

Scheduling and Timing

- Plan ahead for initial training
  - Media fill at least two weeks prior to compounding for patients
  - All gowning and finger tips completed at least three days prior
  - Delay start of live compounding if assessments have to be repeated
- Plan ahead and schedule reassessments
  - Every 6 months for High Risk compounding
  - Every 12 months for Low and Medium Risk compounding
  - Resources for observation
  - Plan/schedule time to read samples
USP <797> - Compliance Challenges & Strategies
Personnel Training and Competency

Documentation

• Sample Forms in USP <797>

Appendix III. Sample Form for Assessing Hand Hygiene and Garbing Related Practices of Compounding Personnel

Printed name and position/title of person assessed:
Name of facility or location:

Hand Hygiene and Garbing Practices: The qualified evaluator will mark (x) each space for which the person being assessed has accepted the described activity, except if the activity is not applicable to the assessment session or N/A if the activity was not observed.

- Presents in a clean, appropriate attire and manner.
- Wears no cosmetics or jewelry (watches, rings, earrings, etc.) piercing jewelry included) upon entry into the area.
- Brings no food or drinks into or stored in the area or the area.
- Is aware of the line of demarcation separating clean and dirty sides and observes required activities.
- Does shoe covers designated clean area shoes one at a time, placing the covered or designated shoe on the clean side of the line of demarcation, as appropriate.
- Does shoe covers if necessary.
- Does hand covering assuming that all hair is covered.
- Does face mask to cover bridge of nose down to include chin.
- Performs hand hygiene procedure by washing hands and forearms and wash and applying soap and warm water for at least 30 seconds.
- Does hands and forearms using lint-free towel or hand dryer.
- Selects the appropriate sized gloves for the any holes, tears, or other defects.
- Does gloves and ensures full closure.
- Disinfects hands using a waterless alcohol-based surgical hand scrub with persistent activity and allows hand to dry thoroughly before donning sterile gloves.
- Does appropriate sized sterile gloves ensuring that there is a tight fit with no excessive glove material at the fingertips.
- Examines gloves ensuring there are no defects, holes, or tears.
- While engaging in sterile compounding activities, routinely disinfects gloves with sterile 70% IPA prior to work in the direct compounding areas (DCA) and after touching items or surfaces which contaminate gloves.
- Removes PPE on the clean side of the area.
- Removes gloves and performs hand hygiene.
- Removes gloves and discards it, or hangs it on hook if it is to be reused within the same work day.
- Removes and discards mask, head cover, and beard cover (if used).

Removes shoe covers or shoe one at a time, ensuring that the uncovered foot is placed on the dirty side of the line of demarcation and performs hand hygiene again. (Removes and discards shoe covers every time the compounding area is exited).

The person assessed is immediately informed of all unacceptable activities (i.e., spaces lacking a check mark, N/A, or N/O) and shown and informed of specific corrections.

Signature of Person Assessed
Printed Name
Date

Signature of Qualified Evaluator
Printed Name
Date

Appendix V. Sample Form for Assessing Cleaning and Disinfection Procedures

Printed name and position/title of person assessed:
Name of facility or location:

Cleaning and Disinfection Practices: The qualified evaluator will mark (x) each space for which the person being assessed has accepted the described activity, print N/A if the activity is not applicable to the assessment session or N/A if the activity was not observed.

Daily Tasks:
- Prepares correct concentration of disinfectant solution according to manufacturer's instructions.
- Uses appropriately labeled container for the type of surface to be cleaned (floor, wall, production bins, etc.).
- Documents disinfectant solution preparations.
- Follows the cleaning procedures when performing any cleaning activities.
- At the beginning of each shift, cleans all ISO Class 5 devices prior to compounding in the following order: walls, IV bar, automated compounders, and work surface.
- Uses a lint-free wipe soaked with sterile 70% IPA or other approved disinfectant solution and allows to dry completely.
- Removes all compounder components and cleans all ISO Class 5 areas as stated above at the end of each shift.
- Cleans all counters and easily cleanable work surfaces.
- Mops floors, using the mop labeled "floors", starting at the wall opposite the room entry door; mops floor surface in even strokes toward the operator. Moves carts as needed to clean entire floor surface. Use of a microfiber cleaning system is an acceptable alternative to mops.
- In the sterile area, cleans sink and all contact surfaces; cleans floor with a disinfectant solution or uses microfiber cleaning system.

Monthly Tasks:
- Performs monthly cleaning on a designated day. Prepares a disinfectant solution as stated in daily tasks that is appropriate for the surfaces to be cleaned.
- Cleans buffer areas and sterile area ceiling, walls, and storage shelves with a disinfectant solution and a mop or uses a microfiber cleaning system.
- Once ISO Class 5 area is clean, cleans compounding room ceiling, followed by walls and ending with the floor. Uses appropriate labeled wipes or microfiber cleaning system.
- Cleans all buffer area toes and storage shelves by removing contents and using a peracetic acid based allowed list free wipe, cleans the inside surfaces of the toe and then the entire exterior surfaces of the toe. Allows toes to dry. Prior to replacing contents into toe, wipes toe with sterile 70% IPA to remove any disinfectant residue. Uses new wipe as needed.
- Cleans all buffer area carts by removing contents and using peracetic acid based allowed list free wipe, cleans all cart starting with the top shelf and top of post, working down to wheels. Cleans the under side of shelves in a similar manner. Uses a new wipe for each cart. Allows to dry. Wipes with sterile 70% IPA wetted lint-free wipe to remove any disinfectant residue. Uses new wipe as needed.
- Cleans buffer area chairs, the interior and exterior of trash bins, and storage bins using disinfectant solution soaked lint free wipe.
- Documents all cleaning activities as to who performed such activities with date and time noted.

Sample Forms From USP <797>
Documentation

- Adapt forms to your facility if needed
- Include space for observations and to document any feedback provided
- Consider “scoring” for elements of aseptic technique

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Trainee Response</th>
<th>Trainee Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Selects appropriate syringe and needle size based on policy or test instructions</td>
<td>5</td>
<td>Accepts values from 0 to 5.</td>
</tr>
<tr>
<td>Opens packages with peel and present technique</td>
<td>0</td>
<td>Accepts values from 0 to 3.</td>
</tr>
<tr>
<td>Attaches needles and syringes and switches components while avoiding touch contamination</td>
<td>10</td>
<td>Accepts values from 0 to 10.</td>
</tr>
<tr>
<td>Avoids touching plunger stem during syringe re-use</td>
<td>10</td>
<td>Accepts values from 0 to 10.</td>
</tr>
<tr>
<td>Demonstrates appropriate use of filters and/or filter needles</td>
<td>5</td>
<td>Accepts values from 0 to 5.</td>
</tr>
</tbody>
</table>

Compounding and Aseptic Technique

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Trainee Response</th>
<th>Trainee Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Places objects and hands to avoid airflow disruptions</td>
<td>10</td>
<td>Accepts values from 0 to 10.</td>
</tr>
</tbody>
</table>
USP <797> - Compliance Challenges & Strategies
Personnel Training and Competency

Documentation
• Clearly document results
USP <797> - Compliance Challenges & Strategies
Personnel Training and Competency

Documentation
• Clearly document results

Fingertip Results

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Trainee Response</th>
<th>Trainee Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hand (Left)</td>
<td>Pass</td>
<td>12 colonies</td>
</tr>
<tr>
<td>Document colonies for left hand.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Passing is no more than 3 colonies on BOTH hands.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Merged colonies must be rated as a fail.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hand (Right)</td>
<td>Pass</td>
<td>over 20 colonies</td>
</tr>
<tr>
<td>Document colonies for right hand.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Passing is no more than 3 colonies on BOTH hands.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Merged colonies must be rated as a fail.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plates read by:</td>
<td></td>
<td>Kathy 7-2-16</td>
</tr>
<tr>
<td>If there is any growth on the plates, document it manually using the attached form.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Return form to manager as soon as possible.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Fingertip Results

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Hand (Left)</td>
<td>Pass</td>
<td>1 colony</td>
</tr>
<tr>
<td>Document colonies for left hand.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Passing is no more than 3 colonies on BOTH hands.</td>
<td></td>
<td></td>
</tr>
<tr>
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<td></td>
<td></td>
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</tr>
<tr>
<td>Plates read by:</td>
<td></td>
<td>zimmer 9/12/16</td>
</tr>
<tr>
<td>If there is any growth on the plates, document it manually using the attached form.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Return form to manager as soon as possible.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
USP <797> - Compliance Challenges & Strategies
Personnel Training and Competency

Documentation

• Document remediation taken
  - Include space on forms
  - Communication to employee
• Keeping track of competency documentation
  - Paper → Employee File
    • Where do the papers go while samples are incubating?
    • How to papers get back to the file?
    • Assure supervisory review
  - Electronic
    • Mechanism to monitor completion
    • Document supervisory review
USP <797> - Compliance Challenges & Strategies

Standard Procedures

Challenges
• Written SOPs
  • Detailed
  • Specific
• Do the SOPs reflect actual practice?

Strategies
• Write SOPs to reflect what is truly expected
• Review and update SOPs regularly to reflect any changes in the details

The People Factor
• Teach it, train it, review it, enforce it
• Create the culture of compliance
  • Constructively correct lapses as they are noticed
  • Hold each other accountable to following the rules
USP <797> - Compliance Challenges & Strategies
High Risk Compounding

Handling and Storage to Maintain Sterility
Assessment of Compounding Risk Levels

- Immediate Use
  - Compounding outside of ISO 5 air in emergency situations
  - Simple transfers meeting Low-Risk criteria
  - Begin administration within 1 hour
- Low Risk
  - Simple volumetric transfers
  - All components are sterile
  - No more than 3 components; no more than 2 entries into any container
- Low Risk with ≤2 hour Beyond Use Date
  - Compounding in ISO 5 air but outside of a clean room
- Medium Risk
  - Transfer from multiple containers to a final container
  - Multiple or complex manipulations
  - All components are sterile
- High Risk
  - Use of non-sterile ingredients or devices
  - Components exposed to worse than ISO 5 air for more than 1 hour

Challenges

- Frequency of competency assessments
- Separate media fill assessment - twice a year
- Sterilization methods
- Completion of required testing when using non-sterile ingredients
  - Pyrogen/Bacterial Endotoxin
  - Filter integrity when sterilizing by filtration

Strategies

- Assess whether high risk compounding is absolutely necessary at your facility
  - If you are going to do it, do it right!
- Maintain competencies and include in initial training and regular reassessments
- Develop expertise in sterilization methodology
- Select sterilization methods appropriate for the product
- Document sterility indicators used and results for sterilization by steam or dry heat
- Complete and document filter integrity tests for sterilization by cold filtration
- Complete endotoxin testing when required
USP <797> - Compliance Challenges & Strategies
Extending BUD

Handling and Storage to Maintain Sterility
Requirements to Extend BUDs

• Stability
  • Published data for the same concentration, fluid, and container
  • Internal data
• Sterility
  • Sterility testing for each batch
    • Methods and sample sizes per USP <71>
  • Quarantine procedures

Challenges
• Sterility testing when extending BUD
  • Appropriate method per USP <71>
  • Samples and volumes to test
• Quarantine mechanism
• Early release procedures
• Recall procedures
• Reporting procedures if a potentially contaminated product was administered to a patient

Strategies
• Don’t do it without developing a full set of procedures
• Develop expertise in sterility testing methods
• Dedicate space for secure quarantine of products undergoing testing
• Plan production to assure that products can remain in quarantine for 14 days
USP <797> - Compliance Challenges & Strategies

Summary

• Understand the requirements and intention of USP <797>
• Train and retrain
  • Understand the “why”
  • Everything ties back to patient safety
• Develop and maintain standard procedures
  • Make reality match the procedures
• Create a culture of compliance
  • Correct lapses immediately
  • Create a culture of mutual accountability
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