ASHRAE Hellenic Chapter TEE

DEDICATED VENTILATION APPLICATIONS

INDUSTRIAL - KITCHEN - SMOKE CONTROL - FILTERS

ILIANA GEORGAKAKOU

Senior Mechanical Engineer at LDK Consultants

"ASHRAE Design Guide for Commercial Kitchen Ventilation - Design Approach and Recommendations"

REINER KELCH

Bereichsleiter / Director Systems and Applications Systemair GmbH Germany

"Effect of new published standard 12101-6 on practical implementation"

IOANNIS TZOURALAS

Senior Mechanical Engineer - Consultant MEP Installations Industrial & Building Sector

"HVAC Systems for Cleanrooms (Pharma)"

WEDNESDAY 11/10/2023 | @17:00-21:00

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HVAC Systems for Cleanrooms (Pharma)

Issues of Air Conditioning and Ventilation systems for "cleanrooms" Section 1

Description of "cleanrooms":

- Biological Laboratories
- Hospitals (Surgeries, etc.)
- Premises of Pharmaceutical production industries
- Semiconductor Production Industry Areas
- Food Industry
- and in general, "cleanrooms" for the production of other Industrial products

Issues of Air Conditioning and Ventilation systems for "cleanrooms"
Section 1

Presentation of current legislative framework:

- Legislation
- Regulations/Directions
- Directives
- Standards

Section 1
Cleanrooms

- Biological Laboratories

Credit CFP

Section 1
Cleanrooms

- Healthcare facilities - Hospitals (Surgeries, etc.)

Credit Sinai Health News and Media

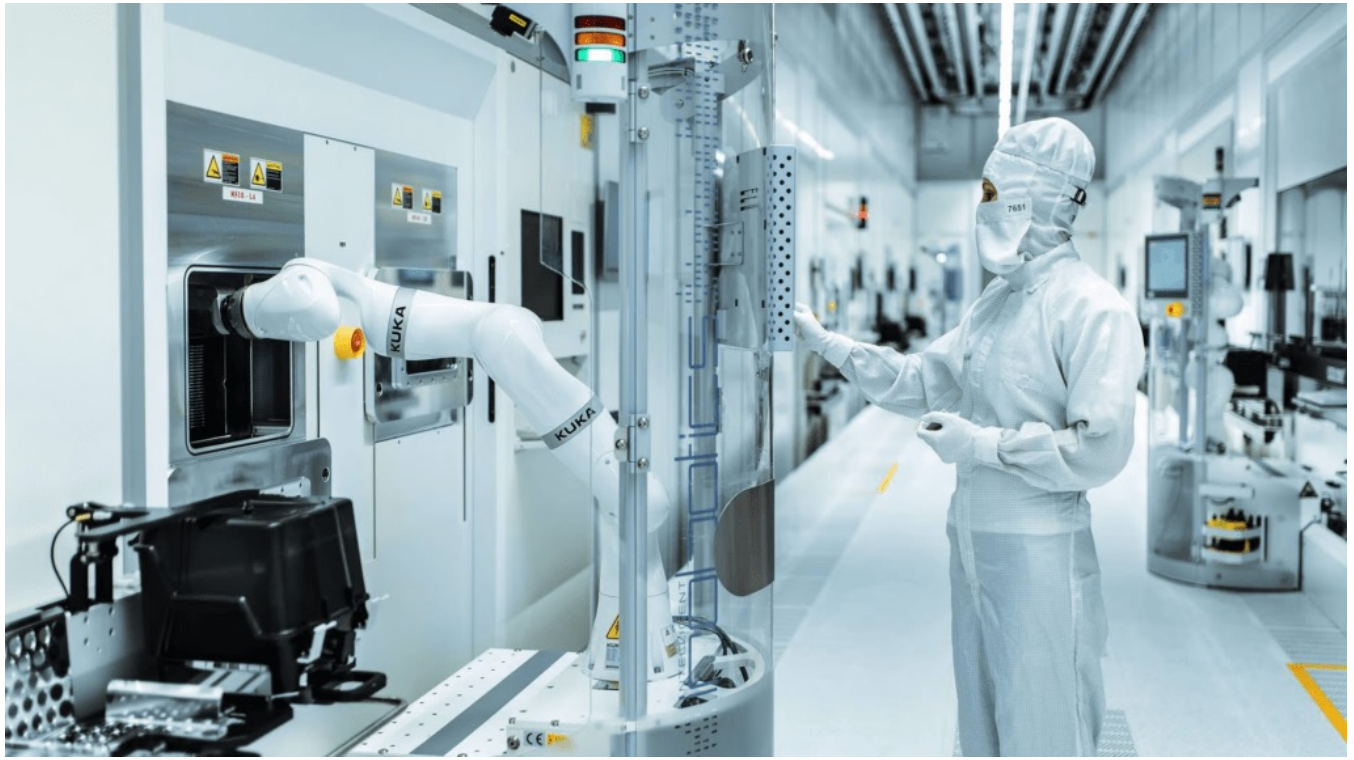
Section 1
Cleanrooms

- Premises of Pharmaceutical production industries

Credit AES Clean Technology, Inc.

Section 1
Cleanrooms

- Areas of Semiconductor Production Industries



Credit KUKA Robotics

Section 1
Cleanrooms

- Biotechnology

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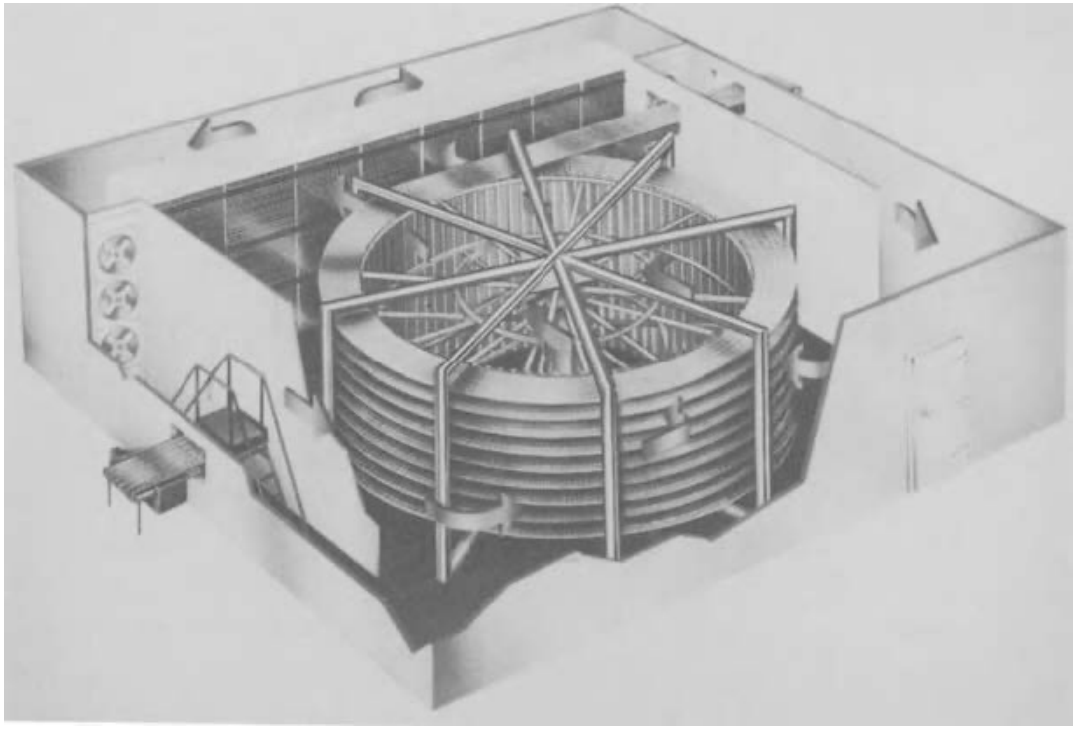
Section 1
Cleanrooms

- Food industry



Section 1
Cleanrooms

- and more generally, "clean" areas for the production of other Industrial products

Credit Plastics News

Section 1
Legislative framework (1of7)

- Law 4600 – Gazette 43A/2019 Modernization and Reform of the Institutional Framework of Private Clinics, Establishment of a National Public Health Organization, Establishment of a National Institute of Neoplasms and other provisions.
- Presidential decree 517 - Gazette 202A/1991 on "Terms of conditions and procedure for the establishment, operation and transfer of Private Clinics".
- General principles for the construction of electro-mechanical installations of buildings under the responsibility of the Ministry of Health and Social Solidarity of the Ministry of Health and Social Solidarity - Decision on approvals ΔΥ8/Β/οικ.10213/27-01-2005 of the Ministry of Health and Welfare.

Section 1
Legislative framework (2of7)

- Other Technical Instructions the Ministry of Health and Social Solidarity.
- DIN 1946-4 1989 Ventilation and Air Conditioning – Part 4: Ventilation in Buildings and Rooms of Health Care.
- EN ISO 14644-1 Cleanrooms and associated controlled environments - Part 1: Classification of air cleanliness by particle concentration (ISO 14644-1).
- EN ISO 14644-2 Cleanrooms and associated controlled environments - Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration (ISO 14644-2).
- EN ISO 14644-3 Cleanrooms and associated controlled environments - Part 3: Test methods (ISO 14644-3).
- ΕΛΟΤ EN ISO 14644-4 Cleanrooms and Associated Control Environments – Part 4: Design, Construction and Start-up

Section 1
Legislative framework (3of7)

- ΕΛΟΤ EN ISO 14644-5 Cleanrooms and Associated Control Environments – Part 5: Operations.
- ΕΛΟΤ EN ISO 14644-6 Cleanrooms and Associated Control Environments – Part 6: Vocabulary.
- ΕΛΟΤ EN ISO 14644-7 Cleanrooms and Associated Control Environments – Part 7: Separative devices (clean air hoods, gloveboxes, isolators and mini-environments).
- ΕΛΟΤ EN ISO 14644-8 Cleanrooms and Associated Control Environments – Part 8: Classification of airborne molecular contamination.
- ΕΛΟΤ EN ISO 14644-9 Cleanrooms and Associated Control Environments – Part 9: Classification of surface cleanliness by particle concentration.

Section 1
Legislative framework (4of7)

- ΕΛΟΤ EN ISO 14644-10 Cleanrooms and Associated Control Environments – Part 10: Classification of surface cleanliness by chemical concentration.
- ΕΛΟΤ EN ISO 14644-12 Cleanrooms and Associated Control Environments – Part 12: Specifications for monitoring air cleanliness by nanoscale particle concentration.
- ΕΛΟΤ EN ISO 14644-13 Cleanrooms and Associated Control Environments – Part 13: Cleaning of surfaces to achieve defined levels of cleanliness in terms of particle and chemical classifications.
- ΕΛΟΤ EN ISO 14644-14 Cleanrooms and Associated Control Environments – Part 14: Assessment of suitability for use of equipment by airborne particle concentration.
- ΕΛΟΤ EN ISO 14644-15 Cleanrooms and Associated Control Environments – Part 15: Assessment of suitability for use of equipment and materials by airborn chemical concentration
- ΕΛΟΤ EN ISO 14644-16 Cleanrooms and Associated Control Environments – Part 16: Energy efficiency in cleanroom and separative devices.

Section 1
Legislative framework (5of7)

- EU GMP (Good Manufacturing Practices) for Cleanrooms.
- ASHRAE Design Guide for Cleanrooms – Fundamentals, Systems and Performance.
- FDA ISO/TC209 as replacement of FS 209E (replaced 2001/11). In the United States in 2000 ISO 14644/2 was adopted as ANSI/IEST/ISO 14644-2:2000.
- FDA 21 CFR (Code of Federal Regulations) Part 314. For FDA approval to market a new drug.
- FDA 21 CFR (Code of Federal Regulations) Part 210. Current Good Manufacturing Practice in Manufacturing Processing, packing, or Holding of Drugs.
- FDA 21 CFR (Code of Federal Regulations) Part 211. Current Good Manufacturing Practice for Finished Pharmaceuticals.
- FDA 21 CFR (Code of Federal Regulations) Part 212. Current Good Manufacturing Practice for Positron Emission Tomography Drugs.
- FDA 21 CFR (Code of Federal Regulations) Part 600. Biological Products: General.

Section 1
Legislative framework (6of7)

- VDI 3803-1 Air-conditioning Central air-conditioning systems - Structural and technical principles (VDI ventilation code of practice).
- VDI 3803-1 “corrections” Air-conditioning Central air-conditioning systems - Structural and technical principles (VDI ventilation code of practice).
- VDI 3803-4 Air-conditioning Central air-conditioning systems - Air filter systems (VDI ventilation code of practice).
- VDI 6022-1 Ventilation and indoor air quality - Hygiene requirements for ventilation and air-conditioning systems and units (VDI Ventilation Code of Practice).
- VDI 6022-1.2 Ventilation and indoor air quality - Hygiene requirements for ventilation & air-conditioning systems & units - Requirements for underground components (VDI Ventilation Code of Practice).
- VDI 6022-1.3 Ventilation and indoor air quality - Hygiene requirements for ventilation & air-conditioning systems & units - Cleanliness of air handling surfaces (VDI Ventilation Code of Practice).
- VDI 6022-3 Ventilation and indoor air quality - Assessment of indoor air quality.

Section 1
Legislative framework (7of7)

- EN ISO 16890-1 - Air filters for general ventilation - Part 1: Technical specifications, requirements and classification system based upon particulate matter efficiency (ePM) (ISO 16890-1).
- EN ISO 16890-2 - Air filters for general ventilation - Part 2: Measurement of fractional efficiency and air flow resistance (ISO 16890-2).
- EN ISO 16890-3 - Air filters for general ventilation - Part 3: Determination of the gravimetric efficiency and the air flow resistance versus the mass of test dust captured (ISO 16890-3).
- EN ISO 16890-4 - Air filters for general ventilation - Part 4: Conditioning method to determine the minimum fractional test efficiency (ISO 16890-4).
- EN 1822-1 - High efficiency air filters (EPA, HEPA and ULPA) - Part 1: Classification, performance testing, marking.

Section 2
Study requirements

- Space "cleanliness" category, "as-built", "at-rest" (15-20min after the end of the operation of the space) / "in-operation"
- (per ISO 14644-1 and FDA ISO/TC209 as a replacement for FS 209E)
- Air exchange requirements
- Fresh air percentage requirements
- Air exchange requirements
- Temperature Requirements
- Relative Humidity Requirements
- Δp requirements between spaces

Section 2
Study requirements

- Laminar flow requirements
- min velocity on working surface
- Positions for installation of inlets (with filters or not)
- Positions for installation of return outlets (with filters or not)
- Equipment requirements (Filters, PPE, Airtightness of Duct/Equipment networks, etc.)

Section 2
Study requirements

National Legislation

The specialization will be done through the analysis of the Legislative framework.

- Law.4600 – Gazette 43A/2019 Modernization and Reform of the Institutional Framework of Private Clinics, Establishment of a National Public Health Organization, Establishment of a National Institute of Neoplasms and other provisions.

Page 1253

- *The cold and hot water production systems for cooling and heating needs will have a reserve of at least 75% in clinics with more than 100 beds, while in the rest the reserve will cover the air conditioning needs of the Surgeries and Intensive Care Units (ICUs, etc).*

Section 2
Study requirements

National Legislation

The requirements for Heating, Cooling, ventilation, air purification (filtering) and noise level from the air conditioning facilities for the various areas of each clinic must be those defined in Table 1 in combination (not mandatory) with the German regulations (DIN 1946 , issue 4, December 1989). In the cases where the air conditions of the premises are not determined by Table 1 since these premises are air-conditioned in accordance with the above, these conditions must be Temperature 26^{o}C in summer, 22^{o}C in winter and Relative Humidity 55% in summer, 35% in winter.

- Presidential decree 517 - Gazette 202A/1991 on "Terms of conditions and procedure for the establishment, operation and transfer of Private Clinics".

Section 2
Study requirements

National Legislation

- General principles for the construction of electro-mechanical installations of buildings under the responsibility of the Ministry of Health and Social Solidarity of the Ministry of Health and Social Solidarity - Decision on approvals ΔΥ8/Β/οικ.10213/27-01-2005 of the Ministry of Health and Welfare.
- Other Technical Instructions the Ministry of Health and Social Solidarity.

for example:

- Presidential decree 235 - Gazette 199A/2000 Special arrangements for the modernization and operation of private clinics subject to Law 2345/95.
- Presidential decree 198 - Gazette 225A/2007 Amendment of P.D. 235/2000 Official Gazette 199/A/2000 Special arrangements for the modernization and operation of private clinics subject to Law 2345/95.

Section 2
Study requirements

National Legislation

- Specifications for Electromechanical Installations of the main Departments of Hospitals of the Ministry of Health and Social Solidarity - Approval decision ΔΥ8/Β/οικ.49727/26-04-2010 of the Ministry of Health and Welfare.
- Building programs for the study and construction of an Integrated Psychiatric Department for Children or Adolescents, Pediatric or at the General Hospital - Decision ΔΥ8/Β/Γ.Π οικ 46103 May 2003 of the Ministry of Health and Welfare.
- Building programs for the study and construction of an Integrated Psychiatric Department for Adults at the General Hospital - Decision ΔΥ8/Β/Γ.Π οικ 22324 May 2003 of the Ministry of Health and Welfare.

Section 2
Study requirements

National Legislation

- Decision Γ1α/Γ.Π.40043 – Official Gazette 2873B/2019 Determination of specifications and operating regulations for Artificial Kidney Units in Health Centers.

Section 2
Study requirements

DIN 1946-4

- **DIN 1946-4 1989** Ventilation and Air Conditioning – Part 4: Ventilation in Buildings and Rooms of Health Care.

DIN 1946-4:2008-12

5.2.1 General

NOTE

…

Supportive measures include the strict application of the dynamic barrier concept, which consists of flooding the area to be protected in the operating room with a low-turbulence flow and flooding the operating room with overspill air directed to adjoining rooms

Section 2
Study requirements

DIN 1946-4

5.2.2 Room class Ia

…

The size of the protected area depends on the type of operations carried out and shall encompass the operating field(s), the table for the sterile instruments and materials, and the operating room team wearing sterile clothing.

In national and international practice protected areas of 3m x 3m, usually achieved by an LTF plenum of 3,2m x 3,2m, have proven sufficient.

Section 2
Study requirements

DIN 1946-4

Any deviation from these dimensions requires a differentiated analysis of the space required for the protected area, including an analysis of the equipment positions, carried out at the planning stage. This analysis shall cover standard scenarios for the location of operating fields, instrument tables with exposed sterile instruments and materials, and the operating team wearing sterile clothing. The hygienist and designer shall be consulted when critically reviewing possible disturbances.

Section 2
Study requirements

DIN 1946-4

NOTE Class Ia operating rooms are recommended for operations such as the following:

- *orthopedic and trauma surgery (e.g. total endoprostheses (TEP) of the knee or hip);*
- *neurosurgery associated with a particularly high risk of infection;*
- *gynecological surgery (e.g. breast prostheses);*
- *general surgery (e.g. net implants for hernia treatment);*
- *cardiovascular surgery (e.g. vascular prostheses);*
- *transplants (e.g. of whole organs);*
- *operations lasting over several hours (e.g. tumor operations with large operation field);*
- *operations where the total operation time is particularly long (including the approximate operating time, sterilization time of instruments, and incision-to-closure time).*

Section 2
Study requirements

DIN 1946-4

5.2.3 Room class Ib

*Class Ib operating rooms are used for operations which **do not require low-turbulence conditions**. For these operating rooms with mixed flow or restricted displacement flow it is not possible to mark off a defined protected area.*

Class Ib rooms can also be used for operations such as inserting small implants (e.g. coronary stents), invasive angiography, heart catheterizing, MIS procedures and endoscopic examinations of sterile body cavities.

Section 2
Study requirements

DIN 1946-4

Class Ib operating rooms shall be operated with a positive air balance with the outside air flow rate being at least 1 200 m3/h. In order to prevent germs and particles from being transmitted through the air when doors to operating rooms are opened and when persons enter the operating room during an operation, it is recommended that an air lock be built-in, particularly where there is a great difference between the air temperature in the operating room and that in adjoining areas. Such air lock-type rooms can be patient preparation rooms or wash rooms, etc. The locking function can by achieved directly (by supply air connection) or indirectly (by overflow from the operating room).

Section 2
Study requirements

DIN 1946-4

6.5 Air handling units

6.5.1 General requirements

….

Air handling unit components shall meet the requirements of DIN EN 1886 and DIN EN 13053.

7.4.2 Requirements for each room class

Hygienic acceptance tests shall be performed for each room class as specified in Table 3.

Table 3 — Minimum scope of the hygienic acceptance test

….

Section 2
Study requirements

EUROVENT Guidebook – Air Handling Units

7.7 Hygiene

Hygienic air handling units put special requirements on planning, manufacture and shipment as well as on the design of the unit. Care is to be taken concerning the choice of inner surface materials and the arrangement of fans, filters and cooling coils with sloping drip trays to ensure proper condensate water drainage, to avoid condensation and biological contamination. Sealing of pockets and gaps to avoid dirt accumulation. There are general requirements for inspection, maintenance and cleaning and especially regarding filter maintenance.

Section 2
Study requirements

EUROVENT Guidebook – Air Handling Units

9.6 National legislation and guidelines

All the described standards and the Ecodesign Regulation 1253/2014 form the normative basis for planning, construction, and conception of AHUs in non-residential buildings.

Additionally, each market participant has to consider national standards. Examples include DIN 1946-4 in Germany, or the quite similar Austrian version ÖNORM H 6020 – to name just a few. They regulate the minimum requirement of AHUs to reduce the microbial contamination in hospitals or surgeries.

Section 2
Study requirements

PHARMA – V model

PHARMA

V model

- Chem engineering uses the V-model for systematic qualification. The GMP critical points of user requirements, system specifications and technical specifications are reflected in the individual tests.

- **Qualification plan:** System-specific qualification activities, responsibilities, scheduling and documents to be created are defined. System specifications (FS, HDS, SDS, R & I / EMSR scheme): Description of the technical equipment as a basis for development, construction and installation.
- **SAT test:** Technical acceptance in the supplier's factory / technical acceptance after delivery and installation by the operator / user.

Section 2
Study requirements

PHARMA – V model

- **Design qualification (DQ):** Documented proof that quality-relevant requirements were taken into account during planning. The compliance with URS and system specifications is checked.
- **Installation qualification (IQ):** Documented proof that equipment and systems have been delivered and installed in accordance with GMP-critical requirements and statutory safety regulations. Measuring and control technology, built-in materials, surfaces and quality-relevant measuring points are tested.
- **Operational qualification (OQ):** Documented proof that the system functionality defined in accordance with the system specifications is completely fulfilled within the entire working area and within specified limits. Qualification report: Approval of the OQ report can be started with a subsequent PQ or process validation.
- **Performance qualification (PQ):** Documented proof that all the relevant plant components and systems meet the defined specifications and requirements in an operating condition.

Section 2
Study requirements

EN ISO 14644 (parts 1-16)

- EN ISO 14644-1 Cleanrooms and associated controlled environments - Part 1: Classification of air cleanliness by particle concentration (ISO 14644-1).

3.3 Occupancy states

3.3.1 as-built

Conditions where the cleanroom or clean zone is complete with all services connected and functioning but with no equipment, furniture, materials or personnel present.

3.3.2 at-rest

Conditions where the cleanroom or clean zone is complete with equipment installed and operating in a manner agreed upon, but with no personnel present.

3.3.1 operational

Conditions where the cleanroom or clean zone is functioning in the specified manner, with equipment operating and with the specified number of personnel present.

Section 2
Study requirements
EN ISO 14644-1

4.3 ISO Class number - Table 1 – ISO Classes of air cleanliness by particle concentration

ISO Class number (N)	Maximum allowable concentrations (particles/m³) for particles equal to and greater than the considered sizes, shown below[a]					
	0,1µm	0,2µm	0,3µm	0,5µm	1µm	5µm
1	10 [b]	d	d	d	d	e
2	100	24 [b]	10 [b]	d	d	e
3	1 000	237	102	35 [b]	d	e
4	10 000	2 370	1 020	352	83 [b]	e
5	100 000	23 700	10 200	3 520	832	d, e, f
6	1 000 000	237 000	102 000	35 200	8 320	293
7	c	c	c	352 000	83 200	2 930
8	c	c	c	3 520 000	832 000	29 300
9 [o]	c	c	c	35 200 000	8 320 000	293 000

[a] All concentrations in the table are cumulative, e.g. for ISO Class 5, the 10 200 particles shown at 0,3µm include all particles equal or greater than this size.

[b] These concentrations will lead to large air sample volume for classification. Sequential sampling may be applied; see Annex D.

[o] Concentration limits are not applicable in this region of the table due to very high particle concentration.
(Too many particles of these sizes – coincidence error)

[d] Sampling and statistical limitations for particles in low concentrations make classification inappropriate.
(Too few particles of these sizes – coincidence error)

[e] Sample collection limitations for both particles in low concentration and sizes greater than 1µm make classification at this particles size inappropriate, due to potential losses in the sampling system.
(Low concentration & losses in sampling)

[f] In order to specify this particle size in association with ISO Class 5, the macroparticle descriptor M may be adapted and used in conjunction with at least one other particle size. (See C.7).
(Particles ≥ 5.0µm not included in ISO Class 5. See clause C7)

[g] This class is only applicable for the in-operation state.

Section 2
Study requirements
EN ISO 14644-1

- **4.3 ISO Class number - Table 1 – ISO Classes of air cleanliness by particle concentration**

Designation ISO Class number; occupancy state; considered particle size(s) for example, **ISO Class 4; at-rest; 0,2μm; 0,5μm** (If measurements are to be made at more one considered particle size, each larger particle diameter (e.g. D2) shall be at least 1,5 times the next smaller particle diameter (e.g. D1), i.e. D2 ≥ 1,5 x D1.
At-rest or operational classification may be performed periodically based upon risk assessment of the application, typically on an annual basis.
Annex C **Counting and sizing of airborne macroparticles** **C2 Considerations or particles larger tan 5μm (macroparticles) – M descriptor.** **C2.2 M descriptor format** The M descriptor may be specified as a complement to the air cleanliness class by particle concentration. The M descriptor is expressed in the format: "ISO M (a; b;); c" Where: a is the maximum permitted concentration of macroparticles (expressed as macroparticles per cubic meter of air); b is the equivalent diameter (or diameters) associates with the specified method for measuring macroparticles

Section 2
Study requirements
EN ISO 14644-1

4.3 ISO Class number - Table 1 – ISO Classes of air cleanliness by particle concentration

(expressed in macroparticles); c is the specifies measurement method. Example: **"ISO M (29; 5μm); LSAPC"**

Sampling measuring devices
• Light scattering device
  • Light Scattering Airborne Particle Counter
  • LSAPC
  • Counts number & Size BY Number and Intensity of flashes
 	
• ISO 21501- 4 specifies performance and calibration of LSAPCs

Section 2
Study requirements
EU GMP

EU-GMP (Volume 4 – Annex 1) Table 1: Maximum permitted total particle concentration for classification

Grade	Maximum limits for total particle ≥ 0.5 µm/m3		Maximum limits for total particle ≥ 5 µm/m3	
	at rest	in operation	at rest	in operation
A	3 520	3 520	Not specified [a]	Not specified [a]
B	3 520	352 000	Not specified [a]	2 930
C	352 000	3 520 000	2 930	29 300
D	3 520 000	Not predetermined [b]	29 300	Not predetermined [b]

[a] Classification including 5µm particles may be considered where indicated by the CCS or historical trends.
[b] For grade D, in operation limits are not predetermined. The manufacturer should establish in operation limits based on a risk assessment and routine data where applicable.

Airborne Particulate Cleanliness Class Comparison								
ISO 14644-1	EU GPM Annex 1		FEDERAL STANDARD 209E					ISO 14644-4
ISO Class	EU Class at-rest	EU Class operational	English	Metric	ACR Air Change Rate (Rajan Jaisinghani 1990s)	Ceiling Coverage (%)	Average Airflow Velocity (m/s)	Air flow type
ISO 1						80-100%	0.305-0.508	UDAF
ISO 2						80-100%	0.305-0.508	UDAF
ISO 3			1	M1.5	360-540	60-100%	0.305-0.457	UDAF
ISO 4			10	M2.5	300-540	50-90%	0.254-0.457	UDAF
ISO 5	A and B	A	100	M3.5	240-480	35-75%	0.203-0.406	UDAF
ISO 6			1 000	M4.5	150-240	25-40%	0.127-0.203	non-UDAF
ISO 7	C	B	10 000	M5.5	60-90	15-20%	0.051-0.076	non-UDAF
ISO 8	D	C	100 000	M6.5	5-48	5-15%	0.005-0.041	non-UDAF
ISO 9			Room Air					non-UDAF

Section 2
Study requirements

EN ISO 14644-2

- EN ISO 14644-2 Cleanrooms and associated controlled environments - Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration (ISO 14644-2).

Risk Assessment

Selection of appropriate risk assessment tool

- HACCP (Hazard analysis and critical control points)
- FMEA/FMECA (Failure Mode and Effects Analysis / Failure Mode, Effects & Criticality Analysis /
- PHA (Process Hazard Analysis)
- FTA (Fault Tree Analysis)
- HAZOP (Hazard and Operability Analysis)

Section 2
Study requirements

EN ISO 14644-2

Monitoring plan (strategy) based on Risk Assessment

- Correctly understand:
- process
- critical areas/locations
- possible sources of Contamination
- elements that may Compromise
  - cleanroom performance or
  - product quality

Section 2
Study requirements

EN ISO 14644-2

- Typical risk assessment takes into consideration
  - Operator movement
  - Previous cleanroom certifications
  - Areas where the product is particularly at risk
- Monitoring can be “continuous”, “sequential” or “periodic” (able to provide clear evidence of cleanroom performance).
  - Sample Point Location
  - Instrument Selection
- Alert and Action Limits
  - Early warning
  - Immediate intervention

Section 2
Study requirements

EN ISO 14644-2

- How to choose the right strategy
  - long term evaluation
  - yearly assessment of limits, method and frequency
- Yearly assessment does not always mean yearly change
- Frequently question whether monitoring plan is still applicable and consistent with the cleanroom's actual performance and activities

Section 2
Study requirements

EN ISO 14644-2 (old)

Old *EN ISO 14644-2:2000 had schedules for:*

Table 1 – Schedule of testing to demonstrate compliance with particle concentration limits

Classification	Maximum time interval	Test method
≤ ISO Class 5	6 months	Annex B in ISO 14644-1:1999
> ISO Class 5	12 months	Annex B in ISO 14644-1:1999
NOTE Particle count tests will normally be performed in the "operational" state, but may also be performed in the "at-rest" state in accordance with the designated ISO classification.		

Section 2
Study requirements

EN ISO 14644-2 (old)

Table 2 – Schedule of additional tests for all classes

Test parameter	Maximum time interval	Test procedure
Airflow volume [a] or airflow velocity	12 months	ISO 14644-3 / Clause B.4
Air pressure difference [b]	12 months	ISO 14644-3 / Clause B.5
NOTE These tests may normally be performed in either the “operational” or “at-rest” state in accordance with the designated ISO classification.		
[a] Airflow volume may be determined by either velocity or volume measurement techniques [b] This test will not apply to clean zones which are not totally enclosed.		

Section 2
Study requirements

EN ISO 14644-2 (old)

Table A.1 – Schedule of optional tests

Test parameter	Class	Suggested maximum time interval	Test procedure
Installed filter leakage	All Classes	24 months	ISO 14644-3 / Clause B.6
Airflow visualization	All Classes	24 months	ISO 14644-3 / Clause B.7
Recovery	All Classes	24 months	ISO 14644-3 / Clause B.13
Containment leakage	All Classes	24 months	ISO 14644-3 / Clause B.14

Section 2
Study requirements

EN ISO 14644-2

Monitoring Plan Alternatives

- **Continuous**
  - Uses multiple particle counters, one for each individual location
  - Continuous flow of data over time
  - Immediate evaluation of unexpected contamination events
- **Periodic**
  - ISO 14644-2:2015 requires the test frequency to be defined and clearly specified
  - Scheduled particle monitoring frequency (i.e. once per week)
- **Sequential**
  - Performed using sequential multiplexing systems.
  - High risk of particle loss in long tubing while measuring particles greater than 1μm
  - Generally unacceptable for pharmaceutical industry

Section 2
Study requirements

EN ISO 14644-3

- EN ISO 14644-3 Cleanrooms and associated controlled environments - Part 3: Test methods (ISO 14644-3).

Table 1 – Requires test for installation

Required tests	Reference in ISO 14644-3:2005			Referenced in
	Principle	Procedure	Apparatus	
Airborne particle count for classification and test measurement of cleanrooms and clean air devices	4.2.1	B.1	C.1	ISO 14644-1 and ISO 14644-2

Section 2
Study requirements

EN ISO 14644-3

Table 1 – Requires test for installation

Required tests	Reference in ISO 14644-3:2005			Referenced in
	Principle	Procedure	Apparatus	
Airborne particle count for ultrafine particles	4.2.1	B.2	C.2	ISO 14644-1
Airborne particle count for macroparticles	4.2.1	B.3	C.3	ISO 14644-1
Airflow test [a]	4.2.2	B.4	C.4	ISO 14644-1 and ISO 14644-2
Airflow pressure difference test [a]	4.2.3	B.5	C.5	ISO 14644-1 and ISO 14644-2
Installed filter system leakage test	4.2.4	B.6	C.6	ISO 14644-2
Airflow direction test and visualization	4.2.5	B.7	C.7	ISO 14644-2
Temperature test	4.2.6	B.8	C.8	ISO 7726
Humidity test	4.2.6	B.9	C.9	ISO 7726
Electrostatic and ion generator test	4.2.7	B.10	C.10	
Particle deposition test	4.2.8	B.11	C.11	
Recovery test	4.2.9	B.12	C.12	ISO 14644-2
Containment leak test	4.2.10	B.13	C.13	ISO 14644-1 and ISO 14644-2

[a] This is a test based on ISO 14644-2. These optional tests are not presented in order of importance. The order in which tests should be performed may be based upon the requirements of specific document or after agreement between customer an supplier.

Section 2
Study requirements

EN ISO 14644-3

- Leakage tests of filters mounted in ducts or air-handling units (AHUs)
- Annex C: Test Apparatus specifications

Section 2
Study requirements

EN ISO 14644-4

- ΕΛΟΤ EN ISO 14644-4 Cleanrooms and Associated Control Environments – Part 4: Design, Construction and Start-up.

3.1.1 air change effectiveness (ACE)

Ratio between the recovery rate at a location or location in cleanroom and the overall recovery rate of the cleanroom after contamination event.

Note 1 to entry: Thew recovery rate is defines and measures in accordance with ISO 14644-3

3.1.2 classification

3.1.3 cleanliness

3.1.4 cleanroom

Section 2
Study requirements

EN ISO 14644-4

3.1.5 clean zone (e.g A + B)

3.1.8 containment removal effectiveness CRE

3.1.10 non-unidirectional airflow

3.1.16 unidirectional airflow

3.1.18 verification

6.1 Cleanroom requirements

- Use, operation to be carried out therein

Section 2
Study requirements

EN ISO 14644-4

- Air cleanliness (ISO 14644-1)
- Recovery time, recovery rate or both (ISO 14644-3)
- Ventilation effectiveness

- Temperature
- Humidity

- Non-unidirectional airflow (non-UDAF)
- Unidirectional airflow (UDAF, direction of air flow: Vertical, Horizontal direction)
- Combined airflow

Section 2
Study requirements

EN ISO 14644-2

- Velocity
- Extra Extract Air (position, flow, pass-through, etc)
- Δp

- Processes and operator comfort
- Equipment
- Materials
- Source of contamination and their strength data (envelope, machinery, equipment, materials, off-gassing materials, process, people, supply air, leakages)

Section 2
Study requirements

EN ISO 14644-4

B.2.1 Zoning

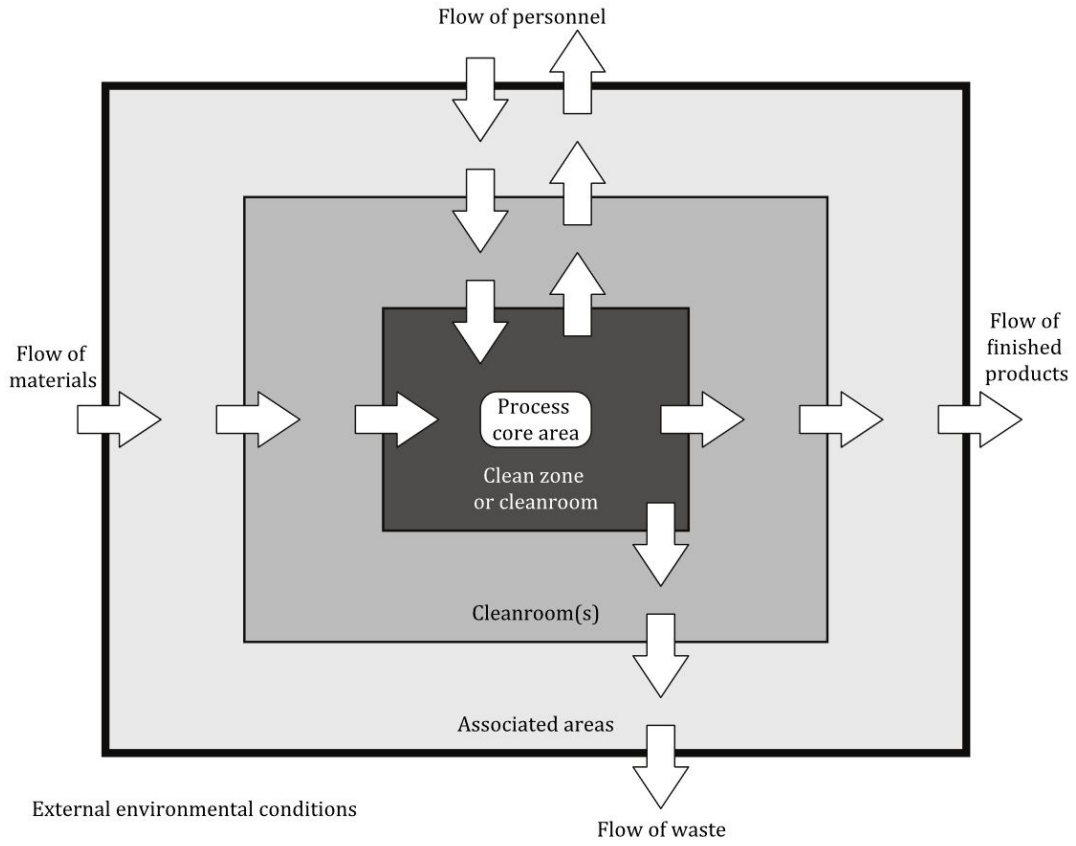
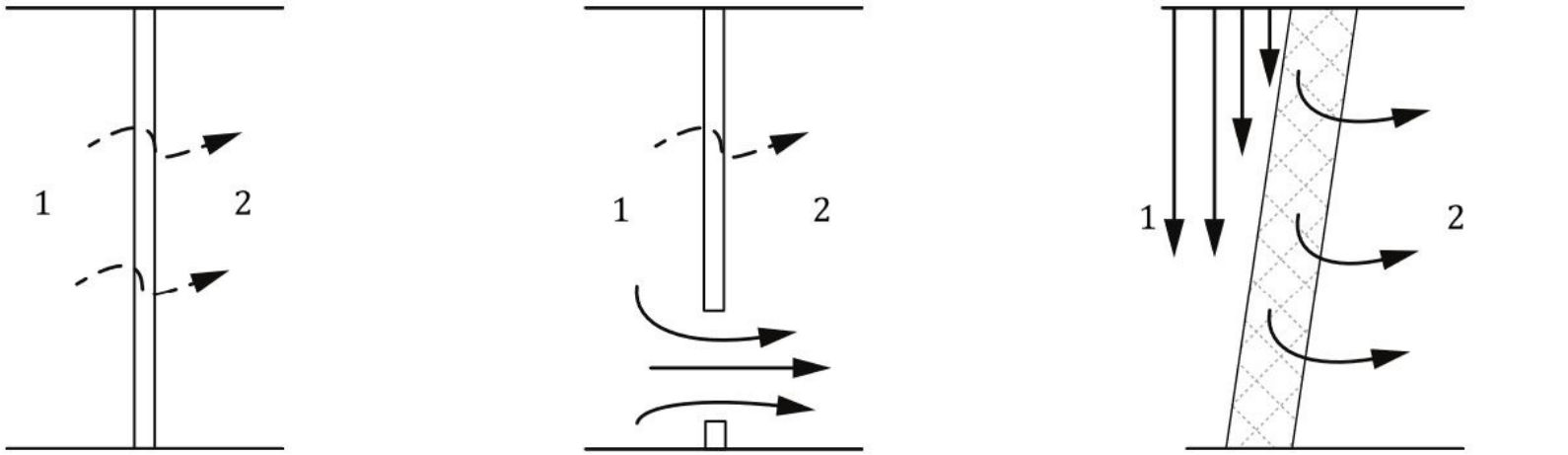


Figure B.1 — Example of a box-in-box contamination control concept

Section 2
Study requirements

EN ISO 14644-4

- **B.2.2.1 Segregation (διαχωρισμός) General**
- Cleanroom installations can consist of multiple zones and/or rooms with different requirements for contamination control (less clean, high clean spaces)



a) By physical barrier with leakage: static pressure $P_1 > P_2$

b) By physical barrier with leakage and overflow: static pressure $P_1 > P_2$

c) Aerodynamic: no practical difference between static pressure P_1 and P_2

Figure B.2 — Concepts of segregation

Section 2
Study requirements

EN ISO 14644-4

b) is for e.g. Continuous product transfer

e.g. Walls Floors, Ceilings Doors, Screens (encloser) Δp 7.5Pa – 15Pa for multiple connected rooms, smaller Δpressure (typically at least 5Pa) Cascade pressure 5, 10, 15, 20, 25, 30, 35Pa

Pressure in gaps 7.5Pa ==> 3.5m/s - 15Pa ==> 5.0m/s

c) Aerodynamic segregation concept (air thermal load between zones, physical obstacles, air exhausts, heat sources, contamination sources)

e) Other: equipment encloser

Section 2
Study requirements

EN ISO 14644-4

B.2.3.1 Airflow concepts

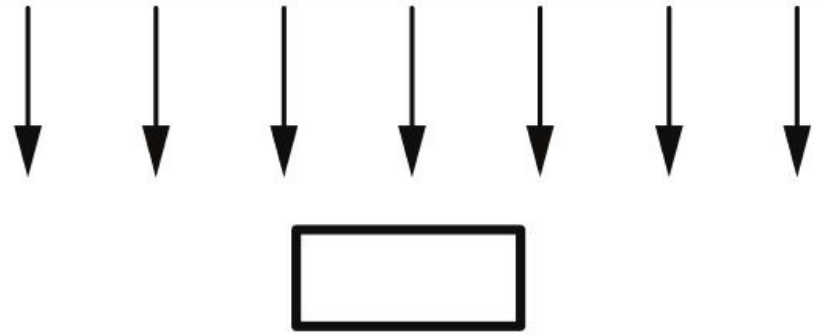
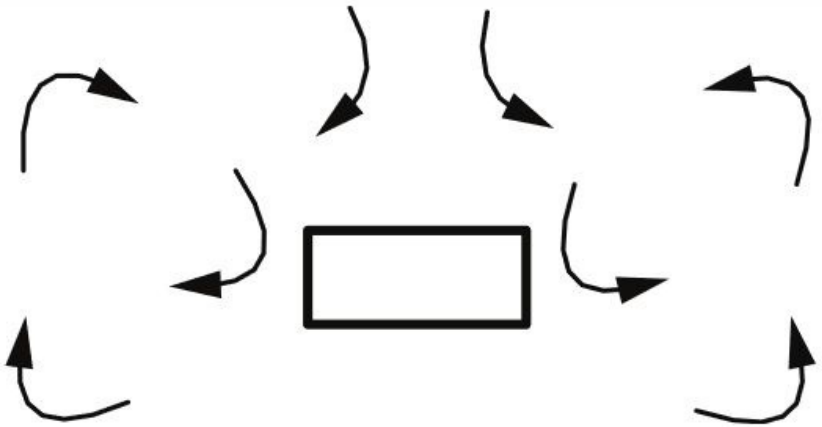
Airflow: unidirectional	Airflow: non-unidirectional
	
Ventilation mechanism: displacement	Ventilation mechanism: dilution

Figure B.3 — Examples of airflow concepts

Section 2
Study requirements

EN ISO 14644-2

Unidirectional airflow (UDAF, direction of air flow: Vertical, Horizontal direction) (ISO class 5 and cleaner classes)

Displacement of contaminates air by the filtered supply of clean air. (vertical/downwards or horizontals, but also diagonal or upwards) with steady velocity till working surface.

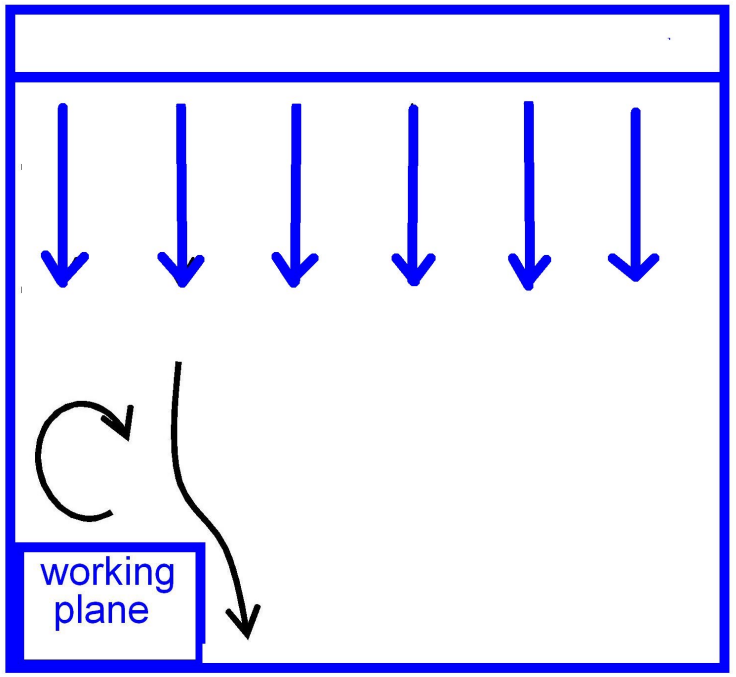
Air Velocity is typically 0.20m/s to 0.60m/s at a test distance of 150mm to 300mm from the supply air inlet face (HEPA, ULPA). Some processed demand 0.45m/s at working surface.

Section 2
Study requirements

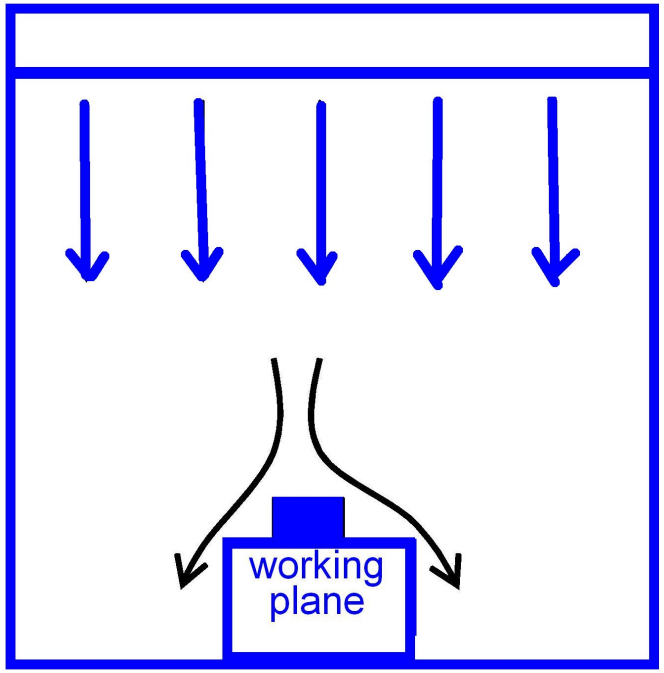
EN ISO 14644-4

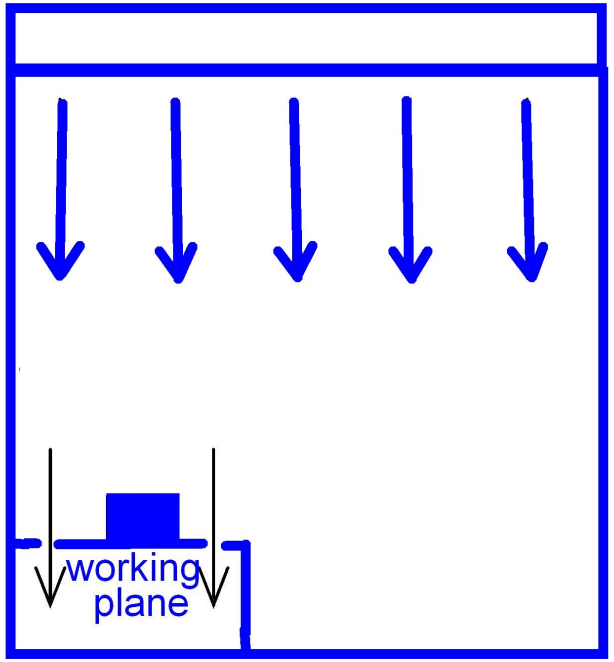
Influence of personnel and objects on UDAF

Air stream pattern disturbance



Improvement throught changes to layout

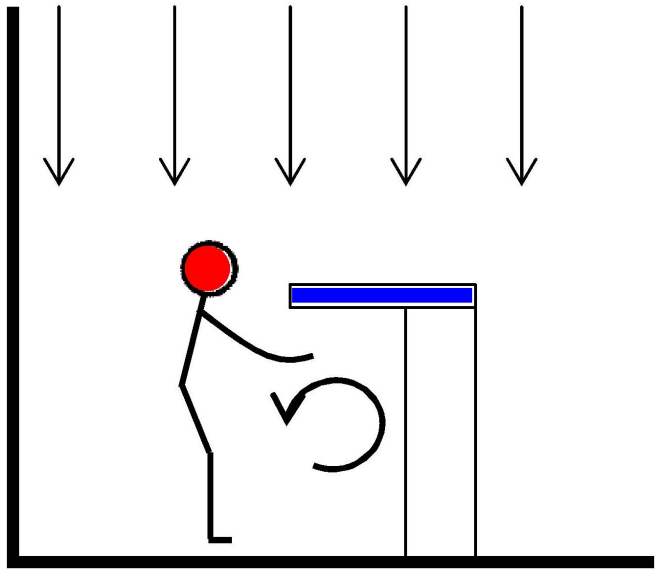




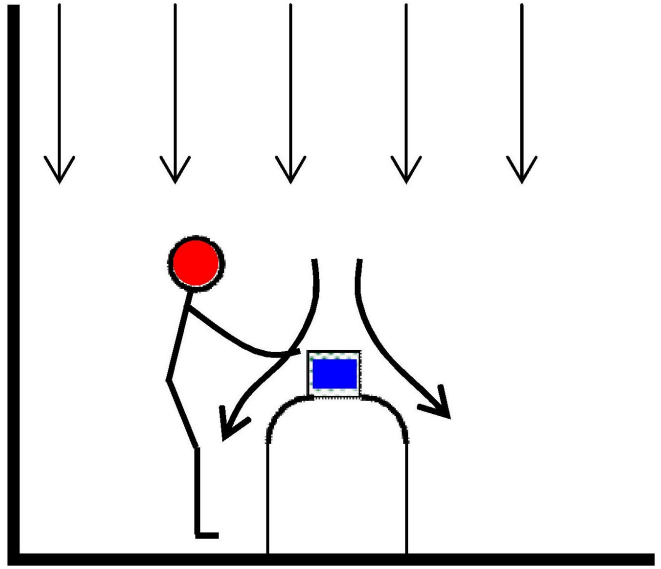
Section 2
Study requirements

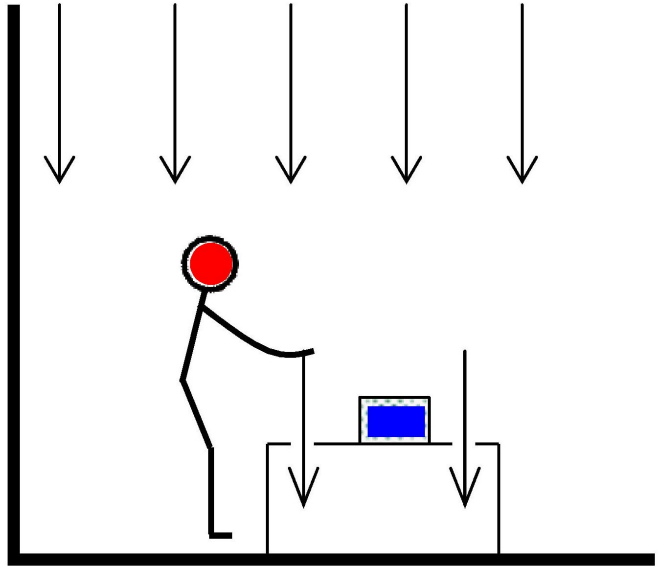
EN ISO 14644-4

Airstream pattern disturbance



Improvement throught changes to structure shape

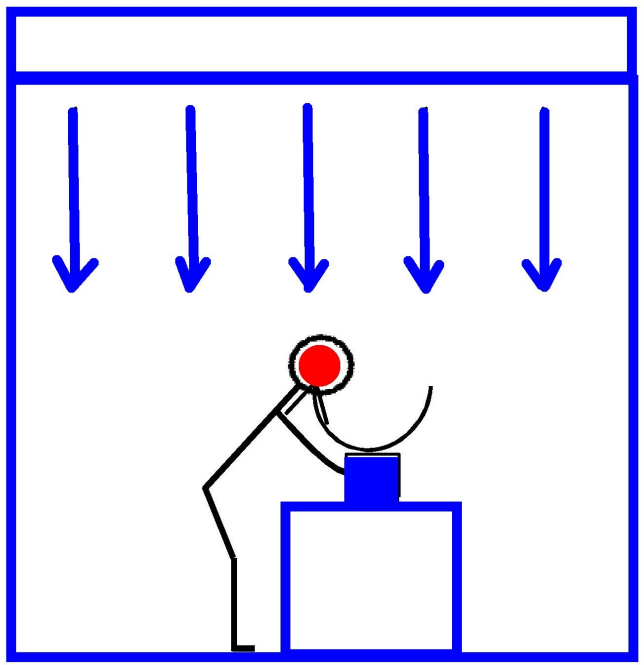




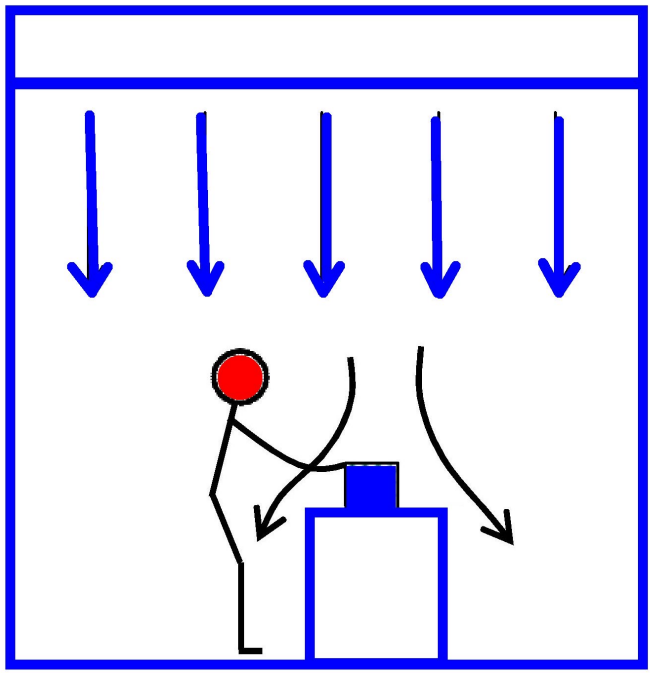
Section 2
Study requirements

EN ISO 14644-4

Airstream pattern disturbance



Improvement throught changes to operator's behaviour



Section 2
Study requirements

EN ISO 14644-4

Non-unidirectional airflow (non-UDAF) (ISO class 6 or less clean)

Non-unidirectional airflow provides control of the environment through dilution of ant airborne contamination by the introduction of clean supply air into the cleanroom, mixed with contaminated room air and then removed away.

Combined airflow for critical areas by means of a separative device such as a UDAF ceiling or enclosure (clean air hoods, gloveboxes, isolators and mini-environments).

Exhaust point placement near contamination sources

Section 2
Study requirements

EN ISO 14644-4

B.3.1 Calculation of air volume for non-UDAF cleanroom

$$Q = \frac{\quad}{) \cdot} \qquad \text{(B.1)}$$

where

Q is supply air volume flow rate to the cleanroom ($m^3 \cdot s^{-1}$);

S is rate of particle emission in cleanroom air (source strength) (number$\cdot s^{-1}$);

C is particle concentration limit in the cleanroom (number$\cdot m^{-3}$);

ε is ventilation effectiveness (dimensionless).

Section 2
Study requirements

EN ISO 14644-4

Plus airflow for the cooling loads.

This formula assumes that the number of particles entering cleanroom or clean zone from supply air is negligible. (HEPA or ULPA filters of combination)

Fresh air 10% (extra humidity - control)

Contamination Control examples (airflow patterns)

- **Protection of products**

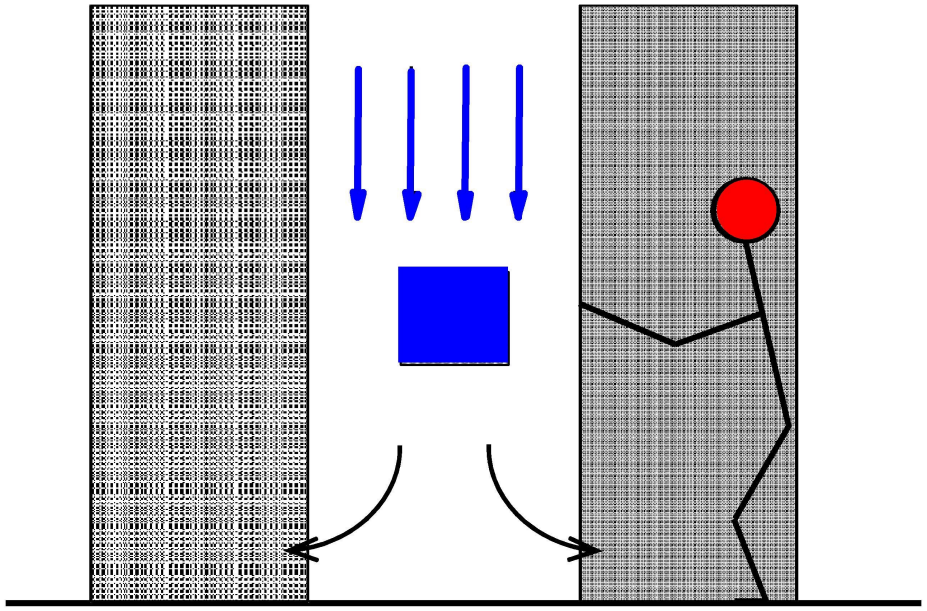
Section 2
Study requirements

EN ISO 14644-4

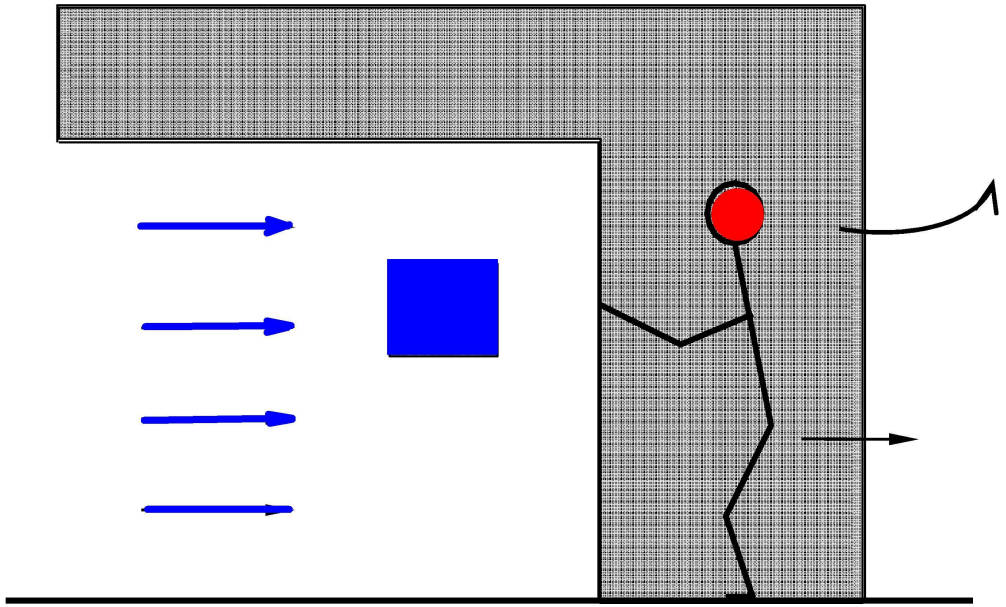
Contamination Control examples (airflow patterns)

Protection of products

Vertical flow



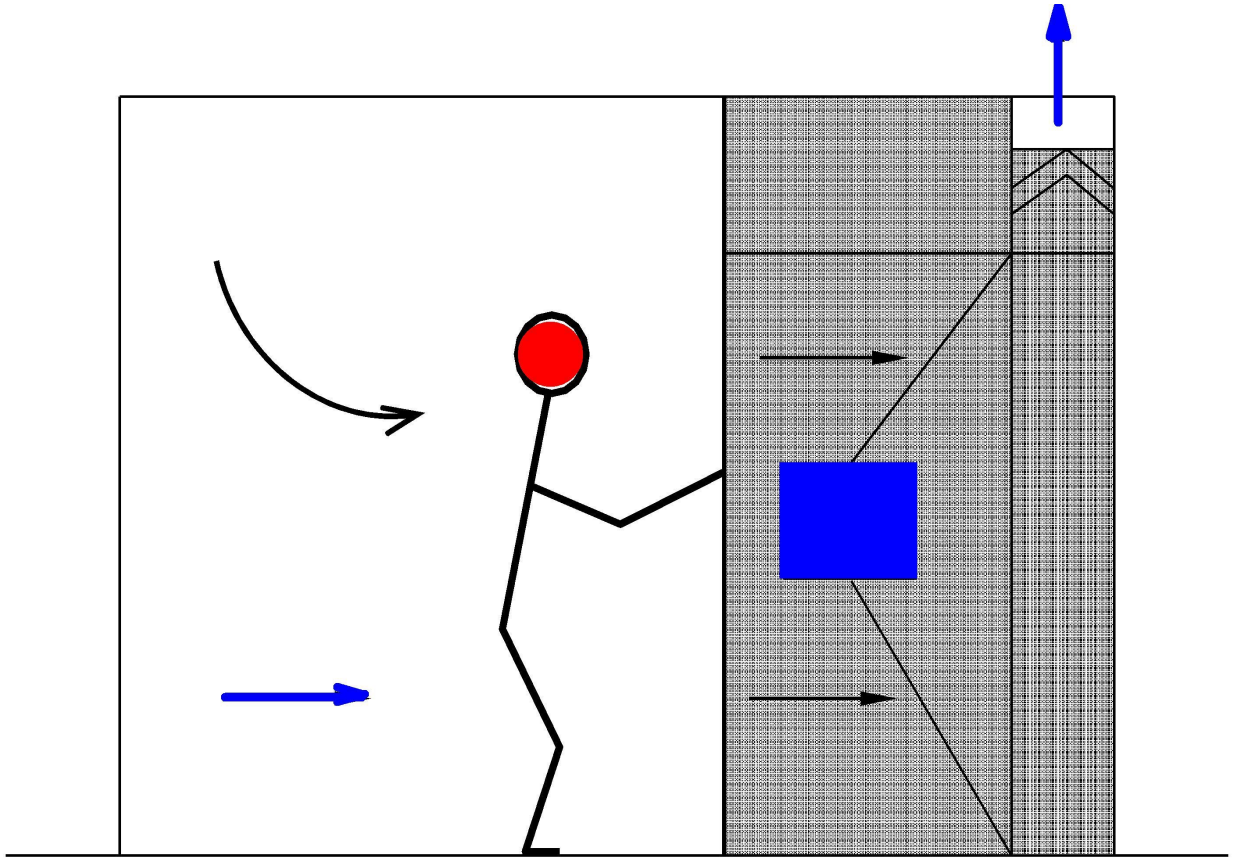
Horizontal flow

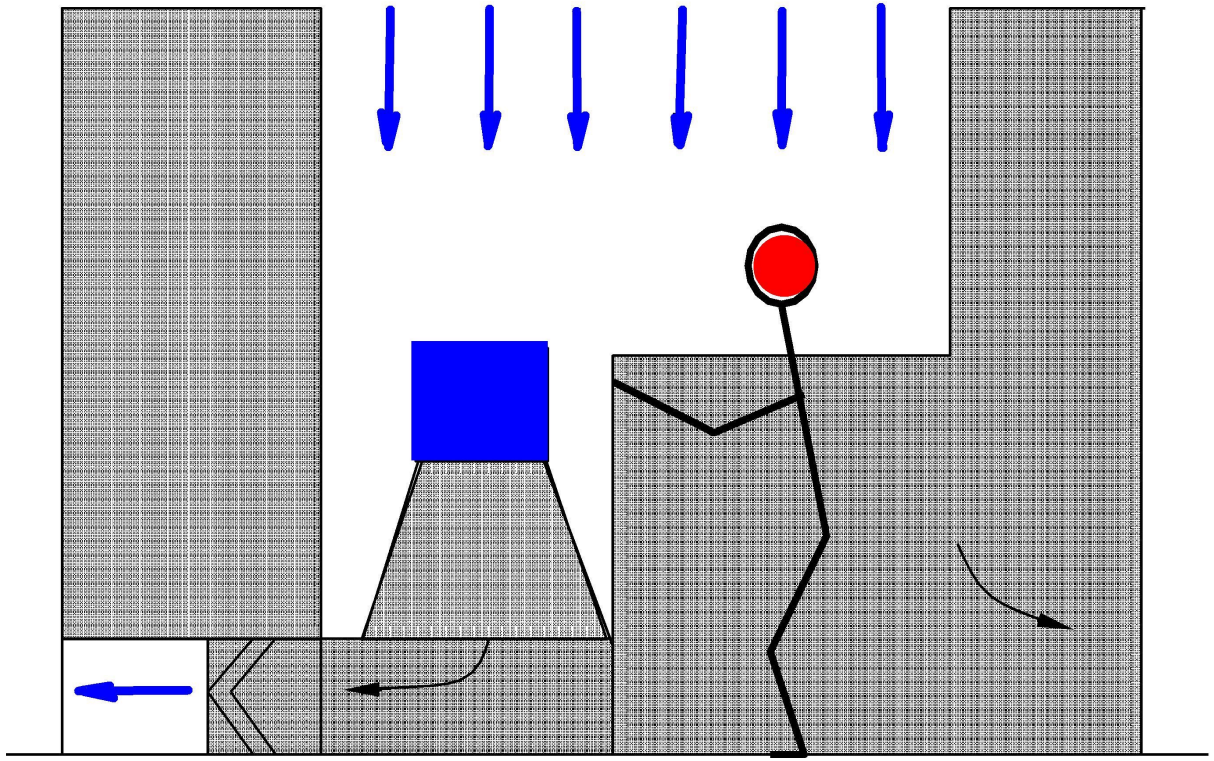


Section 2
Study requirements

EN ISO 14644-4

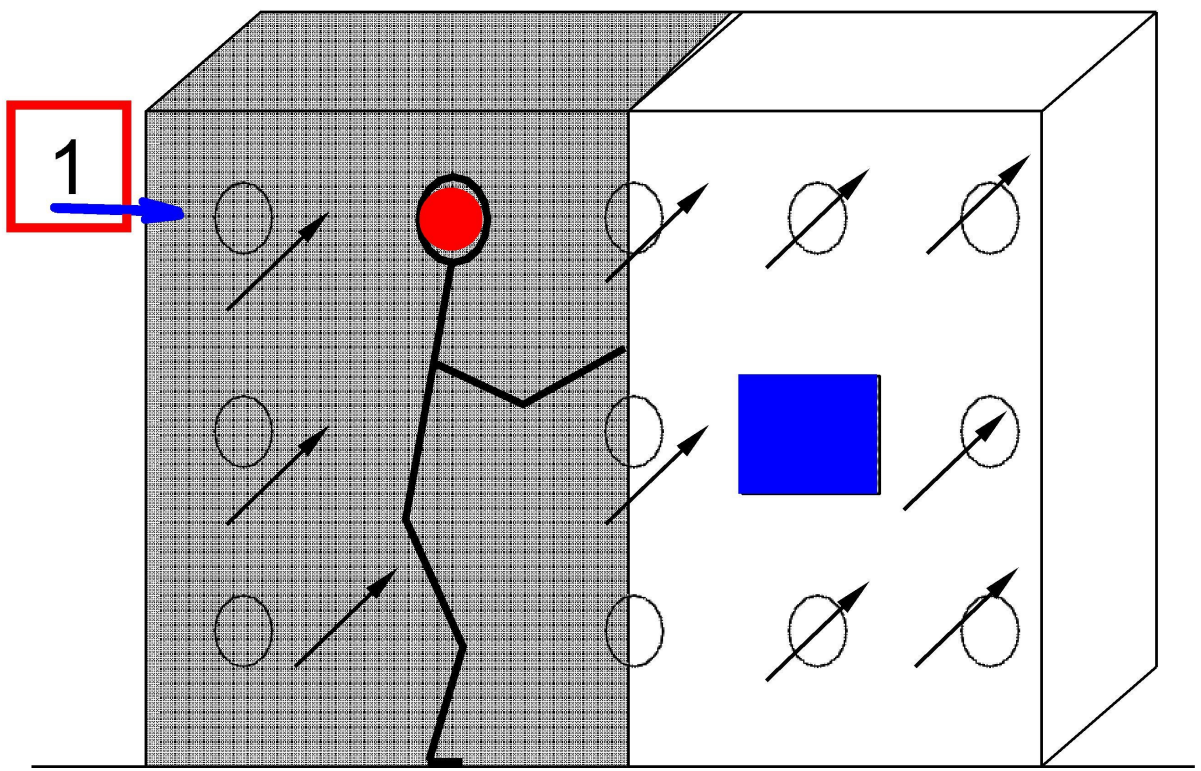
Protection of personnel and environments

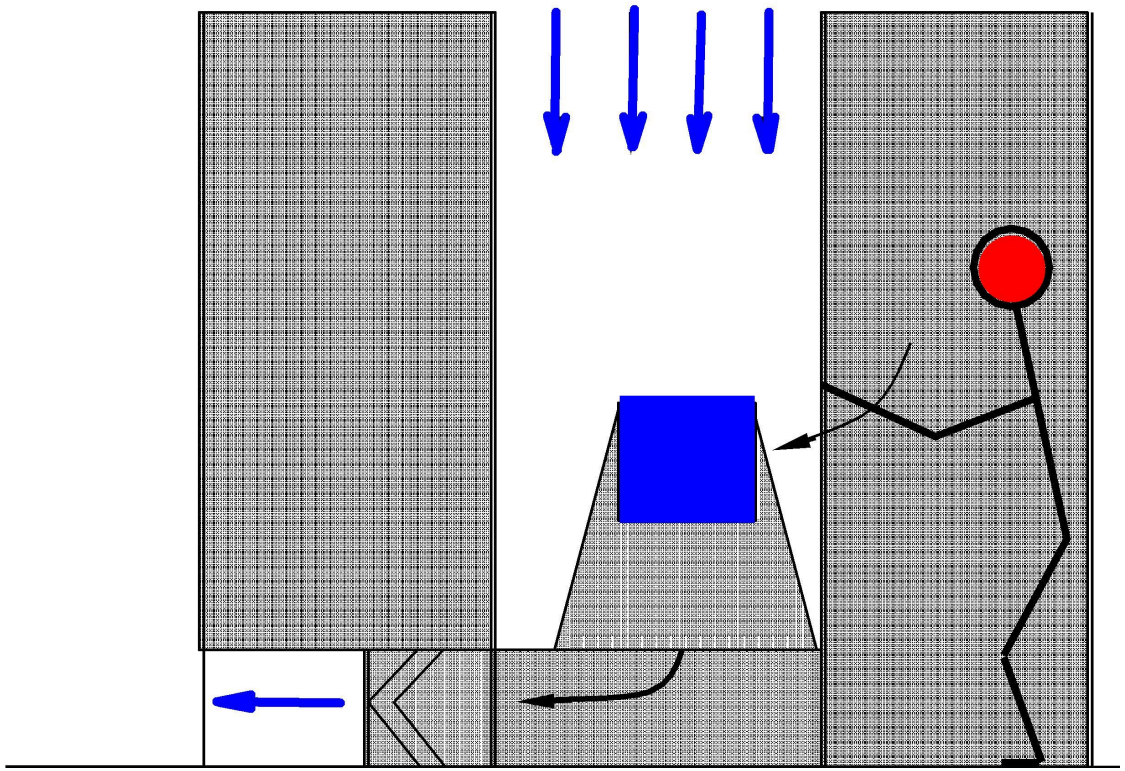




Section 2
Study requirements

EN ISO 14644-4



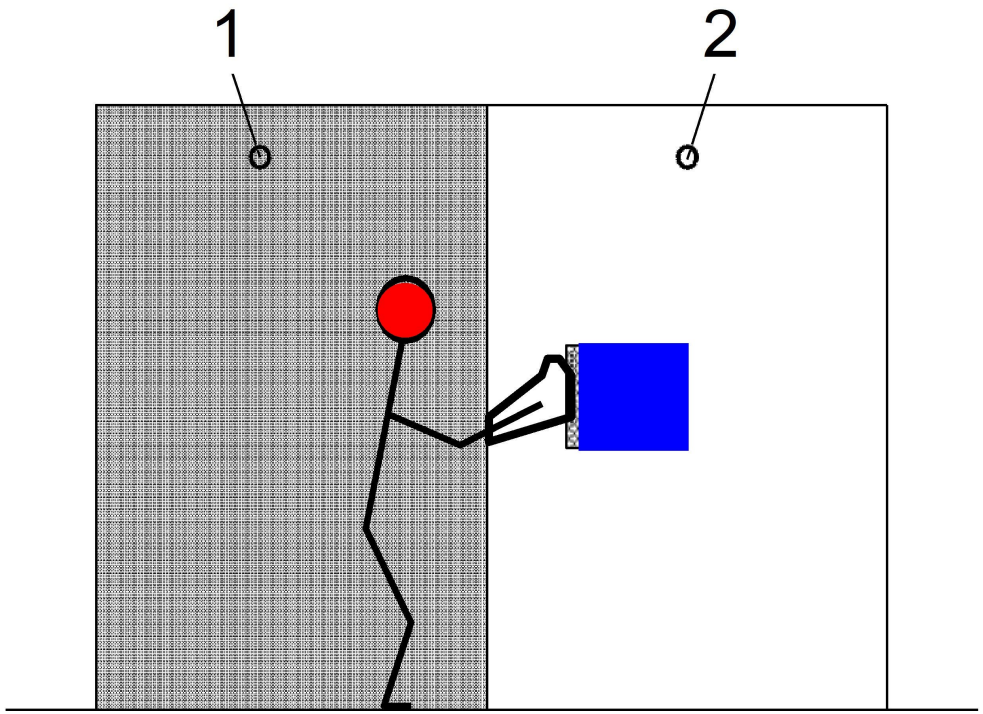


Where: 1 = Flow direction perpendicular to colored plane

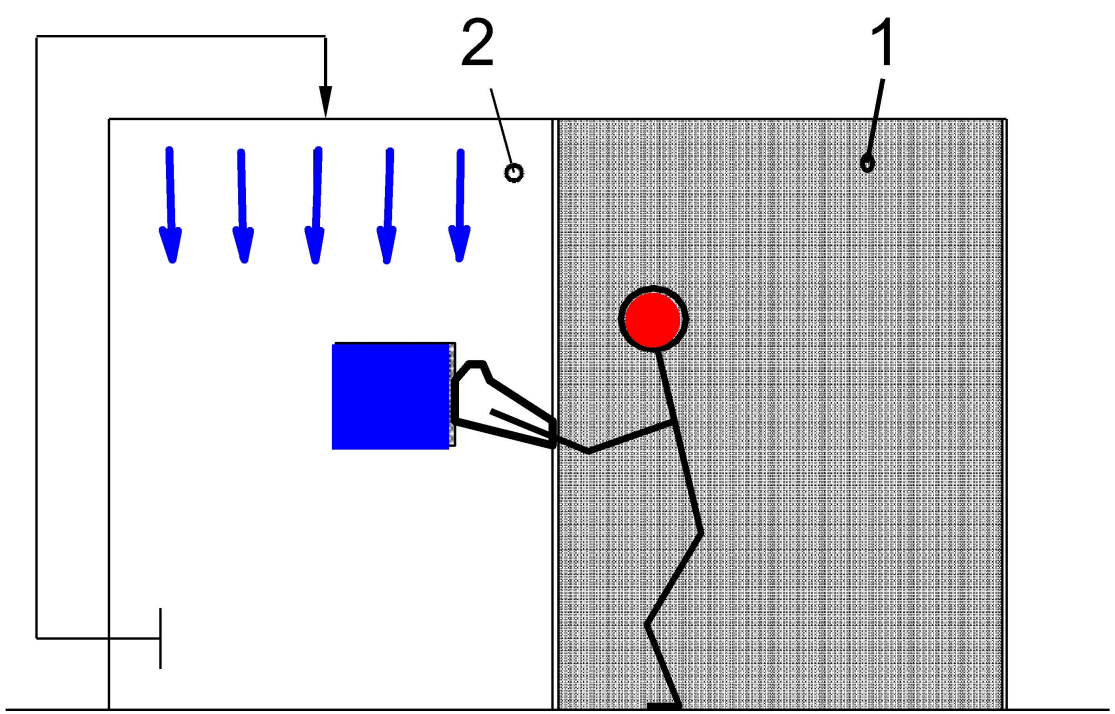
Section 2
Study requirements

EN ISO 14644-4

Passive system



Airflow/Active system



Where: 1 = Safety zone for personnel

2 = Protection zone for product

Section 2
Study requirements

EU GMP – ASHRAE – FDA

- EU GMP (Good Manufacturing Practices) for Cleanrooms.
- ASHRAE Design Guide for Cleanrooms – Fundamentals, Systems and Performance.
- FDA ISO/TC209 as replacement of FS 209E (replaced 2001/11).
- FDA 21 CFR (Code of Federal Regulations) Part 314. For FDA approval to market a new drug.
- FDA 21 CFR (Code of Federal Regulations) Part 210. Current Good Manufacturing Practice in Manufacturing Processing, packing, or Holding of Drugs.
- FDA 21 CFR (Code of Federal Regulations) Part 211. Current Good Manufacturing Practice for Finished Pharmaceuticals.
- FDA 21 CFR (Code of Federal Regulations) Part 212. Current Good Manufacturing Practice for Positron Emission Tomography Drugs.
- FDA 21 CFR (Code of Federal Regulations) Part 600. Biological Products: General.

Section 2
Study requirements

VDI 3803

- VDI 3803-1 Air-conditioning Central air-conditioning systems - Structural and technical principles (VDI ventilation code of practice).
- VDI 3803-1 “corrections” Air-conditioning Central air-conditioning systems - Structural and technical principles (VDI ventilation code of practice).
- VDI 3803-4 Air-conditioning Central air-conditioning systems - Air filter systems (VDI ventilation code of practice).

Section 2
Study requirements

VDI 6022

- VDI 6022-1 Ventilation and indoor air quality - Hygiene requirements for ventilation and air-conditioning systems and units (VDI Ventilation Code of Practice).
- VDI 6022-1.2 Ventilation and indoor air quality - Hygiene requirements for ventilation & air-conditioning systems & units - Requirements for underground components (VDI Ventilation Code of Practice).
- VDI 6022-1.3 Ventilation and indoor air quality - Hygiene requirements for ventilation & air-conditioning systems & units - Cleanliness of air handling surfaces (VDI Ventilation Code of Practice).
- VDI 6022-3 Ventilation and indoor air quality - Assessment of indoor air quality.

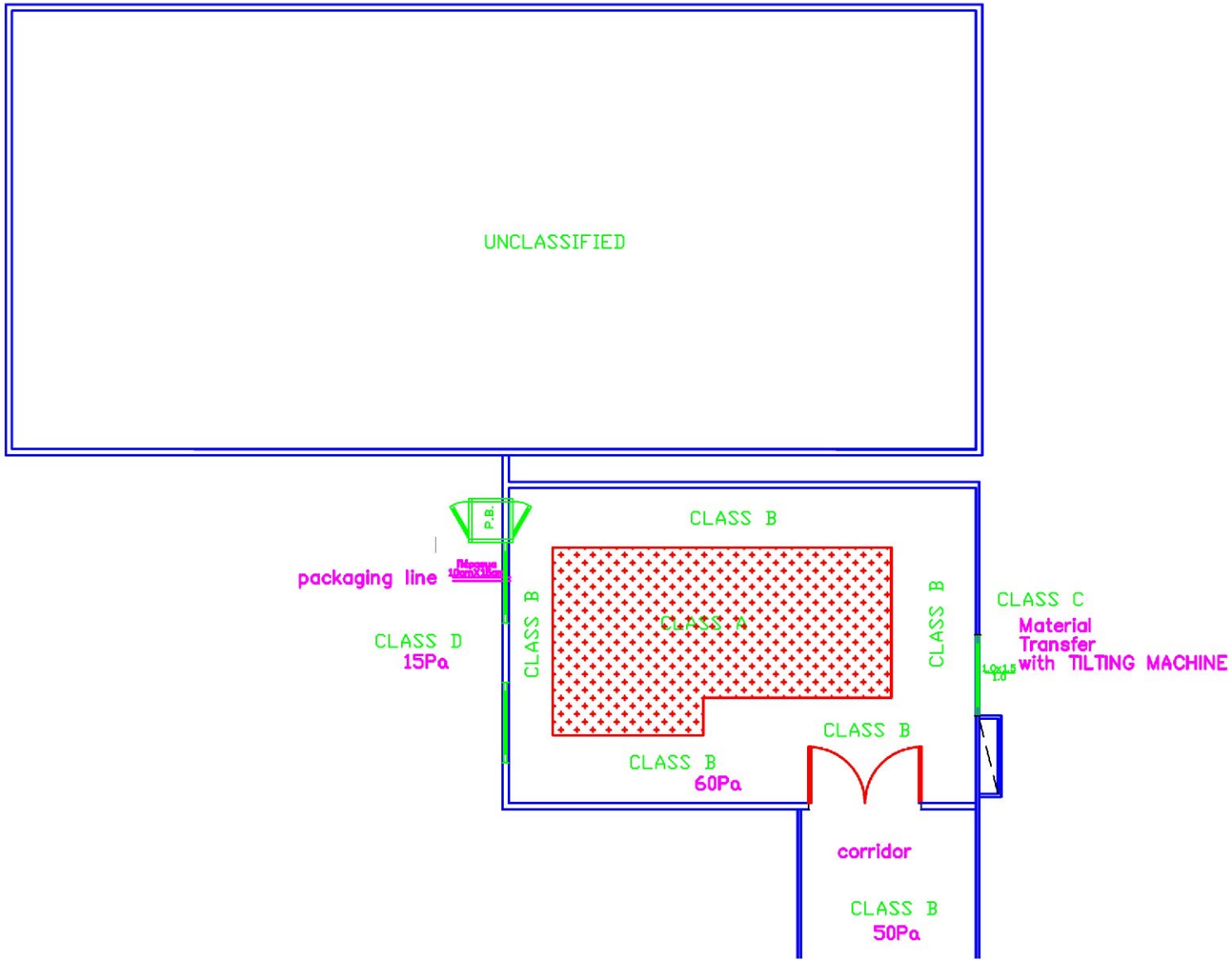
Section 2
Study requirements

EN (FILTERs)

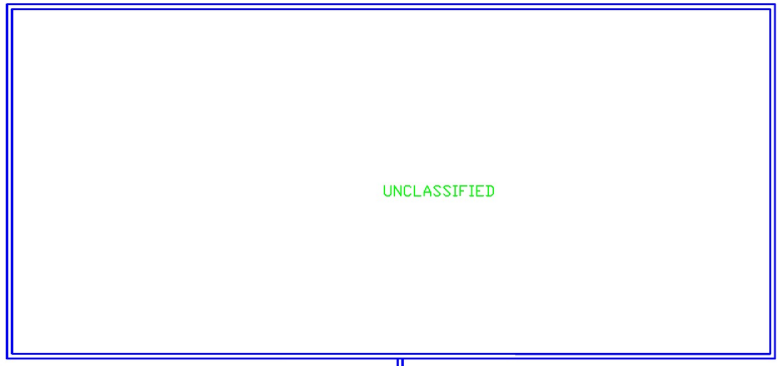
- EN ISO 16890-1 - Air filters for general ventilation - Part 1: Technical specifications, requirements and classification system based upon particulate matter efficiency (ePM) (ISO 16890-1).
- EN ISO 16890-2 - Air filters for general ventilation - Part 2: Measurement of fractional efficiency and air flow resistance (ISO 16890-2).
- EN ISO 16890-3 - Air filters for general ventilation - Part 3: Determination of the gravimetric efficiency and the air flow resistance versus the mass of test dust captured (ISO 16890-3).
- EN ISO 16890-4 - Air filters for general ventilation - Part 4: Conditioning method to determine the minimum fractional test efficiency (ISO 16890-4).
- EN 1822-1 - High efficiency air filters (EPA, HEPA and ULPA) - Part 1: Classification, performance testing, marking.

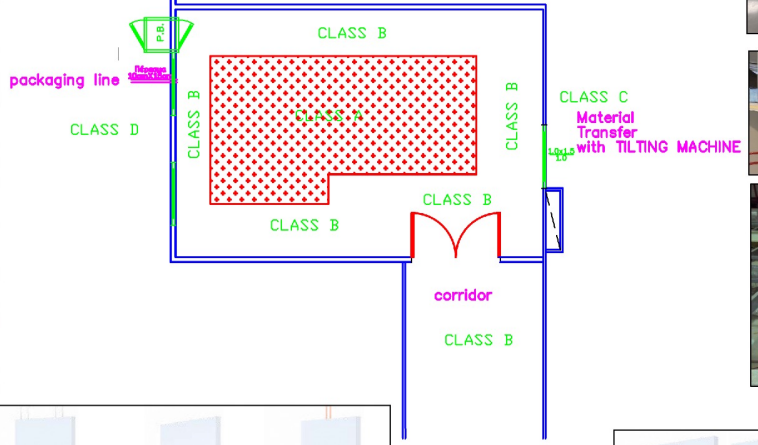
Section 3
Example

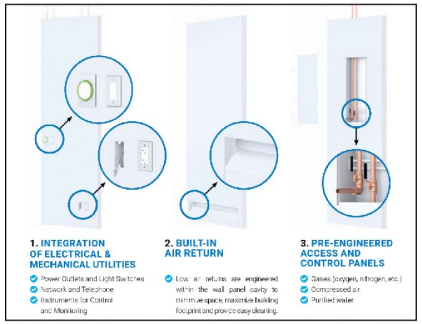
- PHARMA-AB.BLD\01-ARK-C



Section 3
Example

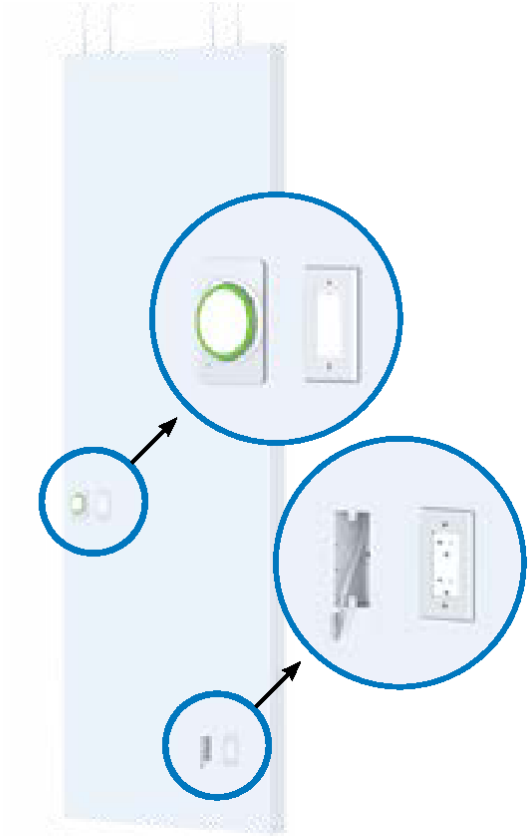






Section 3
Example

Section 3
Example

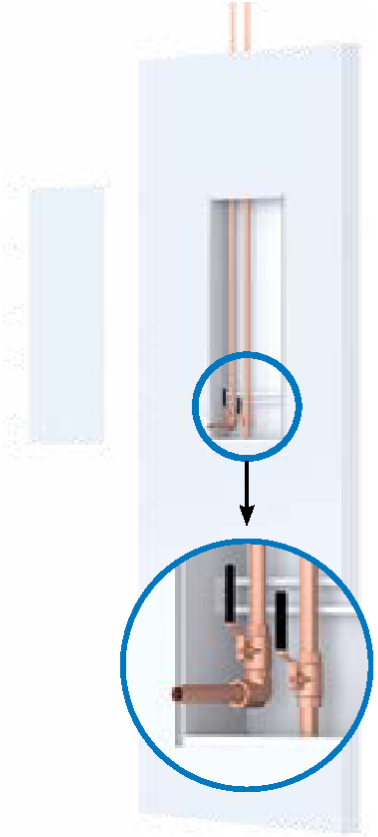


1. INTEGRATION OF ELECTRICAL & MECHANICAL UTILITIES

- Power Outlets and Light Switches
- Network and Telephone
- Instruments for Control and Monitoring

2. BUILT-IN AIR RETURN

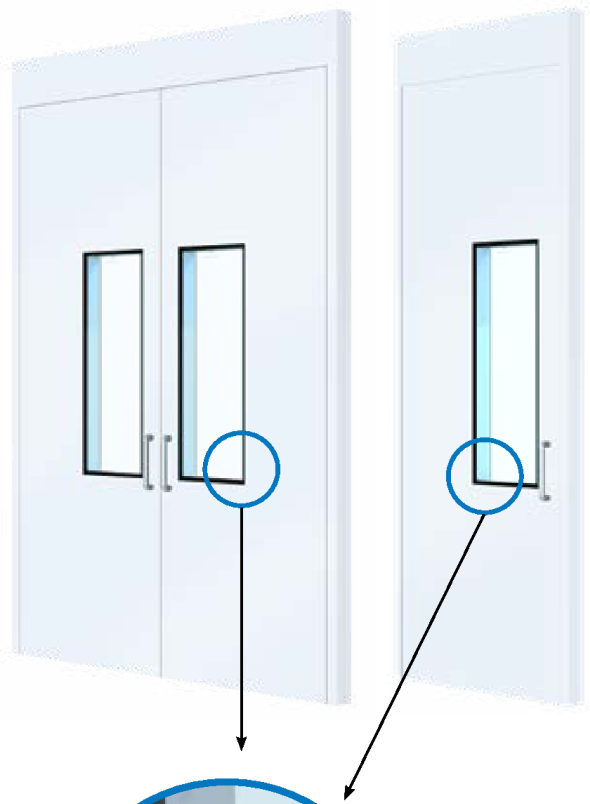
- Low air returns are engineered within the wall panel cavity to minimize space, maximize building footprint and provide easy cleaning.



3. PRE-ENGINEERED ACCESS AND CONTROL PANELS

- Gases (oxygen, nitrogen, etc.)
- Compressed air
- Purified water

Section 3
Example



STAINLESS STEEL HANDLES

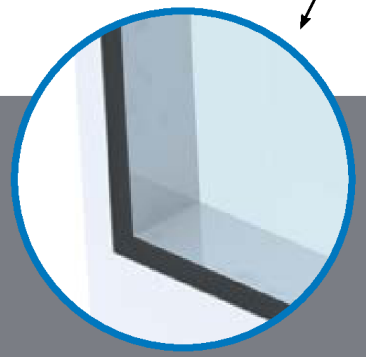
- 9 inch C-shape pull handle on the outside with push plate on the inside
- 3 foot C-shape pull handle on the outside with push plate on the inside
- Custom handles

OTHER OPTIONS

- Stainless steel push plates
- Stainless steel kick plates
- Automated openers (motorized operators)
- Interlocks
- Touchless functionality
- Automatic drop down door seal
- Security control/lock
- Door header

WINDOW DESIGN *(double glazed, tempered glass)*

- No window
- Rectangular design with right angles (16" x 42" or 24" x 60")
- Custom-designed window

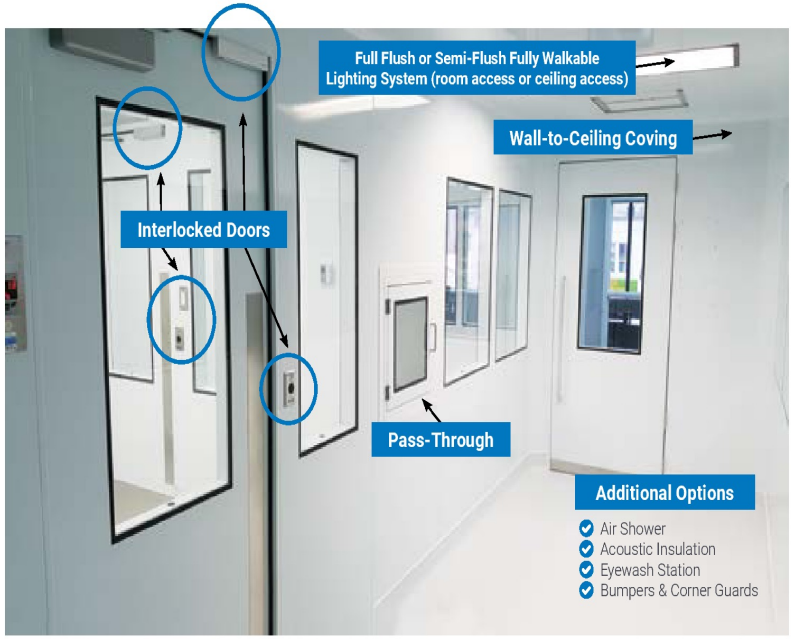


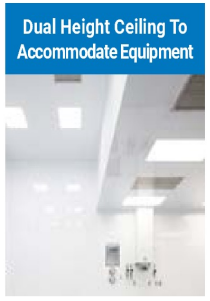
FULLY FLUSH WINDOW

Fully-flush windows are flat against the clean room wall.

The absence of edges makes them easy to clean since there are no corners or edges to collect dust particles and micro-organisms, perfect for GMP applications.

Section 3
Example





Section 3
Example

KLA-CLEAN-ROOMS.xls

Στοιχεία χώρων												Στοιχεία Ποιότητας Αέρα/Φίλτρων																Απώλειες Αέρα Από Χαραμάδες							
A/A	Κωδικός Χώρου	Ονομασία Χώρου	Μήκος=(Μήκος Μηχανής, κλπ)+0.3m (+0.15m για κάθε πλευρά)	Πλάτος=(Πλάτος Μηχανής, κλπ)+0.3m (+0.15m για κάθε πλευρά)	Εμβαδόν	Ύψος (μικτό)	Ύψος (καθαρό)	Αεριζόμενη Ψευδοροφή (π.χ. PLENUM) (ΝΑΙ/ΟΧΙ)	Όγκος (καθαρός)	Ύψος Αναφοράς Επιπέδου εργασίας (Ύψος επιπέδου εργασίας+0.15m)	Διαφορά ύψους Τοποθέτησης Στομίου από ύψος Αναφοράς Επιπέδου εργασίας	Κατηγορία Χώρου (Class κατά EU GMP)	Απαραίτητες Εναλλαγές Αέρα (Πρόταση)	Απαραίτητες Εναλλαγές Αέρα (Επιλογή)	Απαραίτητη Προσαγωγή Αέρα (από εναλλαγές)	Μήκος Απόλυτου Φίλτρου/Στομίου	Μήκος Απόλυτου Φίλτρου/Στομίου	Επιφάνεια Απόλυτου Φίλτρου/Στομίου	Αριθμός Απόλυτων Φίλτρων/Στομίων	Συνολική Επιφάνεια Απόλυτων Φίλτρων/Στομίων	Ποσοστό Καλυπτόμενης Επιφάνειας από Απόλυτα Φίλτρα/Στόμα	Προσαγωγή Αέρα ανά Απόλυτο Φίλτρο/Στόμιο	Υπολογιζόμενη Προσαγωγή Αέρα	Προσαγωγή Αέρα (έμμεση από Class A προς Class B)	Συνολική Προσαγωγή Αέρα Class B	Απαραίτητη Προσαγωγή Αέρα για βελτιωμένες στομίου)	Απαραίτητη Προσαγωγή Αέρα ανά ft² (για βελτιωμένες στομίου)	Πραγματικές Εναλλαγές Αέρα	Έλεγχος Εναλλαγών	Ταχύτητα Αέρα Προσαγωγής στο στόμιο (από κατασκευαστή για τα Laminar Flow)	Ταχύτητα Αέρα Προσαγωγής (στον χώρο και κατά προτίμηση στο Επίπεδο Εργασίας για Class A)	Απαιτούμενη Πίεση	Διαφορά Πίεσης	Μήκος Χαραμάδας	Πλάτος Χαραμάδας	Επιφάνεια Χαραμάδας	Συντελεστής Αποτόνωσης Χαραμάδας	Συνολικές Απώλειες Αέρα από Χαραμάδες ή/και άλλες Απορρίψεις	Ποσοστό επί της Συνολικής Προσαγωγής στο χώρο
			m	m	m^2	m	m		m^3	m	m		ch/h	ch/h	m^3/h	m	m	m^2		m^2		m^3/h	m^3/h	m^3/h	m^3/h	CFM	CFM/ft^2	ch/h		m/sec	m/sec	Pa	Pa	m	m	m^2		m^3/h	
6	AB	Filling Machine MAR (τμήμα Class A)	6,60	3,00	19,80	2,90	2,50	ΟΧΙ	49,50	1,00	1,50	A	480	500	24.750,00	1,135	0,535	0,61	27	16,40	83%	1.115,00	30.105,13			17.708,90	83,13	608,2	Ο.Κ	0,51	0,45	60,0							
7	AB	Filling Machine MAR (τμήμα Class B)	6,60	2,68	17,69	2,90	2,50	ΟΧΙ	44,22	1,00	1,50	B	200	60	2.653,20	1,135	0,535	0,61	3	1,82	10%	990,00	2.970,00	30.105,13	33.075,13			67,2	Ο.Κ	0,45	0,05	60,0							
		ΥΠΟΣΥΝΟΛΟ			**37,49**				**93,72**						**27.403,20**				**30**				**33.075,13**					**352,9**				**60,0**						
		Προσαγωγή Pass Through																	**1**			**500,00**	500,00															
		ΣΥΝΟΛΟ										**Τελική Προσαγωγή συμπερ. της διαφοράς για την διατήρηση υπερπίεσης/υποπίεσης**												**33.575,13**															
		ΚΚΜ-ΑΒ										**Τελική Επιστροφή συμπερ. της διαφοράς για την διατήρηση υπερπίεσης/υποπίεσης**												**32.210,03**															
	B	Sterile corridor																													B - Sterile corridor		50,0	10,0	7,50	0,003	0,023	0,93	238,21	ΕΚΡΟΗ
		Bottles packaging line (Tunnel/Πέρασμα - 10cmX15cm)																								- Bottles packaging line (Tunnel/Πέρασμα - 10cmX15cm)						15,0	45,0	0,10	0,150	0,015	0,93	336,89	ΕΚΡΟΗ
		Κλίβανος - PassThrough																											- Κλίβανος - PassThrough									-500,00	ΕΙΣΡΟΗ
		Material Transfer Device (Tilting Machine)																								- Material Transfer Device (Tilting Machine)											790,00	ΕΚΡΟΗ
		ΕΛΕΓΧΟΣ ΠΙΕΣΕΩΝ																																			**865,10**	**2,6%**
8	B	Sterile corridor (Class B)	6,10	14,47	88,27	2,90	2,40	ΟΧΙ	211,84	1,00	1,40	B	200	60	12.710,45	1,135	0,535	0,61	10	6,07	7%	1.255,00	12.550,00	0,00	12.550,00			59,2	ΠΡΟΣΟΧΗ	0,57	0,04	50,0							
		ΥΠΟΣΥΝΟΛΟ			**88,27**				**211,84**						**12.710,45**				**10**				**12.550,00**					**59,2**				**50,0**						
		Προσαγωγή Pass Through																	**0**			**500,00**	0,00															
		ΣΥΝΟΛΟ										**Τελική Προσαγωγή συμπερ. της διαφοράς για την διατήρηση υπερπίεσης/υποπίεσης**												**12.550,00**															
		ΚΚΜ-Β										**Τελική Επιστροφή συμπερ. της διαφοράς για την διατήρηση υπερπίεσης/υποπίεσης**												**13.241,91**															
		Sterile corridor																													- Sterile corridor		38,0	12,0	7,50	0,003	0,023	0,93	260,95	ΕΚΡΟΗ
		Filling Machine1																													- Filling Machine1		60,0	-10,0	7,50	0,003	0,023	0,93	-238,21	ΕΙΣΡΟΗ
		Filling Machine2																													- Filling Machine2		60,0	-10,0	7,50	0,003	0,023	0,93	-238,21	ΕΙΣΡΟΗ
		Sterile filling																													- Sterile filling		60,0	-10,0	7,50	0,003	0,023	0,93	-238,21	ΕΙΣΡΟΗ
		Any Device (κλπ)																													- Any Device (κλπ)		60,0	-10,0	7,50	0,003	0,023	0,93	-238,21	ΕΙΣΡΟΗ
		ΕΛΕΓΧΟΣ ΠΙΕΣΕΩΝ																																			**-691,91**	**-5,5%**

$\Delta p=(\rho/2)*(\Delta V/A*\mu*3600)^2$ (Bernoulli equation)

Δp (Pa) = Διαφορά Πίεσης μεταξύ των χώρων

ρ (kgr/m^3) = Πυκνότητα αέρα = 1.2

ΔV (m^3/h) = Παροχή αέρα από τις χαραμάδες

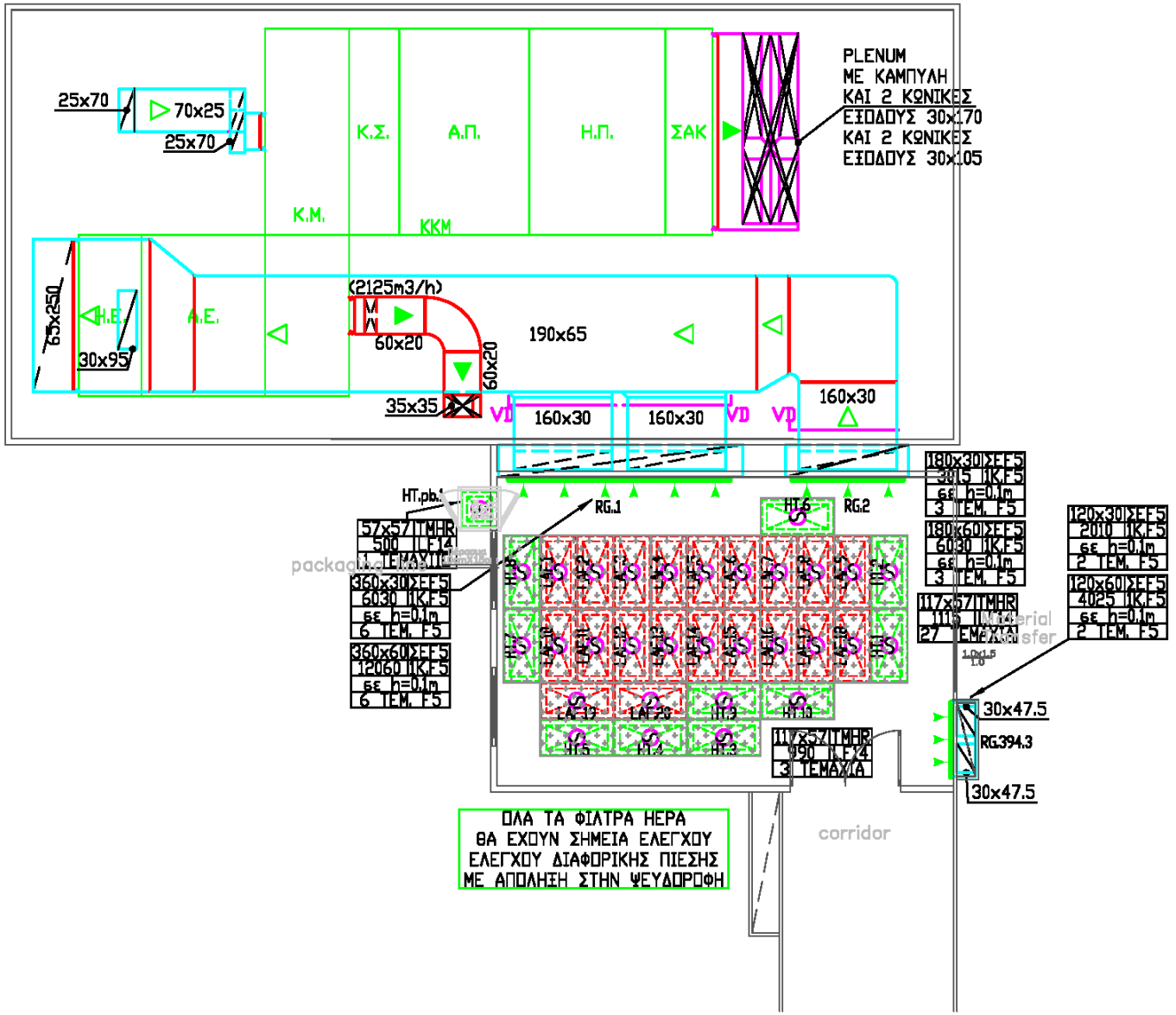
A (m^2) = Συνολικό Εμβαδόν χαραμάδων

μ = Συντελεστής χαραμάδας = 0.72

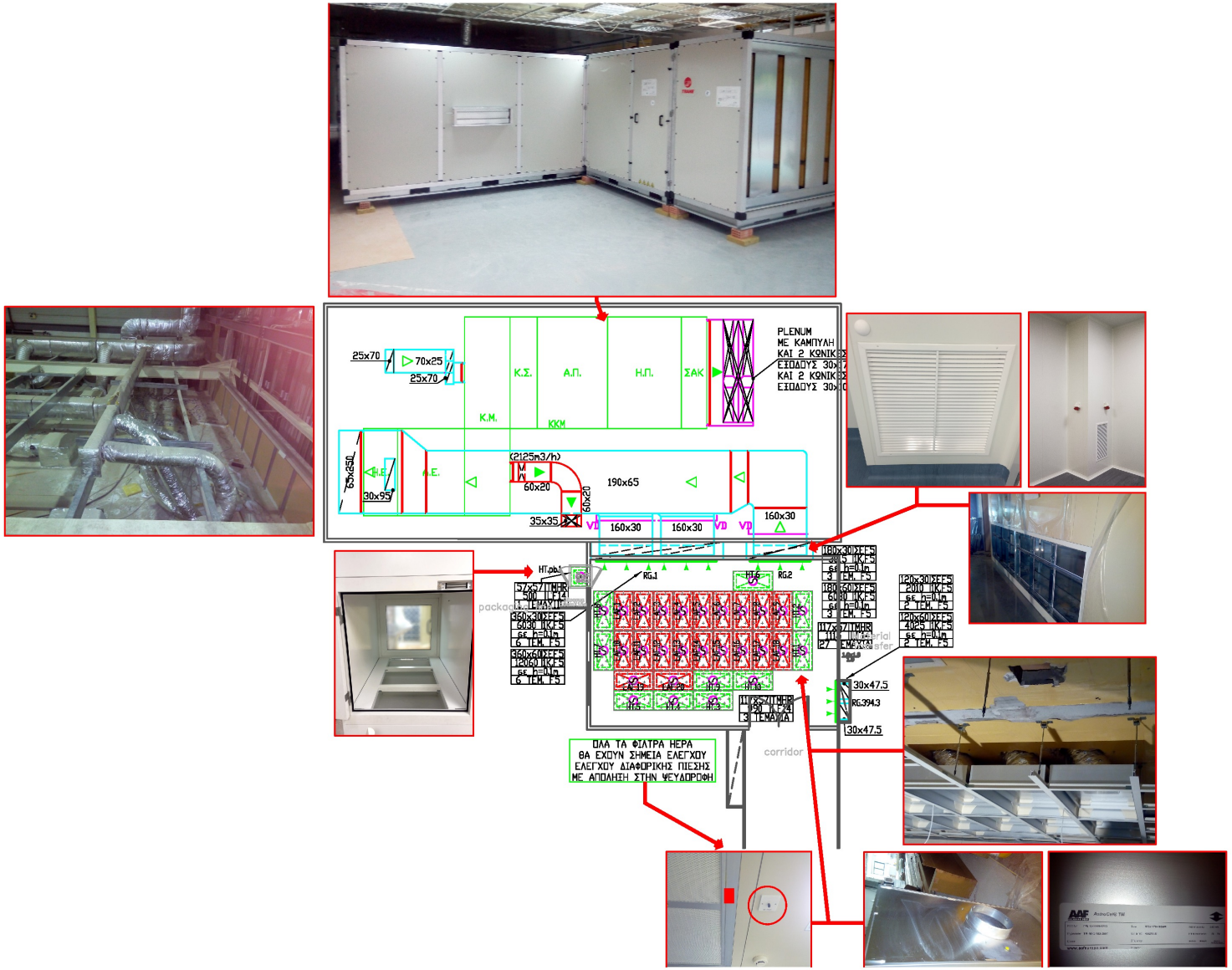
τον μ τον αλλάζω και έτσι χρησιμοποιώ την απλουστευμένη σχέση των Υπολογισμών μου

Section 3
Example

PHARMA-AB.BLD\PHARMA-AB.DWG



Section 3
Example



ASHRAE Hellenic Chapter TEE

DEDICATED VENTILATION APPLICATIONS

INDUSTRIAL - KITCHEN - SMOKE CONTROL - FILTERS

THANK YOU! / Q&A

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