Keeping your Cleanroom “Clean”

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Factors

Humans as the main source of contamination
Cleaning the cleanroom
Cleaning the equipment
People are the major source of contamination

- The average body surface is about 1.75 m².
- Corresponds to about 2,000,000,000 cells.
- The outer layer of skin is replaced in < 24 hours.

Figure 2. Average particle source strength (particle size ≥ 0.5 μm) in function of working activities at different WDS cycles.

Figure 3. Relation of MCPs to ≥0.5μm and ≥0μm particles.


Considerations for reducing particles & microbes

- Daily personal hygiene
- Cosmetics
- Nail polish
- Clothing
- Corrective & protective eyewear

Considerations for reducing particles & microbes

- Handwashing and garbing
- Level of activity
- Illness and allergy season
- Burns and rashes

Individuals with rashes, recent tattoos, oozing sores, conjunctivitis, or active respiratory infection must report these conditions to the designated person(s). The designated person is responsible for evaluating whether these individuals should be excluded from working in compounding areas. USP<797> June 1, 2019
Cleaning the cleanroom

How often?
What products are used and reused?
Who cleans?

<table>
<thead>
<tr>
<th>Site</th>
<th>Cleaning</th>
<th>Disinfecting</th>
<th>Applying Sporicidal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pass-through(s)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Work surface(s) outside the PEC Floor(s)</td>
<td>Daily</td>
<td>Daily&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Sinks (See Section 4.4)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wall(s), door(s), and door frame(s)</td>
<td>Monthly</td>
<td>Monthly&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Ceiling(s)</td>
<td></td>
<td></td>
<td>Monthly</td>
</tr>
<tr>
<td>Storage shelving and bins</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Equipment outside the PEC(s)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Many disinfectants registered by the EPA are one-step cleaning and disinfecting agents, which means that the disinfectant has been formulated to be effective in the presence of light to moderate soiling without a separate cleaning step.

### Table 7. Purpose of Cleaning, Disinfecting, and Sporicidal Agents

<table>
<thead>
<tr>
<th>Type of Agent</th>
<th>Purpose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cleaning agent</td>
<td>An agent used for the removal of residues (e.g., dirt, debris, microbes, and residual drugs or chemicals) from surfaces.</td>
</tr>
<tr>
<td>Disinfectant</td>
<td>A chemical or physical agent used on inanimate surfaces and objects to destroy fungi, viruses, and bacteria.</td>
</tr>
<tr>
<td>Sporicidal agent</td>
<td>A chemical or physical agent that destroys bacterial and fungal spores when used at a sufficient concentration for a specified contact time. It is expected to kill all vegetative microorganisms.</td>
</tr>
</tbody>
</table>
Cleaning v Disinfection v Sporicide Application

- Disinfectants and sporicides are more effective after cleaning removes substances that could reduce effectiveness.
- Contact time matters.
- Products have different contact times for different microorganisms
- Bleach is a sporicide and is cheap.
- Sporicides with detergent are expensive.

- Why 70% IPA?
  - Need water to effectively denature bacterial proteins; also dries more slowly, better contact time.

https://www.cdc.gov/infectioncontrol/guidelines/disinfection/

Factors to consider when choosing cleaning products

Detergents:
- Should be non-foaming, neutral and non-ionic
- Should be compatible with the disinfectant
- Residue should not inactivate the disinfectant

Disinfectants:
- Should have a wide spectrum of activity
- Should have rapid action (Short Contact Time)
- Must be sterile
- Safe to use
- Useable at cleanroom temperatures
- Should not damage equipment
- Rotation of products is no longer required

Sadle,T.:Cleanroom Cleaning and Disinfection: Eight steps for Success 2012
Box 7-1. Procedures for Cleaning and Disinfecting the PEC

- Remove visible debris with SWFI or SWFIrrigation using sterile, low-lint wipers.
- Using a low-lint wiper, apply a cleaning agent, followed by a disinfecting agent, or apply an EPA-registered (or equivalent) one-step disinfectant cleaner to equipment and all interior surfaces of the PEC.
- Ensure the contact time is achieved.
- Using a low-lint wiper, apply sterile 70% IPA to equipment and all interior surfaces in the PEC.
- Allow the surface to dry completely before beginning compounding.

USP<797> June 1, 2019

The Cost of Clean?

- Cost of supplies, equipment and garb
- N95 respirators for cleaning
- Sterile, disposable, “low-lint” wipes
- Labor Costs. Time cleaning takes time away from compounding.
- Time is money- Cleaning products with quicker contact times are usually more costly.
- What is the cost of non-compliance?
A Comparison of 3 Sporicidal Agents

<table>
<thead>
<tr>
<th>Sporicidal Agent</th>
<th>Contact Time</th>
<th>Average Cost</th>
<th>Active Ingredients</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iradecon 32 oz. (Decon Labs)</td>
<td>5 min.</td>
<td>$39.41</td>
<td>0.525% Sod. Hypochlorite 99.475% “other”</td>
<td>Very Strong Bleach Smell</td>
</tr>
<tr>
<td>Clorox Healthcare Bleach Geranicidal Cleaner 32 oz. (Clorox)</td>
<td>3 min.</td>
<td>$11.95</td>
<td>0.65% Sod. Hypochlorite 99.35% “other”</td>
<td>Fruity Floral Bleach smell</td>
</tr>
<tr>
<td>Peridox 32 oz. (Contec)</td>
<td>3 min.</td>
<td>$42.04</td>
<td>Hydrogen Peroxide &amp; Peracetic Acid</td>
<td>Offensive Vinegar Smell. Company recommends Charcoal filtered Masks. ($36.00/8)</td>
</tr>
</tbody>
</table>

What is the cost of non-compliance?

- 12 hour BUD
- Form 483 is posted online after FDA inspection
  - No response → FDA Warning Letter
  - Insufficient improvement → FDA Consent Decree
- State actions?
- Loss of reputation
- Loss of business
**Cleaning Supplies**

Wipers, Sponges, Mop Heads

- Must be “low linting”
- Must be disposable
- If disposable, must be discarded after each cleaning activity
- Dispose with minimal agitation away from work surfaces

Reusable Cleaning Tools (Mop Handles)

- Must be made of cleanable materials (e.g., non-wooden)
- Must be cleaned before and after each use
- Must be dedicated for use in each area
- Must be stored in the area (do not remove, except for disposal)

**WHO CLEANS?**

- Environmental services?
- Pharmacy technicians?
- Outside cleaning company?
- Who trains and supervises?

**THAT’S NOT IN MY JOB DESCRIPTION**
Wipe from clean to dirty

Do What Your Mother Taught You

• Ceilings, then walls, windows, doors
• Using overlapping strokes
• Floors Last
• Start to finish in ISO 7 area first, then ISO 8

Cleanroom Tacky (Sticky) Rollers?

• From one cleanroom vendor
  • The hand held poly tacky roller is used for smooth surfaces. Polyurethane coated film provides an anti microbial agent. The tacky roller has perforated sheets and when each sheet is contaminated it is simply peeled off the roll to uncover a clean sheet. The refill simply slides on and off the core handle.

• From another cleanroom vendor
  • Cleans particles from cleanroom walls and other surfaces
  • Select peel-off adhesive sheets made of polyethylene film (for smooth surfaces) or polyethylene film/foam laminate (for textured surfaces)
  • Handle extensions allow a "reach" of up to 6 feet

No mention of tacky rollers in USP<797>
Cleaning the ceiling
Start at farthest corner from ISO 8 wall (cleanest)
Single pass all the way across

First pass of cleaning
Second pass should overlap first pass

Pattern of overlapping strokes

Same pattern for walls. Start from farthest wall, clean towards ISO 8.
### USP <797> Table 8. Minimum Frequency for Cleaning and Disinfecting Surfaces

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<th>Applying Sporicidal</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEC(s) and equipment inside the PEC(s)</td>
<td>Equipment and all interior surfaces daily and when surface contamination is known or suspected.</td>
<td>Equipment and all interior surfaces daily and when surface contamination is known or suspected. Apply sterile 70% IPA to the horizontal work surface at least every 30 minutes, but do not disrupt compounding.</td>
<td>Monthly</td>
</tr>
<tr>
<td>Removable work tray of the PEC</td>
<td>Work surface of the tray <strong>daily</strong>&lt;br&gt; All surfaces and the area underneath the work tray <strong>monthly</strong></td>
<td>Work surface of the tray <strong>daily</strong>&lt;br&gt; All surfaces and the area underneath the work tray <strong>monthly</strong></td>
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</tr>
</tbody>
</table>

### Procedures for cleaning and disinfecting the PEC

- **Pre-Clean**
  - Remove any debris/drug residue with Sterile Water for Injection OR Sterile Water for Irrigation
  - Use “low lint” wipers
- **Clean**
  - Apply cleaner (sterile) to low lint wiper outside of PEC
  - AVOID spraying
  - Wipe from cleanest to dirtiest
  - Allow for proper contact time
- **Rinse stainless steel surfaces with sterile water**
  - To remove residue that could damage metal
- **Disinfect**
  - Using sterile 70% IPA, leaves no residue
  - Allow to dry completely
- **Clean the PEC with a sporicidal agent Monthly**
Order of Wiping PEC (for a Horizontal LAFS)

- Start at the top in the back.
- Wipe side-to-side from back to front
- Turn wipe to fresh surface
- Wipe bar
- Turn wipe to fresh surface; add more product if necessary
- On one side, start at the top in the back, wipe top-to-bottom using overlapping strokes
- Turn wipe to fresh surface; add more product if necessary
- Repeat on other side
- NEW WIPE for the surface
- Start in the back, wipe side-to-side from back to front

Wipe filter surface at your own risk!

Tips for using wipers

- Wipe spills up immediately
- Clean regularly
- Fold sterile “non-linting” wipes in half or in quarters
  - in half= 4 sides, quarters=8 sides
- Best practice is to wipe in 1 direction with 10% overlap
- Use a damp wiper- not dry or too wet
- Fold the wiper first then apply cleaner
- Do not let the bottle of cleaner touch the sterile wiper

Meadows 2015 Seven deadly sins of cleanroom wiping and how to avoid them https://blog.gotopac.com/2015/01/22/the-seven-deadly-sins-of-cleanroom-wiping-and-how-to-avoid-them/
Administrative Challenges

1. How well does your staff understand their role in reducing particle production?
2. How is this information conveyed?
3. Do your SOPs provide explanation to emphasize significance of human particle generation?
4. How rigorously does your staff adhere to the SOPs?
5. Does adherence trail off over time?
6. Do you have one or more natural leader(s) among your staff who dismiss the need for controls on particles and the role of humans?