Facility Cleaning & Monitoring

Cleaning
GTP Regulations: 21CFR Part 1271.190

- Maintain facility in clean, sanitary & orderly manner
- Establish & maintain procedures for facility cleaning
  - Assign responsibility for cleaning
  - Maintain records for 3 years
- Environmental monitoring where appropriate

GMP Regulations: 21 CFR Part 211.66

- Maintain facility in a clean & sanitary condition
- Written procedures assigning responsibility for sanitation & describing:
  - Cleaning schedule
  - Methods
  - Equipment & materials
- Written procedures for use of pest control, cleaning and sanitization agents.
Classified or Non-Classified Space?

- If you set classification you must meet it!
  - Particle counts
  - Viable counts
  - Alert and alarm levels specified with actions to be taken
  - Formal Cleaning Validation

Setting the Bar Too High?

- No products are handled in an open room - BSC
- Majority of products are terminally tested for sterility
- Many products are irreplaceable
- Little evidence of clinical sequelae from using positive products
- Need for Class 10K facilities?
Every Facility Should Have

- SOP for Cleaning Procedures
- Monitoring if appropriate
- Changeover procedures

Cleaning SOP

- Agents to be used
- Frequency of Cleaning
- Who is to perform cleaning
- How to document cleaning
- Training records
**Choices**

- **Cleaning agents**
  - Know potential contaminants
  - Check with institution infection control
  - Don’t mix phenolic & non-phenolic
  - Rotate regularly
  - Ensure proper use

- **Schedule**
  - Be prepared to explain!

- **Monitoring plan?**

**Selection of Cleaning Agents**

- Met with Infection Control to review organisms
- Selected IC-approved agents with appropriate activity (virus, bacteria, fungus)
  - Vesphene
  - Process LpHst
- Rotated monthly +/- 5% bleach
- Equipment – 3MQuat, 70% ethanol
Cleaning

- Dedicated cleaning crew
- Trained by QC staff and audited
- Formal schedule with sign-off
- Regular clean – floors and counters
- Complete clean – walls, ceilings, windows
- Continuous process
- Equipment – GMP staff

WORKSHEET AW03.2.3: CLEANING OF GMP CONTROLLED ENVIRONMENT

<table>
<thead>
<tr>
<th>SCHEDULE FROM:2/6/06</th>
<th>TO:2/10/06</th>
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</thead>
<tbody>
<tr>
<td>CLEANER TO USE</td>
<td>VESPHENE II</td>
</tr>
<tr>
<td>Lot Number of Selected Disinfectant</td>
<td>C 1130.19</td>
</tr>
<tr>
<td>DAY</td>
<td>MONDAY</td>
</tr>
<tr>
<td>Clean Floors and</td>
<td></td>
</tr>
<tr>
<td>Equipment</td>
<td></td>
</tr>
<tr>
<td>Wipe down Equipment</td>
<td></td>
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<tr>
<td>Gowning Area</td>
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<tr>
<td>Corridors*</td>
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<tr>
<td>COMPLETE CLEANING</td>
<td></td>
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<tr>
<td>Clean Floors, Walls</td>
<td>C 1130.31</td>
</tr>
<tr>
<td>and Ceilings</td>
<td>C 1130.34</td>
</tr>
<tr>
<td>of Room Number</td>
<td>C 1130.43</td>
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<tr>
<td></td>
<td>C 1130.38</td>
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</tbody>
</table>

Special Instructions
* Corridors consist of C1130.23, C1130.37, C1130.13
Wipe down ALL of the door handles with 3MQuat before leaving for the day.
Bleach must be used only on the floor and JM Quat must be used for wiping down the equipment.

CLEANED BY:
Pedro B Pedro B Pedro B Pedro B Pedro B
CLEANED BY: Lucian Lucian Lucian Lucian Lucian
REVIEWED BY: Landrum
DATE: 2-13-06
Disinfectants

- Monitor water for preparation
- Ensure solutions are sterile
- Record preparation of disinfectant

Contaminants

- Predominantly skin flora
- Coagulase-negative staph
- Diphtheroids
- Dematiaceous / Hyaline mould
- Bacillus species
Validation of Cleaning Agents

- Skin organisms main contaminants
- “Dirty” handprints onto surfaces
- RODAC plates before and after cleaning
- Reduction in colonies after cleaning
- Viral validation (more complex)
- Checked sterility of solutions
- Use clean room disposable mops

Changeover Procedure
Cell Processing Facility

- Formal SOPs
- Documented cleaning of all equipment
- Before and after each product is handled
- Removal of all associated paperwork
Changeover Procedure

Vector Facility

- Room closed for manufacturing
- All disposables & reagents removed & discarded
- Room completely cleaned
- Equipment cleaned
- Room restocked with checked disposables & reagents
- Environmental monitoring performed
- Room released for use by QA
SOP for Pest Control

1. Purpose
   1.1. Routine pest control services are performed to comply with public health and other regulatory requirements, and to provide a pest-free environment for all employees and patients.
   1.2. This procedure describes the pest control methods used in the Good Manufacturing Practices (GMP) Facilities.

2. Scope
   2.1. This procedure is to be followed by GMP staff if pests are detected within the GMP facility. Subsequent actions are coordinated by QC in collaboration with TCH and the EPICA (see abbreviations below).

3. Definitions and Abbreviations
   3.1. TOH Texas Children’s Hospital
   3.2. OAMC Quality Assurance and Control
   3.3. EPICA External Pest Control Agency

4. Materials and Equipment
   4.1. External Pest Control Agency
   4.2. TCH Environmental Safety Management System

5. Procedure
   5.1. Pest control services are the responsibility of TCH Environmental Services.
   5.2. A routine inspection and treatment is performed bi-monthly around the perimeter of the building. This is an area where it is clear to use pesticides to keep insects from entering into the hospital.
   5.3. The method of treatment will include power spraying, baiting, and pheromone Insect Growth Regulators in areas to not endanger children or pets. This treatment is to control ants, cockroaches, spiders, and other common indoor pests from entering the hospital.
   5.4. Exterior rodent control will consist of the maintenance of Tamper Resistant Rodent Stations. Inspection and treatment of any accessible burrows and other monitoring procedures will also be implemented if deemed necessary by TCH.
   5.5. A logbook is kept by TCH to log pest control problems and actions taken.
Monitoring

Monitoring Plan

- Required for each facility
- Tailored to the specific facility
- Non-clean room –
  - Monitor cleaning/product contamination
- Clean room – ensure within stated specifications
  - Particle and viable counts in room
  - Fallout plates in hoods
  - Surface monitoring – RODAC plates
  - Staff coats and gloves
CAGT GMP Facility Monitoring

- Class 10,000 maintained
  - 0.5um particle counts <10,000 / cubic foot
  - Alert @ 8,000 counts
- <0.5 viable counts / cubic foot
  - Alert @ 0.4 cfu

Viable counter  
Particle counters

Fallout Plates

- Trypticase Soy [TSA] or Sabouraud Dextrose [SDX] Agar
- Placed in hood during activity
- Minimum exposure 30 minutes
- Maximum exposure 4 hours
- Incubate the TSA plates at 32.5°C for 7 days in a humidified incubator. Incubate SDX plates at 20-25°C
Monitoring Challenges

What data to collect?
- Huge quantities of information
- Results may take days to obtain
- How to relate and manage data?

How often to clean?

How to manage ongoing production

How to respond to contamination?

Monitoring Schedule

Cell Processing Facility
- Weekly room monitoring (static/dynamic)
- Viable and particle counts
- Production monitoring if in progress or required

Vector Production Facility
- As above but monitoring during all productions
  - Viable, particle and fallout plates
Audits & Tracking

- Door charts
- Show
  - Alerts & alarms
  - Counts
  - Temperature
  - Humidity
- Indicate trends
- Early warning

Documentation

- Environmental monitoring database
  - Date, type of cleaning, disinfectant
  - Monitoring counts – particle & viable
  - Results – alerts, alarms, actions, species
  - Activities in facility or suite
  - Used for audits, follow-ups, door reports
Response to Alarms

Particles

- Alert – Remonitor same & different location in room
- Alarm – Close room – monitor product

Viables

- Alert – Schedule complete clean ASAP
- Alarm – Close room – relocate production – monitor product
Audits & Tracking

2003 Environmental Monitoring
CPF 1130.23 Viable Counts

Viable Counts
2 Alarm Readings

2003 Environmental Monitoring
CPF 1130.44 Particle Counts

Particle Counts
Within Specifications

Most events are
Viable Counts >1SD
Mainly in Summer

2003 Environmental Monitoring
Total CPF Events >1SD

2003 Environmental Monitoring Total Alerts/Alarms

Events >1SD
Audits & Tracking

Take Home Messages

- Development & maintenance of a cleaning & monitoring system is possible
- It is complex, costly & labor-intensive
- Large amounts of information need to be processed and acted upon in a timely & consistent manner