



HVAC

Heating, Ventilation &
Air Conditioning

Cleanroom

- Particles
- Bacteria
- Temperature
- Humidity
- Pressure



Environment contaminations

- Dust Particle (0.5 μm – 500 μm)
- Virus (0.006 μm – 0.03 μm)
- Bacteria (0.2 μm – 2 μm)
- Fungi and mould (1 μm – 100 μm)

Bacteria removal and Control

- Dust must be controlled
- Filtration
- Directional air flow and air flushing or dilution
- Surface bacteria cleaning

Uncontrolled environments

- Quality issues
- Product Degradation
- Product Contamination
- Product Rejection

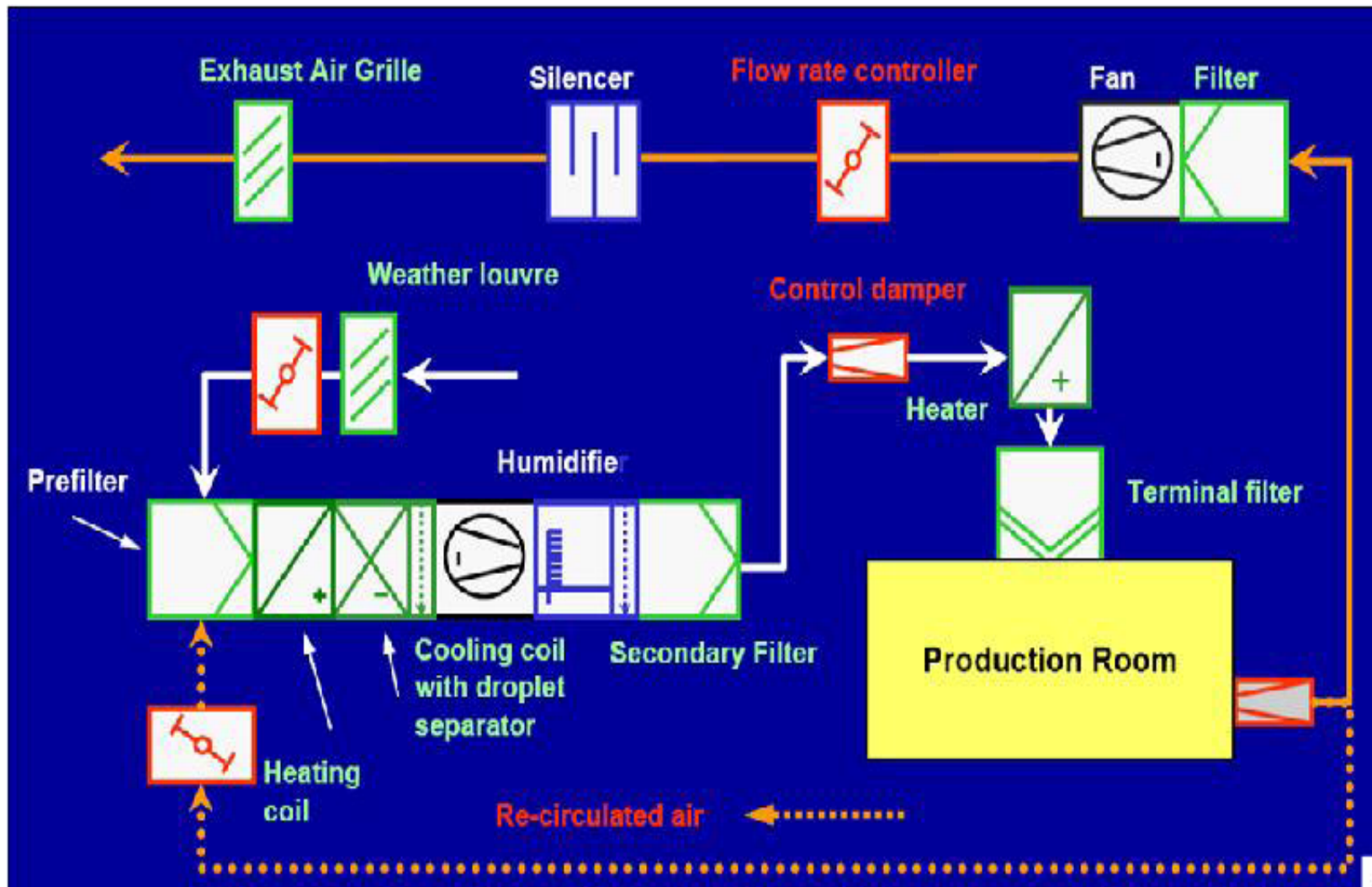
Classification

Grade	Maximum permitted number of particles/m ³ equal to or greater than the tabulated size			
	At rest		In operation	
	0.5μm	5.0μm	0.5μm	5.0μm
A	3,520	20	3,520	20
B	3,520	29	352,000	2,900
C	352,000	2,900	3,520,000	29,000
D	3,520,000	29,000	not defined	not defined

GMP manufacturing considerations

- **Product** protection (contamination, cross-contamination,...)
- **Personnel** protection (dust, fume, comfort,...)
- **Environment** protection (dust, fume, effluent discharge,...)

HVAC Components



HVAC components

- Weather louvre (protection from insects, leaves,...)
- Flow rate controller (automated adjustment of air volume)
- Make up and return air mixer
- Metal filter
- Pre filter (G4)
- Primary Filter (F5 bag filter)
- Heating Coil
- Cooling Coil
- Fan or Blower
- Silencer (noise reduction)
- Humidifier
- Secondary or Final filter F8-F9 or HEPA
- Damper (fixed adjustment of air volume)
- Heater
- Terminal Filter (HEPA)
- Diffuser (ducts)

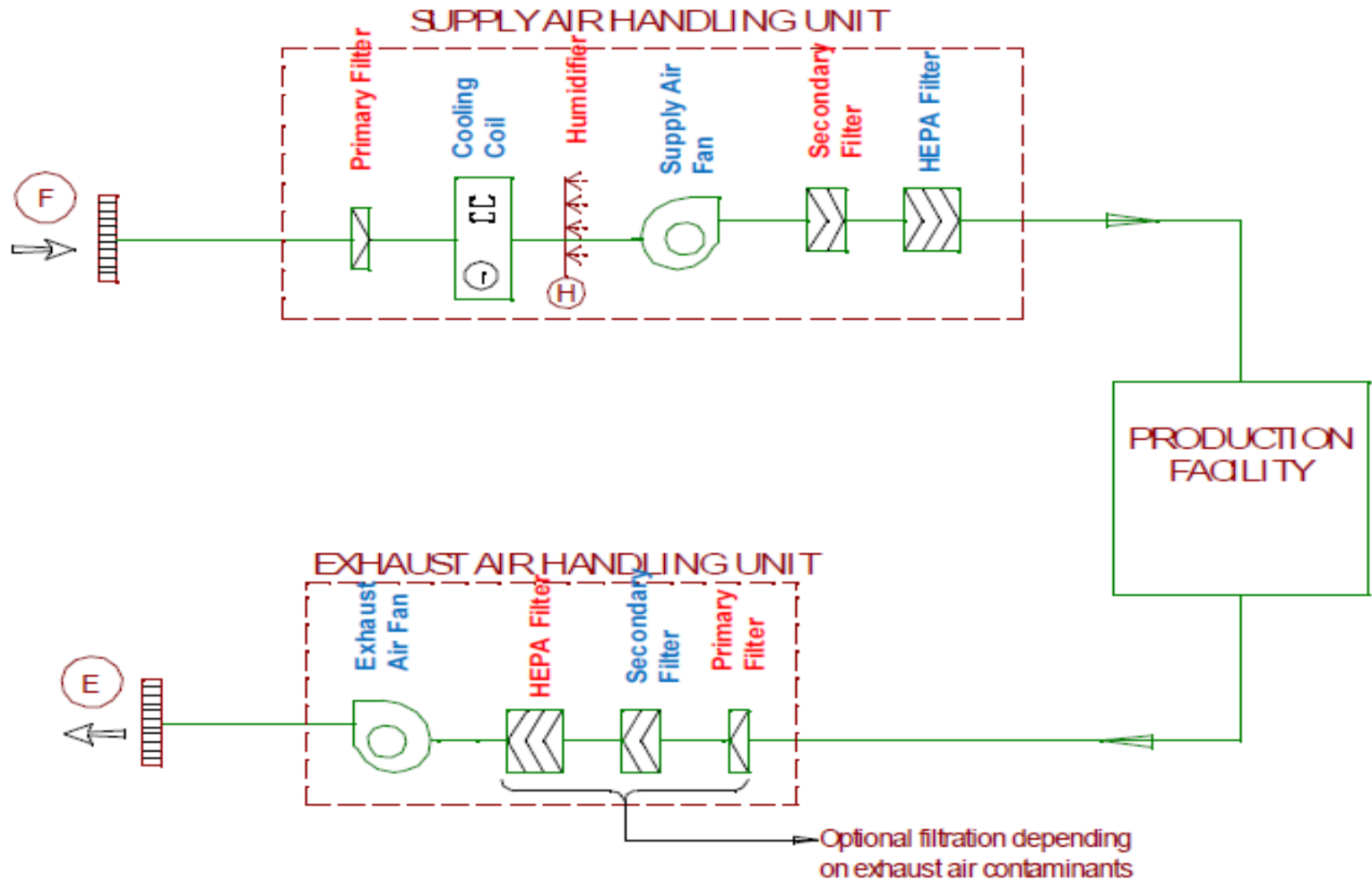
Exhaust unit components

- Pre filter
- Fan
- Air washer (second filter)
- Final filter (HEPA H12(hazardous) or F9 (general))
- Flow rate controller
- Silencer
- Exhaust air grille

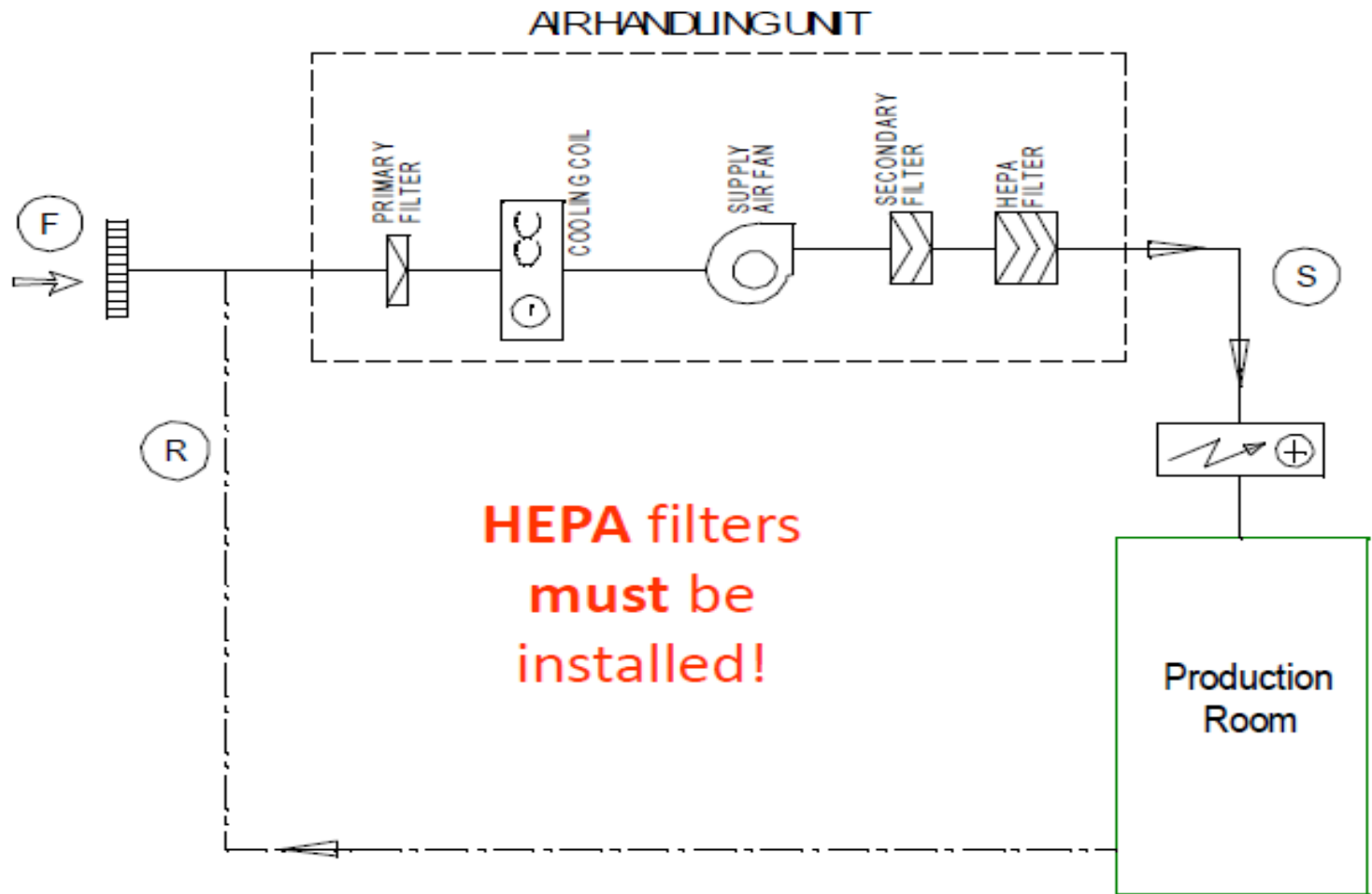
Exhaust air filtration

- Two banks of HEPA in series
- BIBO systems
- Differential pressure gauges
- Monitoring of filters (BMS, BAS, SCADA)
- Air showers or Mist water

Full fresh system



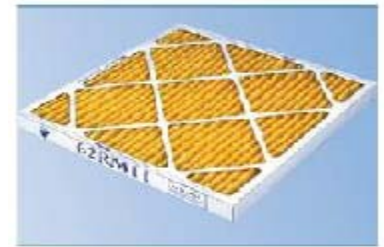
Re-circulation system



Air Filtration

- Level 1 Filtration (Metal filters, leaves, insects): Aluminum, Galvanized steel, Stainless steel
- Level 2 Filtration (G filters or Pre-filtering outside air): 60-65%
- Level 3 Filtration (intermediate filters or F Filters (Secondary Filtering for protection of final filters)): Bag filters
- Level 4 Filtration (F8-F9 or HEPA Filters (Final filtering)): 0.3 – 10 μm
- Level 5 or Terminal filtration (in the filter box on the ceiling of cleanroom): 0.1 – 0.3 μm

Gravimetric Filters



Group Standard	Class	Typical contaminants	Typical application
<p>G</p> <p>Coarse Dust Filters</p> <p>Effective for particles $\geq 10 \mu\text{m}$</p> <p>EN 779</p>	G1	<ul style="list-style-type: none"> • Leaves 	<ul style="list-style-type: none"> • Filter for low grade application (e.g. for protection against insects and leaves) • filter for exhaust air from spray booths • Kitchen exhaust air filters • filter for compact room air conditioners • Prefilter for F7 and F8 filters with heavily contaminated outside air
	G2	<ul style="list-style-type: none"> • Insects 	
	G3	<ul style="list-style-type: none"> • Textile fiber • Human hairs 	
	G4	<ul style="list-style-type: none"> • Sand • Fly ash • Water droplets • Beach sand • Plant spores • Pollen • Fog 	

Fine Filters



Group Standard	Class	Typical contaminants	Typical application
<p>F</p> <p>Fine Dust Filters</p>	<p>F5 or M5</p>	<ul style="list-style-type: none"> • Spores • Cement dust (coarse fraction) • Sedimenting particles 	<ul style="list-style-type: none"> • inlet filter for very low requirement rooms (e.g. production areas, garages, warehouses) • pre-filter for F8 and F9 filters in urban location.
<p>Effective for particles $\geq 1 \mu\text{m}$</p>	<p>F6</p>	<ul style="list-style-type: none"> • Larger bacteria • Germs on carrier particles • PM 10-dust 	<ul style="list-style-type: none"> • inlet filter for rooms with low requirement (e.g. production areas, shops) • pre-filter for F9 and H10 filters. • exhaust air filter to protect heat recovery installation in AC plants.
<p>EN 779</p>	<p>F7</p> <p>F8</p>	<ul style="list-style-type: none"> • Agglomerated soot • lung damaging dust • PM 2.5-dust • Cement dust (fine fraction) 	<ul style="list-style-type: none"> • typical final filter for air conditioned offices and other buildings • filter for recirculated air in AC plants • pre filter for H11 and H12 filters

Fine Filters



Group Standard	Class	Typical contaminants	Typical application
<p data-bbox="305 525 349 596">F</p> <p data-bbox="305 644 494 758">Fine Dust Filters</p> <p data-bbox="305 872 494 1039">Effective for particles $\geq 1 \mu\text{m}$</p> <p data-bbox="305 1139 446 1182">EN 779</p>	<p data-bbox="568 511 620 554">F8</p> <p data-bbox="568 596 620 639">F9</p>	<ul data-bbox="678 515 1166 839" style="list-style-type: none">• tobacco smoke (coarse fraction)• metallurgical fumes (coarse fraction)• oil smoke• bacteria	<ul data-bbox="1193 515 1812 868" style="list-style-type: none">• final filter for medium quality air conditioning system (e.g. pharmaceutical industry, hospitals, EDP and control rooms, etc.)• pre filter for H13 and H14 filters• pre filter for gas adsorption filters

HEPA Filters

- High-Efficiency Particulate Air
- Extended-medium
- dry-type
- rigid frame
- minimum particle collection efficiency of 99.97%



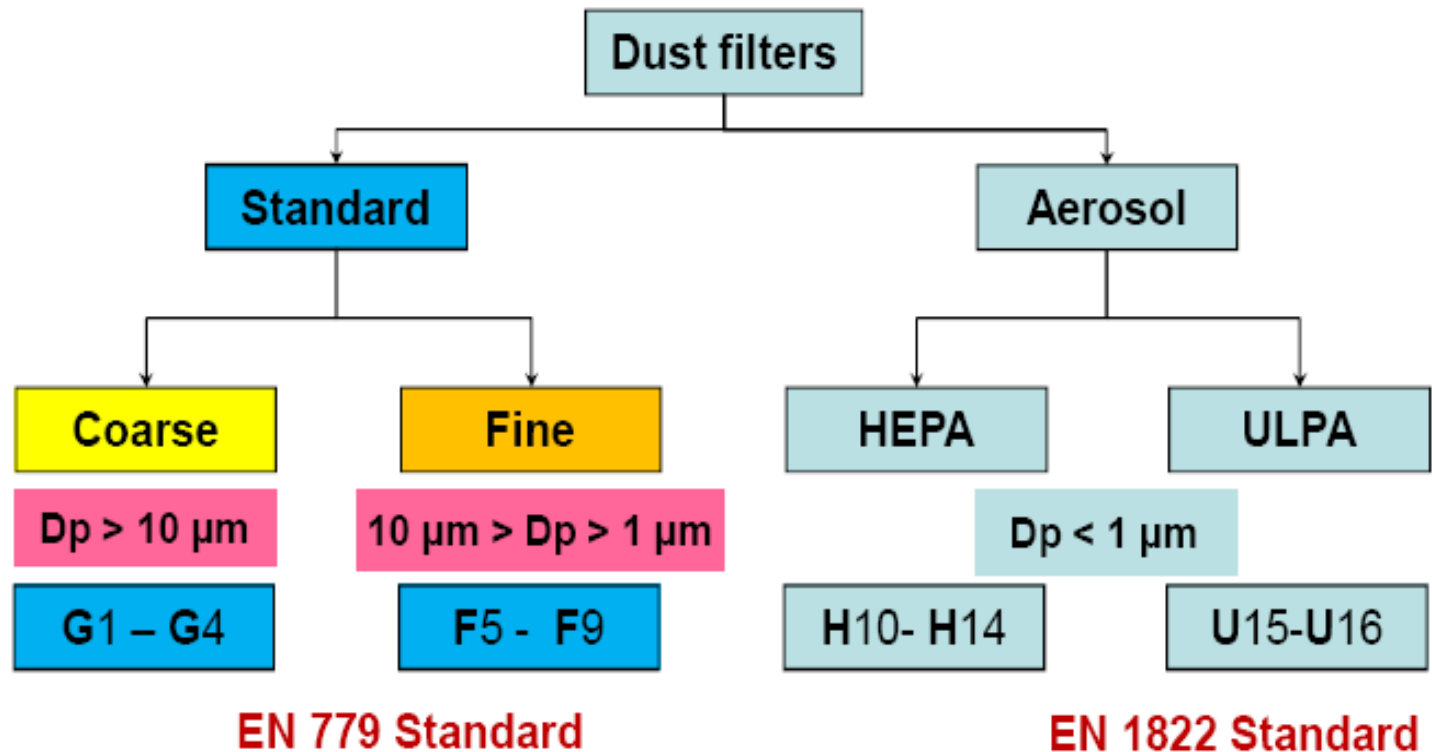
ULPA Filters

- Ultra Low Penetration Air
- Extended-medium
- Dry-type
- Rigid frame
- minimum particle collection efficiency of 99.999% (maximum particle penetration of 0.001%)

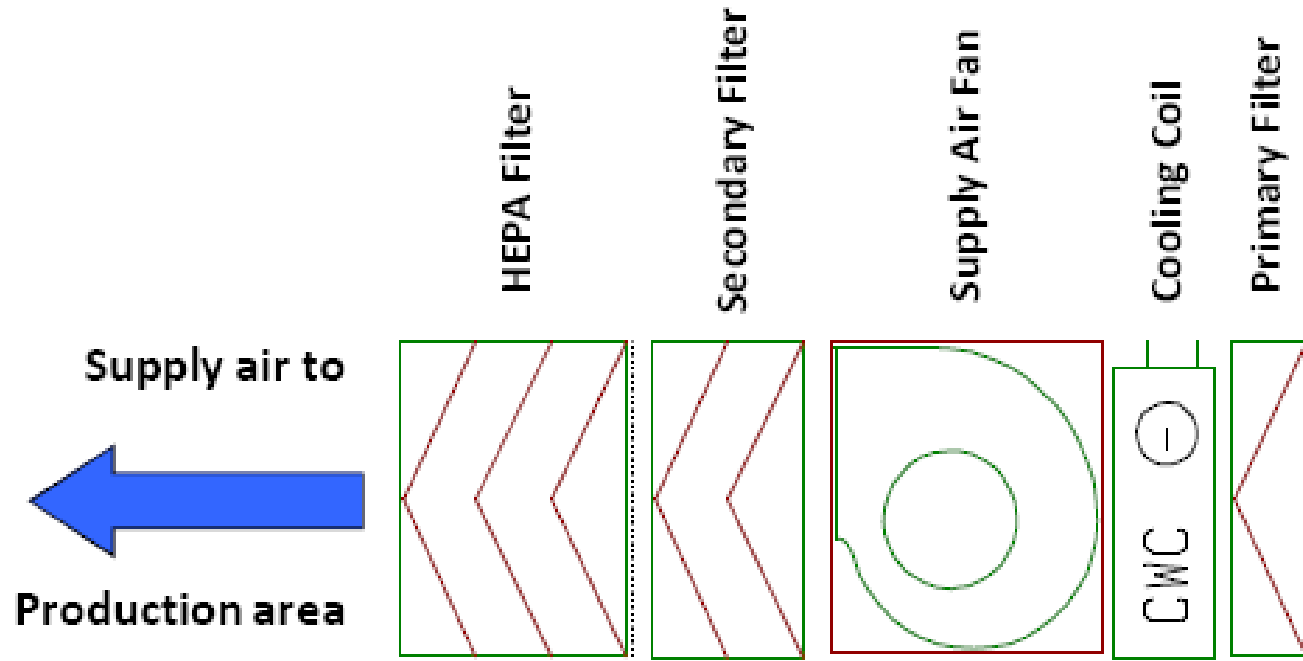
HEPA & ULPA Filters

		MPPS integral values			MPPS local values		
Filter Group	Filter Class	Minimum efficiency (%)	Maximum penetration (%)	Minimum D.C.	Minimum efficiency (%)	Maximum penetration (%)	Minimum D.C.
HEPA	H10	85	15	6.7	---	---	---
	H11	95	5	20	---	---	---
	H12	99.5	0.5	200	---	---	---
	H13	99.95	0.05	2,000	99.75	0.25	400
	H14	99.995	0.005	20,000	99.975	0.025	4,000
ULPA	U15	99.9995	0.0005	200,000	99.9975	0.0025	40,000
	U16	99.99995	0.00005	2,000,000	99.99975	0.00025	400,000
	U17	99.999995	0.000005	20,000,000	99.9999	0.0001	1,000,000

Filters classification



HVAC Assembly



HEPA Filters considerations

- Packaging
- Transportation
- Mechanical Damage
- Storage (Maintenance)
- Inspection
- Fitting
- Leak test

Leak Test

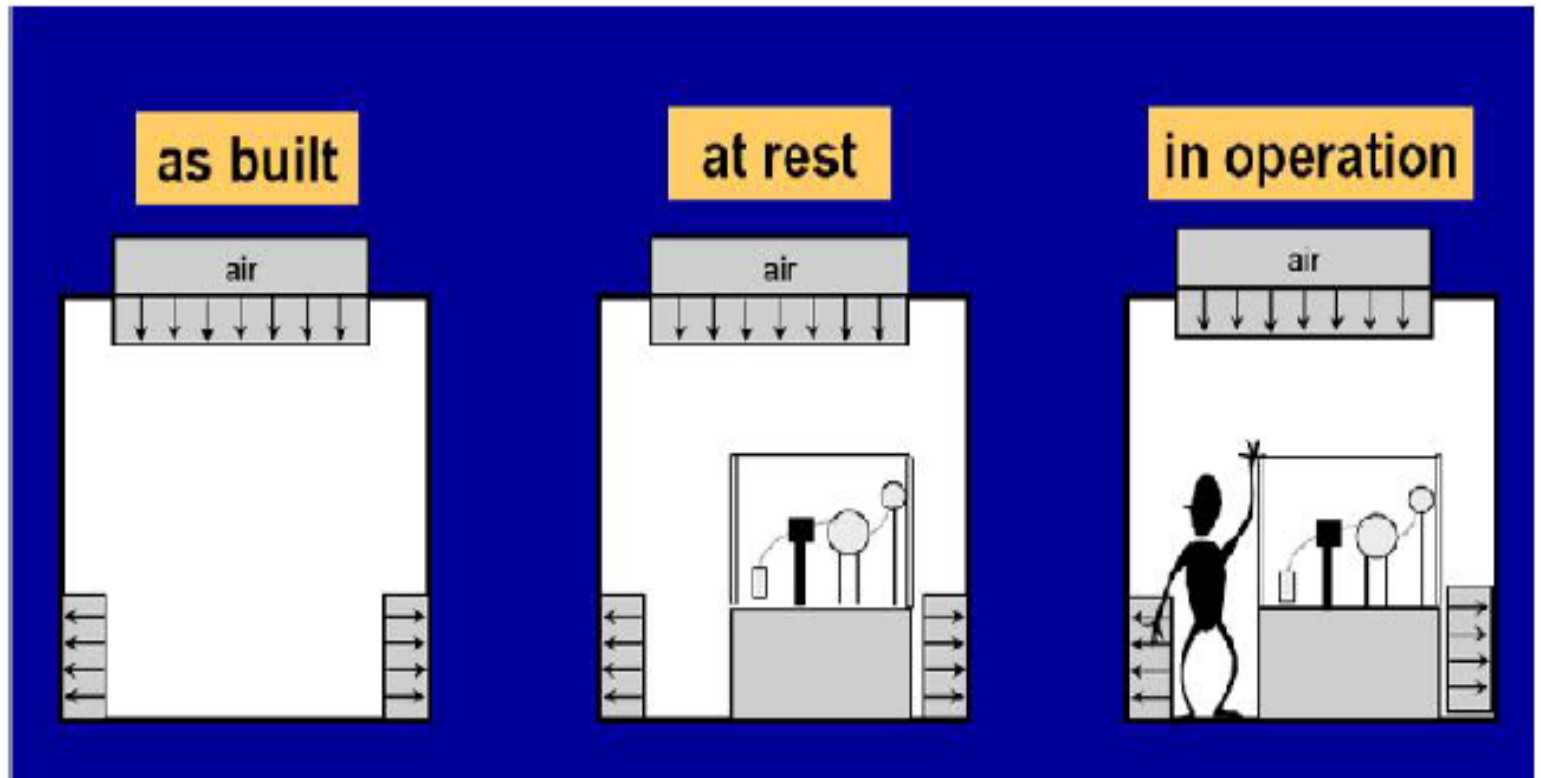
- Cold generated oil test: DOP test
- Hot generated smoke: CO₂
- Particle counting
- Scanning



Production activities

Cleanroom Class	A	B	C	D
Washing of containers				X
Preparation of solution for terminal sterilisation			X	
Preparation of solutions for aseptic filling	X	X	X	
Depyrogenisation of containers	X			
Filling for terminal sterilisation			X	
Filling for aseptic process	X			

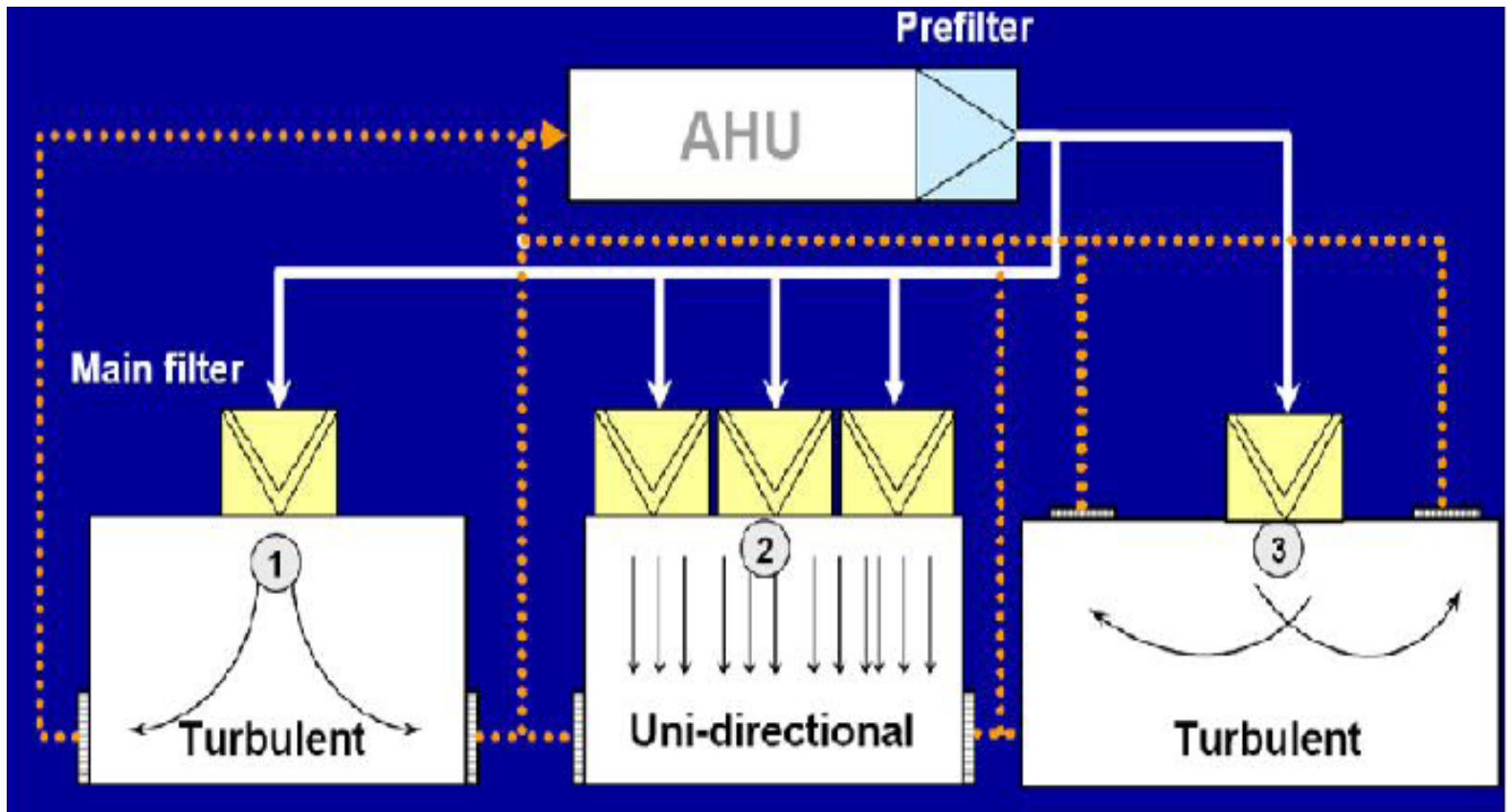
Cleanroom conditions



Cleanrooms

- Increased air supply (ACH: 20 -60)
- HEPA filters
- Terminal filters
- Differential pressure

Air flow



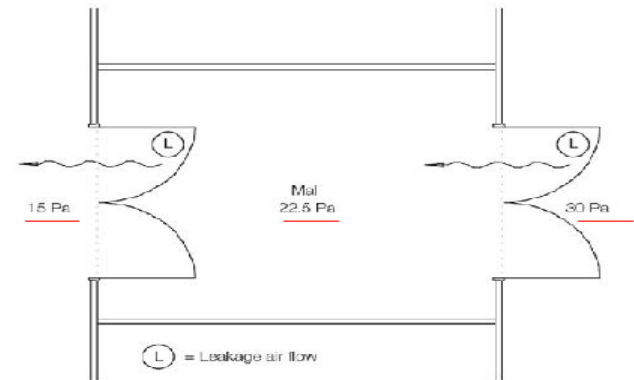
Cleanroom Diffusers

- Swirl
- Perforated

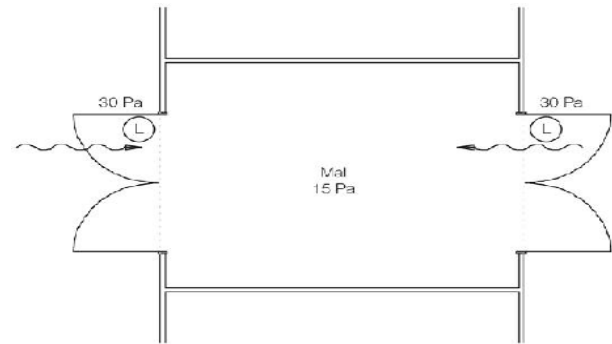


Airlocks

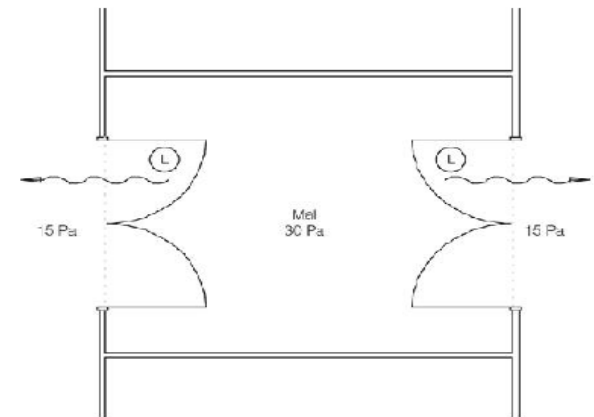
- Cascade



- Sink



- Bubble



Qualification

- HVAC Qualification
- URS
- DQ
- IQ
- OQ
- PQ
- Cleanroom Qualification
- Microbial
- Particle



Thank You

Any Questions?