USP 797: Environmental Testing Plan

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Objectives

- Review requirements for an environmental testing plan
- Identify areas of opportunity for improvement in sterile compounding practice

Why do we need to test?

- The risk of contaminating a compounded sterile product (CSP) under low-risk level and medium-risk level conditions is highly dependent on proper hand hygiene and garbing practices, compounding personnel aseptic technique, and the presence of surface contamination, assuming that all work is performed in a certified and properly functioning ISO Class 5 primary engineering control (PEC) and secondary engineering controls, ISO Class 7 buffer area, and ISO Class 8 ante-area.
- High-risk level CSP's pose the greatest threat to patients because compounding personnel are tasked with the requirement of processing non-sterile components and devices in order to achieve sterility.

The Why continued

- A sampling program in conjunction with an observational audit is designed to evaluate the competency of compounding personnel work practices, allowing for the implementation of corrective actions on an ongoing basis.

Board of Pharmacy Rules

- Documentation Requirements - The following documentation must also be maintained by a drug outlet in which sterile products are prepared
  - Justification of expiration beyond use dates chosen assigned, pursuant to direct testing or extrapolation from reliable literature sources
  - Training records, evidencing that personnel are trained on a routine basis and are adequately skilled, educated, and instructed
  - Audits appropriate for the risk of contamination for the particular sterile product including:
    - Visual inspection to ensure the absence of particulate matter in solutions, the absence of leakage from bags and vials, and the accuracy of labeling with each dispensing;
    - Periodic hand hygiene and garbing competency;
    - Media-fill test procedures (or equivalent), aseptic technique, and practice related competency evaluation at least annually by each compounder or sterile prepackager;

Board of Pharmacy Rules

- Environmental sampling testing at least upon registration of a new drug outlet, following the servicing or re-certification of facilities and equipment, or in response to identified problems with end products, staff techniques or patient-related infections, or every six (6) months including:
  - Total particle counts
  - Viable air sampling
  - Gloved fingertip sampling
  - Surface sampling
  - Sterility testing of high risk batches of more than twenty-five (25) identical packages before dispensing or distributing
  - Temperature, logged daily
  - Beyond use date and accuracy testing, when appropriate
  - Measuring, mixing, sterilizing, and purification equipment inspection, monitoring, cleaning, and maintenance to ensure accuracy and effectiveness for their intended use.

Developing the plan

- The three areas to monitor:
  - **Air testing**
    - Nonviable
    - Viable
    - Air pressures
  - **Surface testing**
    - Primary engineering controls (LFH, CAI, CACI, BSC)
    - Buffer area
    - Ante area
  - **Personnel testing**
    - Post garbing
    - Within the ISO 5 environment
    - Aseptic manipulation

Air testing

Nonviable Air Sampling

- A program to sample nonviable airborne particles differs from that for viable particles in that it is intended to directly measure the performance of the engineering controls used to create the various levels of air cleanliness, for example, ISO Class 5, 7, or 8.
- Total Particle Counts
  - Certification that each ISO classified area is within established guidelines.
  - Performed no less than every 6 months
  - Performed when PEC's are relocated or the physical structure of the buffer area or ante-area has been altered.
  - Must be performed by qualified operators using current, state-of-the-art electronic equipment.

Allowable Particle Counts

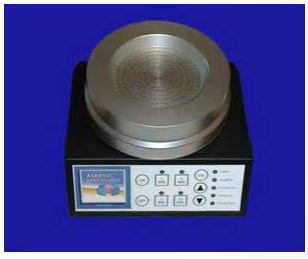
- ISO Class 5
  - Not more than 3520 particles 0.5 µm and larger size per cubic meter of air for any PEC (LAFW, BSC, CAI, and CACI)
- ISO Class 7
  - Not more than 352,000 particle of 0.5 µm and larger per cubic meter of air for any buffer area
- ISO Class 8
  - Not more than 3,520,000 particle of 0.5 µm size and larger per cubic meter of air for any ante-area.

Viable Air Sampling

- An appropriate environmental sampling plan shall be developed for airborne viable particles based on a risk assessment of compounding activities performed.
- Selected sampling sites shall include locations within each ISO Class 5 environment and in the ISO Class 7 and 8 areas and in the segregated compounding areas at greatest risk of contamination (e.g., work areas near the ISO Class 5 environment, counters near doors, pass-through boxes).

How

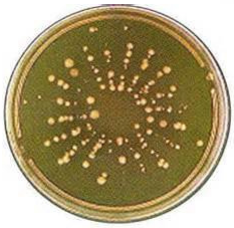
- The plan shall include:
  - Sample location
    - Include greatest risk areas
  - Method of collection
    - Volumetric collection
      - 400 to 1000 liters
    - Impaction vs. settling
    - Appropriate growth medium
      - Soybean-Casein Digest Medium – bacteria
      - Malt extract agar – fungi
    - Can be done internally or outsourced
  - Frequency of sampling
    - At least every 6 months
  - Documentation
  - Time of day as related to activity in the compounding area and action levels.
    - Normal activity should be occurring during testing



Viable Air Action Levels

Classification	Air Sample*
ISO Class 5	> 1 CFU
ISO Class 7	> 10 CFU
ISO Class 8 or worse	> 100 CFU

* CFU per cubic meter [1000 liters] of air per plate.
* Any CFU found must be identified at least to the genus level.



Pressure Monitoring

- 3 types
  - Positive pressure - physical separation (walls, doors, pass-throughs)
    - Monitor for minimum differential positive pressure of 0.02- to 0.05-inch water column.
  - Displacement airflow (line of demarcation between buffer/ante areas)
    - Monitor air velocity of 40 feet per minute or more across line
    - High risk compounding not allowed
  - Negative pressure room (HD preparation)
    - Monitor for negative pressure of not less than 0.01-inch water column

Surface testing

Surface Sampling

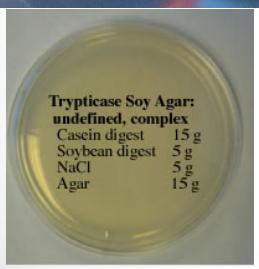
- Surface sampling is an important component of the maintenance of a suitable microbially controlled environment for compounding CSP's., especially since transfer of microbial contamination from improperly disinfected work surfaces via inadvertent touch contact by compounding personnel can be a potential source of contamination into CSP's.
- It is useful for evaluating facility and work surface cleaning and disinfecting procedures and employee competency in work practices such as disinfection of component/vial surface cleaning.

Question

Which of the following is incorrect when establishing guidelines for cleaning PEC surfaces?

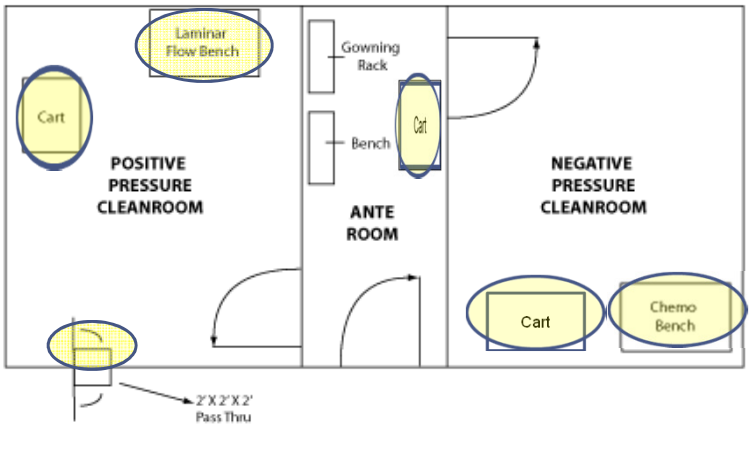
A. Before each batch
B. At the beginning of each shift
C. Every hour during continuous compounding periods of individual CSP's
D. Every 30 minutes during continuous compounding periods of individual CSP's
E. When surfaces are visibly soiled

How



- The Plan should include
  - Locations for surface sampling in all ISO classified areas
    - PEC's
    - Buffer area
    - Ante area
  - Method of collection
    - Plates containing solid agar growth medium containing lecithin and polysorbate 80 24-30 cm in size
  - Frequency of sampling
    - USP 797 – Periodic basis
    - BOP – at least every 6 months
  - Documentation
  - Time of sampling
  - How to address results exceeding acceptable levels

Sample Plan



Surface Sample Action Levels

Classification	Surface Sample
ISO Class 5	> 3 CFU
ISO Class 7	> 5 CFU
ISO Class 8	> 100 CFU

Personnel testing

Gloved Fingertip Sampling

- All compounding personnel shall successfully complete an initial competency evaluation and gloved fingertip/thumb sampling procedure no less than three times before initially being allowed to compound CSP's for human use.
- Re-evaluation of all compounding personnel for this competency shall occur at least annually for personnel who compound low- and medium-risk level CSP's and semi-annually for personnel who compound high-risk level CSP's using one or more sample collections during any media-fill test procedure before they are allowed to continue compounding CSP's for human use.

Question

How often should sterile gloves be disinfected with sterile 70% isopropyl alcohol per USP 797?

A. At least every 30 minutes
B. Routinely throughout the compounding process
C. Only when visibly soiled
D. Whenever nonsterile surfaces are touched
E. B and D

How

- The plan should include
  - Frequency
    - 3 tests initially
    - USP 797 – Annual or semi-annual based upon risk level
    - BOP – Every 6 months
  - Method of collection
    - Agar plates containing lecithin and polysorbate 80
  - Appropriate garbing procedure
    - Use of 70% isopropyl alcohol on sterile gloves prior to test is prohibited
  - How to address results exceeding acceptable levels

Sharing fingertip results with an employee in a timely manner and being able to offer observations of behaviors that can explain growth on the fingertip tests can be a powerful teaching tool.

Fingertip Sample Action Levels

Classification	Fingertip Sample
ISO Class 5	> 3 CFU
ISO Class 7	N/A
ISO Class 8	N/A
Garbing test (ISO Class 7 or 8)	0 CFU

Aseptic Manipulation Competency Evaluation

- After successful completion of an initial Hand Hygiene and Garbing Competency Evaluation, all compounding personnel shall have their aseptic technique and related practice competency evaluated initially during the media-fill test procedure and subsequent annual or semi-annual media-fill test procedures.
- Tests should mimic the most challenging or stressful conditions actually encountered by the personnel being evaluated when they prepare low- and medium-risk level CSP's and when sterilizing high-risk level CSP's.

How

- The plan should include
  - Testing kit
    - Selection based upon highest risk level performed at your facility
    - Soybean-Casein Digest medium
  - Frequency
    - Annually for low- and medium-risk
    - Semi-annually for high-risk
  - Procedure for test
  - Documentation
  - How to address positive test results

Positive Results

Processing Samples

- Request assistance from a laboratory if available
- Process internally
  - This will require the purchase of or having access to an incubator
- Specific temperatures – always consult the manufacturers recommendations for the testing product being used
  - TSA plates should be incubated at 30° to 35° for 48 to 72 hours
  - Malt extract agar or other suitable fungal media should be incubated at 26° to 30° for 5 to 7 days
  - Media fill – Soybean-Casein Digest medium should be incubated at 20° to 25° or at 30° to 35° for a minimum of 14 days.
    - If using 2 different temperatures ensure that the test is exposed to each temperature for at least 7 days

Opportunities for improvement

Cleaning

Site	Minimum Frequency
ISO Class 5 (PEC)	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.
Counters and easily cleanable work surfaces	Daily
Floors	Daily
Walls	Monthly
Ceilings	Monthly
Storage shelving	Monthly

Develop processes which result in good habits

- Identify when items need to be wiped down and wipe them down
  - Transfer into compounding area
  - When placed in PEC
- Have clear processes for garbing and adhere to them
  - Determine when garb items can be re-used vs. discarded and replaced
- Develop a cleaning schedule and follow it.
- Hold yourself and the team accountable
  - Ensure you educate your peers when slips are observed

What can you do better?

Remember who is at the end of the process

References

- United States Pharmacopeal Convention, Inc. <797> Pharmaceutical Compounding – Sterile Preparation, *United Stated Pharmacopeia 36-National Formulary 31*. Rockville, MD: US Pharmacopeal convention, Inc; 2013
- "Education and Training – Negative/Positive photos." *Q.I. Medical*. Accessed March 7, 2015 http://www.qimedical.com/education-training/negative-positive-photos/#prettyPhoto/13/
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