

THE WORLD LEADER IN CLEAN AIR SOLUTIONS



Pharmaceutical Clean Air Solutions

PARTICULATE AND GASEOUS FILTRATION

AAF[®]
INTERNATIONAL

Optimising Process Performance for Protecting Human Health

Globalisation, aging population and economic shifts are transforming the pharmaceutical landscape. New medical needs and therapeutic areas are emerging that will put more pressure on innovation, productivity and time-to-market. At the same time, sustainability has entered the playing field with a focus on energy efficiency, waste management and emission reduction. All these developments shed a new perspective on the role for air filtration.

The Importance of Clean Air

Clean air is something nearly impossible to identify by our human senses. Most airborne particulates are so small that they cannot be perceived with the naked eye. In most cases, we do not know when something is wrong with the air quality until it is already too late and we see the damage that has occurred.

Within the pharmaceutical industry, strict requirements on air purity levels are needed because of the direct effect airborne contamination has on the quality of the pharmaceutical products. Human health and safety depend on it.

The Role for Air Filtration

No clean air is possible without a carefully selected and reliably functioning air filtration system. The performance of installed air filters, whether terminal filters or prefilters, directly determines how effectively harmful contaminants are prevented from entering the airstream in process environments. As such, air filtration represents a vital link in the overall pharmaceutical process chain.

This brochure provides insight into the most important aspects for realising clean air conditions in pharmaceutical applications. The indispensable role for air filtration is explained through the lens of AAF's in-depth expertise, state-of-the-art air filtration solutions and value-added support concepts.

Proven Expertise of AAF

AAF offers the most comprehensive air filtration portfolio in the industry, including particulate and gas-phase filters, that provides a customised clean air solution. Each product is carefully designed, manufactured and tested in full compliance with all applicable standards to meet the most challenging demands at the lowest energy consumption.

AAF manufacturing takes place in ISO 9001 and ISO 14001 certified facilities. AAF HEPA (High Efficiency Particulate Air) filters are produced, tested and packaged in a state-of-the-art ISO 7 or cleaner cleanroom environment for optimised filter performance and quality assurance.

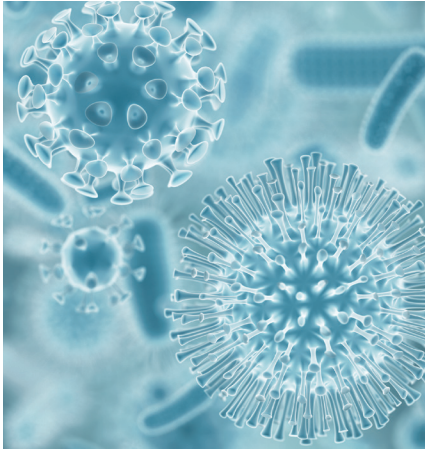
Many pharmaceutical applications today already benefit from AAF's recognised expertise in air filtration. The combination of an extensive product portfolio with high level technical support capabilities has provided significantly improved results for many satisfied customers.



Erik Geertsema
Test Engineer, AAF

We manufacture and individually test all our HEPA filters in a modern cleanroom environment. We believe that only then is product performance assured, through which the most stringent customer requirements can be met.

Controlling Contaminants

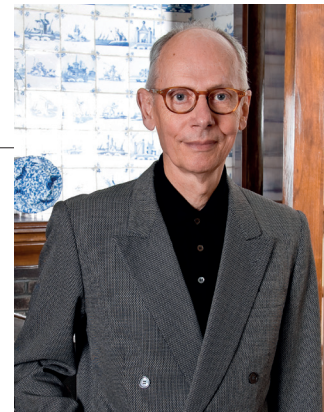


The production of sterile products should be carried out under high levels of air cleanliness. Contamination of raw materials, finished goods or personnel must be avoided at all times through the implementation of appropriate technical and organisational measures. The significance of such contamination risk may vary with the type of contaminant and the product that is being contaminated, but reliable airborne contamination control remains critical in all situations.

Quality of Medicinal Products

Everything that could come into direct contact with a pharmaceutical product is a potential risk toward contamination. Limiting exposure to airborne contaminants is critical, as it may result in health and safety issues. Preventive measures and quality management procedures are described in several industry guidelines: “CFR—Code of Federal Regulations Title 21”, “Guidance for Industry—Sterile Drug Products Produced by Aseptic Processing—Current Good Manufacturing Practice 2004”, and “European Union (EU) Guidelines to Good Manufacturing Practice (GMP) Medicinal Products for Human and Veterinary Use—Annex 1—Manufacture of Sterile Medicinal Products, 2008”. These guidelines are to ensure consistent production and control of pharmaceutical products for human use.

Air filtration plays a critical role in making sure that these objectives are met and that the risk of any adverse effects on product quality is reduced.



Dr. Lothar Gail
GMP and cleanroom consultant VDI.

Mechanical Strength Reduces Contamination Risks

Following the recognised US guidance for Sterile Drug Products Processing, HEPA filters should be tested twice a year for leaks, to demonstrate filter integrity.

A critical leak is given when more than 0.01 percent of the upstream aerosol challenge penetrates a test spot. If a critical leak has been determined, it is customary to evaluate a possible impact on sterile processing. If a local defect is detected, this would require a filter repair or replacement, retesting and finally the evaluation of possible effects on the production line in question.

To avoid leaks, the extremely sensitive surface of traditional HEPA filters used to be protected by a grid on the filter surface. New HEPA filters with the latest generation of membrane media represent a better solution, due to considerably improved mechanical strength and reduced pressure difference, thus increasing the economy and quality of sterile production units. The higher costs of such new filters are justified, since the risk of damages will be considerably reduced.

Balancing High Level Protection With Total Cost of Ownership

No clean air is possible without a carefully selected and reliably functioning air filtration system. The performance of installed air filters, whether terminal filters or prefilters, directly determines how effectively harmful contaminants are prevented from entering the airstream in process environments. However, if the Facility Managers selecting air filters do not also consider the lifetime operating costs of a given product, facilities could be exposed to unnecessary risks and expenses.

Air in critical areas should always be supplied at the terminal stage by HEPA filtered unidirectional airflow, preceded by sequential prefiltration steps. Leak-free and high filtration efficiency performance of the HEPA filter is vital for ensuring that air purity is optimised, the pressure differentials between rooms are met, and healthy working conditions are achieved.

Typical Airborne Contaminants

Airborne contaminants differ in size and impact in a pharmaceutical manufacturing process. Figure 1 shows a typical size range of airborne particles and microorganisms. Each particle size range requires a specific air filtration technique to obtain the required air quality levels.

TCO Diagnostic®

A thorough air filter audit of your HVAC Systems is the first step in order to provide you with professional guidance and analysis for cost savings and risk reduction. By conducting this audit, AAF will be able to understand your current state and then utilise TCO Diagnostic®, an advanced analytical software tool, to identify how you can perform even better.

The purpose of TCO Diagnostic is to assist you in selecting the best filters for your air handling systems and to understand their sensitivity to your operating conditions, in order for your system to operate in the most optimal and effective manner.



TCO Diagnostic provides the insight to identify improvement opportunities, find the optimised options and tailor to your specific needs for a comprehensive purchase perspective—improving air quality, energy savings and operational flexibility while reducing Total Cost of Ownership.

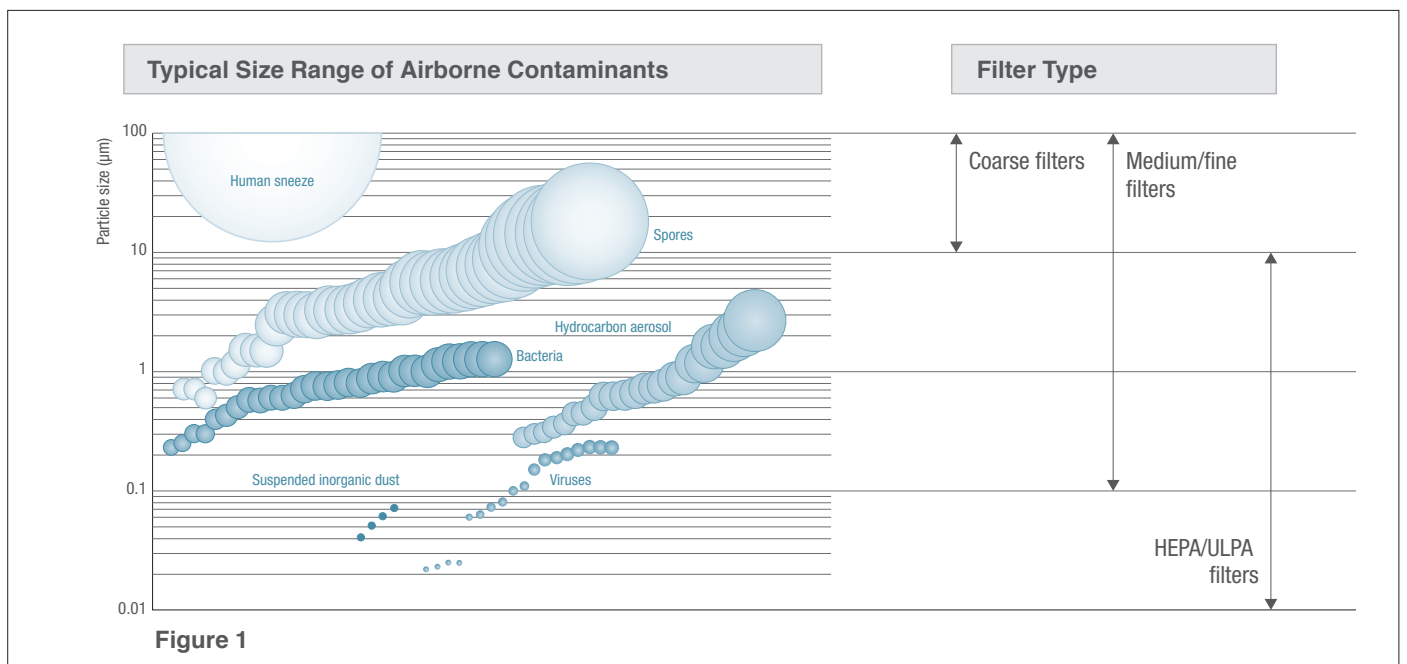


Figure 1

Classifying Air Filters

The type of activity within a particular pharmaceutical processing environment will determine the level of cleanliness that is required. To ensure that the stringent air quality levels for safely manufacturing medicinal products are met, a carefully designed air filtration system is vital. Based on their efficiency performances, air filters are classified according to these accepted European standards, the EN779:2012, ISO 16980 and EN1822:2009.

EN779:2012

The EN779:2012 standard defines the performance of particulate air filters for general ventilation purposes. The air filters are grouped under three categories; Coarse, Medium and Fine. Depending on the category, limits for the average arrestance or efficiency are set for each filter class. Fine filters additionally need to meet a Minimum Efficiency (ME) requirement. This ME is defined as the lowest value of three different tests for 0,4 µm particles; initial efficiency, efficiency throughout the test's loading procedure and discharged efficiency.

AAF offers a broad range of EN779:2012 compliant and energy efficient air filters as pre-filtration to final HEPA filters. The choice of pre-filtration will determine the cleanliness of the air going through the final filter and therewith its lifetime.

Eurovent Certification of AAF

Eurovent is the official European association that certifies the performance of air filters rated and sold as Medium and Fine filter classes M5 up to F9.

AAF's Medium and Fine filters are Eurovent certified for filtration efficiency, operating resistance and energy efficiency. It guarantees customers that the performance is independently validated and delivered as promised.

More information about Eurovent certification and an overview with certified air filters of AAF: www.eurovent-certification.com



Air filter classification according to EN779:2012

Category	Filter class	Final Pressure Drop (Pa)	Average arrestance (A_m) of synthetic dust %	Average efficiency (E_m) of 0,4 µm particles %	Minimum Efficiency of 0,4 µm particles %
Coarse	G1	250	$50 \leq A_m < 65$	-	-
	G2	250	$65 \leq A_m < 80$	-	-
	G3	250	$80 \leq A_m < 90$	-	-
	G4	250	$90 \leq A_m$	-	-
Medium	M5	450	-	$40 \leq E_m < 60$	-
	M6	450	-	$60 \leq E_m < 80$	-
Fine	F7	450	-	$80 \leq E_m < 90$	35
	F8	450	-	$90 \leq E_m < 95$	55
	F9	450	-	$95 \leq E_m$	70

Measuring Real Life – ISO 16890 replaces EN779:2012



International Standards Organisation issues a new standard for filter testing and rating



ISO coarse – filters allocated to this range capture less than 50% of PM10 particles.



PM10 – Refers to the particle size fraction in the range from 0,3 µm up to 10 µm.



PM2,5 – Refers to the particle size fraction in the range from 0,3 µm up to 2,5 µm.



PM1 – Refers to the particle size fraction in the range from 0,3 µm up to 1 µm.

The precise definition of PM10, PM2,5 and PM1 is quite complex and not simple to measure. Public authorities, like the US EPA or the German Federal Environmental Agency (Umweltbundesamt), increasingly use in their publications the simpler denotation of PM10 as being the particle size fraction less or equal to 10 µm. Since this deviation to the above-mentioned complex “official” definition does not have a significant impact on a filter elements particle removal efficiency, the ISO 16890 documents refer to this simplified definition of PM10, PM2,5 and PM1.

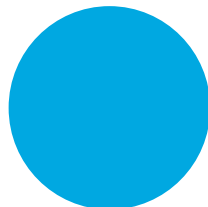
More Than Logic— ISO 16890 Measures Reality!

The world’s leading health-related organisations consider PM10, PM2,5 and PM1 fine dust fractions as the most important and dangerous for humans. Their official documentation to the public always refers to these PM levels.

It is more than logic that filter test methods and classifications follow this approach to demonstrate filtration performance towards the most harmful fine dusts.



The Main Difference Between EN779 and the ISO 16890



10 µm



2,5 µm



1 µm



0,4 µm



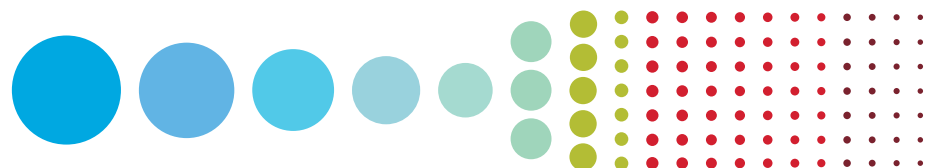
0,3 µm

According to **EN779** filter test procedures are considering only particles in the size of 0,4 µm

According to **ISO 16890** filter test procedures are considering the range from 10 µm–0,3 µm

Due to their Harmfulness, Permanence and Frequency, Particles Smaller or Equal to 1µm Need the Most Attention!

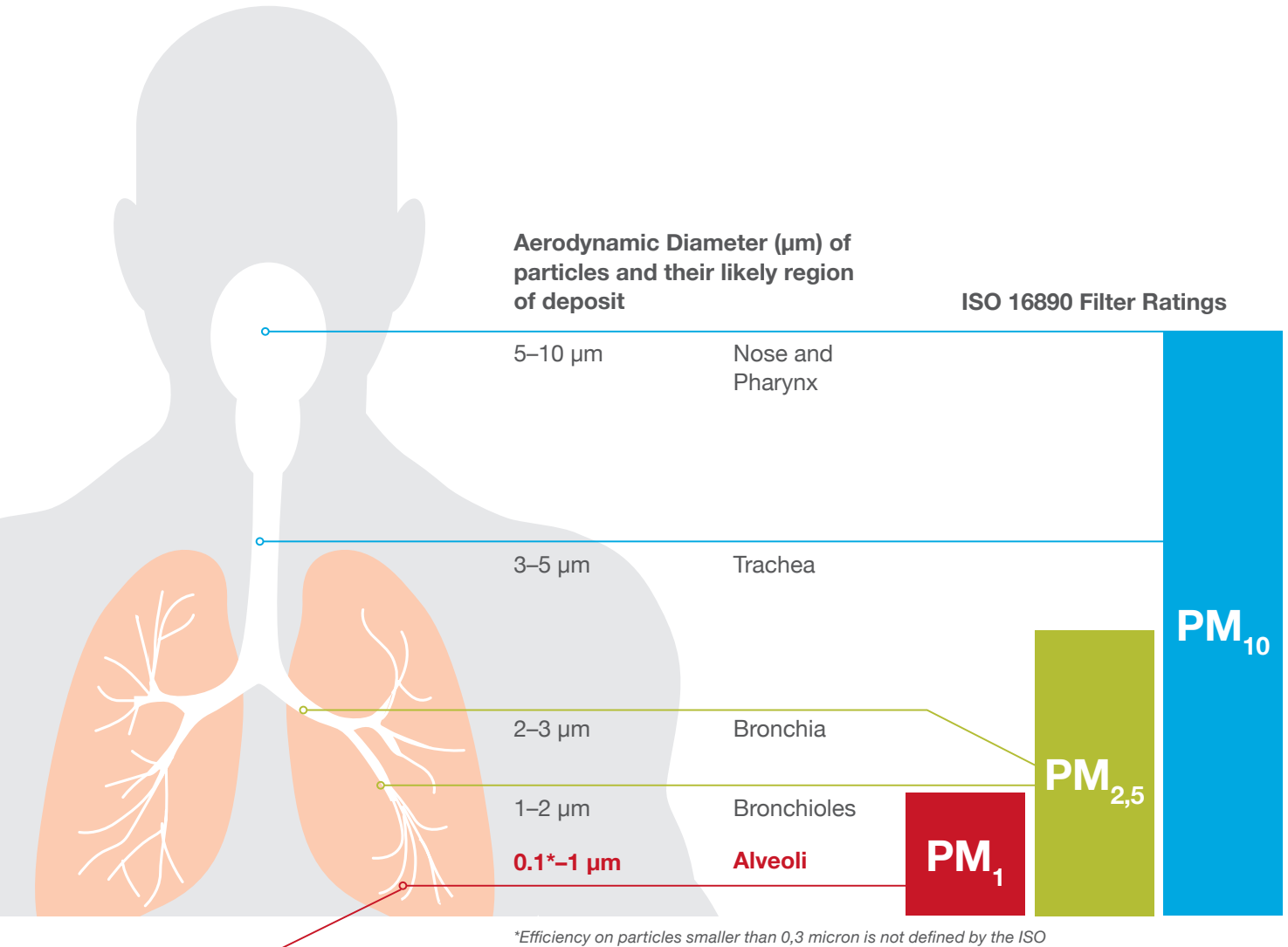
The lighter and smaller a particle is, the longer it stays in the air.



Particles smaller than **1 micron** contribute only a few % to the mass, at the same time contributing to **over 90% of the numbers**.

Classifying Air Filters

ISO 16890 Classifications Are Based On Where Particles Are Deposited in the Human Lung



PM₁ – The Smaller the More Dangerous!

A variety of studies are focusing on the health effects of PM1 particles:

“ Particles smaller or equal to 1 micron in diameter are small enough to find their way through the cell membranes of the alveoli into the human blood stream. ”

“ Fine particles in the air measuring between 0,25 to 0,5 microns in diameter have a closer relationship to human health, especially an increased risk of cardiovascular diseases. ”

“ Smaller particles in the body can harm the regulation of the human nervous system. ”

ISO 16890 Testing and Classification Procedure



Step 1

Filter efficiency is measured on 0,3 to 10 µm of the clean (not conditioned) filter.



Step 2

The filter is conditioned in an isopropanol vapour atmosphere to eliminate electrostatic charge.



Step 3

Filter efficiency is measured again on 0,3 to 10 µm – now of the conditioned filter.



Step 4

Actual efficiency per PM size is calculated as the average of the conditioned and the unconditioned filter.

Important:
For a certain PM classification, the filter needs to show a minimum efficiency of 50% for the unconditioned and the conditioned filter.



Step 5

Values are allocated to ISO groups.

ISO Efficiency
Size Range, µm

coarse	> 10
ePM10	0,3 ≤ x ≤ 10
ePM2,5	0,3 ≤ x ≤ 2,5
ePM1	0,3 ≤ x ≤ 1

For ISO coarse filters Initial Gravity Arrestance is measured by loading the filter with synthetic test dust. This step is voluntary for filters classified as ePM10, ePM2,5 or ePM1.



Step 6

The reporting value for the filter is the combination of the selected ISO group and the efficiency value measured for this group – always rounded down in 5% steps.

Example:

A filter shows the following average efficiency values:

Efficiency class	Value
ISO ePM ₁₀	89%
ISO ePM _{2,5}	63%
ISO ePM ₁	49%

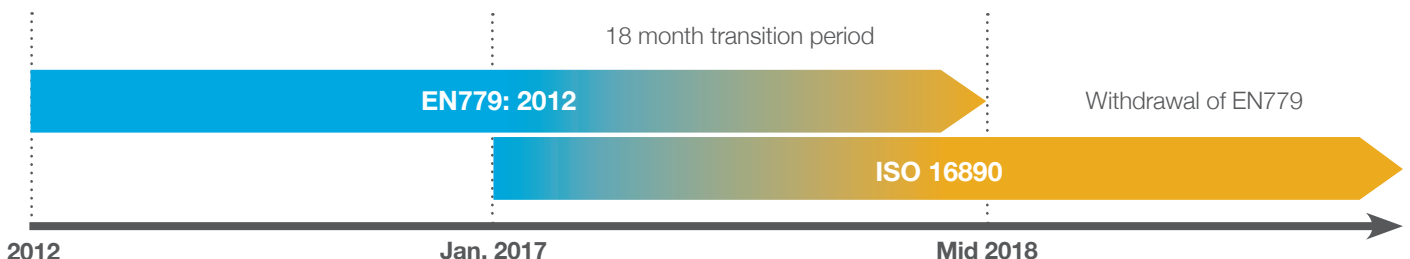
- Minimum efficiency of 50% is achieved for ISO ePM10 and ISO ePM2,5 – but only 49% for ISO ePM1, which is not fulfilled.
- Possible ISO groups are therefore ISO ePM2,5 and ISO ePM10.
- If, for example, ISO ePM2,5 group is selected, value of 63% is rounded down to 60%.

As a result, the filter is classified as:

Classification
ISO ePM _{2,5} 60%

Meaning this filter is able to capture 60% of the particles smaller or equal to 2,5 micron!

ISO 16890 Timeline



Classifying Air Filters

EN1822:2009

To ensure the highest levels of air purity, pharmaceutical processes need to rely on high efficiency particulate air filters as terminal filter. These air filters are subject to classification according to the European EN1822:2009 standard.

EN1822:2009 distinguishes between eight filter classes, which are distributed over three filter groups; EPA, HEPA and ULPA.

EN1822:2009 filter groups	
Group E:	EPA (Efficient Particulate Air filter)
Group H:	HEPA (High Efficiency Particulate Air filter)
Group U:	ULPA (Ultra Low Penetration Air filter)

Air filter classification according to EN1822:2009				
Filter class	Integral Value		Local Value	
	Efficiency %	Penetration %	Efficiency %	Penetration %
E10	≥ 85	≤ 15	–	–
E11	≥ 95	≤ 5	–	–
E12	≥ 99,5	≤ 0,5	–	–
H13	≥ 99,95	≤ 0,05	≥ 99,75	≤ 0,25
H14	≥ 99,995	≤ 0,005	≥ 99,975	≤ 0,025
U15	≥ 99,9995	≤ 0,0005	≥ 99,9975	≤ 0,0025
U16	≥ 99,99995	≤ 0,00005	≥ 99,99975	≤ 0,00025
U17	≥ 99,999995	≤ 0,000005	≥ 99,9999	≤ 0,0001

Testing Capabilities of AAF

All HEPA and ULPA filters produced by AAF are tested in an ISO 7 cleanroom environment with full compliance to the EN1822:2009 standard. In a modern EN1822 test rig, each air filter is individually tested before shipment to the customer.

HEPA and ULPA filters are leak tested by using a DEHS aerosol. The test results are documented in a test report that is supplied with each individual HEPA or ULPA filter. It gives full information about the tested air filter, test parameters (airflow, test method and aerosol) and the test results according to EN1822:2009. Air filter labels include the identification of the air filter type, a serial number for full traceability, the test standard used, the filter class according to EN1822:2009 and the nominal airflow rate at which the air filter has been classified.

Strict quality procedures ensure that all HEPA and ULPA filters leaving the AAF factory are leak-free, perform according to applicable standards and are consistent with the individual customer requirements.

EN1822:2009 establishes a procedure for determining the filtration performance according to the efficiency of MPPS (Most Penetrating Particle Size) particles. It provides a standardised classification of these air filters on the basis of their integral value (for EPA) or their integral value and local value (for HEPA and ULPA).

EN1822-3:2009 governs the determination of the efficiency of a flat sheet of media for a range of particle sizes at nominal velocity. From the generated efficiency versus particle size curve, the MPPS is established. The MPPS differs per media type and air velocity applied. In EN1822-4:2009, the individual testing of filter elements of groups H and U is described for absence of leaks at their nominal airflow rate (leaks are specified as maximum allowable local penetration at the MPPS and must not exceed 5 times the overall penetration). Filter elements of group H are leak tested using an aerosol probe or alternatively a visual oil thread leak test method. Filter elements belonging to group U are leak tested using an MPPS scanning method with a particle counter probe. How to measure the overall efficiency of a filter element at its nominal airflow rate, using the MPPS test aerosol, is defined in EN1822-5:2009. For air filters of groups H and U, this has to be done on each individual filter element.



Air Filter Classification According to IEST-RP-CC001

Table 3: Recommended Test and Minimum Rating for Filters Types A Through K.

Filter Type	Penetration Test		Last (Scan) Test ¹			Minimum Efficiency Rating	Designated Leak Penetration
	Method	Aerosol	Method	Aerosol	Comments		
HEPA (type A)	MIL-STD-282	Thermal DOP	None	None		99.97%	n/a
HEPA (type B)	MIL-STD-282	Thermal DOP	None	None	Two-flow leak test	99.97%	n/a
HEPA (type C) ¹	MIL-STD-282	Thermal DOP	Photometer	Polydisperse DOP/PAO		99.99%	0.010%
HEPA (type D) ¹	MIL-STD-282	Thermal DOP	Photometer	Polydisperse DOP/PAO		99.999%	0.0050%
HEPA (type E) ¹	MIL-STD-282	Thermal DOP	None	None	Two-flow	99.97%	n/a
HEPA (type F) ¹	IEST-RP-CC007	Open	Particle Counter	Open		99.9995% at 0.1-0.2 or 0.2-0.3 µm	0.00250%
HEPA (type G) ¹	IEST-RP-CC007 ²	Open	Particle Counter	Open		99.9999% at 0.1-0.2 or 0.2-0.3 µm	0.0010%
HEPA (type H) ¹	IEST-RP-CC007	Open	None	None		99.97% at 0.1-0.2 or 0.2-0.3 µm	n/a
HEPA (type I) ¹	IEST-RP-CC007	Open	None	Open	Two-flow leak test	99.97% at 0.1-0.2 or 0.2-0.3 µm	n/a
HEPA (type J) ¹	IEST-RP-CC007	Open	Particle Counter or Photometer	Polydisperse DOP/PAO		99.99% at 0.1-0.2 or 0.2-0.3 µm	0.010%
HEPA (type K) ¹	IEST-RP-CC007	Open	Particle Counter Photometer	Polydisperse DOP/PAO		99.995% at 0.1-0.2 or 0.2-0.3 µm	0.0080%

¹Either of the two scan test methods or an alternative method may be used for filter types C, D, F, and agreed. Designated leak details for these filter types are given in IEST-RP-CC034.

²Filter medium tested at most-penetrating particle size (MPPS) prior to filter assembly. All filters are leak-tested but in some instances may not be tested for overall penetration. The MPPS for testing this filter type is determined from the media according to IEST-RP-CC021.

Testing Capabilities of AAF

All HEPA and ULPA filters produced by AAF are built in an ISO 7 cleanroom environment and tested in an ISO 4 cleanroom with full compliance to IEST standards. In a modern test rig, each air filter is individually tested by well-trained AAF personnel before shipment to the customer.

HEPA and ULPA filters are leak tested using a challenge aerosol. The test results are documented in a test report for each individual HEPA or ULPA filter. This report gives full information about the tested air filter, test parameters (airflow, test method and aerosol) and the test results according to IEST-RP-CC001, and are available for every filter when requested. Air filter labels include the identification of the air filter type, a serial number for full traceability, the test standard used, the filter class and the nominal airflow rate at which the air filter has been classified.

Strict quality procedures ensure that all HEPA and ULPA filters leaving the AAF factory are leak-free, perform according to applicable standards and are consistent with the individual customer requirements.

Filters that meet the requirements of IEST-RP-CC001 are suitable for use in clean air devices and cleanrooms that fall within the scope of ISO 14644, and for use in supply air and contaminated exhaust systems that require extremely high filter efficiency (99.97% or higher) for submicrometer (µm) particles.

IEST-RP-CC001 describes 11 levels of filter performance and six grades of filter construction. The level of performance and grade of construction required should be specified. The filter efficiency required should also be specified if it is not covered by the performance level specified in this RP (Table 3).



Classifying Cleanrooms

The production of sterile pharmaceuticals is subject to special requirements in order to minimise risks of particulate and microbial contamination. Manufacturing is carried out in clean areas within which the concentration of airborne particles needs to be controlled. The classification and monitoring of such clean areas follow the ISO 14644 standard and the EU GMP Directive 2003/94/EC.

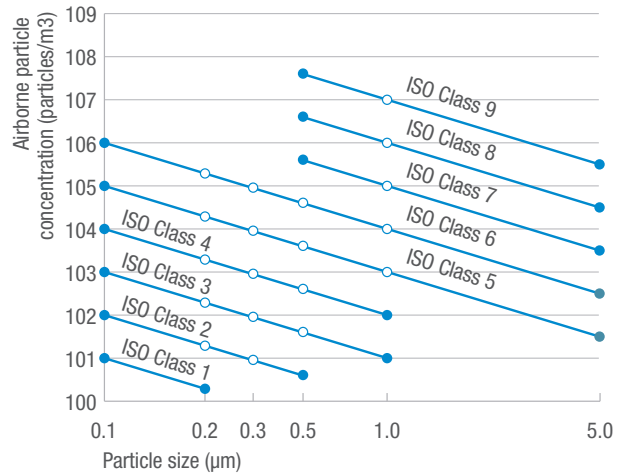
Classification Standards

Pharmaceutical cleanrooms and clean air devices are classified according to ISO 14644-1. The level of airborne particulate cleanliness, applicable to a clean area, is expressed as an ISO class. The lower the classification number, the higher the level of cleanliness. The ISO class represents maximum allowable concentrations for considered particle sizes, ranging from 0.1 µm up to 5.0 µm. Figure 2 shows a graphic illustration of the nine ISO cleanroom classes with the concentration limits for the given particle sizes. Different room classes are typically necessary for the various pharmaceutical clean areas and production steps taking place.

For the operational environmental monitoring of the production of sterile preparations, EU GMP distinguishes four alpha grades. Each grade is assigned maximum permitted airborne particle concentrations for sizes $\geq 0.5 \mu\text{m}$ and $\geq 5.0 \mu\text{m}$ 'at-rest' and 'in operation' state. Particles of $0.5 \mu\text{m}$ and larger can be considered as the most critical particle sizes that need to be effectively filtered out by HEPA filtration for obtaining the required aseptic process conditions. GMP grade A is the most stringent classification and equals ISO 5 according to ISO 14644-1. This type of area is expected to be almost completely free from particle sizes $\geq 5.0 \mu\text{m}$, both 'at-rest' and 'in operation' condition.

Figure 2:

ISO 14644-1 Cleanroom Class Particulate Concentration Limits



The graph shows the minimum and maximum particle size limits acceptable for each of the ISO classes shown. The classification lines do not represent actual particle size distributions found in cleanrooms and clean zones.

Sterile Manufacturing Activities

The pharmaceutical industry is expected to take proactive steps in ensuring that products are safe and effective. EU GMP regulations require building a quality approach into the manufacturing process, to minimise or eliminate risk of cross-contamination and errors (Table 4).

Table 4: Typical Cleanroom Activities for Terminal Sterilisation and Aseptic Preparation

GMP Grade	Examples of Typical Activities	
	Terminal Sterilisation	Aseptic Preparation
A	Filling of products for sterilisation (unusual risk profile)	Handling of sterile starting materials and components Preparation of materials and products (non-sterile filtering) Handling and filling of aseptically prepared products
B	–	Background area for grade A zones
C	Filling of products for sterilisation (usual risk profile) Preparation of materials and products (sterile filtering)	Preparation of components (unusual risk profile)
D	Preparation of components (usual risk profile)	Handling of components after washing

Monitoring Microbial Contamination EU GMP Annex 1

Clean areas for the production of sterile products are classified according to the required characteristics of the environment. Each manufacturing operation requires an appropriate environmental cleanliness level for minimising the risks of particulate and microbial contamination of the concerning starting material or product. EU GMP Annex 1 sets limits for microbial contamination for each of the four identified cleanroom grades (Table 5).

The air in risk zone areas, particularly vulnerable to biocontamination, needs to be protected from viable particles, consisting of one or more live organisms. Methods for evaluation and control are provided by ISO 14698 (Biocontamination Control).

Monitoring microbial contamination according to EU GMP Annex 1

Grade	Recommended limits for microbial contamination (average values)			
	Air sample cfu/m ³	Settle plates (diameter 90 mm) cfu/4 hours	Contact plates (diameter 55 mm) cfu/plate	Glove print 5 fingers cfu/glove
A	< 1	< 1	< 1	< 1
B	10	5	5	5
C	100	50	25	–
D	200	100	50	–

The Role for Air Filtration

Especially for aseptically prepared parenteral medicine (such as injectables and infusions), no contamination can be accepted, otherwise severe harm or life-threatening health risks to the patient can result. It is exactly in this area where air filtration comes in as the critical link in the overall chain.

Air in critical areas should always be supplied at the terminal stage by HEPA filtered unidirectional airflow, preceded by sequential prefiltration steps. A leak-free and high filtration efficiency performance of the HEPA filter is vital for ensuring that air purity is optimised, the pressure differentials between rooms are met and healthy working conditions are achieved.



Table 5: Cleanroom Classification According to EU GMP Annex 1

Maximum Permitted Number of Particles /m ³ Equal to or Greater than the Tabulated Size					International Cleanroom Standard Comparison for "At-rest"		
Grade	At-rest		In Operation		FED 209E	FED 209D	ISO 14644
	0.5 µm	5.0 µm	0.5 µm	5.0 µm			
A	3,520	20	3,520	20	M 3.5	Class 100	ISO 5
B	3,520	29	352,000	2,900	M 3.5	Class 100	ISO 5
C	352,000	2,900	3,520,000	29,000	M 5.5	Class 10,000	ISO 7
D	3,520,000	29,000	Not Defined	Not Defined	M 6.5	Class 100,000	ISO 8

Qualifying HEPA Filters

Pharmaceutical cleanrooms require an extensive validation procedure before medicinal production can be started up. In pre-defined intervals the process is then to be re-validated. Validation and revalidation both serve to determine if the process is capable of reproducible commercial manufacturing. For HEPA terminal filtration this implies initial qualification and periodic re-qualification of its performance characteristics.

Qualification Procedure

EU GMP Annex 15 describes the principles of validation and qualification which are applicable to the production of medicinal products. The procedure typically follows a v-shaped model, consisting of three sequential steps. Each of these steps would pose its own stringent demands on HVAC installations in general and HEPA filtration in specific. Selecting high quality manufactured HEPA filters will enhance the probability of success and will limit the risk of failure.

✔ Installation Qualification (IQ): does the HEPA filter specification match with what I had ordered and expected?

Examples of HEPA filter requirements

- Individual test report according to EN1822:2009
- Complete and accurate labeling including serial number for traceability
- Correct packaging and testing information

✔ Operational Qualification (OQ): does the HEPA filter perform according to functional specifications during at-rest operation?

Examples of HEPA filter requirements

- Absence of any visual damage to filter media, gasket and frame
- Successful in-situ test result with confirmed filter integrity
- Actual initial resistance performance consistent with specification

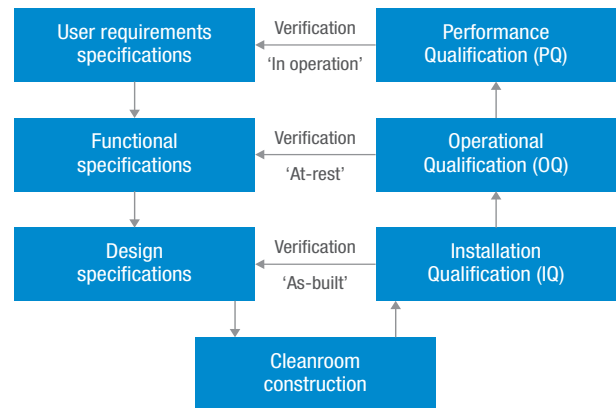
✔ Performance Qualification (PQ): does the HEPA filter demonstrate a reliable performance during full-scale operation?

Examples of HEPA filter requirements

- Absence of leakage (e.g. media) and bypass (e.g. gasket seal)
- Consistent particulate collection efficiency over time
- Absence of particle shedding that could cause contamination

Figure 3:

Cleanroom Validation Procedure, Derived from ISO 14644-4



Installed HEPA Filter Integrity Testing

The purpose of installed HEPA filter integrity testing, also called in-situ testing, is to confirm a flawless performance during normal operation. Filter integrity measurements encompass tests for installed filter leakage, such as in the media or sealant to frame, and bypass, such as in the frame, gasket or grid system. As such, this testing differs from factory leak testing that focuses on measuring filter integrity under laboratory conditions.

Both filter leakage and bypass can result in a penetration of contaminants that exceeds the expected value of downstream concentration. As these situations may seriously harm the sterility of critical parameters, and therefore the quality of medicinal products, periodic requalification of terminal HEPA filters is required. Subject to risk assessment of the cleanroom activity, this interval is typically set at six months for GMP grade A aseptic processes.

The most commonly used methods for testing the integrity of installed HEPA filters are described in the ISO 14644-3 standard: Aerosol Photometer (AP) and Discrete Particle Counter (DPC). The AP method typically uses a high concentration 10-40 ug/litre of oil-based aerosol for scanning air filters for leakage.

A low concentration aerosol challenge exposure is always recommended, as this testing leads to a less contaminated filtration system and therefore an optimised energy efficiency and improved HEPA filter lifetime expectancy.

Dedicated Support From AAF

With AAF's patent-pending ePTFE Filtration Technology, filters can now be scan tested with the industry standard photometer at the standard aerosol concentrations set forward, as well as the low aerosol concentration DPC method. AAF engineers work with state-of-the-art test equipment and can provide a project team or supervisor on site for practical assistance. As AAF firmly believes that independency in testing is critical, its core policy is to educate staff and test agencies locally for transferring knowledge and sharing best practices.

Please contact your local AAF affiliate office for more details on the in-situ testing support that AAF can provide to ensure that terminal filter performance is optimised for its purpose.

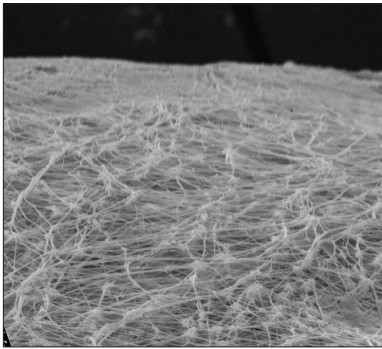


ePTFE Filtration Technology

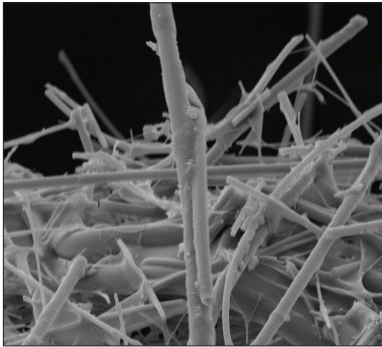
AAF ePTFE Filtration Technology represents the latest advancement in high-end air filtration. Developed and marketed by AAF, HEPA filters with ePTFE Filtration Technology give value-added benefits to pharmaceutical applications operating under classified conditions. The result is a more sustainable performance with lower energy consumption and reduced operational risk.

Industry-Leading Durability

Independent tests have shown that filters with ePTFE Filtration Technology have superior mechanical strength over filters with traditional ultrafine microglass media. This superior durability and tensile strength is 84 times the pleated strength of microglass.



Resilient ePTFE Technology media at fold tip @ 10,000x magnification.



Fractured ultrafine microglass media fibers at fold tip @ 10,000x magnification.

Reduce Operational Risk/Increase Uptime

The superior mechanical strength is demonstrated by a high tensile strength, burst pressure and abrasion resistance. ePTFE membrane media retains its integrity with a high resistance to any potential damage, for example due to errors in handling or installation. In daily practice this means that the risk of filter media failure is minimised and that fibre shedding, which could cause contamination when entering the airstream, is eliminated.

As a consequence, there will be less likelihood of hazardous contaminants entering cleanroom environments. Protection of sterile medicine and cleanroom personnel is optimised. It gives critical pharmaceutical applications the possibility to improve their quality risk management systems for a consistent supply of quality products, a reduction of failure costs and an overall increase of facility uptime.

Manufactured in ISO 7 Clean Facilities

ePTFE media is manufactured by AAF. By doing so, we control the quality and consistency of the media. This media is produced in an ISO 7 cleanroom to ensure the purity and cleanliness of the product. The filter is then assembled, tested and packaged in an ISO 7 clean manufacturing facility, resulting in unparalleled product performance and operational efficiency.



**Source: Pharmaceutical Manufacturing Magazine (2004).*

Particulate Filtration Solutions

HEPA and ULPA Filters

HEPA filters are the most efficient air filters commercially available. They are used in pharmaceutical manufacturing and other applications requiring ultra-clean air—semiconductor, electronics, cleanroom, food processing, hospitals and labs. AAF HEPA filters are individually tested before shipment to ensure they meet rated efficiency and resistance. AAF HEPA and ULPA filters are available in a variety of efficiencies— from 99.97% tested on .3 μm particles to 99.9995% and higher tested on .1 to .2 μm particles. All filters are available scan-tested.

High Temperature HEPA Solutions

To prevent endotoxin contamination in sterile conditions, containers and closure surfaces need to be depyrogenated. Endotoxins are removed by applying dry heat sterilisation, where the air is cleaned by a reliable HEPA filtration system. AAF high temperature HEPA filters are designed to provide excellent protection of this critical depyrogenation process.



The HEPA/ULPA Filter line delivers:

- Built according to EN1822:2009
- Designed to meet the demanding requirements of the most critical applications
- ePTFE Filtration Technology provides superior durability
- Chemical-resistant capabilities for highly corrosive environments
- High-capacity, space-saving designs
- Filters designed specifically for high airflow applications requiring HEPA efficiency at an ultra low pressure drop



High Temperature HEPA Filters feature:

- High temperature resistance with a steel frame construction
- Thorough heat-cycle tests confirm damage-free construction and consistent performance
- Unique combination of high temperature operation and superior durability, optimising process results and limiting unscheduled downtimes
- The right solution for ensuring that strict air cleanliness conditions are met



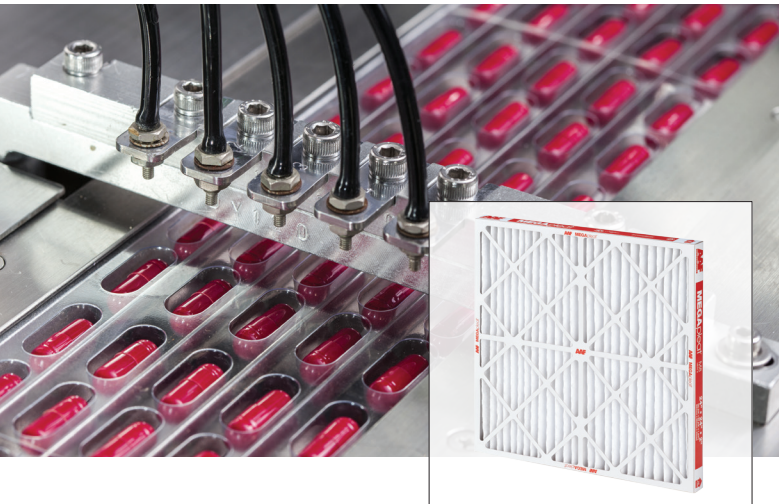
Particulate Filtration Solutions

High Efficiency Extended Surface Filters

These rigid, high-efficiency extended surface filters are ideal for use in all high-efficiency applications. The supported pleat filters provide strength and integrity in high-flow, turbulent, and variable airflow conditions.

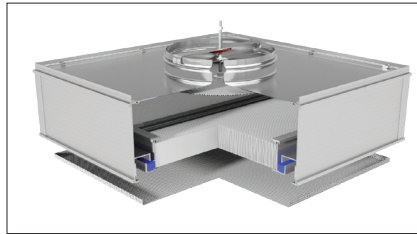
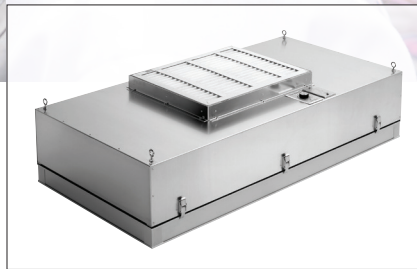
Disposable Ceiling Modules

HEPA and ULPA filters are available in a variety of configurations to fit the highest efficiency filter requirements for new, existing and retrofitted cleanroom applications.



The High Efficiency Extended Surface Filter line provides:

- Filter classes M6–E10 (EN779:2012; EN1822:2009)
- ISO ePM_{2,5} to ePM₁ (ISO 16890)
- Lowest life cycle pressure drop and highest Dust Holding Capacity (DHC) reduces energy consumption and total operating costs
- Patented Impress® Technology delivers a higher DHC and a lower pressure drop for greater energy efficiency
- Heavy duty construction and high performance in tough operating conditions



Disposable Ceiling Modules feature:

- Designed for pharmaceutical and biotech applications requiring an easily replaceable HEPA filter cartridge without risk of bypass leakage
- Self-contained fan/HEPA filter modules for critical applications
- Roomside replaceable HEPA/ULPA filter modules that are lightweight, low-profile ducted units

Gaseous Filtration Solutions

AAF has assumed an industry-leading position with the development of its innovative SAAF™ (pronounced as “SAFE”) product line designed to reduce or eliminate harmful gaseous contaminants. In combination with our expertise in airborne particulate filtration, SAAF products and solutions allow us to develop unique and effective total filtration solutions to protect people, processes and equipment.



No other company offers this combination of experience, expertise, innovation and capability to combat airborne contaminants, particulate and/or gaseous, and deliver the best clean air solutions.

The SAAF product line features:

- Patented chemical media cassettes with superior sealing and energy savings. These cassettes also fit in most legacy units. The housings are designed for quiet operation and durability.
- Complete chemical media line – adsorbents, oxidants and blends configured by and produced under the supervision of our world-class global research and development teams.
- Environmental Measurements related to the ISA Standard S71.04: “Environmental Conditions for Process Measurement and Control Systems. Airborne Contaminants to determine types of contaminants and their relative concentrations.”
- RoHS-compliant Corrosion Control
- Comprehensive, industry-leading software – SAAF Tech Tools analyses applications, develops solutions, configures equipment and media, and delivers a complete technical proposal.

Cleanroom Components

For guaranteeing an efficient installation and effective operation of terminal air filtration systems, AAF offers a broad range of matching cleanroom components. These components vary from ceiling grids to light fixtures.

Please contact your local AAF affiliate office for tailored advice and a custom-made solution, designed by AAF cleanroom specialists.

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AAF has a policy of continuous product research and improvement and reserves the right to change design and specifications without notice.

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