Q&A
• How many personnel (of different grade) are usually present in ONE single clean room?
  – The less the better.
• HVAC system:
  – How often should HEPA filters be changed?
    • 5 years in general.
  – How to identify items and frequency of environment monitoring for HVAC system PQ?
  – Do we need to develop a list of qualified manufacturers of HEPA filters? And manage the manufacturers like we do with raw materials? What are the rules?
    • Yes. Difficult to manage as raw materials. No actual rules, make sure you do testing on HEPA filters yourselves.
• What should be the length of Probe tube for particle counter?
  – Tube should be around 2m minimum, exceeding 4-5m, not OK.
How often should grade A and grade B area be cleaned?

- After every use. 1 hour everyday after use, it is the job of the operator, people from outside are not allowed to do clean grade A and B area.
- Daily: clean surfaces
- Weekly: wall (peroxide and alcohol).
- Monthly: all (including ceiling)
• Function and design specification provided by WHO? Manufacturer or contractor?
• How do we decide whether to use trap door/wall or pressure door/wall?

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• “First air” concept design in HVAC input and output (inlets and returns)?
  – Input should be directly above working area.
  – Return far away from work area.
• For personnel working in Grade C and Grade D areas, should “medium trial” be carried out on gowning?
• About products of sterile filtration. During a mock medium filling, should the medium undergo sterile filtration step?
  – If the basic process requires the medium to go through sterile filtration, then yes.
• If for some reason the RABS was shut down, do we always need to redo the medium fill validation?
  – Yes. Because different methodology, so need to revalidate and do medium refill.
• In case of remodeling of some rooms, do we need to redo process validation even if the process stays unchanged?
  – The likelihood that the remodeling would affect the process is high, restart with risk assessment, to see whether the remodeling affects the process.
• Should the laminar hood be on at all times in Grade C area (C background)?
  – No, not in Grade C, only 15-20 minutes before working to clean the air in the hood. But yes in Grade A.
• Do we need to do the “in operation” monitoring when the process is done in laminar hood (Grade A) in Grade C area (C background)?
  – Yes, we need to make sure the aseptic transfer does not cause contamination.
• Our Grade C clean room is closed during the summer (water and HVAC). Is there a guideline we can refer to for qualification of clean room and water system before re-starting production?
  – Never turn off water system (can be slowed down to 1.5m/second, but never off). HVAC should also be on at all times to prevent contamination, if off, you need to requalify.
• We know the monitoring points “at rest” should be evaluated before validation and monitoring. What about “in operation”?  
  – Simulate in operation in Grade B (5 people maximum), run the machines and the process, but not the product.  
  – You can also run it in actual operation.
• Does every exposure process need to be handled under HEPA?
  – Yes.
• How can we define “Airlock Grade”? And shower room?
  – Transition room C/D.
  – A clean room is better than air shower.
• How can we evaluate risk level?
  – See handout on Aseptic RA Qualitative Report A3 from workshop.
  – Use documented process.
• How do we assure aseptic operators?
  – Clean hands, come to work after shower, sensitize hands before gowns, garment, under garment, test contact hotspots for bugs.
  – Operators need to be trained and monitored constantly.
  – Check garments for bugs when out of the room.
• If colony is found in Grade A, does it mean the product is “non aseptic”?
  – If found at filling point and stopper point, discard batch.
  – if found somewhere else, you need to find the source of the bug.
• During ONE MFT run, how many times should regulatory or non-regulatory intervention activity be run?
• Do we need to monitor airflow velocity at a regular basis? If so, how often?
  • Every 6 months in Grade A.
  • Every 2 months in Grade B.
• Do we need to monitor air input and output (inlets and exhaust) in each room? If so, how often?
  – Air input velocity in Grade A and B.
  – Air input integrity in Grade C and D.
  – Air output does not have to be monitored.