

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

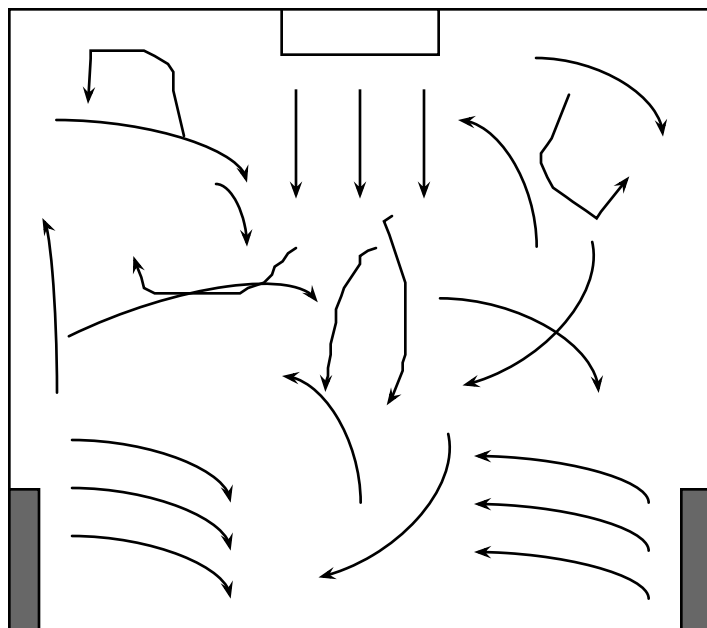
- Turbulent or uni-directional airflows
- Filter position
- Air re-circulation vs fresh air
- Return air systems (positions)
- Overpressure requirements



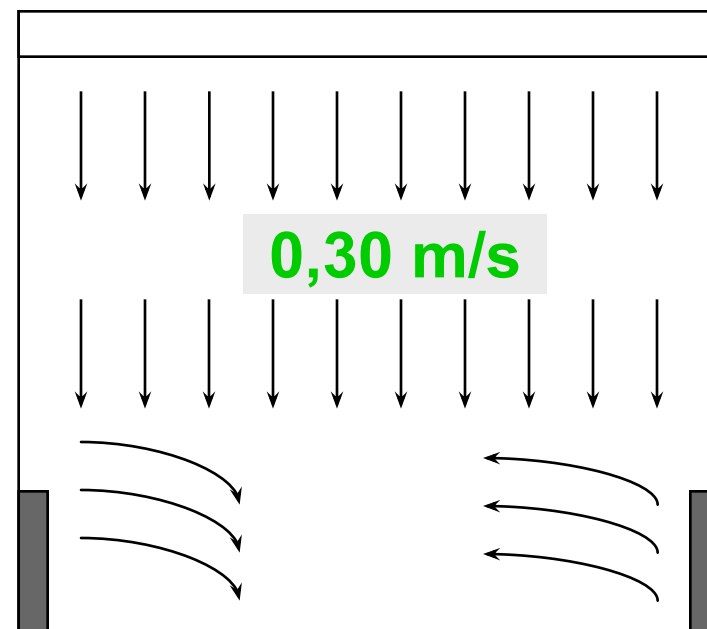
Air Handling Systems

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*

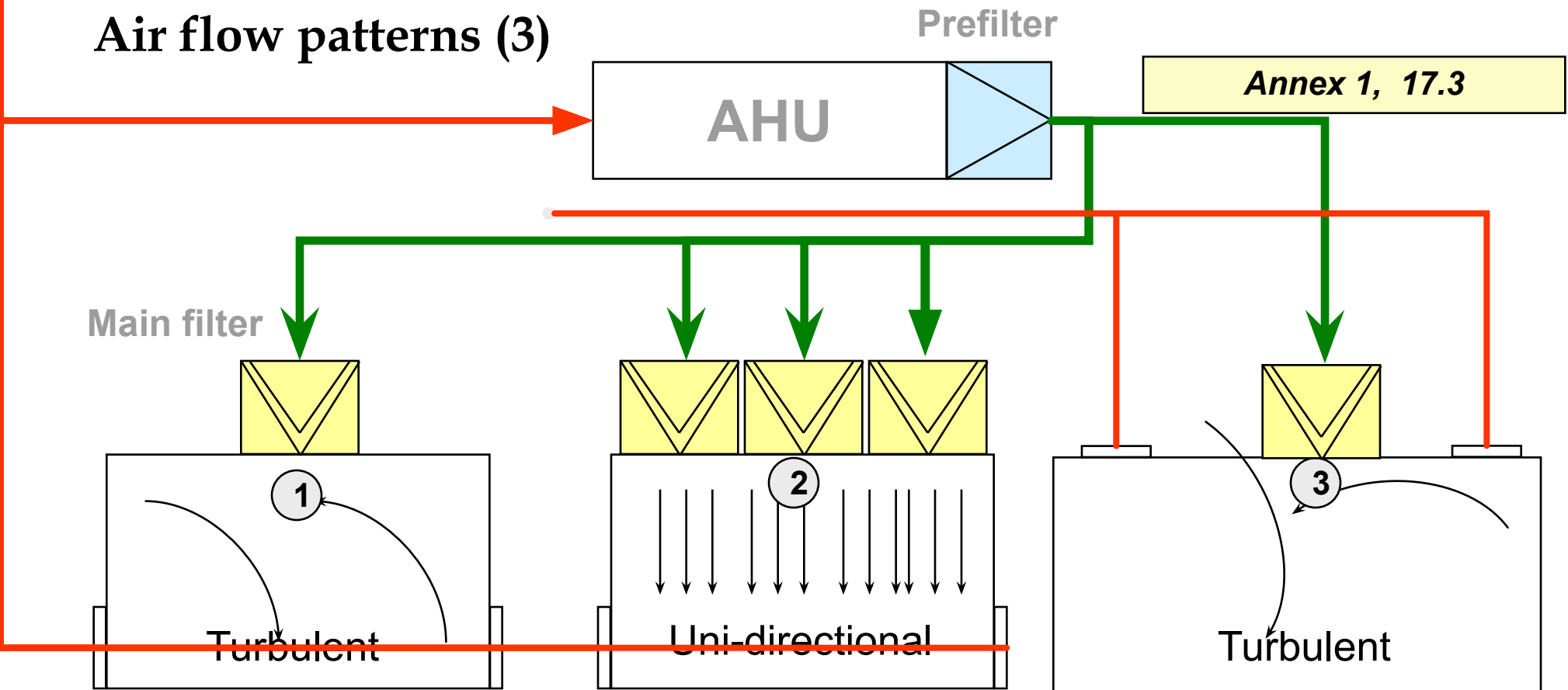
New technologies: barrier technology/isolator technology.

Annex 1, 17.3, 17.4



Air Handling Systems

Air flow patterns (3)



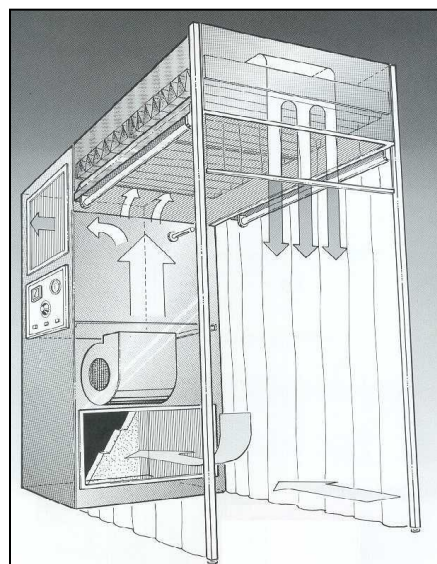
Air Handling Systems

Air flow patterns (4)

Workbench (vertical)



Cabin/ booth



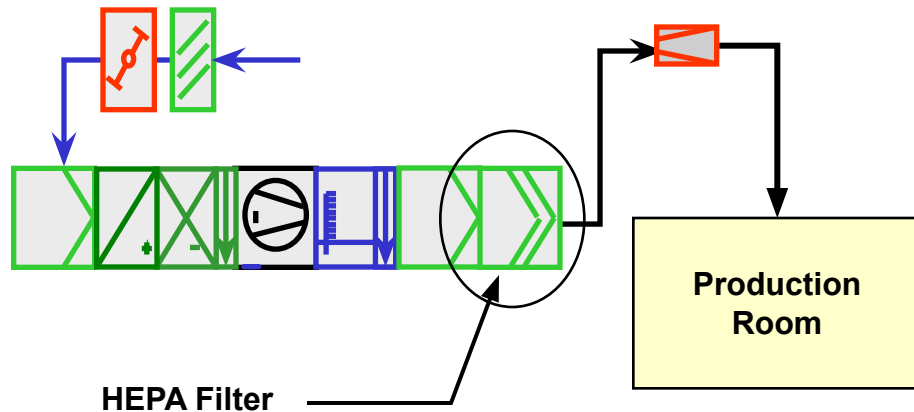
Ceiling



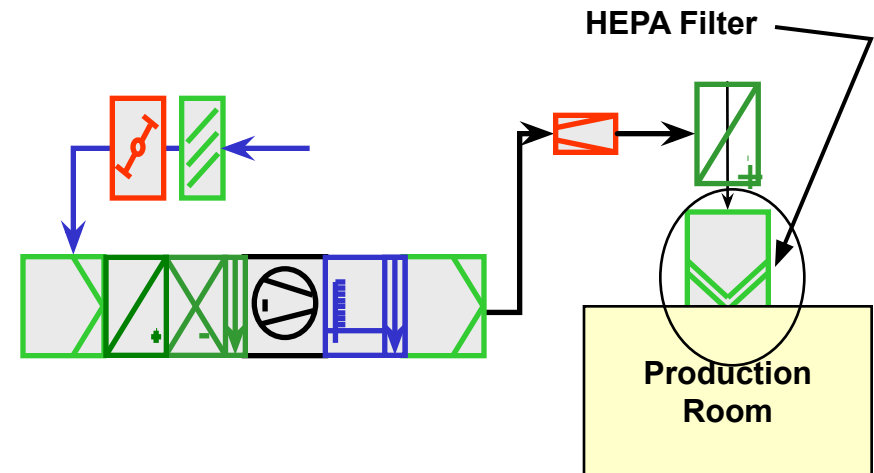
Air Handling Systems

Positioning of filters (1)

AHU mounted final filter

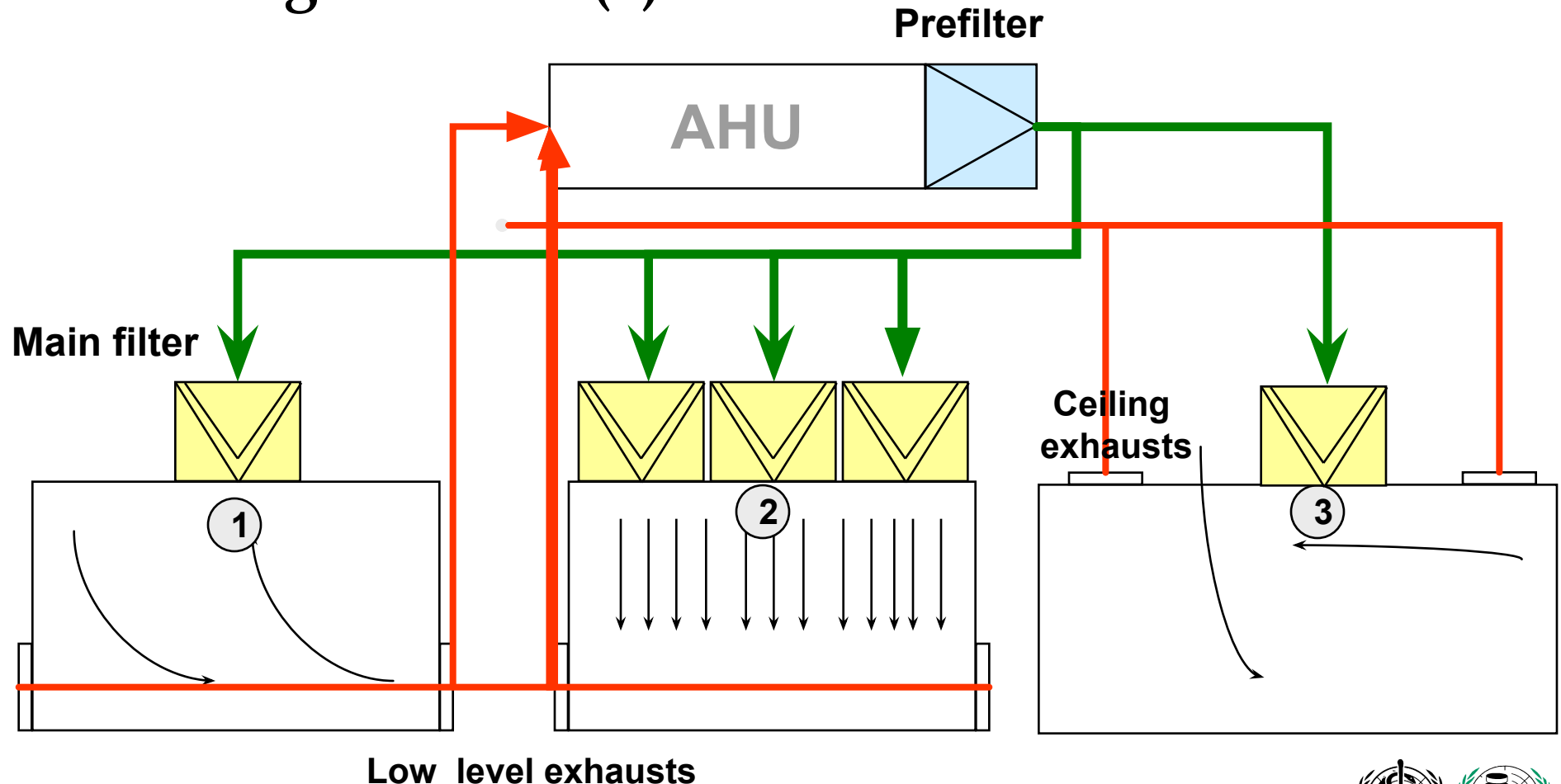


Filter in terminal position



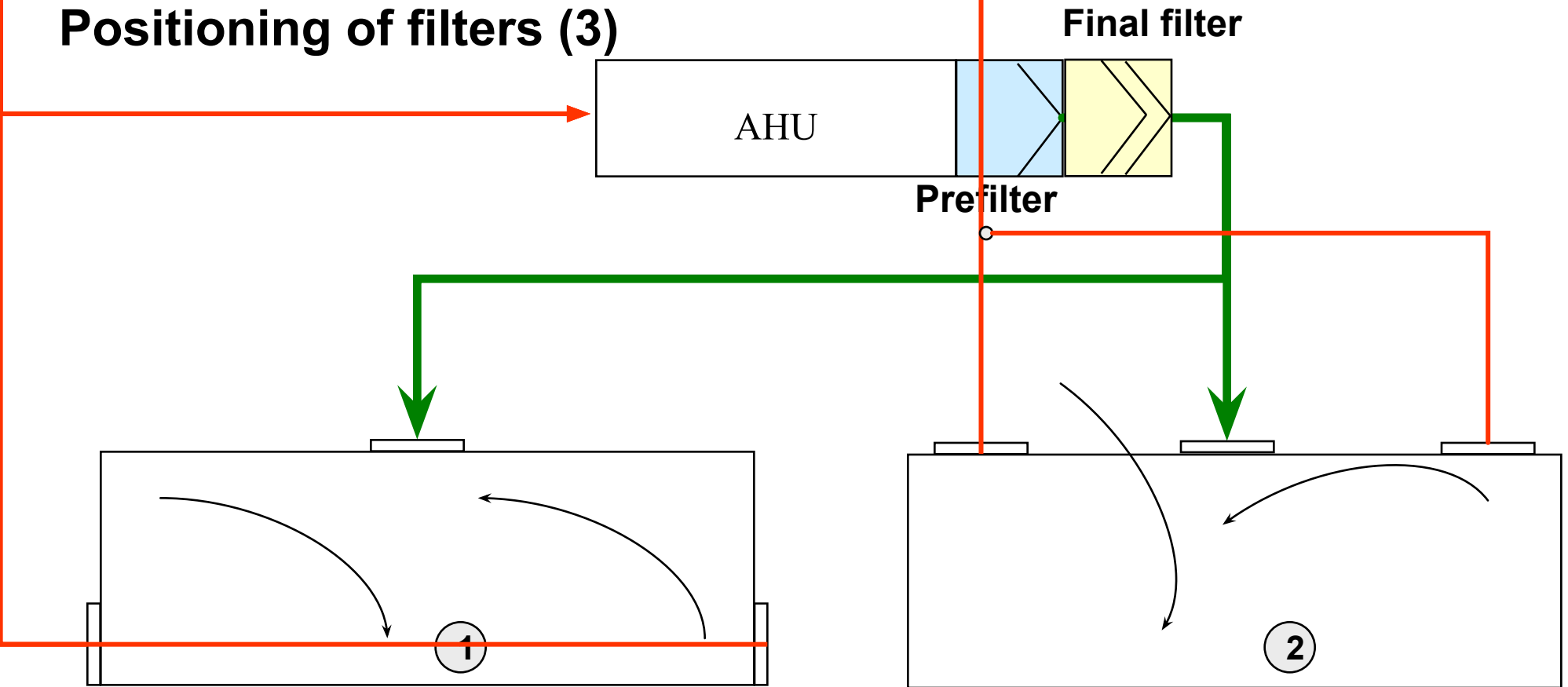
Air Handling Systems

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

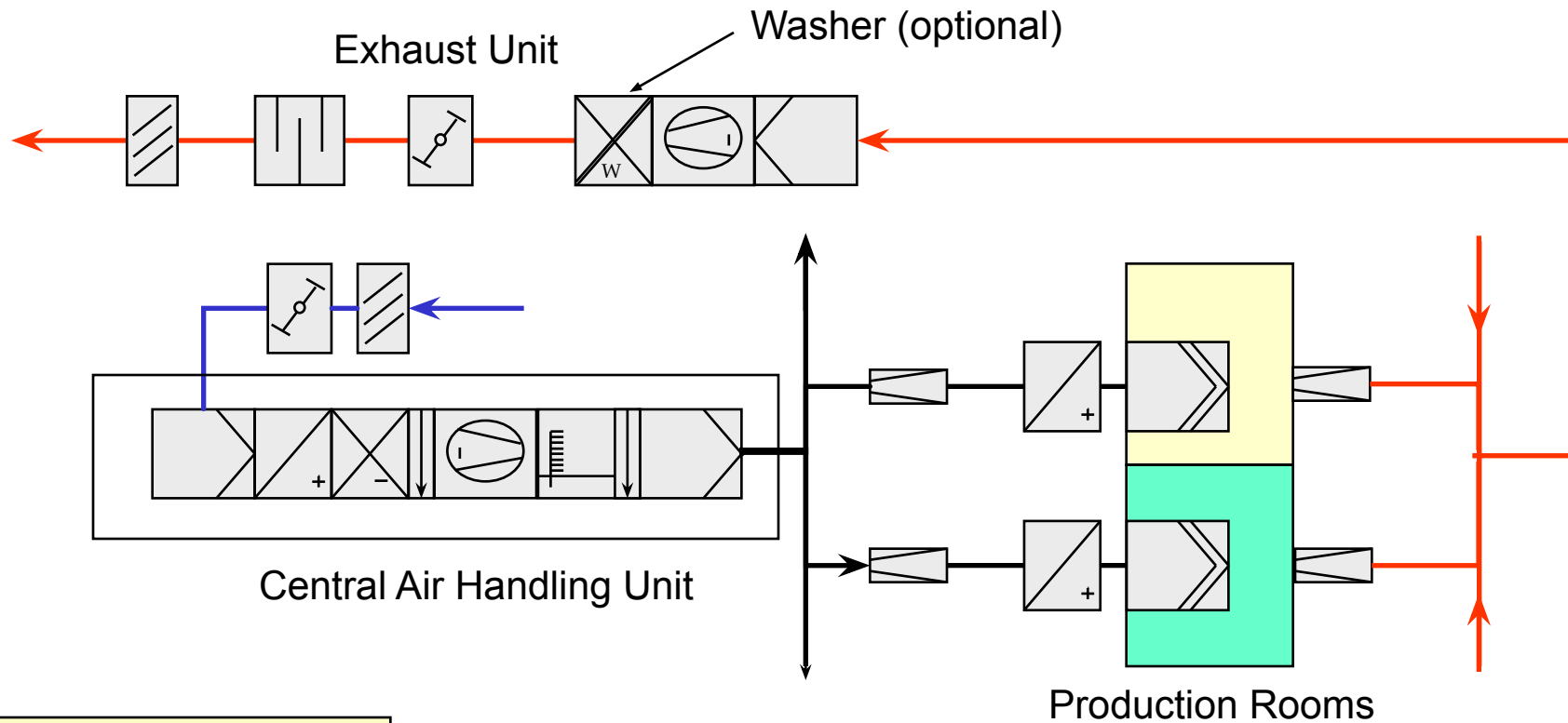
- 100% exhausted or
- a proportion re-circulated
 - *GMP aspect*
 - *economical reasons*

Annex 1, 15.10, 17.24



Air Handling Systems

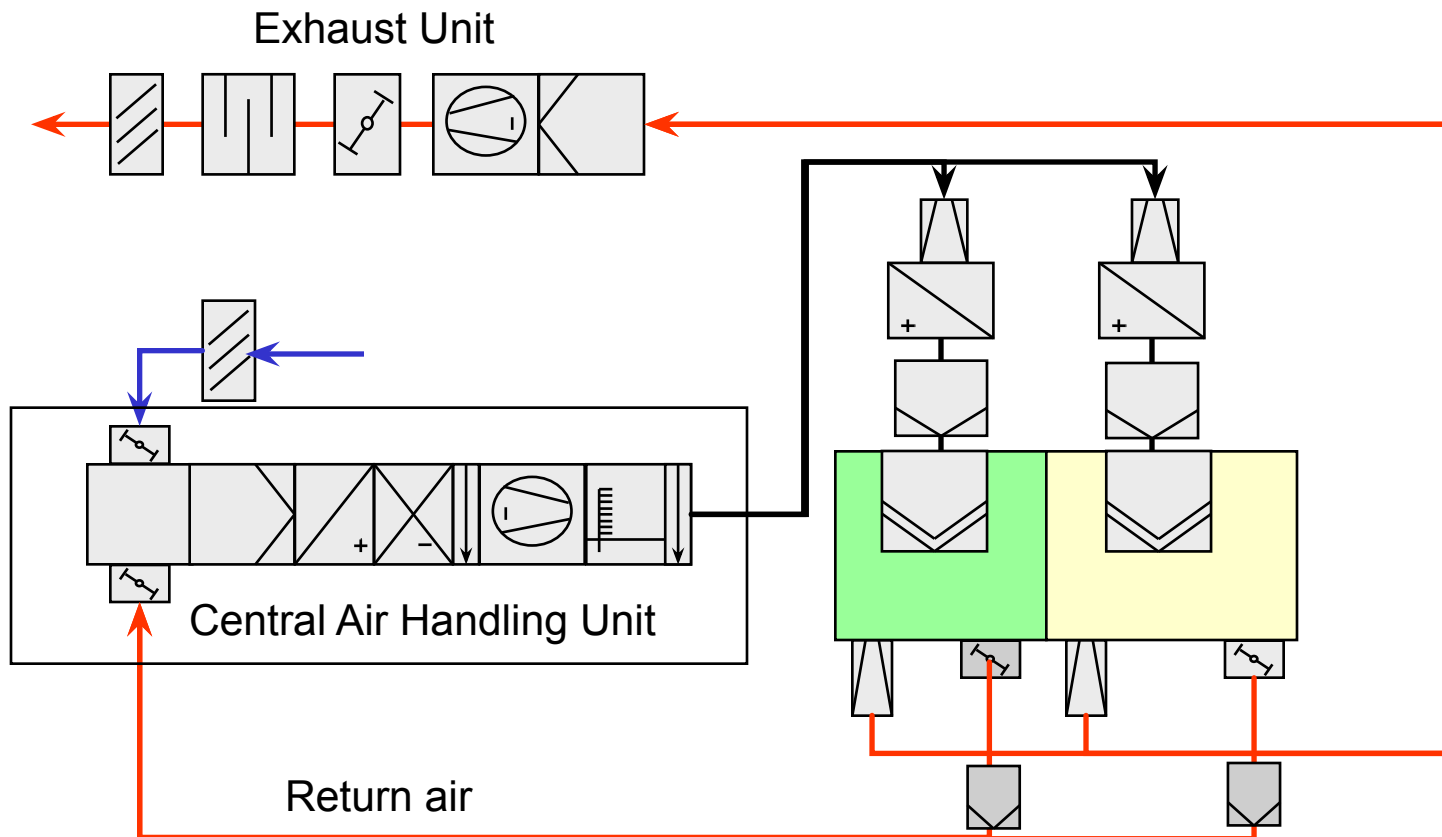
Ventilation with 100% fresh air (no air re-circulation)



Annex 1, 17.24

Air Handling Systems

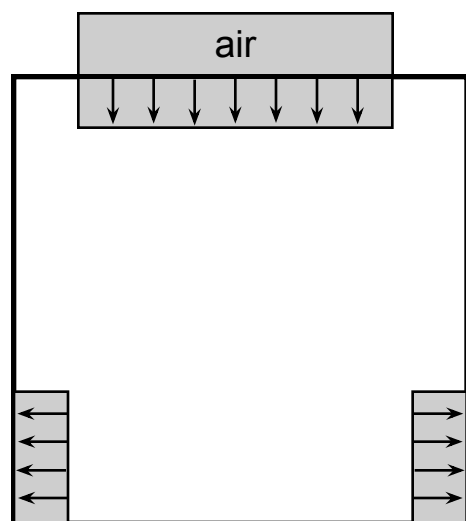
Ventilation with re-circulated air + make-up air



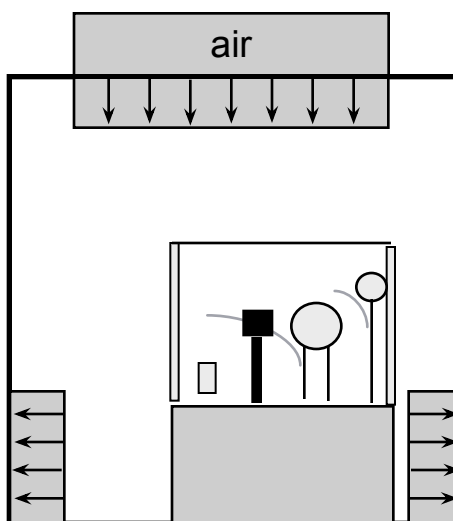
Air Handling Systems

Definition of Conditions

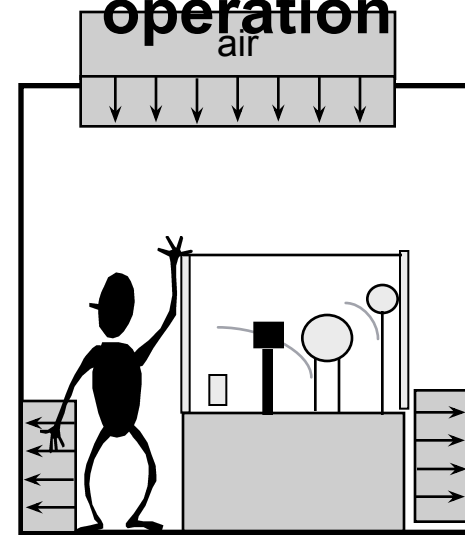
as built



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



Air Handling Systems

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



Air Handling Systems

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



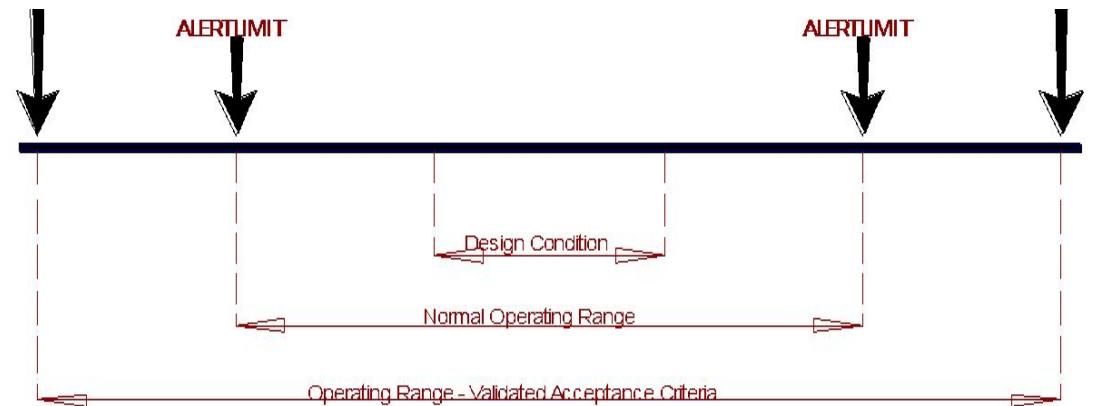
Air Handling Systems

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



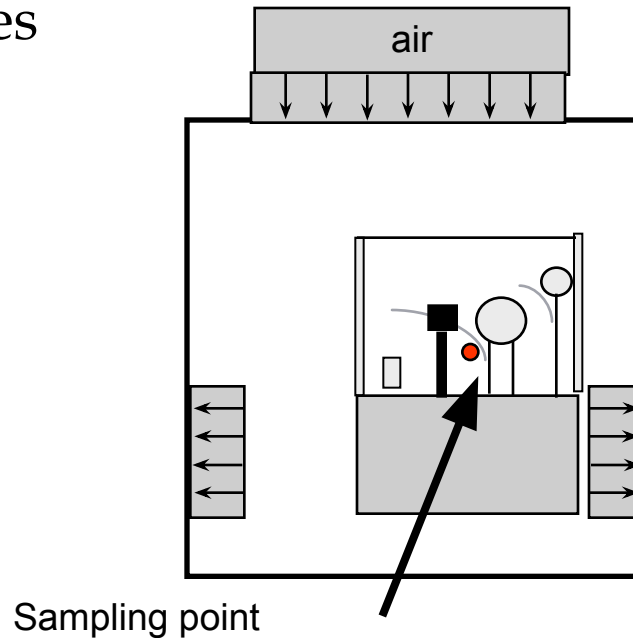
Ask the question:
“What are the alert and action Limits and what procedures are followed if these points are exceeded?”



Air Handling Systems

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



Air Handling Systems

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 |



Air Handling Systems

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

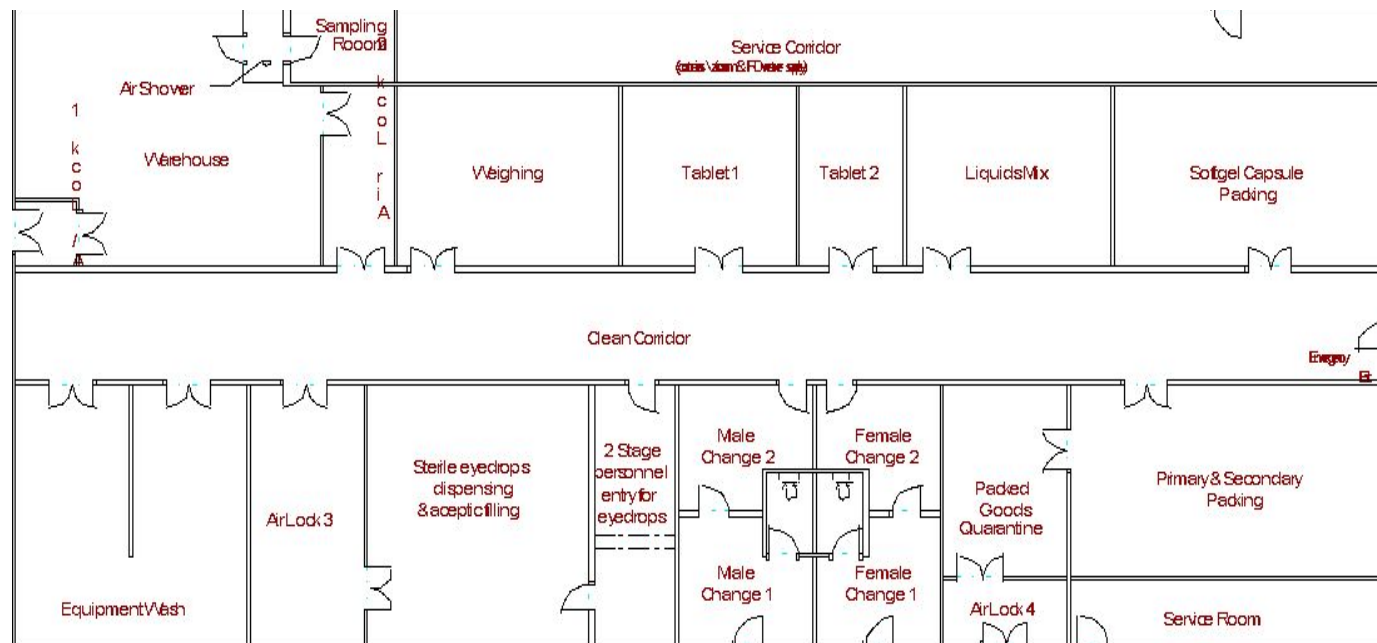
This series of explanations will now be followed by:

- Group discussion, with a simple exercise
- Short test



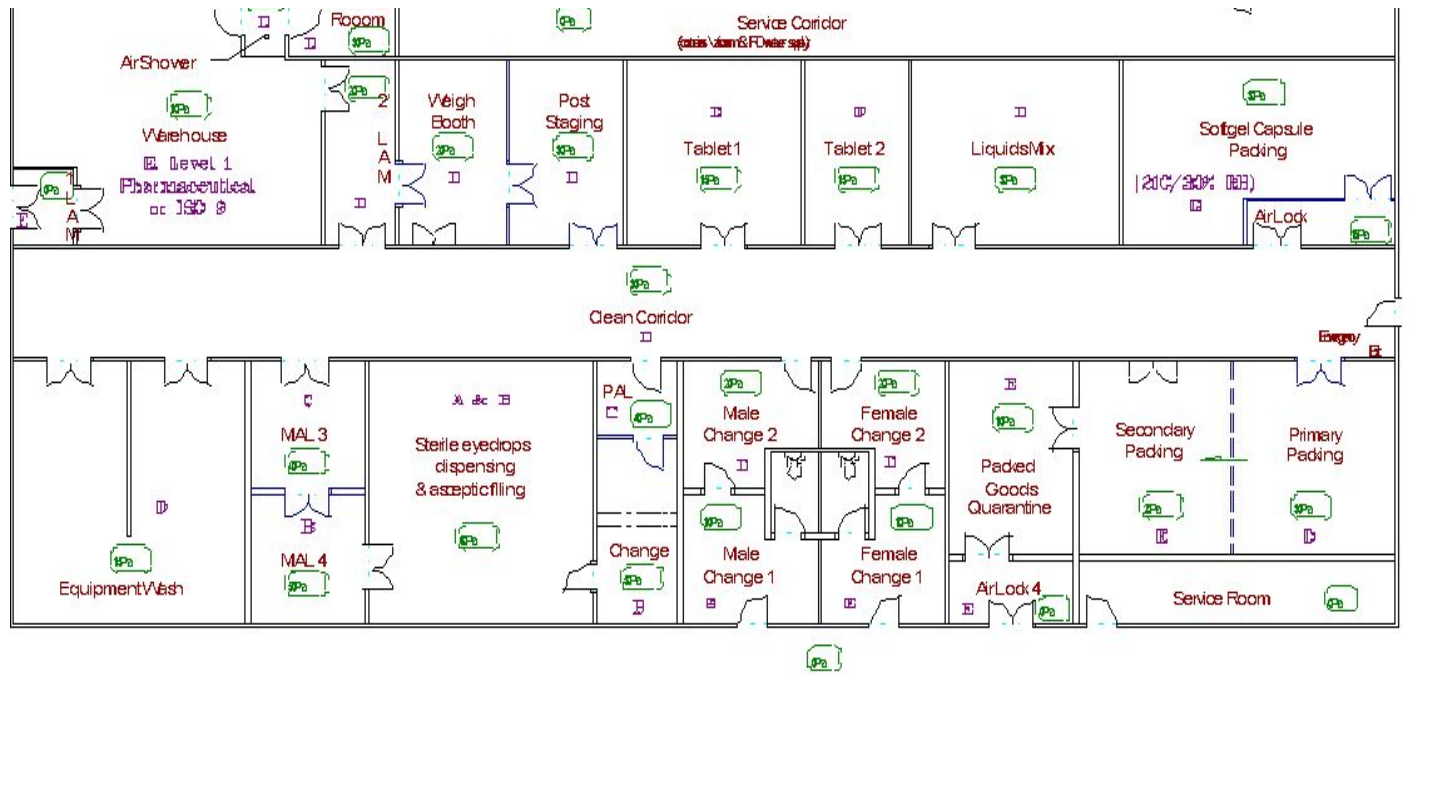
Air Handling Systems

Group Session



Air Handling Systems

Group Session – modified layout



MAL = Material Air Lock

PAL = Personnel Air Lock

