Sterile Compounding Inspection Algorithm

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October 10, 2013
<table>
<thead>
<tr>
<th>ISO Class 5 Primary Engineering Controls</th>
<th>ISO Class 7 Buffer Area (cleanroom)</th>
<th>ISO Class 8 Ante-area (serving only non HD buffer areas)</th>
<th>ISO Class 7 Hazardous Drug Buffer Area (cleanroom)</th>
<th>ISO Class 7 Anteroom (required if serves HD buffer)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Air flow: Air Changes per Hour (ACPH)</td>
<td>Varies NSF-ANSI 49 CAG-002-2006</td>
<td>≥ 30 ACPH</td>
<td>Not specified but usually ≥ 20 ACPH</td>
<td>Not specified but usually ≥ 20 ACPH</td>
</tr>
<tr>
<td>HEPA Filter Leak Test</td>
<td>All HEPA filters in the secondary engineering controls are tested at each certification. Maximum allowable leakage is 0.01% of the upstream aerosol concentration.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Viable Particle Counting*</td>
<td>≤ 3,520</td>
<td>≤ 352,000</td>
<td>≤ 3,520,000</td>
<td>≤ 352,000</td>
</tr>
<tr>
<td>Segregation by: Pressure differential or air displacement (open air architecture)</td>
<td>LAFW/CAI + BSC/CACI - ≥ 0.02 positive to anteroom</td>
<td>≥ 0.02 positive to adjacent spaces</td>
<td>≥ 0.01 negative to anteroom</td>
<td>≥ 0.02 positive to adjacent spaces</td>
</tr>
<tr>
<td>Airflow velocity manuf. specs.</td>
<td>40 feet/minute across entire opening</td>
<td>may not be used in HD compounding</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Airflow Smoke Pattern Testing</td>
<td>Buffer rooms must be segregated from the ante-area and all other adjacent spaces with the doors close using smoke to observe airflow under dynamic operating conditions (with pharmacy staff compounding). Use smoke in PECs to visualize airflow under dynamic operating conditions to confirm laminarity of the air is undisturbed</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Viable Air Sampling* (CFU/1000 liters) (400-1000 liters/location)</td>
<td>Action Level &gt;1</td>
<td>Action Level &gt;10</td>
<td>Action Level &gt;100</td>
<td>Action Level &gt;10</td>
</tr>
<tr>
<td>Viable Surface Sampling* (CFU/plate)</td>
<td>Action Level &gt;3</td>
<td>Action Level &gt;5</td>
<td>Action Level &gt;100</td>
<td>Action Level &gt;5</td>
</tr>
<tr>
<td>Gloved Fingertip Sampling (GFS)* (CFU/both hands)</td>
<td>Initial: (GFS) Action Level &gt; 0 CFU x 3 consecutive times during hand hygiene and garbing after donning sterile gloves Ongoing: Action Level &gt; 3 CFU in association with annual/semi-annual MFT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Media Fill Testing (MFT)*</td>
<td>All compounding employees, no growth detected; annually low/medium risk; twice yearly high risk Must mimic most complex compounding procedure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All CFU ID’d to Genus</td>
<td>No mold, yeast, coagulase positive staphylococcus, or gram negative rods detected</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table adapted with permission from table called “Quick Reference” by Denise Frank for NABP.

*When Action Levels are triggered for ES or Media Fill/GFS there must be evidence of a logical set of actions taken and retesting performed.
Type of Operation

• Type of pharmacy operation
  – Hospital
  – Home Infusion
  – Retail
  – Specialty Compounding
CSP types

- PCA
- Cardioplegia
- Inhalation
- TPN
- Eye Drops
- Nonsterile preparations
  - Solid oral dosage
  - Liquids
Conducting an Inspection

• There are a variety of ways to organize a sterile compounding pharmacy audit or inspection.

• Be organized and respectful of the organization’s time.

• Most information falls into one of these categories
  – Facility
  – Compounding Processes
  – Personnel/Training
  – Equipment
  – Materials
  – Documentation related to above
• Visit the Bathroom
  – The way a business treats its facilities is a reflection of its operating standards.
  – In one recent Cintas survey, more than 75% of respondents said they would not return to a restaurant if the restrooms were not well kept.
Gain Access to Certain Documents

- Policy and Procedures (electronic or paper)
  - Sterile compounding
  - Personnel training may be separate manual
- Ask if logs are found in binders in the pharmacy (if so you can pull them yourself)
Why start with PnP?

Policy and Procedure tells you 2 very important things about an organization

• Alpha gap:
  – difference between what regulations require and written PnP
  – Are PnPs current?

• Beta gap:
  – difference between written PnP and actual practice in the work setting

\[
\alpha = 0 \\
\beta = 0
\]
Documentation: Facility Related

• Temperature/Humidity Logs
• Pressure Differential Logs
• Cleaning Logs
  – Check Daily and Monthly Cleaning
• Environmental Sampling Plan and Diagram
  – Viable Air Sampling (if they do it more than at certification)
  – Surface Sampling and GFS (see Personnel related)
  – Environmental Sampling Action Reports
• Certification Report
  – All controlled room environments
  – Each primary engineering control
  – Check to see that documentation on PECs matches
Documentation: Personnel Related

• Initial orientation and training to sterile compounding
• Didactic Training and evidence of training on PnPs
• Testing
• Documentation of observation of staff
• Competencies
  – Hand hygiene and Garbing Competency (including GFS on initial)
  – Aseptic Technique
  – Cleaning and Disinfecting
  – Other relevant competencies such as to particular types of equipment
• Gloved Fingertip Sampling: initial and ongoing
• Media Fill Testing
• Surface Sampling associated with employees
• HD Training, Competency and Acknowledgement of Risk Form
Documentation: Compounding Related/Materials

- Signature Log
- Certificates of Analysis
- Compounding Worksheets or Batch Records
  - Sufficient compounding instruction detail
  - Does it capture staging double checks, weighing, calibration, calculations and independent double-check
  - Lot numbers and expiration dates
  - Testing results: FIT, Sterility, BET, etc.
- Beyond-use Dating Substantiation for CSPs
- Controlled Substances Perpetual Inventory
- Component Disposal
- Delivery Logs
Documentation: Materials

• Is a Certificate of Analysis (COA) received with every bulk API?
  – COAs kept on file for each
  – Bulk API have an expiration date; date receive, opened documented
  – Are the API documented on the batch record

• Cleaning supplies/materials (PnP and observe)
  – Non-shedding/Low linting
  – Dedicated for use
  – Germicidal detergent; containers to measure
  – Gowns correct type
  – Sterile gloves and sIPA

• Media types
Documentation: Equipment Related

- Calibration logs (if not captured elsewhere)
- Prefilter change logs
- Evidence of annual certification according to NIST standards for incubators, refrigerators, freezers, etc.
- Evidence of staff training on equipment use:
  - Automated compounding equipment
  - Syringe fillers
  - Workflow automation such as DoseEdge
- Certification Reports on PECs
Forms review

- Correct form
- Correct information on form
- Form is complete
- Information is legible
- Demonstrates conformity: ZERO GAP between actual performance and established policy

![Cleaning Solutions Preparation Log](image)
Documentation rules

1. If it isn’t written down, it didn’t happen.

2. If it isn’t written down correctly, it still didn’t happen.

3. Don’t forget rules 1 and 2.
Get familiar and look for the following areas:

- Bulk inventory/warehouse
- Inventory Receiving Area
- Bulk inventory
- Quarantine, Return, Biomedical and RCRA Hazardous Waste
- General Prep Area
- Uncartonned inventory
- Order staging
- CSP Labeling
- Refrigerated, frozen and room temperature storage
- Controlled substance safe
- Hazardous Drug Storage
- Controlled Environments
  - Non hazardous BA
  - HD BA
  - Ante-room
  - Garbing room?
  - Mop/Bucket Closet?
- Incubators
- Autoclave
- Nonsterile processing area
Strategies to employ...ask them

• What do you do?
• How you do it?
• Show me how you do it.
• Show me the data.
• Show me the policy and procedure (PnP) that tells you to do it that way.
• Point me to the documentation that demonstrates you did it
Ask “What do you do?”

- Staff will describe their normal day-to-day operation
- Helps to demonstrate the individuals’ level of knowledge and comprehension of their respective jobs
- Their description may identify inconsistencies with current established procedures.
“Show me allows you to evaluate if...

1. the data supports the compounding steps and QC analysis
2. the data supports the successful execution of the defined specifications described in protocols
3. the data documents inconsistency or does not support the requisite compounding steps and the QC analysis

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By showing you, they will help you identify...

- whether or not written PnP is followed
- if compounding steps are successfully executed with the required specifications and acceptance criteria achieved
- inconsistencies based on described in the protocols
- procedures are consistent with 797 or other regulations
Spend time in the anteroom and cleanroom...

- Perform hand hygiene and garbing
- Look around the anteroom and cleanroom
  - State of repair of facility
  - Cleanliness (check bins, corners and returns)
  - Look for clues and ask questions
- Observe staff as unobtrusively as possible
- Plan to get in cleanroom during compounding (preferably when it’s as busy as possible)
- Observe aseptic technique
  - Frequency gloves are resanitized
  - Vial decontamination
  - Use of First Air
Spend time in cleanroom... (continued)

- Look at compounding worksheet
- Observe staff conduct
- Notice how components for batch come into cleanroom
- Evaluate supervision of compounding
Use Tracer Methodology

- Select a particular patient or order for a CSP and use that as a roadmap to assess all facets of sterile compounding pharmacy operations.
- Retrace all the steps from receipt of the order through delivery to the customer
  - BUD
  - Compounding Methodology
  - Final release checks and tests
  - Labeling
- Facilitates meaningful evaluation of the quality and completeness of compounding documentation.
Staff interviews...

- One on one
- Try to keep them informal
- Use open ended questions
- Always ask staff to:
  - “Tell me about your orientation to the pharmacy”
Key Item: Quality Assurance Program

• Whether it is called PI, QA or CAPA, the pharmacy must have a mechanism to identify, track, correct and evaluate the effectiveness of any changes made to correct and prevent each error.

Hopefully, whatever you do find will be more meaningful that this cartoon!

"Now slap a little quality on, and we'll ship this sucker out."

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Keys to a successful inspection...

• Organization
  – take the time to document as you go
  – keep a running list of questions as they come up
  – get the PnP manuals, QA meeting logs, facility logs, personnel files
  – request them early on

• Ability to multi-task
  – Often you will pick up a variety of information all at once (for example when you are in the clean room and anteroom)
  – Develop the ability to capture it

• Take extra care to be consultative (no matter how lacking in compliance the pharmacy seems to be)