Sterile Compounding 2016

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Disclosure

Julie Nelson and Tony Palmer do not have any relevant financial relationship with any commercial interests
Learning Objectives

- Review cleaning frequency schedule for the environment of the clean room
- Review sterile compounding personnel procedural testing and sampling
- Review the risk levels of compounded sterile products (CSP)
- Review CSP end product testing and beyond use dating (BUD)
- Describe current standards for sterile compounding
- Consider future standards for sterile compounding
- Construct an exceptional policy and procedure manual for sterile compounding
- Review a case study related to the design and construction of a clean room, sterile compounding work flow schematics, federal and state compliance, and continuous education and training of sterile compounding professional pharmacists and technicians

The Environment

- Air quality measured by total number of particles and the number of viable microorganisms and evaluated by a quality operator every 6 months
- International Organization of Standardization (ISO) Classes 4 (barrier isolator aka “glovebox), 5 (Laminar Airflow Hood), 7 (Buffer aka Clean room), and 8 (Clearly demarcated Ante area/room)
Cleaning, Sanitizing, and Disinfecting

- Purpose to protect the patient by preventing microbial contamination and cross-contamination
- Purpose to maintain facilities
- Purpose to protect the product
- Purpose to protect the compounding personnel

Personnel training

- Attention to detail
- Clean room design and airflow
- Proper gowning
- Clean room conduct
- Cleaning, sanitizing, disinfectant protocol
- The Standards of Performance (SOP)
Which of the following best describes the purpose of your cleaning program?

- to protect the patient by preventing microbial contamination and cross-contamination
- to maintain facilities
- to protect the product
- to protect the compounding personnel

Risk levels of compounded sterile products (CSP)

- The three levels are described and assigned according to the probability of contaminating a CSP
- Low Risk Level CSP’s
- Medium Risk Level CSP’s
- High Risk Level CSP’s
Risk levels of compounded sterile products (CSP)

- Compounded with aseptic manipulations within ISO Class 5 or better air quality using only sterile ingredients, products, components, and devices
- Risk conditions description
- BUD description
- Quality Assurance practices
- Media fill test procedures

Sterile compounding personnel procedural testing and sampling

- Media-fill challenge testing used to assess the quality of the aseptic skill of compounding personnel
- When? Initially. Annually for low and medium risk level compounding and semi-annually for high risk level compounding
- What happens if my media-fill challenge test results in gross microbial contamination? Immediate re-instruction and re-evaluation by expert compounding personnel to ensure correction of all aseptic practice deficiencies
CSP end product testing and beyond use dating (BUD)

- TSBP 291.133: 318-331

Current Standards for Sterile Compounding

- USP 797
- FDA
- Texas State Board of Pharmacy
USP 797

- Intent: “to prevent harm and fatality to patients” by anyone in any practice setting who prepares, stores, and dispenses sterile preparations
- Traditionally recognized as the standard of practice
- The Texas State Board of Pharmacy
- FDA, CDC, OSHA, Joint Commission, ASHP, and ASPEN recognize and enforce it
- Lawyers know it

Compounding personal responsibilities articulated by USP 797

- Aseptic handwashing
- Garbing
- Disinfecting compounding surfaces and equipment
- Precisely identify, weigh, and measure compounded ingredients
- Precisely manipulate sterile products aseptically avoiding touch contamination and critical site exposure
- Sterilize high-risk level CSP’s
- Label and quality inspect CSP’s
- Assign beyond-use dates based on direct testing and/or reliable literature
Handwashing refresher

- Remove all jewelry, watches, etc.
- Start water and adjust to hot temperature
- Use sufficient antimicrobial cleanser throughout the washing process
- Scrub hands starting with the fingernails first using a scrub brush
- Clean all four surfaces of each finger
- Clean all surfaces of hands, wrist, and arms up to the elbow using a circular motion
- Do not touch sink, faucet, or other objects that may contaminate hands
- Rinse off all soap residue; holding hands upright and allowing water to drip down to elbow
- Do not turn off water until hands are completely dry
- Turn water off with a clean, dry, lint-free paper towel
- Do not touch faucet or sing while turning off water

Garbing refresher (prior to entering clean room)

- Remove lab, jackets, makeup, jewelry
- Thoroughly wash hands as per handwashing refresher
- Don clean, no shedding attire including hair covers, shoe covers, coats, sterile suites, powder free sterile gloves, face masks and or shields, goggles
- Resanitize gloves frequently with sterile isopropyl alcohol frequently
- Upon leaving the clean room the coat is to be hung inside out for regarbing upon entry and all other attire must be discarded
Future Standards for Sterile Compounding

- USP 800
- USP 797
- FDA
- Texas State Board of Pharmacy issued 388 warning notices for absence of or incomplete Policy and Procedure Manual

Policy and Procedure Manual Table of Contents (TOC)

- Lab Technician Training Manual-Sterile Compounding
- Compounding SOP-Adverse Events
- Compounding SOP-Allergies
- Compounding SOP-Labeling and Assigning Beyond Use Dates
- Compounding SOP-Clean-Up of Accidental Chemical Spills
- Compounding SOP-General Cleanliness of Lab
Policy and Procedure Manual
TOC Continued

- Compounding SOP-Cleaning Reusable Devices and Glassware
- Compounding SOP-Controlled Substance Perpetual Inventory
- Compounding SOP-Documentation
- Compounding SOP-Dry-Heat Oven Operation
- Compounding SOP-Electronic Balance
- Compounding SOP-Equipment and Supplies

Policy and Procedure Manual
TOC Continued

- Compounding SOP-Expired Stock Removal Policy
- Compounding SOP-FDA Inspection
- Compounding SOP-Horizontal Laminar Air Flow Hood
- Compounding SOP-Non-sterile Compounding Enclosure
- Compounding SOP-Inventory Management
- Compounding SOP-Media Fill Testing
Policy and Procedure Manual
TOC Continued

- Compounding SOP-Medications Similar to Commercial Available Products
- Compounding SOP-Non-Sterile Personnel Training and Documentation
- Compounding SOP-Patient-Related Medical Records
- Compounding SOP-pH Meter
- Compounding SOP-Compounding: Physician Office Use Requirement
- Compounding SOP-Ensuring Environmental Quality for CSPs

Policy and Procedure Manual
TOC Continued

- Compounding SOP-Recall for Compounded Products
- Compounding SOP-Receiving Controlled Substances
- Compounding SOP-Refrigerators and Freezers
- Compounding SOP-Safety
- Compounding SOP-Scheduled (Controlled) Drug Compounding Operating Procedures
- Compounding SOP-Shipping
Policy and Procedure Manual

TOC Continued

- Compounding SOP-Sterile Personnel Training and Competency Evaluation of Garbing and Aseptic Work Practice
- Compounding SOP-Sterilization
- Compounding SOP-Expired Stock Removal
- Compounding SOP-Testing
- Compounding SOP-New Technician Training Log
- Compounding SOP-USP Chapter 795 Compliance
- Compounding SOP-USP Chapter 797 Compliance
Part II

- Review History of “Sterile Compounding”
- IV admixture services in hospitals
- IV compounding pharmacies
- Pharmacist/technician education
- IV Certification

Case Studies

- New England Compounding Center
  - 10/20/2012 CDC reports 281 cases with 23 deaths of fungal meningitis from compounded methylprednisolone acetate injection.
Case Studies

- Specialty Compounding LLC Cedar Park
  - FDA inspected March 2013
  - August 11, 2013 nationwide recall of sterile products.
  - 15 patients from 2 Texas Hospitals who received infusions containing Calcium Gluconate from Specialty Compounding developed Rhodococcus equi septicemia

Case Studies

- Franck’s Laboratories Oclala, Florida
  - FDA announced recall of sterile products on 5/24/2012.
  - March reports of fungal endophthalmitis in patients who received Brilliant Blue G dye injections and in April eye infections in patients who received compounded triamcinolone injections.
Case Studies

- Apothecure Compounding Pharmacy Dallas, Texas
- 2007 colchicine injection sold to a Portland, Oregon medical center: 3 patients died.
- Some of the vials were superpotent and some subpotent.
- Gary D. Osborn, owner criminally prosecuted under Park Doctrine as the responsible corporate officer.

Case Studies

- Preferred Homecare, Nevada 2014
- Pediatric TPN failed to be compounded according to the prescription.
- Pediatric patient had seizures and died from hyperglycemia
- Executrix of decedent’s estate sued the home care provider and 3 individual pharmacists who were involved.
Federal legislation

- June 2013 new proposed law required compounding pharmacies to adhere to USP 797 and USP 795.
- Excluded drugs on an FDA list of products subject to shortages from the definition of “essentially copies of a commercially available drug”.

Federal legislation

- Proposed legislation would allow compounding for office use subject to notification to the compounding of patient specific information within 7 days.
Federal Law: DCQA

- Drug Quality and Security Act signed into law November 27, 2013.
- Bipartisan effort to bolster FDA oversight of compounding pharmacies.
- Created voluntary registration process for facilities wishing to engage in certain compounding activities.

DQSA

- Pharmacies wishing to compound medications without a prescription could register with the FDA as “outsourcing facilities”. 503B facilities
- Drugs compounded by licensed pharmacists at registered FDA outsourcing facilities exempt from FDCA under the DQSA: adequate directions for use, new drug requirements and tracing provisions.
To qualify for the exemptions, outsourcing facilities had to voluntarily register, pay registration fees, adhere to specific labeling and reporting requirements and undergo periodic inspections.

Entities that chose to not register as an outsourcing facility could be exempt from FDCA requirements ONLY if they compound pursuant to a prescription.

Some cases of “anticipatory compounding” allowed if reasonable anticipation of receiving a prescription.
DQSA

- FDA commissioner sent open letters to hospital purchasers and state officials on 1/8/2014 urging them to require the compounding pharmacies that supplied them drugs to register as outsourcing facilities.
- Despite this, the FDA’s website indicated less than 20 compounding pharmacies had registered.

DQSA

- January 14, 2014 first warning letter issued by FDA to a compounding pharmacy.
- FDA started using its enforcement authority to encourage compounding pharmacies to register.
Changes coming

- Current FDA interpretations of DQSA have been controversial, attracting Congressional Scrutiny.
- In August 2016, FDA announced a change for investigating 503A pharmacies
  - FDA inspectors are now required to assess whether a pharmacy is compounding under 503A exemptions before issuing a 483 inspection report.

Changes coming

- Pharmacies compounding pursuant to 503A will not be cited for violations of FDA’s good manufacturing practices (CGMP)
  - Previously, on 483 inspection reports, FDA was citing 503A pharmacies for violations of CGMP requirements that are not legally applicable to 503A pharmacies.
Case Studies

IV Specialty LLC Austin, Tx.
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