HYGIENE ZONING ... GENERAL PRINCIPLES

1. All manufacturing activities must take place in the appropriate class of environment (A, B, C, D or ISO 4.8, 5, 7, 8).

2. Different classes must be segregated from each other to reduce contamination (airlocks, changing rooms etc.)

3. Each class of environment has its own design criteria to meet the required level of performance.

4. Each class of environment has its own disciplines and practices to maintain the level of cleanliness.

5. Each class of environment has its own monitoring requirements to demonstrate that the desired performance is actually achieved.
ENVIRONMENTAL CLASSIFICATION IS NOT ONLY BASED ON AIR (HVAC) REQUIREMENTS, BUT REPRESENTS A HOLISTIC APPROACH, COVERING...

<table>
<thead>
<tr>
<th>Design Features</th>
<th>Facility Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Facility to be correctly designed for clean/sterile operations</td>
<td>Facility monitored to demonstrate class requirements</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HVAC Specifications</th>
<th>Operations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Air system to supply appropriate environmental conditions</td>
<td>Facility operated in compliance with current expectations</td>
</tr>
</tbody>
</table>
ENVIRONMENTAL CLASSIFICATION IS NOT ONLY BASED ON AIR (HVAC) REQUIREMENTS, BUT REPRESENTS A HOLISTIC APPROACH, COVERING...

### Design Features
- Walls/floors/ceilings
- MALs & PALs
- Material/people flows
- Equipment
- Hatches
- Drains
- Gases

### Monitoring
- Particles
- Viables
- Surfaces
- People
- Pressure/temperature/RH
- Requalification

### HVAC Specifications
- Filters
- Pressures/RH/°C
- Air velocity
- Air changes
- Air flows

### Operations
- Clothing
- Disinfectants
- Cleaning
- Material supply
- Training
REQUIREMENTS
### CLASS A

<table>
<thead>
<tr>
<th>Definition</th>
<th>Aseptic filling zone. Must be surrounded by Class B area.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Air flow</td>
<td>Laminar under the filter. Practically unidirectional at work station.</td>
</tr>
<tr>
<td>Air velocity</td>
<td>0.45 m/s ± 20% @ 15-30 cm below filter face (WHO-2011). NLT 0.36 m/s @ working level (WHO-2011)</td>
</tr>
<tr>
<td>Design features</td>
<td>No drains, sinks. Smooth impervious surfaces.</td>
</tr>
<tr>
<td>Non viable air count</td>
<td>3520 @ 0.5 μ and 20 @ 5 μ /m³ in operation and at rest.</td>
</tr>
<tr>
<td>Particle monitoring frequency</td>
<td>Continuous</td>
</tr>
<tr>
<td>Clean up period</td>
<td>N/A</td>
</tr>
<tr>
<td>Viable air count</td>
<td>&lt; 1 cfu/m³ in operation (and at rest if tested). &lt;1 cfu/4 hr settle plate (90 mm).</td>
</tr>
<tr>
<td>Surface counts</td>
<td>&lt;1 cfu/55 mm contact plate (no recommendations for swabs).</td>
</tr>
<tr>
<td>Gloves counts</td>
<td>&lt; 1 cfu/5 fingers during normal operations.</td>
</tr>
<tr>
<td>Gowns counts</td>
<td>No recommendations. Company to define strategy and specification.</td>
</tr>
<tr>
<td>Gown type</td>
<td>Full, sterilised, low particles, specially laundered, goggles, gloves.</td>
</tr>
<tr>
<td>Disinfectants</td>
<td>Sterile prior to use.</td>
</tr>
<tr>
<td>Supply of material</td>
<td>Only appropriately wrapped, sterilised materials via adjacent Class B area.</td>
</tr>
<tr>
<td>Personnel qualification</td>
<td>At least annually with a media fill in addition to “normal” training requirements for on-the-job skills.</td>
</tr>
</tbody>
</table>
# CLASS B

<table>
<thead>
<tr>
<th>Definition</th>
<th>Aseptic area surrounding the Class A filling zone.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Air flow</td>
<td>Away from critical points. Turbulence minimised.</td>
</tr>
<tr>
<td>Air velocity</td>
<td>0.45 m/s ± 20% at filter face.</td>
</tr>
<tr>
<td>Design features</td>
<td>No drains, sinks. No differences to Class A.</td>
</tr>
<tr>
<td>Non viable air count</td>
<td>3520 @ 0.5 μ, 29 @ 5 μ /m³ at rest and 352 000 @ 0.5 μ, 2900 @ 5 μ /m³ in operation.</td>
</tr>
<tr>
<td>Particle monitoring frequency</td>
<td>Continuous recommended but not mandatory</td>
</tr>
<tr>
<td>Clean up period</td>
<td>15-20 minutes</td>
</tr>
<tr>
<td>Viable air count</td>
<td>10 cfu/m³ in operation (and at rest if tested) and/or &lt;5 cfu/4 hr settle plate (90 mm).</td>
</tr>
<tr>
<td>Surface counts</td>
<td>5 cfu/55 mm contact plate.</td>
</tr>
<tr>
<td>Gloves counts</td>
<td>5 cfu/5 fingers during normal operations.</td>
</tr>
<tr>
<td>Gowns counts</td>
<td>Also called: Exit count</td>
</tr>
<tr>
<td></td>
<td>No recommendations (company to define strategy and specifications).</td>
</tr>
<tr>
<td>Gown type</td>
<td>As for Class A.</td>
</tr>
<tr>
<td>Disinfectants</td>
<td>Sterile prior to use.</td>
</tr>
<tr>
<td>Supply of material</td>
<td>Through double ended sterilisers or multiple wrapping strategy, or “spray and pray” with validation data.</td>
</tr>
<tr>
<td>Personnel qualification</td>
<td>As for Class A.</td>
</tr>
<tr>
<td>Class Requirements</td>
<td></td>
</tr>
<tr>
<td>----------------------------</td>
<td>-----------------------------------------------------------------</td>
</tr>
<tr>
<td><strong>Definition</strong></td>
<td>High grade clean room.</td>
</tr>
<tr>
<td><strong>Air flow</strong></td>
<td>Away from critical activities. Some turbulence.</td>
</tr>
<tr>
<td><strong>Air velocity</strong></td>
<td>0.45 m/s ± 20% at filter face.</td>
</tr>
<tr>
<td><strong>Design features</strong></td>
<td>No sinks. Closed drains permitted. Water supply permitted.</td>
</tr>
<tr>
<td><strong>Non viable air count</strong></td>
<td>352,000 @ 0.5 μ and 2900 @ 5 μ /m³ at rest. 3,520,000 @ 0.5 μ and 29,000 @ 5 μ in operation.</td>
</tr>
<tr>
<td><strong>Particle monitoring frequency</strong></td>
<td>No recommendation on frequency.</td>
</tr>
<tr>
<td><strong>Clean up period</strong></td>
<td>15-20 minutes.</td>
</tr>
<tr>
<td><strong>Viable air count</strong></td>
<td>100 cfu/m³ in operation (and at rest if tested) and/or 50 cfu/4 hr settle plate (90 mm).</td>
</tr>
<tr>
<td><strong>Surface counts</strong></td>
<td>25 cfu/55 mm contact plate.</td>
</tr>
<tr>
<td><strong>Gloves counts</strong></td>
<td>No recommendations.</td>
</tr>
<tr>
<td><strong>Gowns counts</strong></td>
<td>No recommendations.</td>
</tr>
<tr>
<td><strong>Gown type</strong></td>
<td>Single or two piece. Sterilisation not required. Low particulates.</td>
</tr>
<tr>
<td><strong>Disinfectants</strong></td>
<td>Regularly monitored.</td>
</tr>
<tr>
<td><strong>Supply of material</strong></td>
<td>Through MAL as needed. Sterilisation not required to protect environment but determined by process requirements.</td>
</tr>
<tr>
<td><strong>Personnel qualification</strong></td>
<td>Normal training requirements.</td>
</tr>
<tr>
<td><strong>Definition</strong></td>
<td>Clean area.</td>
</tr>
<tr>
<td>---------------------</td>
<td>----------------------</td>
</tr>
<tr>
<td><strong>Air flow</strong></td>
<td>No requirements.</td>
</tr>
<tr>
<td><strong>Air velocity</strong></td>
<td>No requirements.</td>
</tr>
<tr>
<td><strong>Design features</strong></td>
<td>Basic hygiene. All equipment permitted. Local LAF protection if needed.</td>
</tr>
<tr>
<td><strong>Non viable air count</strong></td>
<td>3,520,000 @ 0.5 μ and 29,000 @ 5 μ /m³ at rest. No specification in operation.</td>
</tr>
<tr>
<td><strong>Particle monitoring frequency</strong></td>
<td>No requirements.</td>
</tr>
<tr>
<td><strong>Clean up period</strong></td>
<td>No requirements.</td>
</tr>
<tr>
<td><strong>Viable air count</strong></td>
<td>200 cfu /m³ in operation (and at rest if tested). 100 cfu/4 hr settle plate.</td>
</tr>
<tr>
<td><strong>Surface counts</strong></td>
<td>50 cfu/55 mm contact plate.</td>
</tr>
<tr>
<td><strong>Gloves counts</strong></td>
<td>No requirements.</td>
</tr>
<tr>
<td><strong>Gowns counts</strong></td>
<td>No requirements.</td>
</tr>
<tr>
<td><strong>Gown type</strong></td>
<td>Head/foot cover, general protective garment.</td>
</tr>
<tr>
<td><strong>Disinfectants</strong></td>
<td>Regularly monitored.</td>
</tr>
<tr>
<td><strong>Supply of material</strong></td>
<td>Through MAL as needed. Basic hygiene rules apply.</td>
</tr>
<tr>
<td><strong>Personnel qualification</strong></td>
<td>Normal training requirements.</td>
</tr>
</tbody>
</table>
## Classification of Air Cleanliness

Selected airborne particulate cleanliness classes for clean rooms and clean zones.

### Classification by formula
Illustrated by a table

<table>
<thead>
<tr>
<th>Classification numbers Numbers (N)</th>
<th>Maximum concentration limits (particles/m³ of air) for particles equal to and larger than the considered sizes shown below</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.1 μm</td>
</tr>
<tr>
<td>ISO 1</td>
<td>10</td>
</tr>
<tr>
<td>ISO 2</td>
<td>100</td>
</tr>
<tr>
<td>ISO 3</td>
<td>1 000</td>
</tr>
<tr>
<td>ISO 4</td>
<td>10 000</td>
</tr>
<tr>
<td>ISO 5</td>
<td>100 000</td>
</tr>
<tr>
<td>ISO 6</td>
<td>1 000 000</td>
</tr>
<tr>
<td>ISO 7</td>
<td></td>
</tr>
<tr>
<td>ISO 8</td>
<td></td>
</tr>
<tr>
<td>ISO 9</td>
<td></td>
</tr>
</tbody>
</table>

**ISO 4.8 = Class A**
### EXAMPLE OF OPERATIONS VS. CLASSIFICATION

<table>
<thead>
<tr>
<th>Grade</th>
<th>Examples of operations for terminally sterilised products (see par 17-EU, 4.7.9 WHO)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Filling of products, when unusually at risk</td>
</tr>
<tr>
<td>C</td>
<td>Preparation of solutions, when unusually at risk. Filling of products.</td>
</tr>
<tr>
<td>D</td>
<td>Preparation of solutions, when unusually at risk. Filling of products.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Grade</th>
<th>Examples of operations for aseptic preparations</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Aseptic preparation and filling.</td>
</tr>
<tr>
<td>C</td>
<td>Preparation of solutions to be filtered.</td>
</tr>
<tr>
<td>D</td>
<td>Handling of components after washing.</td>
</tr>
</tbody>
</table>

DESIGN CRITERIA
## HVAC DESIGN CRITERIA

<table>
<thead>
<tr>
<th>Issue</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constant volume or pressure</td>
<td>No preference if adequately validated</td>
</tr>
<tr>
<td>Air inlet/outlet strategy</td>
<td>No preference if adequately validated</td>
</tr>
<tr>
<td>Prefiltration configuration</td>
<td>No preference if adequately validated</td>
</tr>
<tr>
<td>Humidification</td>
<td>Preferably steam injection – 55% ± 10%</td>
</tr>
<tr>
<td>Temperature</td>
<td>23° C ± 5%</td>
</tr>
<tr>
<td>Prefilters</td>
<td><strong>EN779</strong></td>
</tr>
<tr>
<td>HEPA filters</td>
<td><strong>EN1822, H13 (D/C) H14 (B/A)</strong></td>
</tr>
<tr>
<td>Position of HEPAs</td>
<td>Class A-C: Terminal, Class D: central</td>
</tr>
<tr>
<td>Air change rates</td>
<td>No specification – guidance values only</td>
</tr>
<tr>
<td>Air pressure differentials</td>
<td>• Minimum 10-15 Pa Guidance value</td>
</tr>
<tr>
<td></td>
<td>• Practically: 12.5 Pa ± 2.5 Pa</td>
</tr>
<tr>
<td></td>
<td>• Required at class interfaces only (&quot;interclass&quot; ΔP)</td>
</tr>
<tr>
<td></td>
<td>• &quot;Intraclass&quot; pressure differentials not specified</td>
</tr>
<tr>
<td></td>
<td>• Continuous monitoring at class interfaces by either manual or</td>
</tr>
<tr>
<td></td>
<td>automatic means (minimum daily)</td>
</tr>
<tr>
<td></td>
<td>• Positive pressures for all areas &lt;BL3 and below (no containment)</td>
</tr>
<tr>
<td></td>
<td>• Negative pressures for all areas BL3 and above (containment)</td>
</tr>
<tr>
<td></td>
<td>• Negative “sink” concept for all other applications.</td>
</tr>
</tbody>
</table>
## HVAC DESIGN CRITERIA

<table>
<thead>
<tr>
<th>Issue</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Air velocity</td>
<td>• 0.45 m/sec (± 20%) at the filter face (design specification).</td>
</tr>
<tr>
<td></td>
<td>• 0.45 ± 20% at working height for guidance only. If laminarity is</td>
</tr>
<tr>
<td></td>
<td>demonstrated at higher or lower velocities this can be accepted.</td>
</tr>
<tr>
<td></td>
<td>• Velocities should be homogeneous.</td>
</tr>
<tr>
<td></td>
<td>• Velocities checked twice per year for Class A/B. Annually for Class C.</td>
</tr>
<tr>
<td>Air flow patterns</td>
<td>• Smoke studies in Class A/B areas only. Should show even flow of air</td>
</tr>
<tr>
<td></td>
<td>in predicted direction. Workstation should show “practically” laminar</td>
</tr>
<tr>
<td></td>
<td>flow.</td>
</tr>
<tr>
<td></td>
<td>• Studies repeated only after breakdown/change.</td>
</tr>
<tr>
<td>Zoning concept issues</td>
<td>• Class D → Class B: 3 chamber changing area (PAL)</td>
</tr>
<tr>
<td></td>
<td>2 chamber airlock (MAL)</td>
</tr>
<tr>
<td></td>
<td>• Class C → Class B: 2 chamber PAL</td>
</tr>
<tr>
<td></td>
<td>1 chamber MAL</td>
</tr>
<tr>
<td></td>
<td>• Unclassified → Class B: Not permitted (2 changing rooms required)</td>
</tr>
<tr>
<td>Air clean up rates</td>
<td>• After challenge, class should be re-established in 15 minutes</td>
</tr>
<tr>
<td></td>
<td>• Test in Class A-C only</td>
</tr>
<tr>
<td></td>
<td>• Test performed at IQ, OQ stage only and after breakdown or change</td>
</tr>
</tbody>
</table>
These are the key items about cleanrooms in the GMPs:

- Particle classification
- Biocontamination control (if required)
- HEPA filter selection
- Filter testing
- Room pressurization
- Uni-directional airflow (UDAF) system velocity
- Dynamic Passboxes
- Performance monitoring
- Clean room validation
ROOM DESIGN CRITERIA

Principle of an airlock

- Physical separation between the areas
- Pressure differential
  - 10 - 15 Pa
  - Continuous monitoring
  - Be aware of special processes!!
- Doors must not be open simultaneously
- Sufficient air changes for the operation
ROOM DESIGN CRITERIA

Principle of an airlock

- Cleanroom clothing – changing principles for each step
- Incoming and outgoing materials flow
- Incoming and outgoing people flow
  - Changing principle for cleanroom clothing
- Disinfection for each step
- Final step at rest equivalent to the production area
AIRLOCK CRITERIA

EU-51 (Annex 1) comparable with WHO TRS961 (11.7)

• Changing rooms: airlocks providing physical separation.
• Flushed with sufficient air
• .....The final stage of the changing room should be in at-rest state, be the same grade as the area into which it leads....
• ....In general hand-washing facilities should be provided only in the first stage of the changing room.....

SC = Social Clean (unclassified but clean)
OPERATIONAL ASPECTS
ROOM DESIGN CRITERIA
Design of a clean room (Class A)
• Process Flow Diagram and/or Manufacturing Diagram to be prepared.

• Mapping of:
  – Personnel Flow
  – Raw Material Flow
  – Flow of utensils/devices
  – Finished Product Flow
  – Waste Flow
  – Cleaning Utensils
  – …..

• Checks/Reviews on Cross-flows and
OPERATIONAL ASPECTS

1. Operator gowning
2. Operator training / qualification
3. Cleaning and sanitisation practices
4. Material movement across clean zones
5. Operator behaviour / attitude
GOWNING REQUIREMENTS

EU-43 (Annex 1) comparable with WHO TRS961 (10.8)

- **Grade D:** Hair and, where relevant, beard should be covered. A general protective suit and appropriate shoes or overshoes should be worn. Appropriate measures should be taken to avoid any contamination coming from outside the clean area.

- **Grade C:** Hair and where relevant beard and moustache should be covered. A single or two-piece trouser suit, gathered at the wrists and with high neck and appropriate shoes or overshoes should be worn. They should shed virtually no fibres or particulate matter.

- **Grade A/B:** Headgear should totally enclose hair and, where relevant, beard and moustache; it should be tucked into the neck of the suit; a face mask should be worn to prevent the shedding of droplets. Appropriate sterilised, non-powdered rubber or plastic gloves and sterilised or disinfected footwear should be worn. Trouser-legs should be tucked inside the footwear and garment sleeves into the gloves. The protective clothing should shed virtually no fibres or particulate matter and retain particles shed by the body.
GOWNING REQUIREMENTS

EU-44 (Annex 1) comparable with WHO TRS961 (10.6)

- Outdoor clothing should not be brought into changing room leading to Grade B AND Grade C rooms. For every worker in a Grade A/B area, clean sterile (sterilized or adequately sanitized) protective garments should be provided at each work station. Gloves should be regularly disinfected during operations. Masks and gloves should be changed at least every working session. Operations working in Grade A and B areas should wear sanitized goggles.
MINIMUM PERSONNEL

EU-36 (Annex 1) comparable with WHO TRS961 (10.1)

• Only the minimum number of personnel required should be present in clean areas; this is particularly important during aseptic processes. As far as possible, inspections and controls should be conducted from outside such areas.
MATERIAL MOVEMENT ACROSS CLEAN ZONES

- Double ended sterilisers
- Multiple wrapping
- Spray and pray
- Active airlocks
- H₂O₂ airlocks
- UV lights

ALL DESIGNED TO ENSURE THAT CONTAMINATION IS NOT TAKEN INTO CLEAN AREAS
THE "V MODEL": A THEORATICAL FRAMEWORK

DEFINITION

USER SPECIFICATION (URS)

FUNCTIONAL SPECIFICATION (FS)

DESIGN SPECIFICATION

CONSTRUCTION AND TESTING

USER

SUPPLIER

SUPPLIER

OPERATIONAL QUALIFICATION

INSTALLATION QUALIFICATION

PERFORMANCE QUALIFICATION

USE
VALIDATION DOCUMENTATION

Validation Policy & Guidelines

Validation Master Plan (VMP) (EU GMP Annex 15)

Validation protocol

Validation Report

Validation checklists

Validation SOPs

URS ➔ DQ ➔ IQ ➔ OQ ➔ PQ ➔ Chg. Ctr.
SEQUENCE OF QUALIFICATION STEPS AND VALIDATION ACTIVITIES

VALIDATION PROJECT ACCORDING TO VALIDATION MASTER PLAN (VMP)

- URS
- Project Master Plan
- Risk Analysis (e.g. HACCP)
- DQ
- IQ
- OQ
- Qualification Report
- System Suitability Test
- PQ1 Micro. Qualif. Oper.
- PQ2 Mediaf ills
- Validation Report

SEQUENCE (TIME)
A URS document clearly defines what the user(s) of a clean room expect:

- Aseptic/terminal sterilisation
- Bulk/finished products
- EU/US compliance
- Product types
- Production volume and mix
- Production Processes
- Sterilisation processes
- Number of operators
- Single/multiple shifts
- Monitoring requirements
- Automation requirements
- Safety/environmental issues
- Waste management
- Logistical issues
- Multipurpose/dedicated

All the above will impact on design specifications.
The Functional Specifications are a technical interpretation of the URS. For clean rooms, they should typically include:

- Room conditions (temperature, humidity, light, noise)
- Room classification (A,B,C,D and/or 100/10.000/100.000 or ISO)
- Room pressurisation
- Recirculation versus fresh air
- Filter specification
- Layouts
- Airlocks
- Changing rooms
- Construction details
- Walls, floors, ceilings
- Drains
- Garment types
- Monitoring:
SOME TYPICAL OFFICIAL FUNCTIONAL SPECIFICATIONS APPLICABLE TO CLEAN ROOMS

- ISO 13408
  - Chapter 5: Facility Design Features
  - Chapter 6: Aseptic Processing Area (APA)
  - Chapter 7: Support Areas outside APA
- BS 5295
  - Environmental cleanliness in enclosed spaces, Parts 1-4
- ISO 14644
  - Clean rooms and associated controlled environments
- US Pharmacopoeial
  - Microbiological Evaluation of Clean Rooms
  - Chapter <1116>
- US FDA
  - Guideline on aseptic Processing
- EU Annex 1
  - Manufacture of Sterile Products
- WHO TRS 961
  - GMP for Sterile Pharmaceutical Products
• A qualification milestone in which the URS and the Functional Specifications are formally approved.
• Change Control applies after DQ to manage changing requirements or functional specifications as the project proceeds.
• DQ forms the basis for all following qualifications (IQ/OQ) and validation (PQ) requirements.
• DQ often regarded as the first official GMP document (in conjunction with URS).
DESIGN SPECIFICATIONS

- Often referred to as Detailed Engineering
- Converts the Functional Specifications into specific requirements for each component
- Calculates air requirements
- Defines materials of construction
- Provides technical specifications on all components

DESIGN QUALIFICATION ALSO POSSIBLE AFTER THIS STAGE
FAT/SAT

• FAT: Factory Acceptance test (at site of vendor)
• SAT: Site Acceptance test (at site of vaccine-facility)

• Newly introduced in Annex 15 EU as precursor for IQ/OQ
• In general, if qualified, information in FAT/SAT maybe used for IQ/OQ
HVAC SYSTEM
- Software
- Hardware
- Drawings
- Certificates and documentation
- Filter types and position

MONITORING DEVICES
- Temperature probes
- RH probes
- Pressure probes
- Particles
- Certificate and documentation

ACCESSORIES
- Magnahelics
- Automatic interlocks
- UV lamps
- Air showers
- Certificate and documentation

PERSONNEL
No particular action required

ROOMS
- Construction material
- Condition of floors, walls, ceilings
- Doors, hatches

PROCESS
No particular action required
HVAC SYSTEM
Full testing to functional specifications:
- Static conditions
- Class compliance (particles and viabes)
- Filters (velocity integrity penetration)
- Clean up rates
- Air volumes/change rates
- Pressure differentials
- Smoke studies
- Light, noise, temperature, humidity

ROOMS
No particular action required

OQ

ACCESSORIES
Correct functioning of all accessories, such as:
- Airlocks
- Lamps
- Showers

PERSONNEL
No particular action required

PROCESS
No particular action required

MONITORING DEVICES
- Calibration of all probes/gauges
- Activation of alarms sequentially
- Activation of parallel alarms
HVAC SYSTEM
Partial testing to functional specifications:
- Particle counts in dynamic state
- Smoke studies during simulated activity
- Microbiological air counts
- Regular review of pressure differentials
- Temperature / humidity

ROOMS
Floors and surfaces of all rooms intensively monitored for viable contaminants

ACCESSORIES
No particular action required

MONITORING DEVICES
- No specific additional activities required
- Regular review of data for alarm situations

PQ1
Area operational but not productive

PROCESS
Initial engineering runs for optimization

PERSONNEL
- Gowning qualification
- Micro-monitoring
HVAC SYSTEM
Intensified routine monitoring:
• Microbiological air counts
• Particle counts
• Pressure differentials
• Temperature / humidity

ROOMS
Intensified microbiological monitoring of floors/walls surfaces

PROCESS
• HACCP analysis / risk assessment
• Media fill studies (3x)
• Simulated interventions

PERSONNEL
• Intensified microbiological monitoring of hands/body
• Close supervision of cleanroom practices

ACCESSORIES
No particular action required

MONITORING DEVICES
• No specific additional activities required

PQ2
Area operational and productive
HVAC SYSTEM
- Calibration of all probes/gauges yearly
- Testing of alarm system, yearly requalification
- Media fills 2x/year for each process
- Revalidation after major change
- Revalidation after failure

ROOMS
- Microbiological monitoring of clinical surfaces for each aseptic batch
- Regular monitoring of floors/walls

PROCESS
- Media fills 2x/year for each process
- Revalidation after major change
- Revalidation after failure

MONITORING DEVICES
- Calibration of all probes/gauges yearly
- Testing of alarm system, yearly requalification

ACCESSORIES
- No particular action required

PERSONNEL
- Participation in media fill at least yearly
- Ongoing training in Micro Hygiene, Clean room practices
- SOP training as required
- Microbiological monitoring for each aseptic batch

STEADY STATE
- Particle counts, batch related for A/B areas
- Particle counts, time based for C/D areas
- Microbiological air counts during activity
- Pressure differentials continuous
- Temperature / humidity continuous
- Filter integrity 2x/year
- Filter velocity 2x/year
THANK YOU FOR YOUR ATTENTION