Supplementary Training Modules on GMP

Air Handling Systems

Heating
Ventilation and
Air Conditioning (HVAC)

Part 3: Design, qualification and maintenance

Air Handling Systems

Characteristics of air handling systems

In the following slides, we will study alternatives in air handling systems

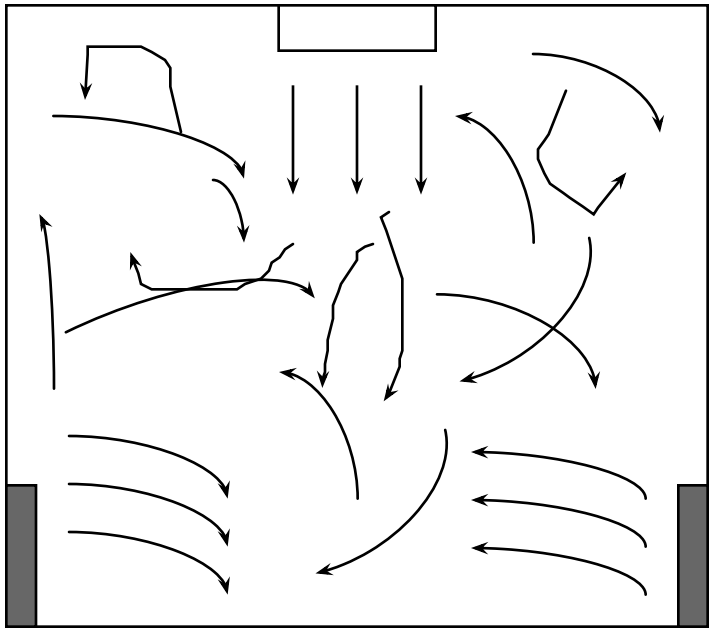
- Turbulent or uni-directional airflows
- Filter position
- Air re-circulation vs fresh air
- Return air systems (positions)
- Overpressure requirements

Air Handling Systems

Air flow patterns (1)

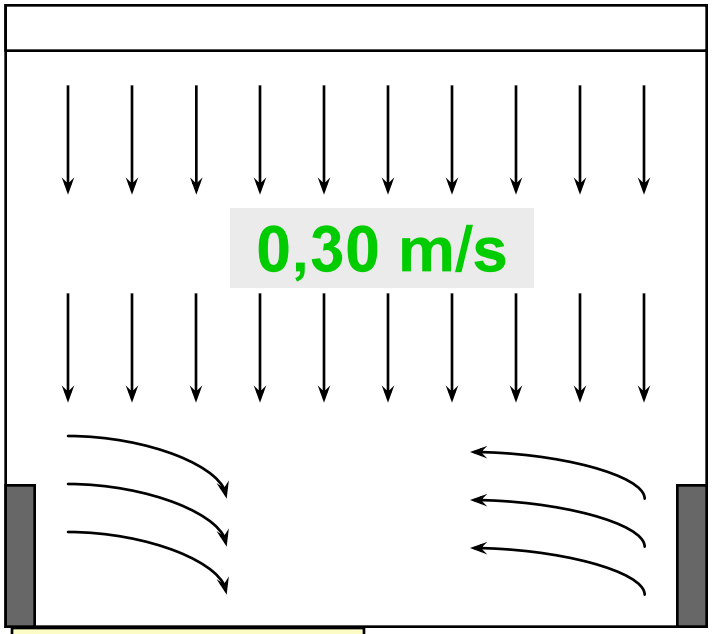
Turbulent

dilution of dirty air



Uni-directional / laminar

displacement of dirty air



Annex 1, 17.3

Air Handling Systems

Air flow patterns (2)

Filtered air entering a production room or covering a process can be

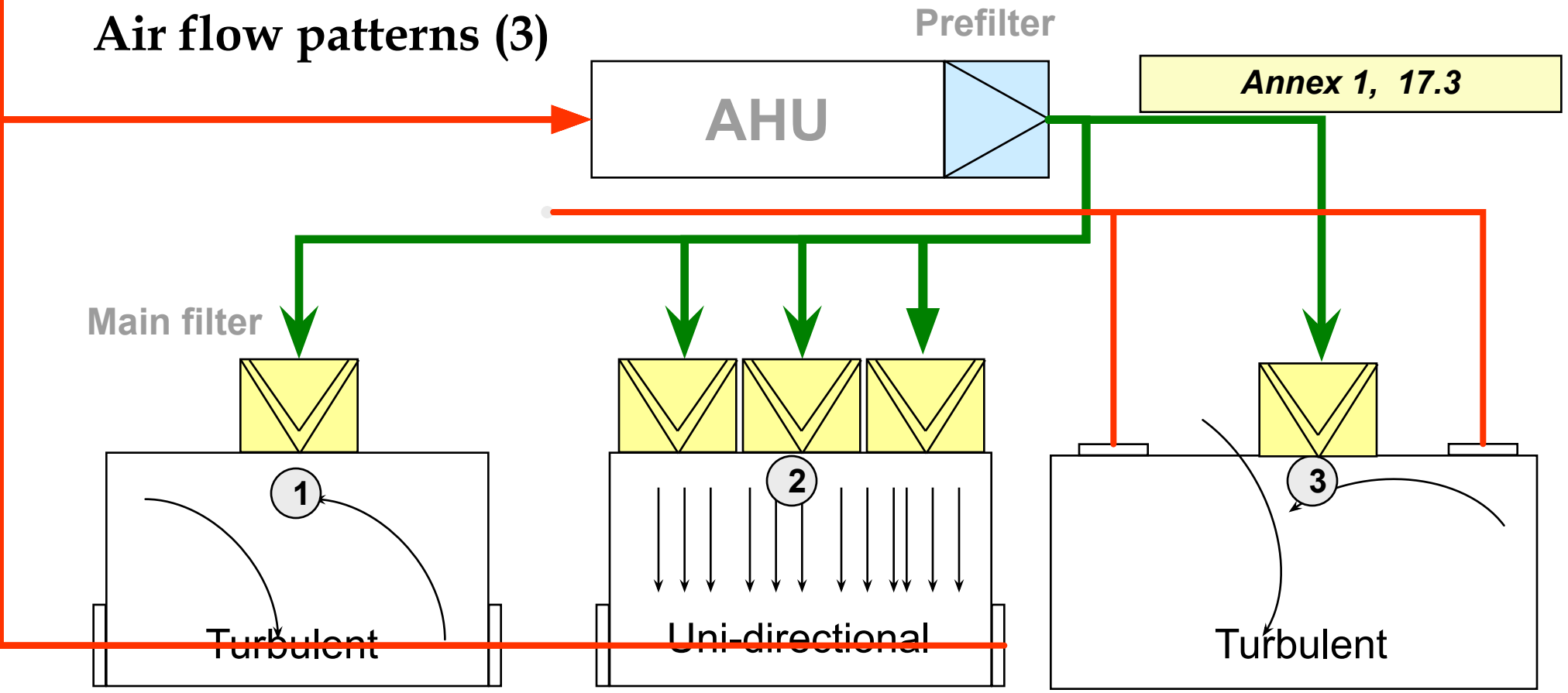
- turbulent
- uni-directional (laminar)
  - *GMP aspect*
  - *economical aspect*

New technologies: barrier technology/isolator technology.

Annex 1, 17.3, 17.4

Air Handling Systems

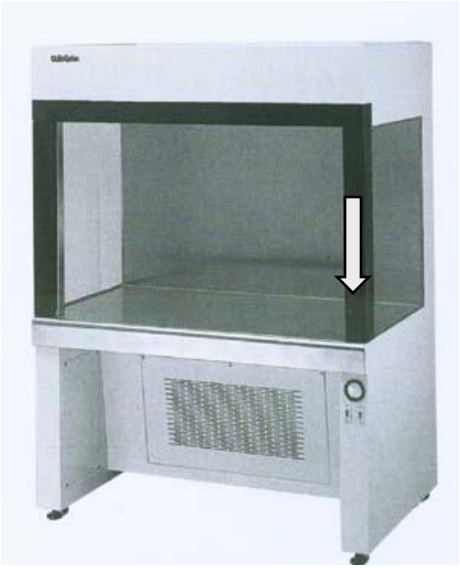
Air flow patterns (3)



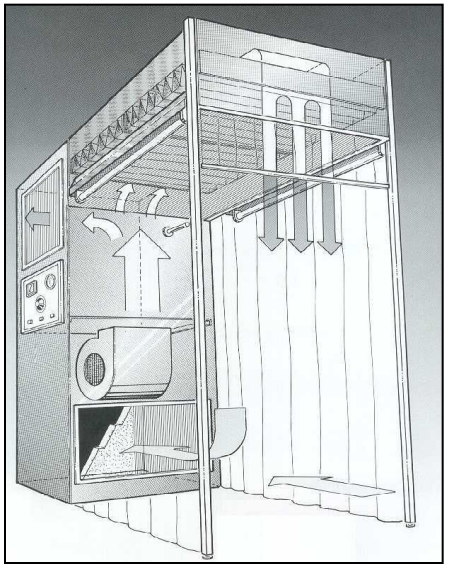
Air Handling Systems

Air flow patterns (4)

Workbench (vertical)



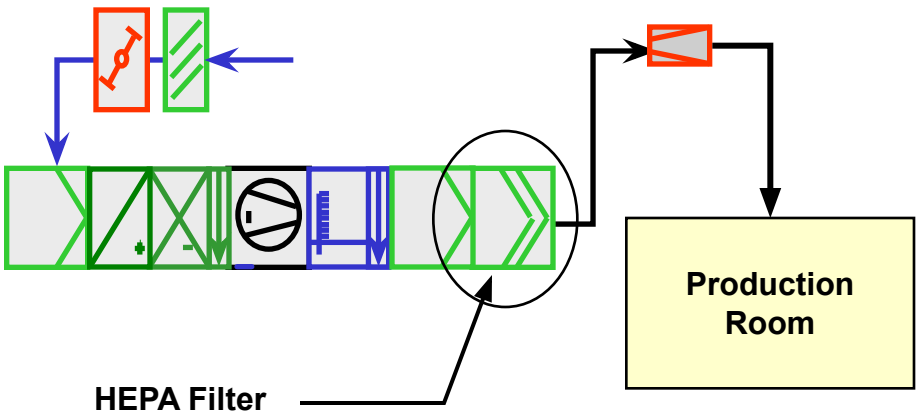
Cabin/ booth



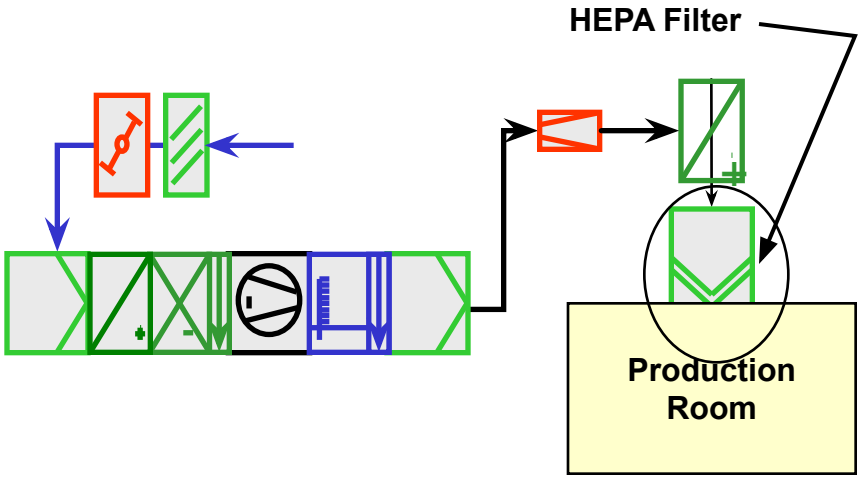
Ceiling

Positioning of filters (1)

AHU mounted final filter

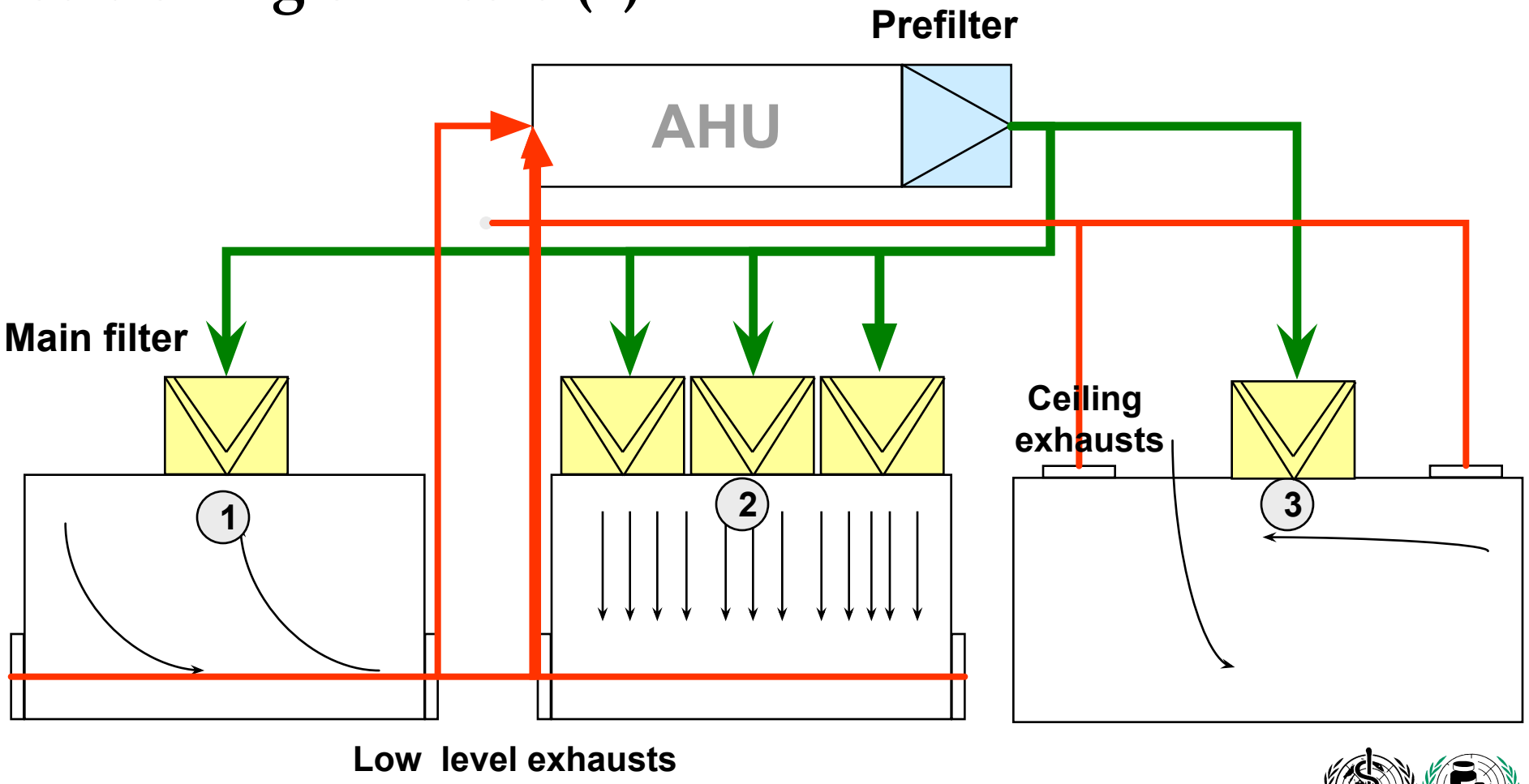


Filter in terminal position



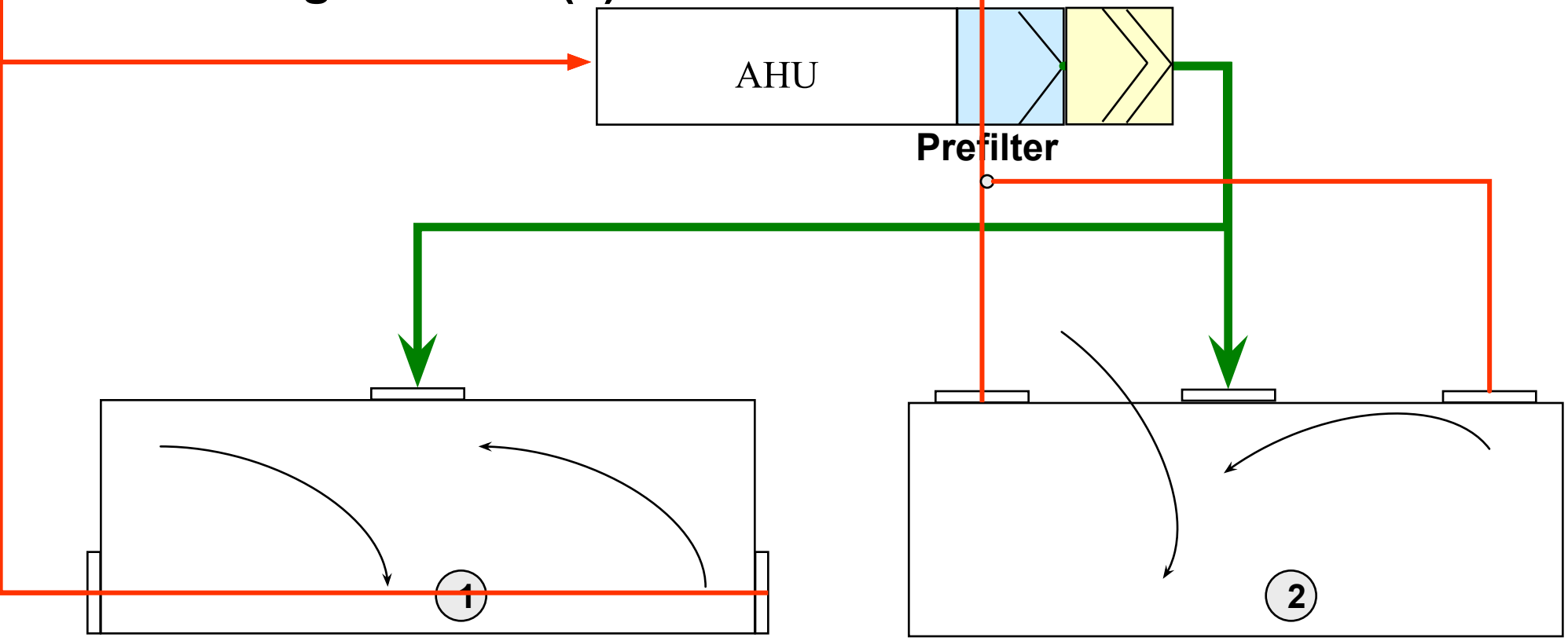
Air Handling Systems

Positioning of filters (2)



Air Handling Systems

Positioning of filters (3)



Air Handling Systems

Air re-circulation

The filtered air entering a production room can be

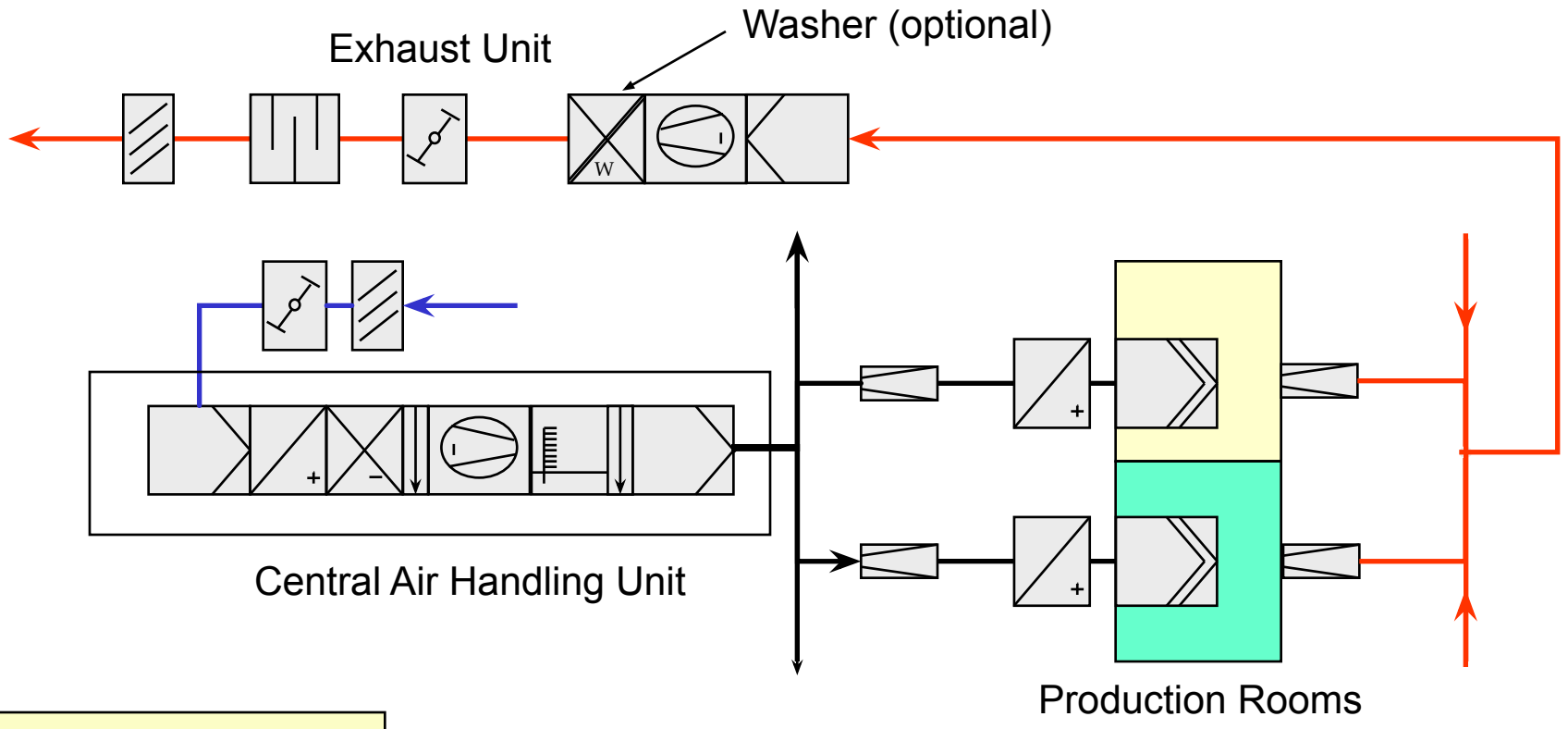
- 100% exhausted or
- a proportion re-circulated

  - *GMP aspect*
  - *economical reasons*

Annex 1, 15.10, 17.24

Air Handling Systems

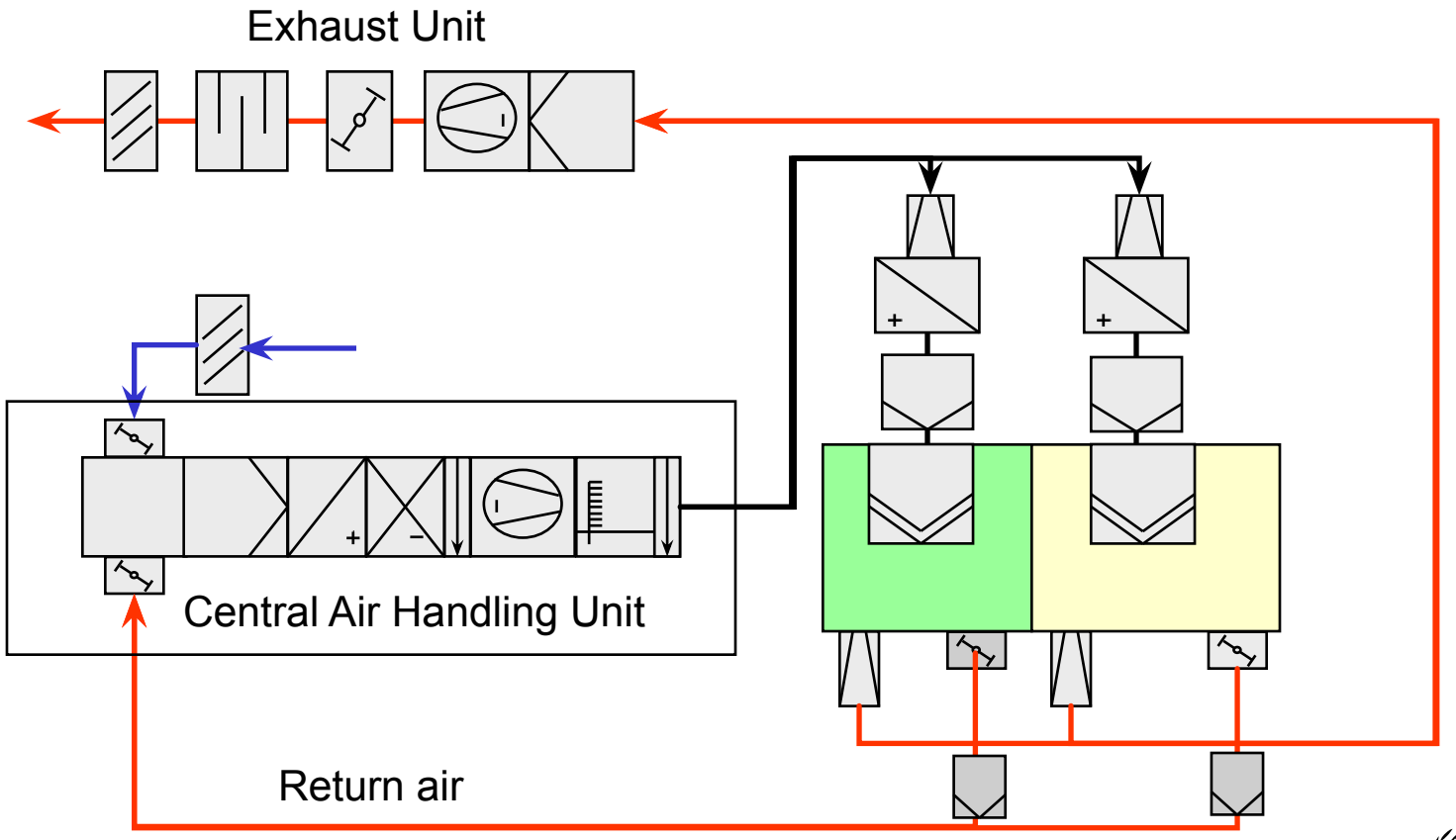
Ventilation with 100% fresh air (no air re-circulation)



Annex 1, 17.24

Air Handling Systems

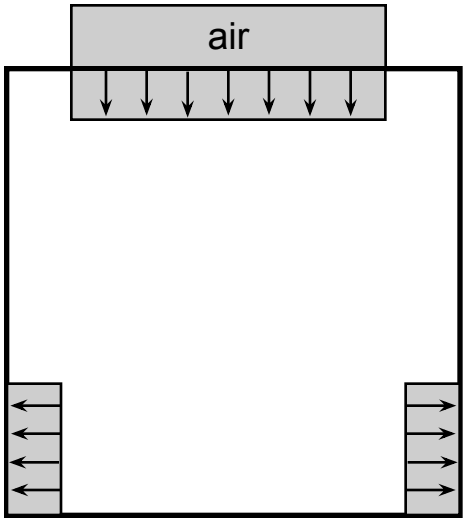
Ventilation with re-circulated air + make-up air



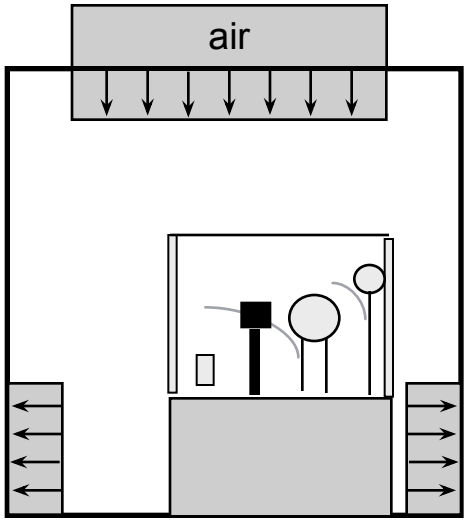
Air Handling Systems

Definition of Conditions

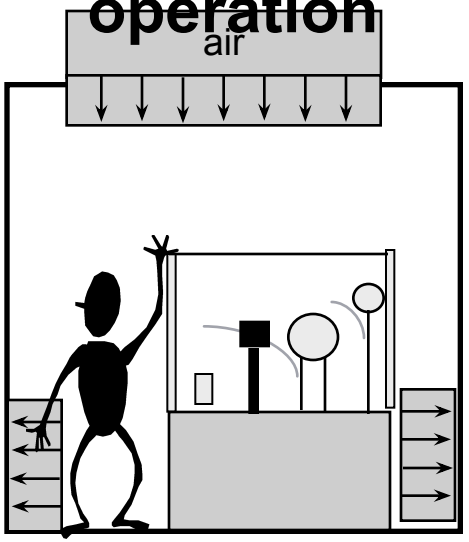
as built



at rest



in operation



Air Handling Systems

Qualification / Validation issues

A good design is essential, but it has to be complemented by:

- Qualification of air handling systems
- Process validation
- Maintenance and periodic re-qualification
- Adequate documentation

Qualification (OQ, PQ) (1)

Test	Uni-directional airflow / LAF	Turbulent / mixed airflow	Description
Differential pressure on filters	2	2	1 := As built (ideally used to perform IQ) 2 = At rest (ideally used to perform OQ) 3 = Operational (ideally used to perform PQ)
Room differential pressure	N/A	2, 3	
Airflow velocity / uniformity	2, 3	Optional	
Airflow volume / rate	2	2	
Parallelism	2	N/A	
Air flow pattern	2	3	

Annex 1, 17. 4

IQ tests are not mentioned on this slide

Qualification (OQ, PQ) (2)

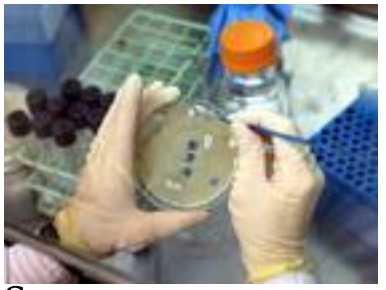
Test	Uni-directional airflow / LAF	Turbulent / mixed airflow	Description
Recovery time	N/A	2	1 := As built (ideally used to perform IQ) 2 = At rest (ideally used to perform OQ) 3 = Operational (ideally used to perform PQ)
Room classification (airborne particle)	2	2,3	
Temperature, humidity	N/A	2,3	

Annex 1, 17. 4

IQ tests are not mentioned on this slide

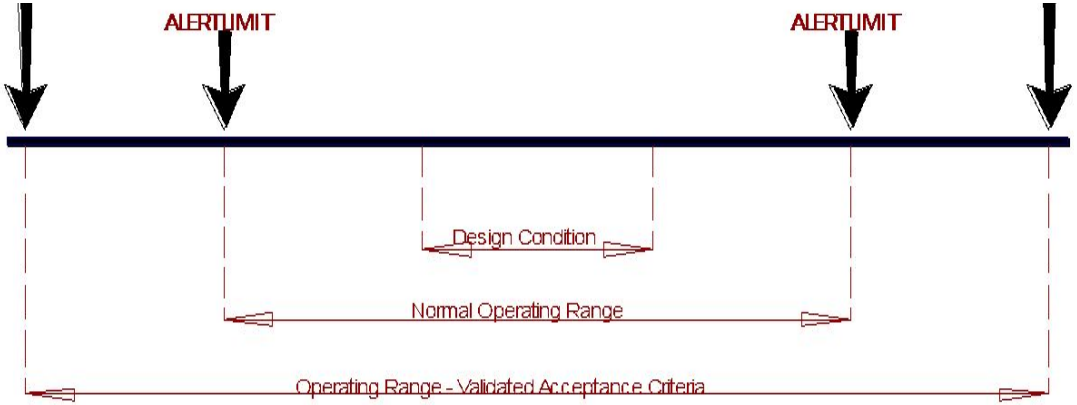
Air Handling Systems

Microbiological validation



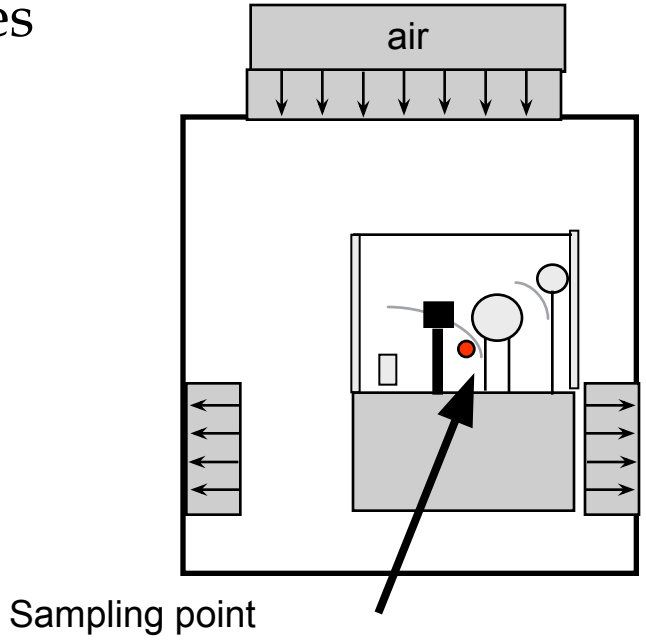
1. Definition of alert / action limits as a function of cleanliness zone
1. Identification and marking of sampling points
2. Definition of transport, storage, and incubation conditions

Ask the question: "What are the alert and action Limits and what procedures are followed if these points are exceeded?"



Cleanroom monitoring program (1)

Cleanrooms should be monitored for micro-organisms and particles



Air Handling Systems

Cleanroom monitoring program (2)

Routine monitoring program as part of quality assurance

Additional monitoring and triggers

1. Shutdown
2. Replacement of filter elements
3. Maintenance of air handling systems
4. Exceeding of established limits

Annex 1, 17.37

Cleanroom maintenance program (1)

Schedule of Tests to Demonstrate Continuing Compliance			
Test Parameter	Class	Maximum Time Interval	Test Procedure
Particle Count Test	A, B <= ISO 5	6 Months	ISO 14644 -1 Annex A
	C, D > ISO 5	12 Months	ISO 14644 -1 Annex A
Air Pressure Difference	All Classes	12 Months	ISO 14644 -1 Annex B5
Air Flow	All Classes	12 Months	ISO 14644 -1 Annex B4

Cleanroom maintenance program (2)

Schedule of Additional Optional Tests			
Test Parameter	**Class**	**Maximum Time Interval**	**Test Procedure**
Installed Filter Leakage	All Classes	24 Months	ISO 14644-1 Annex B6
Containment Leakage	All Classes	24 Months	ISO 14644-1 Annex B4
Recovery	All Classes	24 Months	ISO 14644-1 Annex B13
Air Flow Visualisation	All Classes	24 Months	ISO 14644-1 Annex B7

Air Handling Systems

Documentation requirements

1. Description of installation and functions
2. Specification of the requirements
3. Operating procedures
4. Instructions for performance control
5. Maintenance instructions and records
6. Maintenance records
7. Training of personnel (program and records)

Air Handling Systems

Inspecting the air handling plant

1. Verification of design documentation, including
   - *description of installation and functions*
   - *specification of the requirements*
2. Operating procedures
3. Maintenance instructions
4. Maintenance records
5. Training logs
6. Environmental records
7. Discussion on actions if OOS values
8. Walking around the plant

Air Handling Systems

Conclusion

Air handling systems:

1. Play a major role in the quality of pharmaceuticals
2. Must be designed properly, by professionals
3. Must be treated as a critical system

Air Handling Systems

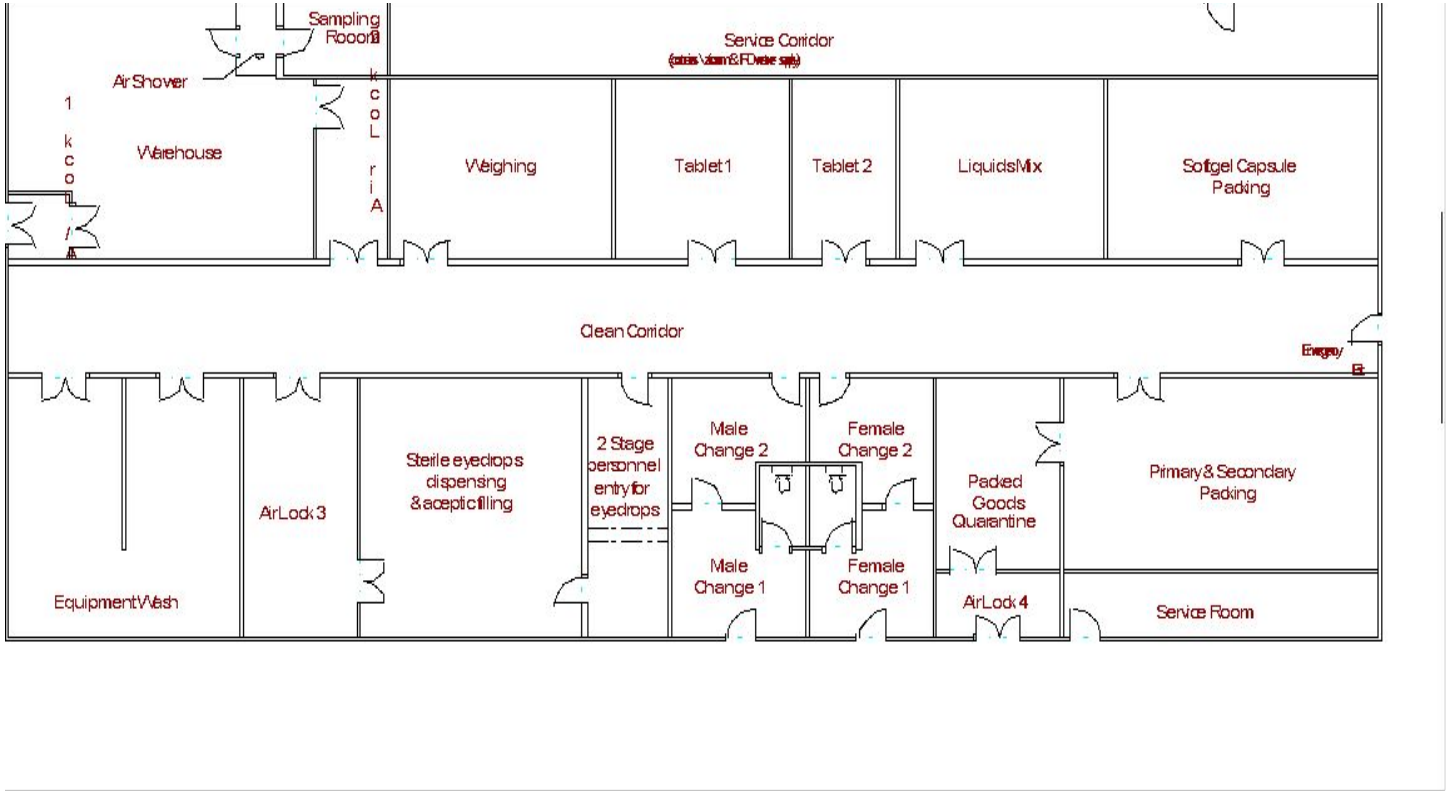
Further proceedings

This series of explanations will now be followed by:

- Group discussion, with a simple exercise
- Short test

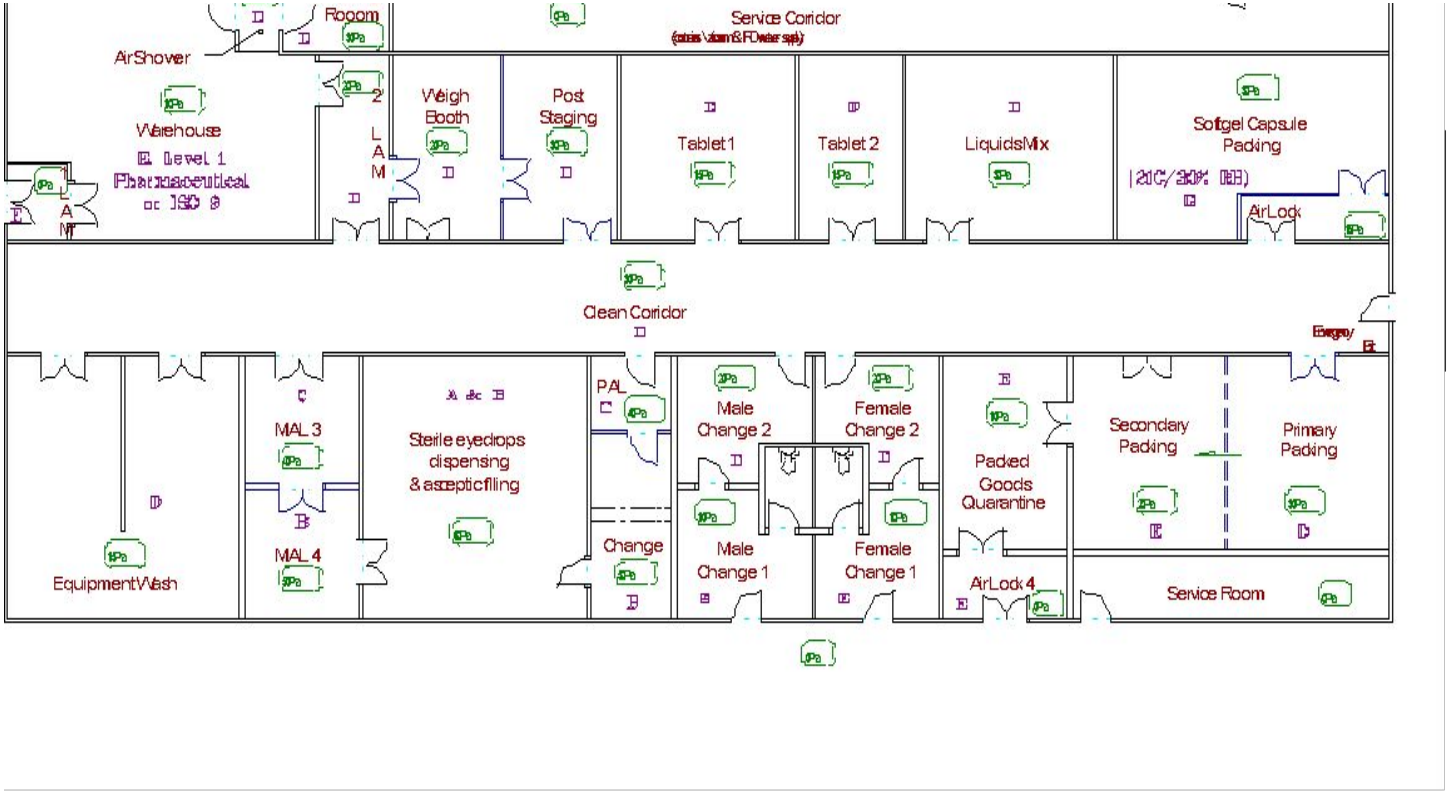
Air Handling Systems

Group Session



Air Handling Systems

Group Session – modified layout



MAL = Material Air Lock

PAL = Personnel Air Lock