Management Case Study:

Strategies To Investigate Unacceptable Levels of Viable Air in Clean Room Environments: Minimizing Environmental Risk Factors To Compounded Sterile Preparations

Vaiyapuri Subramaniam, Pharm.D, M.S., FCP, FASHP, FASCP
Brenda S. Jensen, CPhT, CNMT, M.B.A.
Linda F. McElhiney, Pharm.D., M.S., FASHP, FIACP, FACA

Learning Objectives

- Identify three structural issues that may affect viable air results in clean room environments.
- Describe five requirements for clean room certification.
- State three work practice deficiencies that may affect viable air results in clean room environments.

Disclaimer

The views and opinions expressed are those of the speakers and do not necessarily represent those of their organizations and any practices or policies in which they are affiliated.

True or False Self-Assessment Questions

- Exhaust vents located in ceilings may negatively affect viable air results in clean room environments due to “dead areas” that do not receive adequate air changes.
- Viable air results showing fungal growth are acceptable as long as action levels are not exceeded.
- Gowning and hand hygiene are not necessary in ante areas if you are not compounding.

Certificate of Compliance

Certification report should include:

- Nonviable air counts in each ISO area under dynamic working conditions
- Viable air counts in each ISO area under dynamic working conditions
- Chart showing buffer area is positive to ante area and ante area is positive to non-ISO area.
- Pressure of at least 0.02 inches of water
- 30 ACPH (15 ACPH may come from the PEC)
- Leak testing of HEPA filters
- Pertains to positive pressure ISO areas. Negative pressure ISO area requirements differ.

Viable Airborne Particle Testing

- Collected in each ISO area under dynamic conditions
- 400 – 1000 Liters of air sample size
- Air sample for measuring bacterial load: Use TSA
- Air sample for measuring fungal load: Use MEA
- High-risk level compounding requires testing for two media: TSA and MEA (or other suitable fungal media)
- Growth identified and reported in cfu per cubic meter

TSA: Tryptic Soy Agar; MEA: Maltose Extract Agar
cfu: Colony Forming Units

USP <797> Recommended Action Levels for Viable Microbial Sampling of Air

- ISO Class 5 > 1 cfu
- ISO Class 7 >10 cfu
- ISO Class 8 (or worse) >100 cfu

- Per USP <797>, "Regardless of the number of cfu identified in the pharmacy, further corrective actions will be dictated by the identification of microorganisms recovered."
- "Highly pathogenic microorganisms (e.g., Gram-negative rods, coagulase positive staphylococcus, molds and yeasts) can be potentially fatal to patients receiving CSPs and must be immediately remedied."

Investigation

- Evaluation of physical structure
- ACPH
- Pressures
- HEPA integrity
- Personnel garbing and hand hygiene
- Cleaning and disinfection procedures
- Environmental monitoring
- Aseptic technique

Contributing Factors (Structural)

- Poor location of ante room doors
- Lack of adequate HEPA filtration
- Inadequate ACPH
- Low pressure
- Air leaks through uncaulked ceiling
- Inappropriate placement of vents
- Surfaces not smooth and/or nonshedding

Contributing Factors (Personnel)

- Failure to perform proper garbing and hand hygiene
- Failure to disinfect gloves with sterile IPA after touching nonsterile surfaces
- Failure to stage components into each ISO area
- Inappropriate disinfectant choice
- Failure to observe disinfectant contact times

Case Study

- Community pharmacy that performs nonhazardous high-risk level sterile compounding
- ISO 7 buffer room containing 4 ft LAFW
- ISO 8 ante room containing sink, powder-containment hood with electronic balance and limited supplies

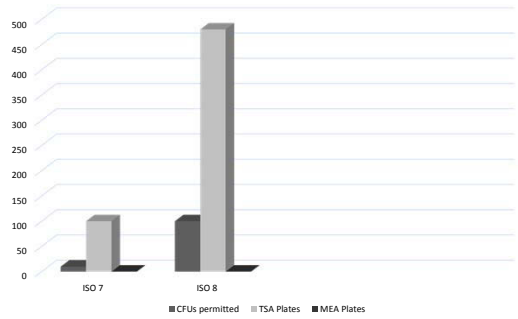
Certification Reports Prior to June 2014

- Performed under 'occupational' conditions
- Nonviable and viable air counts within limits
- Pressures and pressure relationships acceptable
- Air changes per hour not reported
- Leak testing on HEPA filters not performed

Certification Report June 2014

- Performed under 'occupational' conditions
- Nonviable air counts within limits
- Viable air counts outside limits
- Pressures and pressure relationships acceptable
- Air changes per hour reported as passing
  - Buffer room 60.73 ACPH
  - Ante room 23.84 ACPH
- No leaks detected in HEPA filters

Viable Growth



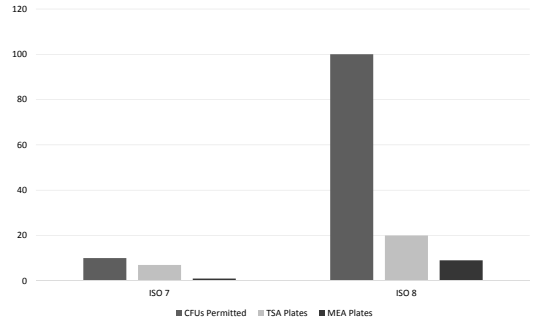
Investigation of Work Practices

- Staff training and validations complete
- Garbing and hand hygiene acceptable
- Aseptic technique acceptable
- Staging not performed into each ISO area
- Ante room door remained open for prolonged periods
- Two disinfectants with sporicidal activity rotated
- Disinfectant contact times adequate
- Cleaning order from cleanest to dirtiest

Other Concerns Identified

- Certification personnel donned garb but did not perform hand hygiene
- Same garb worn in and out of ante room while bringing in certification equipment
- Ante room door left open while bringing in certification equipment
- Certification equipment not staged
- HEPA filter accessed through ceiling from ISO areas

Repeat Viable Air Testing



Growth Identified

- ISO 7 Micrococcus 5 cfu
- ISO 7 Coag-negative staphylococcus 2 cfu
- ISO 7 Pithomyces 1 cfu

- ISO 8 Coag-negative staphylococcus 14 cfu
- ISO 8 Cladosporium 7 cfu
- ISO 8 Micrococcus 6 cfu
- ISO 8 Pithomyces 2 cfu

New Employee Break Area

Conclusion

- Safety of compounded sterile preparations starts with the cleanliness of clean rooms
- Knowledge of clean room certification requirements is essential
- Assess clean rooms for structural problems
- Address employee work practices

Recommendations

- Evaluate compounding personnel
  - garbing and hand hygiene
  - aseptic technique
  - cleaning and disinfection procedures
  - media fill testing and fingertip sampling
  - didactic training with written quiz
- Frequency of evaluations
  - every 6 months for high-risk sterile compounding
  - annually for low/medium-risk sterile compounding
- Evaluation forms available in appendix of USP<797>

Recommendations

- Restrict access to ante and buffer rooms
  - No non-essential personnel allowed
  - Minimize opening of ante room door
  - Only materials needed for compounding ensuring proper staging into each ISO area
- Monitor room environment and document results
  - Check of temperature, humidity and pressure by compounding staff every shift
  - Viable surface sampling in each ISO area by compounding staff
  - Every 6 months check of nonviable and viable air counts, pressure relationships, ACPH and filter integrity by contractor

Recommendations

- Standard operating procedures (SOPs) are written and readily accessible
  - Compounding personnel read and understand SOPs
  - SOPs reviewed annually for accuracy
- Monitor cleaning procedures
  - Consult with environmental services or microbiologist about disinfectant choice
  - Routinely rotate different types of disinfectants
  - Use a disinfectant with sporicidal activity

Recommendations

- Choose a reliable certification contractor
  - Performs all required USP <797> testing
  - Provides a detailed report of results
- Read the report and take appropriate actions
  - Ensure that the results are within USP <797> specifications
  - Investigate any cfu, especially if it exceeds the action levels
  - Find the source of the contamination, eliminate it, clean and disinfect the environment, and re-test

Self-Assessment Question 1

- Exhaust vents located in ceilings may negatively affect viable air results in clean room environments due to "dead areas" that do not receive adequate air changes.

Answer: True

Self-Assessment Question 2

- Viable air results showing fungal growth are acceptable as long as action levels are not exceeded.

Answer: False

Self-Assessment Question 3

- Gowning and hand hygiene are not necessary in ante areas if you are not compounding.

Answer: False

Key Takeaways

- Key Takeaway #1
  - Constantly monitor the operations, environment, and personnel for compounding sterile preparations
- Key Takeaway #2
  - Rotate disinfectants and use a sporicidal
- Key Takeaway #3
  - Document and review all test results, environmental readings, cleaning procedures, and investigations

Thank You!

- Vaiyapuri Subramaniam, Pharm.D., M.S., FCP, FASHP, FASCP
  - Associate Chief Consultant, Pharmacy Benefits Management Service, Veterans Health Administration, Washington, DC
  - Member, USP <797> Expert Panel (vpuris@gmail.com)
- Brenda S. Jensen, CPhT, CNMT, M.B.A.
  - Owner, Compounding Consultants, LLC, Canton, SD (jensen_brenda@yahoo.com)
  - Member USP <797> Expert Panel
- Linda F. McElhiney, Pharm.D., M.S., FASHP, FIACP, FACA
  - Compounding Pharmacy Operations Coordinator, Indiana University Health, Indianapolis, IN (lmcelhin@iuhealth.org)
  - Member, USP Committee of Experts for Compounding