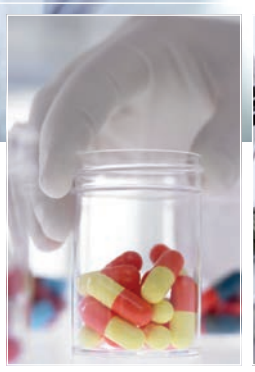
THE WORLD LEADER IN CLEAN AIR SOLUTIONS



Pharmaceutical Clean Air Solutions

PARTICULATE AND GASEOUS FILTRATION

AAF® INTERNATIONAL

BETTER AIR IS OUR BUSINESS®

Optimizing Process Performance for Protecting Human Health

Globalization, 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 realizing 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, covering particulate and gas-phase filters, in offering a customized 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 optimized filter performance and quality assurance.

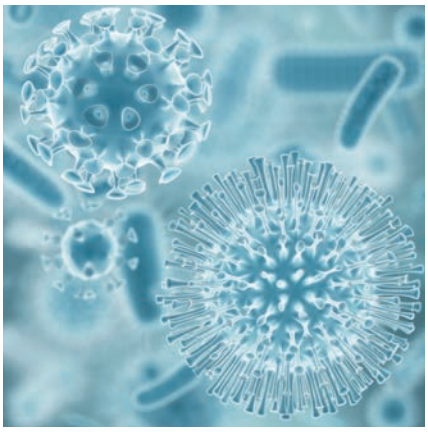
Many pharmaceutical applications today already benefit from AAF's recognized expertise in air filtration. The combination of an extensive product portfolio with high level technical support capabilities has provided significantly improved results for many satisfied customers.

AAF has an in-depth understanding of the challenges and opportunities for pharmaceutical and medical device manufacturing processes. This understanding and technical ability makes AAF the preferred partner in optimizing process performance for protecting human health.

Erik Geertsema
Test Engineer,
AAF International

We manufacture and individually test all our HEPA filters in a modern cleanroom environment. We believe that only then, product performance is 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 organizational 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

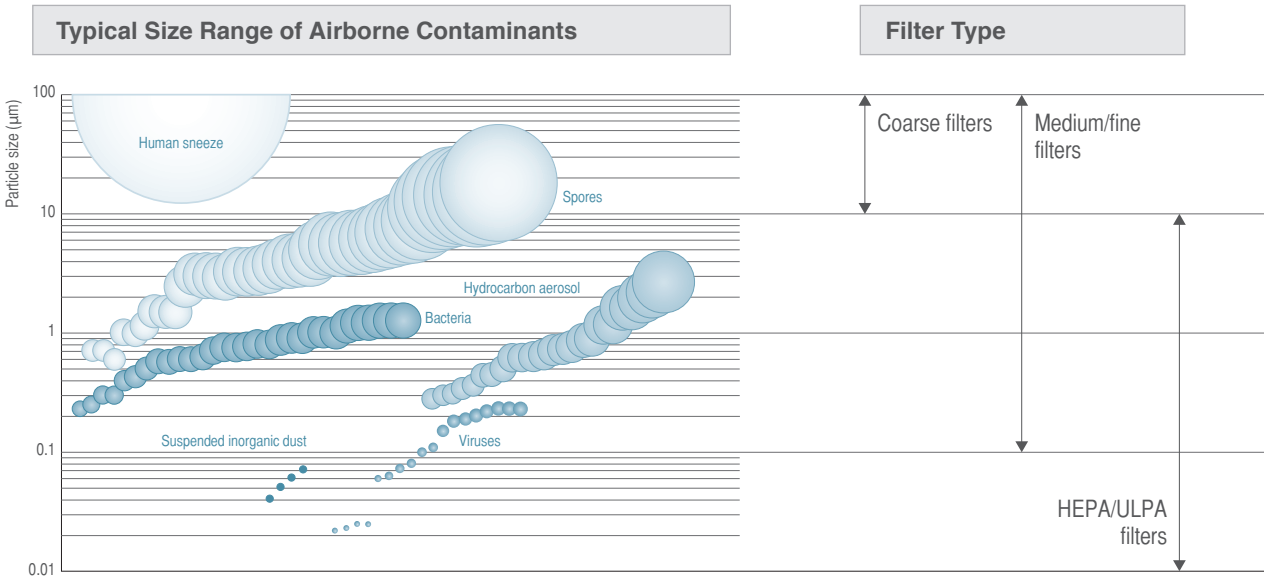
Everything that could come into direct contact with a pharmaceutical product is a potential risk toward contamination. Limiting exposure to airborne contaminants is critical, as they may result in health and safety issues. Preventive measures and quality management procedures are described in several 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.

Typical Airborne Contaminants

Airborne contaminants differ in size and impact on 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.

Figure 1:



Classifying Air Filters

The type of activities within a particular pharmaceutical processing environment will determine the level of cleanliness that is required. To ensure that stringent air quality levels for safely manufacturing medicinal products are met, a carefully designed air filtration system is vital. Based on their performance efficiency, air filters are classified according to two widely accepted standards, ASHRAE 52.2 and the Institute of Environmental Sciences and Technology (IEST) Recommended Practice (RP) IEST-RP-CC001. Internationally EN1822 and the ISO standard 29463 (High Efficiency Filters and Filter Media for Removing Particles in Air) is the accepted classification method (table 1).

ASHRAE 52.2

ASHRAE Standard 52.2 (Method of Testing General Ventilation Air-cleaning Devices for Removal Efficiency by Particle Size) describes a method of laboratory testing to measure the performance of air filters as a function of particle size. The method of testing measures the performance of air filters in removing particles of specific sizes as the filters become loaded by standard loading dust. The dust is fed at intervals to simulate accumulation of particles during service life. The standard defines procedures for generating the aerosols required for conducting the test. The standard also provides a method for counting airborne particles of 0.3 micrometers to 10 micrometers upstream and downstream of the air filter in order to calculate removal efficiency by particle size. The overall reporting value of the air filter is expressed as Minimum Efficiency Reporting Value (MERV) (table 2).

AAF offers a broad range of ASHRAE 52.2 compliant and energy efficient air filters as prefiltration to final HEPA filters. The choice of prefiltration will determine the cleanliness of the air entering the final filter and therefore its lifetime.

Table 1: ISO 29463 Filter Classes and Equivalents

ISO Filter Class	Efficiency	IEST*	EN 1822
ISO 15 E	>95%	-	H 11
ISO 20 E	>99%	-	
ISO 25 E	>99.5%	-	H 12
ISO 30 E	>99.9%	-	
ISO 35 H	>99.95%	-	H 13
-	>99.97%	A,B,E,H,I	-
ISO 40 H	>99.99%	C,J(K)	
ISO 45 H	>99.995%	K	H 14
ISO 50 U	>99.999%	D	
ISO 55 U	>99.9995%	F	U 15
ISO 60 U	>99.9999%	G	
ISO 65 U	>99.99995%	G	U 16
ISO 70 U	>99.99999%	G	
ISO 75 U	>99.999995%	G	U 17

**IEST Type A, B, C, D, and E are classified per test results using photometers (Mil Std 282). Types F, G, H, I, J, and K are classified per test results using particle counters.*

Table 2: Air Filter Classification per ASHRAE 52.2.

Standard 52.2 Minimum Efficiency Reporting Value (MERV)	Complete Average Particle Size Efficiency, % in Size Range, μm			Average Arrestance, %, Addendum B
	Range 1 0.30 - 1.0	Range 2 1.0 - 3.0	Range 3 3.0 - 10.0	
1	n/a	n/a	$E_3 < 20$	$A_{avg.} < 65$
2	n/a	n/a	$E_3 < 20$	$65 \le A_{avg.} < 70$
3	n/a	n/a	$E_3 < 20$	$70 \le A_{avg.} < 75$
4	n/a	n/a	$E_3 < 20$	$75 \le A_{avg.}$
5	n/a	n/a	$20 \le E_3 < 35$	n/a
6	n/a	n/a	$35 \le E_3 < 50$	n/a
7	n/a	n/a	$50 \le E_3 < 70$	n/a
8	n/a	n/a	$70 \le E_3$	n/a
9	n/a	$E_2 < 50$	$85 \le E_3$	n/a
10	n/a	$50 \le E_2 < 65$	$85 \le E_3$	n/a
11	n/a	$65 \le E_2 < 80$	$85 \le E_3$	n/a
12	n/a	$80 \le E_2$	$90 \le E_3$	n/a
13	$E_1 < 75$	$90 \le E_2$	$90 \le E_3$	n/a
14	$75 \le E_1 < 85$	$90 \le E_2$	$90 \le E_3$	n/a
15	$85 \le E_1 < 95$	$90 \le E_2$	$90 \le E_3$	n/a
16	$95 \le E_1$	$95 \le E_2$	$95 \le E_3$	n/a

IEST-RP-CC001

To ensure the highest levels of air purity, pharmaceutical processes need to rely on high efficiency particulate air filters as terminal filters. These air filters are subject to classification according to IEST-RP-CC001 (HEPA and ULPA filters). This recommended practice (RP) covers basic provisions for HEPA and ULPA filter units as a basis for agreement between customers and suppliers.

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%

[1]Either 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.
[2]Filter 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.

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 costruction. A customer should specify the level of performance and grade of construction required. A customer should also specify the filter efficiency required if it is not covered by the performance level specified in this RP (table 3).

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. It 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.

Classifying Cleanrooms

The production of sterile pharmaceuticals is subject to special requirements in order to minimize 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.

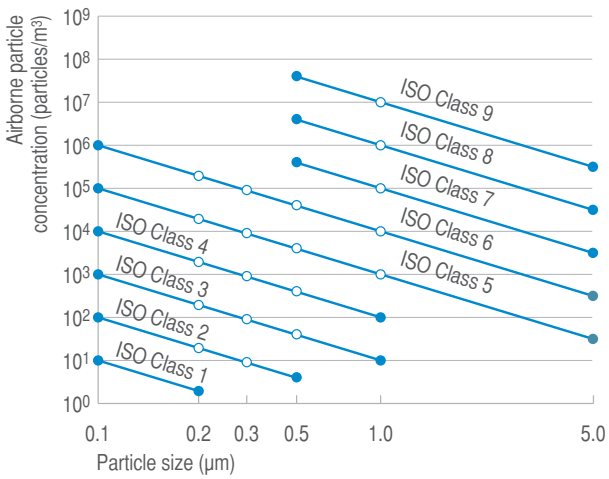
Classification Standards

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 graphical 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 ≥ 0.5 µm and ≥ 5.0 µm 'at-rest' and 'in operation' state. Particles of 0.5 µm 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 ≥ 5.0 µm, 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 minimize or eliminate risk of cross contamination and errors (table 5).

Table 4: Cleanroom Classification According to EU GMP Annex 1

Maximum Permitted Number of Particles /m³ Equal to or Greater than the Tabulated Size					International Cleanroom Standard Comparison for 'At-rest'		
	At-rest		In Operation				
Grade	0.5 µm	5.0 µm	0.5 µm	5.0 µm	FED 209E	FED 209D	ISO 14644
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

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 minimizing 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 4).

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).

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 optimized, the pressure differentials between rooms are met, and healthy working conditions are achieved.

Table 5: Typical Cleanroom Activities for Terminal Sterilization and Aseptic Preparation

GMP Grade	Examples of Typical Activities	
	Terminal Sterilization	Aseptic Preparation
A	Filling of products for sterilization (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 sterilization (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

Qualifying HEPA Filters

Pharmaceutical cleanrooms require an extensive validation procedure before initiating pharmaceutical production. The process then has to be revalidated in predefined intervals. 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 requalification of its performance characteristics.

Qualification Procedure

FDA cGMP Guidelines: Sections IV-Buildings and Facilities; Section IX-Validation of Aseptic Processes; and Section X-Laboratory Controls describe the principles of validation and qualification that are applicable to the production of medicinal products. The procedure typically follows a V-shaped model, consisting of three sequential steps (figure 3). 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 what I had ordered and expected?

Examples of HEPA filter requirements:

- Individual test report according to IEST-RP-CC001
- 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

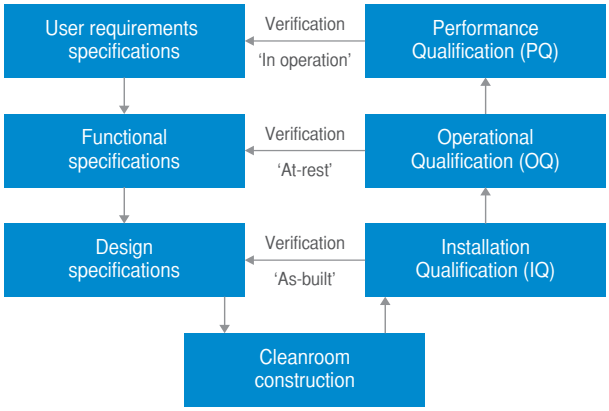
Performance Qualification (PQ): does the HEPA filter demonstrate reliable performance during full-scale operation?

Examples of HEPA filter requirements:

- Absence of leakage (e.g., media) and bypass (e.g., gasket seal) according to IEST-RP-CC034
- Consistent particulate collection efficiency over time
- Absence of fiber 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, it 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/liter of oil-based aerosol, for scanning air filters for leakage.

A low concentration aerosol challenge exposure is always recommended as it gives a less contaminated filtration system and therefore an optimized energy efficiency and improved HEPA filter lifetime expectancy.

Dedicated Support from AAF

With AAF's new Nelior® 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 optimized for its purpose.

Pharmaceutical Process Application

Design Considerations and AAF Air Filtration Solutions

1

Preparation and Cleaning

FDA GMP Classification: Grade C (ISO 7)

Activities:

Support area with medium risk preparation activities such as cleaning, for conveyance into a dry heat sterilization tunnel, before entering the aseptic filling and closing area.

Cleanroom Parameters:	
Room height (ft.)	9
Area per occupant (sq. ft.)	100
Equipment in room	30% floor
Occupant activity	occasional movement
Traffic in/out per hour	2-6
Room over pressure	0-0.06 in. w.g. (0-15 Pa)
Air changes per hour	20-40
Air lock	small
Airflow pattern	non-unidirectional
Clean air inlets as % of ceiling area	10-20
Clean air inlet locations	ceiling
Terminal velocity at clean air inlet	30-90 FPM (0.15-0.45 m/s)
Return air location	low sidewall

2

Sterile Filling and Closing

GMP Classification: Grade A (ISO 5)

Activities:

Process core isolator environment with high risk aseptic filling and closing operations for parenteral products such as prefilled syringes, cartridges, and vials in a GMP grade B controlled background area.

Cleanroom Parameters:	
Room height (ft.)	N/A
Area per occupant (sq. ft.)	300
Equipment in room	minimum
Occupant activity	minimum
Traffic in/out per hour	N/A
Room over pressure	0.06 in. w.g. (15 Pa)
Air changes per hour	500
Air lock	yes
Airflow pattern	unidirectional
Clean air inlets as % of ceiling area	90
Clean air inlet locations	ceiling (wall)
Terminal velocity at clean air inlet	60-90 FPM (0.30-0.45 m/s)
Return air location	low sidewall

3

Checking and Packaging

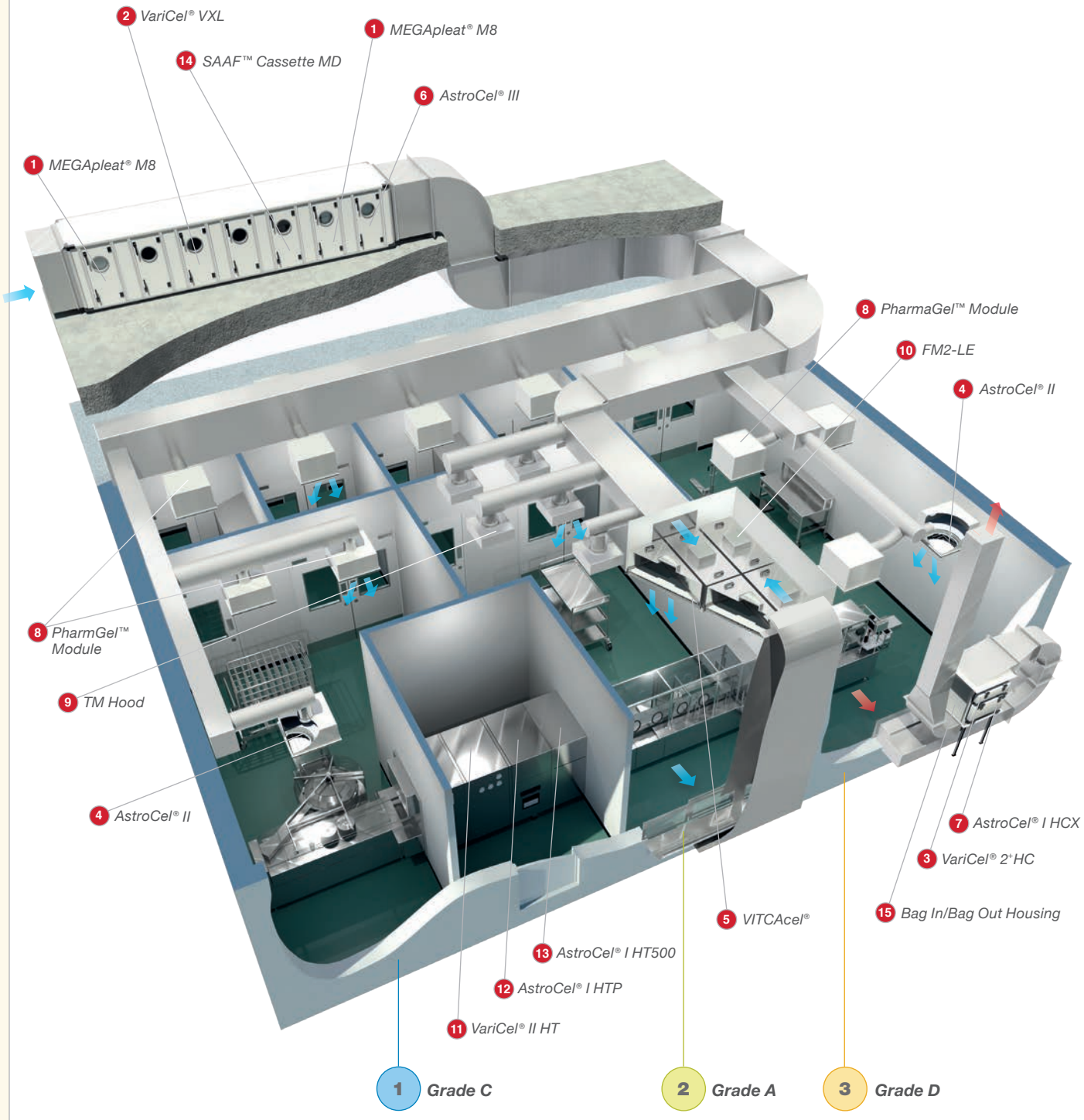
GMP Classification: Grade D (ISO 8)

Activities:

Support area with medium risk activities such as visual checks of the aseptically prepared products, batch quality inspections, labeling, and secondary packaging.

Cleanroom Parameters:	
Room height (ft.)	7.5
Area per occupant (sq. ft.)	50
Equipment in room	50% floor
Occupant activity	constant activity
Traffic in/out per hour	more than 6
Room over pressure	0.02-0.04 in. w.g. (5-15 Pa)
Air changes per hour	10-20
Air lock	no
Airflow pattern	non-unidirectional
Clean air inlets as % of ceiling area	5-10
Clean air inlet locations	ceiling / high sidewall
Terminal velocity at clean air inlet	30-90 FPM (0.15-0.45 m/s)
Return air location	sidewall

AAF Air Filtration Solutions



The illustration represents a simplified aseptic manufacturing process with the aim of visualizing AAF's air filtration solutions. Its exact design and the air filtration system installed, will always be application specific. Please contact your local AAF affiliate office for a custom-made solution.

AAF Air Filtration Solutions

1 MEGApleat® M8

Strongest and longest-lasting MERV 8 pleated filter. Lower pressure drop and higher DHC means reductions in energy consumption and operating costs.

Recommended Application:
First stage prefiltration and post stage filtration in central air handling unit.
Brochure AFP-1-200

Optional product option: PerfectPleat® HC M8

Configuration and Performance:

- MERV 8
- Media: 100% synthetic fiber blend
- Filter frame: High wet-strength beverage board
- Metal backing: Heavy-duty, galvanized expanded metal
- Available in 1", 2" and 4" models

2 VariCel® VXL

Minipleat V-bank design with the lowest average resistance and highest DHC over the life of the filter.

Recommended Application:
Second stage of filtration in central air handling unit.
Brochure AFP-1-162

Optional product option: VariCel®

Configuration and Performance:

- MERV 15, MERV 14, MERV 13, and MERV 11
- Media: Moisture-resistant, dual-density microglass
- Filter frame: High impact polystyrene plastic
- Temperature limit: 176°F / 80°C

3 VariCel® 2+HC

Extended surface mini-pleat filter with low pressure drop and slim-line design for low space access or space saving issues.

Recommended Application:
First stage filtration in Bag In/Bag Out housing.

Configuration and Performance:

- MERV 15, MERV 14, and MERV 11
- Media: Embossed synthetic
- Filter frame: High impact polystyrene plastic
- Temperature limit: 150°F / 66°C

4 AstroCel® II

High efficiency mini-pleat filter individually factory tested for guaranteed performance.

Recommended Application:
Terminal filtration for PharmaGel Hood in GMP grade C-D cleanrooms.
Brochure AFP-1-404

Configuration and Performance:

- HEPA or ULPA efficiency
- Media: Ultrafine microglass
- Filter frame: Anodized aluminum “C” channel
- Seal: Gel, neoprene gasket, or knife edge

5 VITCAcel®

Individually tested pharmaceutical mini-pleat filter with an extremely low resistance and superior mechanical media strength.

Recommended Application:
Terminal filtration for TM Hood or FM2-LE in GMP grade A-B cleanrooms.

Configuration and Performance:

- HEPA or ULPA Efficiency
- Media: Nelior
- Filter frame: Anodized aluminum
- Seal: Gel, neoprene gasket, or knife edge

6 AstroCel® III

High efficiency filter in a V-shaped configuration with optimized fiberglass media packs for handling high airflow rates.

Recommended Application:
Final stage filtration in central air handling unit.
Brochure AFP-1-405

Configuration and Performance:

- HEPA Efficiency
- Media: Ultrafine microglass
- Filter frame: Extruded aluminum
- Seal: Gasket or gel

7 AstroCel® I HCX

High capacity filter in separator style configuration for handling high airflow rates at an extremely low resistance.

Recommended Application:
Final stage filtration in Bag In/Bag Out housing.
Brochure AFP-1-110

Configuration and Performance:

- HEPA Efficiency
- Media: Ultrafine microglass
- Filter frame: Metal or wood
- Seal: Gasket or gel

8 PharmaGel™ Module

Rigid and leak free filter housing available in multiple executions and designed for easy filter installation and exchange.

Recommended Application:
Terminal filtration module in GMP grade C-D cleanrooms.
Brochure AFP-1-408

Configuration and Performance:

- Construction: Aluminum
- Connection: Top inlet
- Seal: Gel
- Filter type: AstroCel II or VITCAcel

9 TM Hood

Hermetically sealed and light weight filter module individually factory tested for guaranteed high filtration performance.

Recommended Application:
Terminal filtration module in GMP grade B cleanrooms.

Brochure AFP-1-475

Configuration and Performance:

- Construction: Anodized aluminum
- Seal: Gasket or gel
- Filter type: AstroCel II or VITCAcel

10 FM2-LE

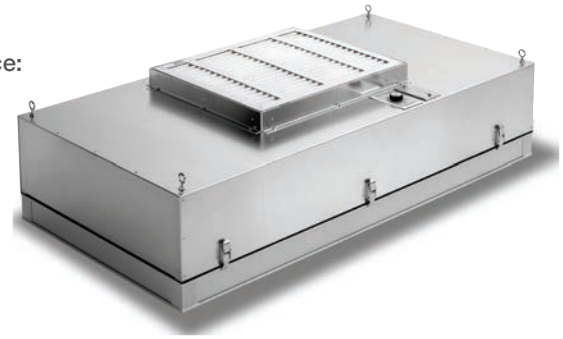
Self-contained, energy efficient ceiling filter unit available in multiple sizes with a high performance and low sound level fan motor system.

Recommended Application:
Terminal filtration module in GMP grade A cleanrooms.

Brochure AFP-1-420

Configuration and Performance:

- Construction: 16-gauge mill finish aluminum
- Fan motor: AC motorized impeller
- Speed controller: Variable
- Filter type: AstroCel II or VITCAcel



11 VariCel® II HT

Extended surface mini-pleat filter designed for high temperature operation.

Recommended Application:
High temperature filtration for dry heat sterilization and depyrogenation.

Configuration and Performance:

- MERV 11, MERV 13, and MERV 14
- Media: Dual-density Microglass
- Filter frame: Aluminized steel
- Temperature limit: 350°F - 500°F / 176°C - 260°C

12 AstroCel® I HTP

Deep-pleat high temperature HEPA filter in a robust construction for superior durability and reliable operation.

Recommended Application:
High temperature filtration for dry heat sterilization and depyrogenation.

Brochure AFP-1-115

Configuration and Performance:

- ≥99.97% minimum efficiency on 0.3 micrometer particles
- Media: Ultrafine microglass
- Filter frame: Stainless steel with support bars
- Seal: Fiberglass
- Temperature limit: 662°F / 350°C (750°F / 400°C 1h peak)

13 AstroCel® I HT500

High capacity filter in separator style configuration designed for high temperature applications.

Recommended Application:
High temperature filtration for dry heat sterilization and depyrogenation.

Brochure AFP-1-115

Configuration and Performance:

- ≥99.97% minimum efficiency on 0.3 micrometer particles
- Media: Ultrafine microglass
- Filter frame: Stainless steel or aluminum
- Seal: Gel
- Temperature limit: 500°F / 260°C

14 SAAF™ Cassette MD

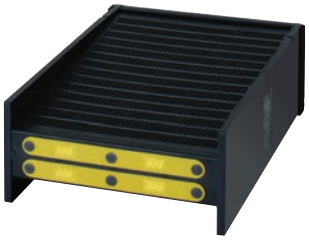
Patented V-bank gas-filtration cassette designed for optimal gas removal.

Recommended Application:
Gas-phase filtration in central air handling unit.

Brochure GPF-1-108

Configuration and Performance:

- Construction: 100% recyclable/ incinerable High Impact Polystyrene (HIPS) plastic
- Chemical media: SAAFBlend GP



15 Bag In/Bag Out Housing

Side loading filter system for removing contaminated particulate filters and/or gas absorbers.

Recommended Application:
Safe change of contaminated filters by radioactive, pathogenic, or toxic substances.

Brochure APC-1-260

Configuration and Performance:

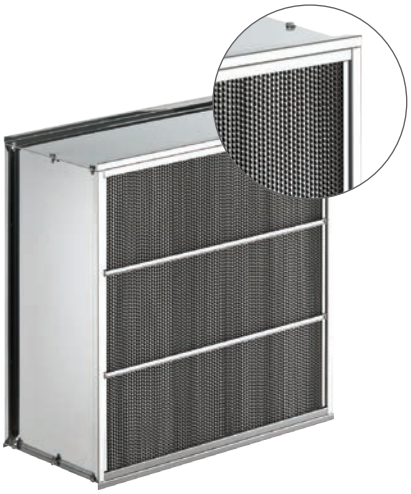
- Casing: 14 gauge, 304 stainless steel
- Modularity: Up to six filters wide
- Temperature: 150°F / 66°C

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.

High Temperature HEPA Solution

To prevent Endotoxin contamination in sterile conditions, containers and closure surfaces need to be depyrogenated. Endotoxins are removed by applying dry heat sterilization, for which the air is to be cleaned by a reliable HEPA filtration system. The new AstroCel I HTP high temperature HEPA filter is designed to provide excellent protection of this critical depryogenation process.



New AstroCel® I HTP high temperature HEPA filter.

Reliable High Temperature Operation

In continuous service, the AstroCel I HTP filter offers a maximum temperature resistance of 662°F / 350°C, with a peak of 752°F / 400°C for one hour. Its robust stainless steel structure prevents potential damage of components that could occur from the heat stretching during temperature rising and falling. Thorough heat-cycle tests have confirmed a damage-free construction and a consistent performance in pressure drop and dust holding capacity at 662°F / 350°C.

Two strong vertical support bars, inside the media pack, make sure that the media pack stays fully intact, preventing winding of the pleats at the bottom. The sloped design of the stainless steel separators reduces media stretching, which causes particle shedding. The AstroCel I HTP filter offers a unique combination of high temperature operation and superior durability, optimizing process results and limiting unscheduled downtimes.

High Air Quality Conditions

The high temperature HEPA filter provides a high air quality level with a particulate collection efficiency of ≥ 99.97% for 0.3 µm particles at a nominal airflow of 1236 CFM. With the possibility of this high airflow rate, ventilation can be optimized for enabling a speedy temperature control. The silicone free construction of the AstroCel I HTP filter further enhances the air purity level during the various steps of the drying process, without the risk of denaturation by siloxane contamination caused by the filter itself.

For critical pharmaceutical aseptic process applications, in which no concessions can be accepted to sterility and product quality, the AstroCel I HTP filter provides the right solution for ensuring that the strict air cleanliness conditions are met.

Certified Cleanrooms

It is critical that any filter manufacturer produce high efficiency filters to the same level of quality and under similarly controlled production, test, and packaging area conditions. The risk of contamination and expense resulting from failure is too great to ignore. Filters introduced into a pharmaceutical cleanroom directly affect the performance and viability of performance of that clean area.

AAF State-of-the-Art Cleanroom

An essential part of contamination prevention is adequate separation of operation areas. To maintain air quality, it is important to achieve a proper airflow from area of higher cleanliness to adjacent less clean areas (from the FDA cGMP Guidelines).

Contamination can be the difference between success or failure. Not only does the particulate collection performance of the high efficiency filter need to comply with industry specifications, but also contamination resulting from the filter itself must be eliminated. This requires manufacturing, testing, and packaging of high efficiency filters under clean conditions for meeting the most demanding customer expectations. AAF has acknowledged this importance, and constructed several new cleanroom areas within its Columbia, Missouri manufacturing facility.

The entire Columbia Cleanroom area covers 9,247 square feet and consists of four core process steps: filter media pleating, assembly, testing, and packaging.

By controlling our processes and maintaining a regimented quality program, including manufacturing, testing, and packaging in cleanroom environments, we provide our customers a total package for their most stringent requirements.

Nelior® Filtration Technology

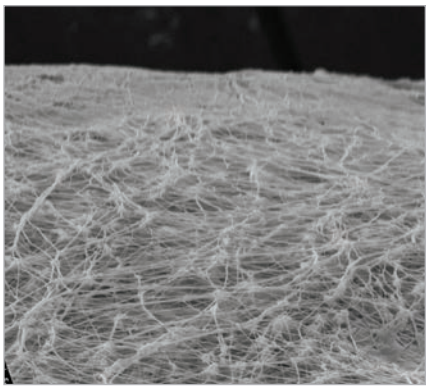
AAF VITCAcel filters feature Nelior Filtration Technology; the latest advancement in high-performance air filtration, exclusively developed and marketed by AAF. HEPA filters with Nelior Filtration Technology provide significant benefits for pharmaceutical applications that operate under strictly controlled conditions.

About Nelior® Filtration Technology

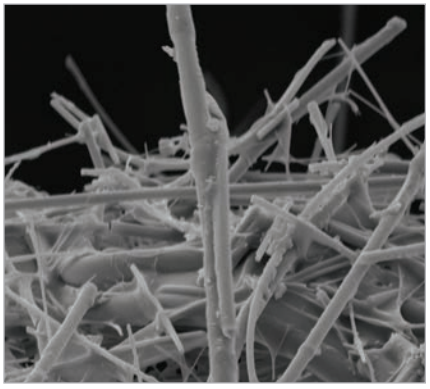
Nelior Filtration Technology is based on a patented membrane air filtration media. It features a superior composition and mechanical strength that give unique performance characteristics to HEPA filtration, unmatched by any other air filtration media currently available on the market.

The media is composed of an evenly distributed layer of fibers with nanometer-scale diameters. It provides up to 50% lower operating resistance than traditional HEPA filters in combination with an excellent overall particulate collection efficiency. The superior mechanical strength is demonstrated by a high tensile strength, burst pressure, and abrasion resistance. Nelior membrane media retains its integrity with high resistance to any potential damage from filter handling prior to, at installation, or during operation. This means that filter media failure risk can be minimized from elements within the airstream during operation and the contamination risk from microglass media shedding fibers downstream can be eliminated.

With AAF Nelior Filtration Technology pharmaceutical applications can rely on a sustainable performance with reduced operational risk, less energy consumption, and substantial cost savings. For full details, please contact your local AAF affiliate office.



Resilient Nelior® media at fold tip @ 10,000x magnification.



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

High Value Areas:

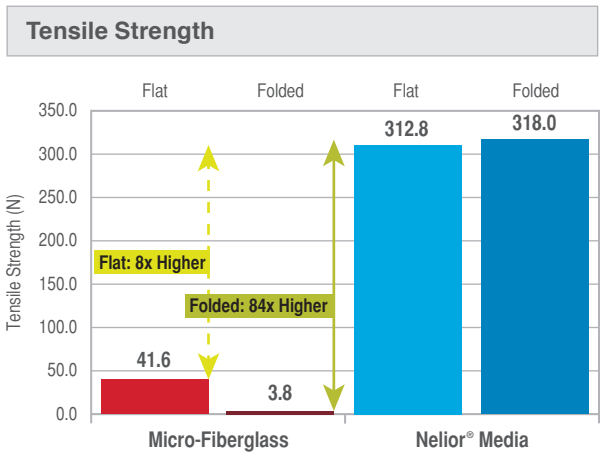
Consistent Air Quality
Providing a reliably high air quality to optimize contamination control and meet the stringent conditions in clean environments.

Environmental Savings
Reducing operating resistance and extending life expectancy to minimize energy consumption, CO_2 equivalents, and waste.

Improved Process Performance
Limiting risk of failures to enhance product quality and prevent negative effects from unnecessary process interruptions.

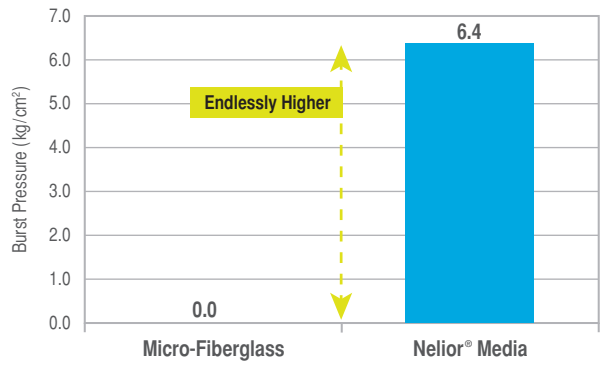
Beneficial Total Cost of Ownership
Improving process reliability and overall efficiency to save life cycle costs and improve profitability performance.

Figure 4:



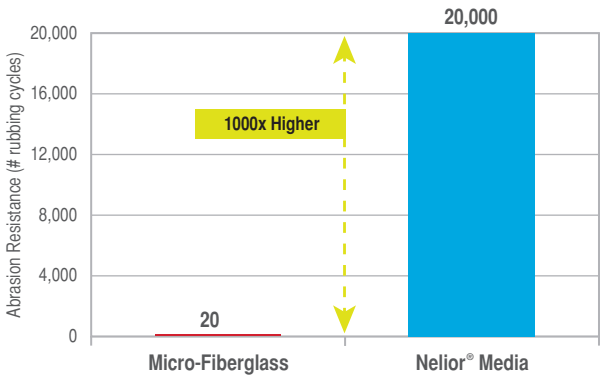
Results based on Test Standard DIN EN 29073-3.

Figure 5:



Results based on Test Standard DIN EN 13938-2.

Figure 6:



Results based on Test Standard DIN EN 12947-2.

Mechanical Strength Reduces Contamination Risks

Following the recognized 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 being 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 latest generation of membrane media represent a better solution due to considerably improved mechanical strength and reduced pressure difference, thus increasing economy and quality of sterile production units.

Higher costs of such new filters are justified, since the risk of damages, which might be detected not before the following semi-annual leak testing cycle will be considerably reduced - a good example for “Best available technology not entailing excessive costs.”

Dr. Lothar Gail
GMP and cleanroom consultant VDI.

Pharmaceutical Clean Air Solutions

Air Filtration Glossary

Air filter
Unit installed in an air handling system designed to remove particulates from the air passing through it.

Airflow
Distribution of air passing through a filter element per unit of time. Airflow rate is usually expressed in ft^3/min or CFM (m^3/h or m^3/s).

Airborne particles
Liquid or solid matter that is suspended in the air. Sizes of airborne particles vary and are expressed in micrometer (µm).

Arrestance
Removal of standard test dust expressed as weight percentage. Average value is used for classification of coarse filters.

Coarse filter
Air filter classified in one of the classes G1 to G4 according to EN779:2012 based on removal of synthetic loading dust. See ASHRAE 52.2.

Efficiency
Removal of the number of defined particles by the air filter in relation to the upstream concentration expressed in a percentage.

Energy efficiency
Ability of the air filter to minimize electricity consumption as a function of its operating resistance and operating conditions.

Face velocity
Airflow rate divided by the effective media area of a filter element. Face velocity is usually expressed in FPM (m/s).

Filter class
Indication of the air filtration performance measured according to test procedures compliant to ASHRAE 52.2 and IEST RP CC001.

Filter integrity
The degree to which the air filter demonstrates a consistent performance according to specification without leakage.

Filter qualification
Action of proving that the HEPA filter functions in line with expectations by using methods according to ISO 14644-3:2005.

Fine filter
Air filter classified in one of the classes F7 to F9 according to EN779:2012 based on minimum efficiency of 0.4 µm particles.

HEPA filter
High Efficiency Particulate Air filter classified with a minimum efficiency of 99.97% when challenged with particles sized at 0.3 micrometers.

HVAC
Heating, Ventilation and Air Conditioning. Regulating system including air filtration to control indoor air quality and comfort.

Life Cycle Valuation
Comparative calculation of air filters demonstrating the provided environmental and financial cost during the installation period.

Mechanical strength
Indication of the elastic or inelastic behavior of air filtration media under pressure demonstrating resistance to damage.

Media
Fibrous material used to remove solid or gaseous particulates from the air passing through a filter element.

MPPS
Most Penetrating Particle Size. Represents the particle size at which penetration of particles through the filter media is highest.

Nelior® Filtration Technology
Patented air filtration media based on fine nanometer-scale membrane fibers, exclusively developed and marketed by AAF.

Operating resistance
Difference in pressure between upstream and downstream airflow through an air filter. Also referred to as pressure drop.

Prefilter
Air filter installed for removal of larger particles from the passing air to protect the higher efficiency air filters in the next stage.

Terminal filter
High efficiency air filter used as final filtration stage to critical process areas that require strict contamination control.

Test aerosol
Suspension of liquid or solid particles used to challenge air filter media for factory efficiency tests and in-situ integrity tests.

ULPA filter
Ultra Low Penetration Air filter classified with a minimum efficiency 99.999% when tested in accordance with the methods of IEST-RP-CC007.

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