



Clean air in the Pharmaceutical Industry

Optimizing process performance
for protecting human health



Application solutions guide

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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 practically impossible to identify by our human senses. Most airborne particulates are that 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, in worst case unrecoverable, damage that has occurred.

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

The role for air filtration

No clean air without a carefully selected and reliably functioning air filtration system. The performance of installed air filters, either terminal filters or pre-filters, 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 insights in 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, its state-of-the-art air filtration solutions and its 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 for offering a customized clean air solution. Each product is carefully designed, manufactured and tested in full compliance with applicable standards to meet the most challenging demands at lowest energy consumption.

The European manufacturing takes place in ISO 9001, ISO 14001 and OHSAS 18001 certified facilities. AAF's HEPA filters are produced, tested and packaged in a modern ISO 7 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 its extensive product portfolio with high-level technical support capabilities has provided significant improvement results for many satisfied customers.

AAF has a thorough understanding of the challenges and opportunities for medicine manufacturing processes. It makes AAF the preferred partner in optimizing process performance for protecting human health.

AAF
quality
statement

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 medicine should be carried out under high levels of air cleanliness. Any contamination of starting material, final product or personnel must be avoided at all times by implementing appropriate technical and organizational measures. Where the significance of such contamination risk may vary with the type of contaminant and the product that is being contaminated, reliable airborne contamination control remains critical.

Quality of medicinal products

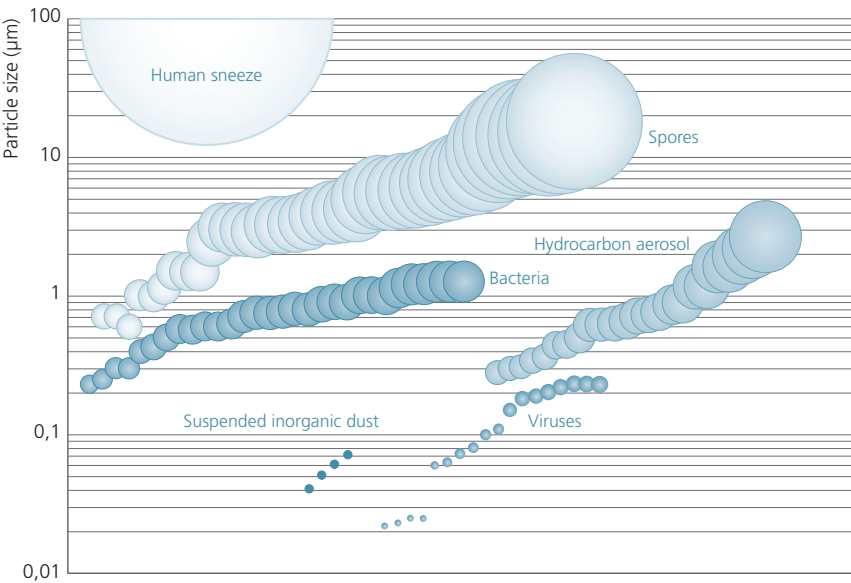
Everything that could come into direct contact with a medicinal product is a potential risk for causing contamination. Limiting exposure to airborne contaminants is critical as they can result in health and safety issues. Preventive measures and detailed quality management procedures are described in several industry guidelines, such as EU GMP Directive 2003/94/EC (Good Manufacturing Practices) and ICH (International Conference on Harmonisation), with the aim to ensure a consistent production and control of medicinal products for human use.

Air filtration plays a central 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. The figure below shows a typical size range of airborne particles and microorganisms. Each particle size range requires a specific air filtration technique for obtaining the required air quality levels.

Typical size range of airborne contaminants

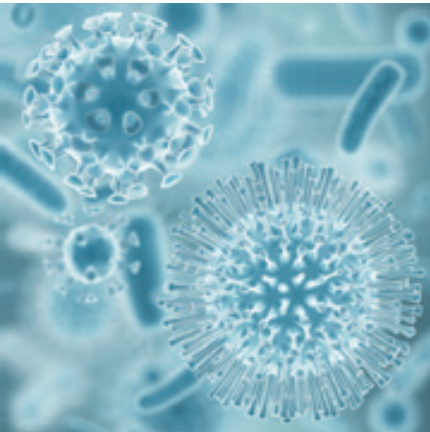


Air filtration techniques

Coarse filters

Medium/Fine filters

HEPA/ULPA filters



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 two widely accepted European standards, the EN779:2012 and the 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

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	≥ 99,99999	≤ 0,0001

EN1822:2009 establishes a procedure for determining the filtration performance according to the efficiency of MPPS (Most Penetrating Particle Size) particles. It provides a standardized 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.



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.

Voice of the expert

Conor Murray
Head of Delegation for Ireland at ISO TC 209 and Subject Matter Expert on Working Groups WG 01 (Airborne Cleanliness Classification), WG 02 (Biocontamination Control) and WG 03 (Cleanroom Testing)



HEPA filtration is at the core of best practice GMP Engineering Controls and should be part of an integrated Life Cycle design including TCO (Total Cost of Ownership).

Careful selection is required to meet the specified GMP performance and application, including critical control points such as air velocity uniformity, airflow distribution and clean up times. From a cleanroom and contamination control standards perspective EN1822:2009 along with ISO 14644 and ISO 14698 are very important standards relating to HEPA filtration. The update and revisions to ISO 14644-1 (Classification by Airborne Particles) and -2 (Ongoing Environmental Monitoring of Airborne Particulate Cleanliness) and -3 (Test Methods) are close to completion. ISO 14698 on Biocontamination control is currently being revised and updated to reflect latest best practices in ongoing Environmental Monitoring, testing methods (referred to ISO 14644-3) and airborne and surface microbiological contamination control.

HEPA filtration is at the forefront of the engineering control in GMP cleanrooms and now with the alignment and harmonisation of filter testing and cleanroom and biocontamination control standards this is an important junction in this technology.

Finally, the support of an air filtration vendor with a significant level of product and applications knowledge is equally critical to ensuring best practice GMP compliance in a cost effective manner.

Classifying cleanrooms

The production of sterile medicine 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 in terms of an ISO class *N*. The ISO class represents maximum allowable concentrations for considered particle sizes, ranging from 0,1 µm up to 5,0 µm. The figure on the right 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 inside.

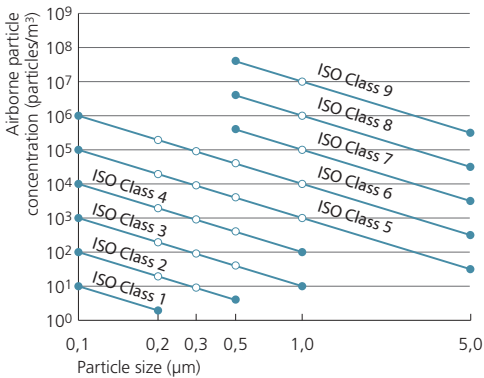
For the operational environmental monitoring of the production of sterile preparations, EU GMP distinguishes four alpha grades. Each grade is assigned maximum permitted airborne particle concentrations for sizes ≥ 0,5 µm and ≥ 5,0 µm ‘at-rest’ and ‘in operation’ state. Particles of 0,5 µm and larger 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.

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 in a quality approach into the manufacturing process, to minimize or eliminate risk of (cross)contamination and errors.

Cleanroom classification according to EU GMP Annex 1				
Maximum permitted number of particles /m³ equal to or greater than the tabulated size				
	At-rest		In operation	
Grade	0,5 µm	5,0 µm	0,5 µm	5,0 µm
A	3.520	20	3.520	20
B	3.520	29	352.000	2.900
C	352.000	2.900	3.520.000	29.000
D	3.520.000	29.000	Not defined	Not defined

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.

International cleanroom standard comparison for ‘at-rest’:		
FED 209E	FED 209D	ISO 14644
M 3.5	Class 100	ISO 5
M 3.5	Class 100	ISO 5
M 5.5	Class 10.000	ISO 7
M 6.5	Class 100.000	ISO 8

Monitoring microbial contamination according to EU GMP Annex 1

Grade	Recommended limits for microbial contamination (average values)			
	Air sample cfu/m³	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	-

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.

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 the ISO 14698 standard.

The role for air filtration

Especially for aseptically prepared parenteral medicine (such as injectables and infusions) no contamination can be accepted, as otherwise severe harm or life-threatening health risks to the patient can be the 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 laminar flow air, preceded by sequential pre-filtration 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.



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 components (unusual risk profile)	Preparation of materials and products (sterile filtering)
D	Preparation of components (usual risk profile)	Handling of components after washing

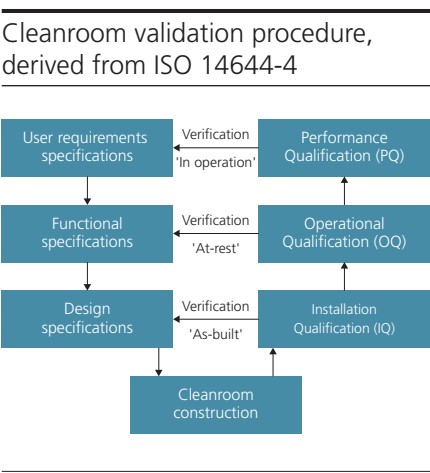
Qualifying HEPA filters

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 labelling 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



Installed 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 efficiency 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 therewith the quality of medicinal products, periodic re-qualification of terminal HEPA filters is required. Subject to risk assessment of the cleanroom activity, this interval is typically set on 6 months for GMP grade A aseptic processes.

The two 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 - 100 mg/m³ oil-based aerosol, such as DOP, PAO or DEHS, for scanning air filters for leakage. In contrast, the sensitive DPC method measures HEPA filter integrity by recording and counting discrete particles for a specific volume for which a much lower upstream concentration is required. For this method, solid PSL particles can also be used as upstream test aerosol. Although the AP and DPC test methods have both proven to provide steady and repeatable outcomes, the test results obtained are not directly comparable.

Irrespective of the test method, a low concentration aerosol challenge exposure is always recommended as it gives a less contaminated filtration system and therewith an optimized energy efficiency and improved HEPA filter lifetime expectancy.

Dedicated support from AAF

Where AAF executes its factory tests in full compliance with EN1822:2009, AAF can also provide dedicated support in designing and executing installed HEPA filter integrity tests.

Based on its experience in the pharmaceutical industry, AAF has developed a DPC test procedure according to ISO 14644-3 in cooperation with the United Kingdom Accreditation Service (UKAS). The DPC test method is required for in-situ testing HEPA filters with AAF's unique NELIOR® membrane media, but is also perfectly suited for traditional HEPA filters. The engineers of AAF's European Technical Support Group 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

EU 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 (m)	: min. 2,75
Area per occupant (m²)	: 10
Equipment in room	: 30% floor
Occupant activity	: occasional movement
Traffic in/out per hour	: 2 - 6
Room over pressure (Pa)	: 10 - 15
Air changes per hour	: 20 - 40
Air lock	: small
Airflow pattern	: turbulent
Clean air inlets as % of ceiling area	: 10 - 20
Clean air inlet locations	: ceiling
Terminal velocity at clean air inlet (m/s)	: 0,15 - 0,45
Return air location	: low sidewall

2

Sterile filling and closing

EU 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 (m)	: N/A
Area per occupant (m²)	: 30
Equipment in room	: minimum
Occupant activity	: minimum
Traffic in/out per hour	: N/A
Room over pressure (Pa)	: 15
Air changes per hour	: 500
Air lock	: yes
Airflow pattern	: laminar
Clean air inlets as % of ceiling area	: 90
Clean air inlet locations	: ceiling (wall)
Terminal velocity at clean air inlet (m/s)	: 0,30 - 0,45
Return air location:	: low sidewall

3

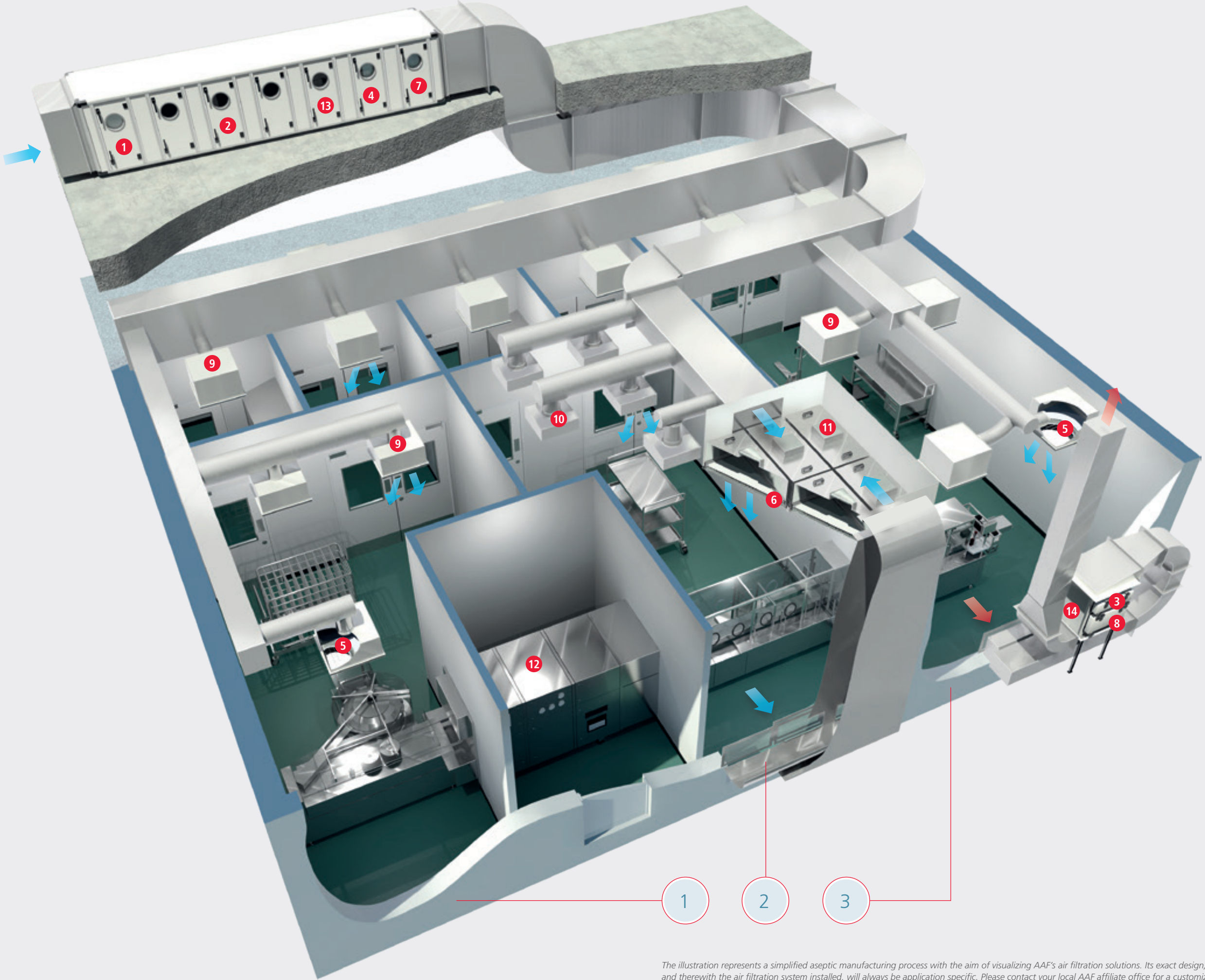
Checking and packaging

EU 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 (m)	: min. 2,25
Area per occupant (m²)	: 5
Equipment in room	: 50% floor
Occupant activity	: constant activity
Traffic in/out per hour	: more than 6
Room over pressure (Pa)	: 5 - 10
Air changes per hour	: 10 - 20
Air lock	: no
Airflow pattern	: turbulent
Clean air inlets as % of ceiling area	: 5 - 10
Clean air inlet locations	: ceiling / high side wall
Terminal velocity at clean air inlet (m/s)	: 0,15 - 0,45
Return air location	: sidewall



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

AAF air filtration solutions

1 DriPak® GX

Pocket filter made of fibreglass in a new tapered design for very low pressure drop and high filtration efficiency

Recommended application:
First stage pre-filtration (class M5) in central air handling unit

- Configuration and performance:
- Filter class EN779/EN1822: M5 - F7, F9
 - Media: fibreglass
 - Filter frame: polystyrene plastic or galvanized steel
 - Optional: dry seal gasket
 - Temperature limit: 70 °C
 - Energy efficiency class: **A**



NEW

2 DriPak® NX

Highly efficient synthetic pocket filter in a new tapered design with extremely low pressure drop and long service life

Recommended application:
Second stage pre-filtration (class F7) in central air handling unit

- Configuration and performance:
- Filter class EN779/EN1822: F7, F9
 - Media: highly efficient synthetic
 - Filter frame: injection moulded polyurethane, polystyrene plastic or galvanized steel
 - Optional: dry seal gasket
 - Temperature limit: 70 °C
 - Energy efficiency class: **A**



3 VariPak

Mini-pleat filter with ultrafine fibreglass media pack, low pressure drop and available with various configuration options

Recommended application:
First stage filtration (class M6) in RPT safe change housing

- Configuration and performance:
- Filter class EN779/EN1822: M6 - F9
 - Media: fibreglass
 - Filter frame: anodized extruded aluminium or MDF
 - Optional: dry seal or gel seal gasket
 - Temperature limit: 70 °C



4 VariCel® VXL

Air filter with high capacity in a robust V-shaped configuration with a lightweight and fully combustible plastic construction

Recommended application:
Third stage pre-filtration (class F9) in central air handling unit

- Configuration and performance:
- Filter class EN779/EN1822: M6 - F9
 - Media: fibreglass
 - Filter frame: combination of HIPS and ABS
 - Optional: dry seal gasket / reverse airflow
 - Temperature limit: 70 °C



5 AstroCel® II

High quality and space-saving mini-pleat filter, individually tested for guaranteed filtration performance

Recommended application:
Terminal filtration (class H14) for PharmaGel Hood in GMP grade C or D cleanrooms

- Configuration and performance:
- Filter class EN779/EN1822: H14 - U17
 - Media: fibreglass
 - Filter frame: anodized extruded aluminium
 - Also available: TM Hood (terminal module)
 - Gasket: dry seal, gel seal or knife edge
 - Temperature limit: 70 °C



6 VITCAcel®

Individually tested mini-pleat filter with a very low pressure drop and a risk-reducing superior mechanical strength

Recommended application:
Terminal filtration (class H14) for TM Hood (terminal module) or Fan Filter Unit in GMP grade A or B cleanrooms

- Configuration and performance:
- Filter class EN779/EN1822: H14 - U16
 - Media: NELIOR membrane
 - Filter frame: anodized extruded aluminium
 - Also available: TM Hood (terminal module)
 - Gasket: dry seal, gel seal or knife edge
 - Temperature limit: 70 °C



7 AstroCel® III

Highly efficient filter in a V-shaped configuration with optimized media packs of fibreglass, suitable for high airflow rates

Recommended application:
Final stage pre-filtration (H14) in central air handling unit

- Configuration and performance:
- Filter class EN779/EN1822: E12 - H14
 - Media: fibreglass
 - Filter frame: steel
 - Gasket: dry seal or gel seal
 - Temperature limit: 70 (regular version) - 120 °C (nuclear grade)



8 MEGAcel® III

Highly efficient filter in a V-shaped configuration for handling high airflow rates at an extremely low pressure drop

Recommended application:
Final stage filtration (H14) in RPT safe change housing

- Configuration and performance:
- Filter class EN779/EN1822: H13 - H14
 - Media: NELIOR membrane
 - Filter frame: galvanized steel or ABS
 - Gasket: dry seal
 - Temperature limit: 70 °C



9 PharmaGel Hood

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

Recommended application:
Terminal filtration module for AstroCel II in GMP grade C or D cleanrooms

- Configuration and performance:
- Construction: mild or stainless steel
 - Connection: circular top or side inlet
 - Seal: knife
 - Filter type: fluid seal mini-pleat up to 128 mm



10 TM Hood

Hermetically sealed and lightweight filter module individually factory tested for guaranteed high filtration performance

Recommended application:
Terminal filtration module with VITCAcel (class H14) in GMP grade B cleanrooms

- Configuration and performance:
- Filter class EN779/EN1822: H14 - U17
 - Filter type: AstroCel II or VITCAcel
 - Filter frame: anodized extruded aluminium
 - Seal: dry or knife
 - Temperature limit: 70 °C



11 Fan Filter Unit

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

Recommended application:
Terminal filtration module for VITCAcel (class H14 - U16) in GMP grade A clean-rooms

- Configuration and performance:
- Construction: cleaned bright aluminium
 - Fan motor: single or three phase AC or EC motor
 - Speed controller: five step or stepless
 - Filter type: AstroCel II or VITCAcel



NEW

12 AstroCel® I HTP

Silicone-free HEPA filter with superior durability, highly reliable operation and performance in compliance with FDA / GMP guidelines

Recommended application:
High temperature filtration in the 'hot zone' of dry heat sterilization and depyrogenation tunnels

- Configuration and performance:
- Efficiency: ≥ 99,99% at 0,3 µm, ≥ 99,95% at MPPS
 - Media: fibreglass
 - Filter frame: stainless steel
 - Gasket: fibreglass
 - Temperature limit: 350 °C (400 °C 1h peak)



13 VariSorb® XL

Fully incinerable combination filter for particulate and molecular filtration with a wide range of chemical media options

Recommended application:
Molecular pre-filtration in central air handling unit

- Configuration and performance:
- Filter class EN779/EN1822: M5
 - Media: synthetic with activated carbon
 - Filter frame: combination of HIPS and ABS
 - Relative humidity: 10 - 95%
 - Temperature limit: 55 °C



14 RPT Housing

Modular safe change housing with a single or double stage filtration system and a leak tight construction for maximum protection

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

- Configuration and performance:
- Casing: reinforced steel
 - Modularity: maximum 5 units
 - Test flange: DIN gasket seal test groove
 - Optional pre-filter bay
 - Temperature limit: 60 °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's cleanroom specialists.

The presented energy efficiency classes are based on Eurovent Guideline 4/21 2014 and RS 4/C/001-2015 and may differ per filter class.

NELIOR® Filtration Technology

NELIOR Filtration Technology represents the latest advancement in high-end air filtration. Exclusively developed and marketed by AAF, HEPA filters with NELIOR 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.

Lower energy consumption

NELIOR Filtration Technology is based on a patented membrane air filtration medium that provides unique performance characteristics, unmatched by any other air filtration medium currently available on the market.

HEPA filters with NELIOR membrane media feature a lower pressure drop than traditional fibreglass media, reducing up to 50% depending on the exact conditions. At the same time, the overall filtration efficiency for NELIOR membrane media has proven to be higher than for fibreglass media.

The lower pressure drop and improved efficiency are achieved from an evenly distributed layer of fibres with very fine nanometer-scale diameters. Air molecules can efficiently pass through the fibres and airborne particles can be captured more easily. The result: air quality is further optimized and energy costs are substantially reduced.

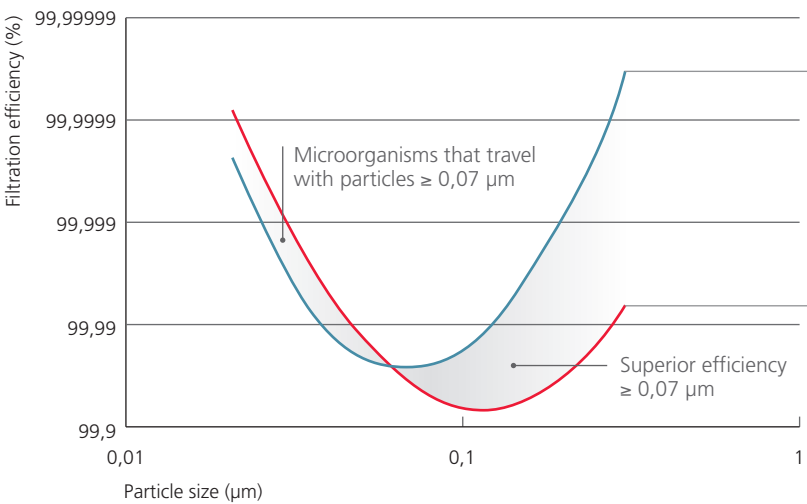


Winner of the annual cleanliness technology award by Fraunhofer IPA



VITACel mini-pleat HEPA filter

High particulate collection efficiency



NELIOR media (HEPA), Traditional media (HEPA)

Low pressure drop

Pressure drop: 150 Pa at 5,3 cm/s

Pressure drop: 300 Pa at 5,3 cm/s

50% savings

Voice of the expert

Dr. Lothar Gail
GMP and cleanroom consultant
VDI (The Association of German Engineers)



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, re-testing and finally the evaluation of possible effects on the production line in question.

To avoid leaks, the extremely sensitive surface of traditional (fibreglass) 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."

Reduced operational risk

Scientific research has shown that AAF’s HEPA filters with NELIOR membrane media have superior mechanical strength over traditional fibreglass media.

The superior mechanical strength is demonstrated by a high tensile strength, burst pressure and abrasion resistance. NELIOR 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 minimized 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 clean-room personnel is optimized. It gives critical pharmaceutical applications the possibility to improve their quality risk management systems for a consistent supply of quality products and a reduction of failure costs.

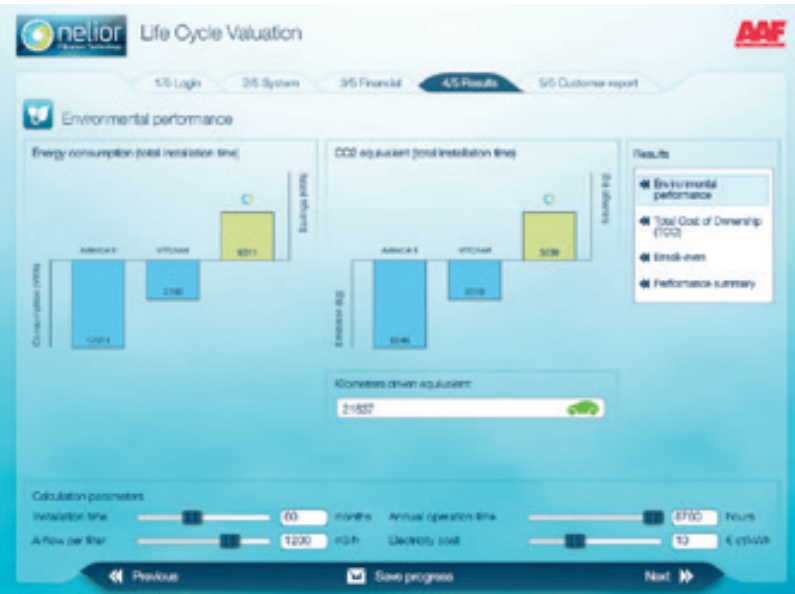
For more information, please visit: nelior.com

NELIOR® Life Cycle Valuation

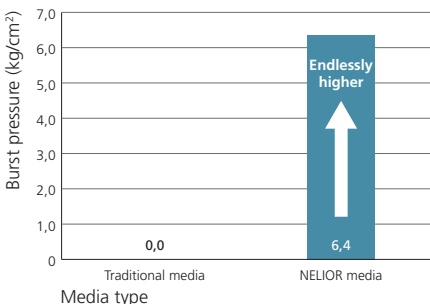
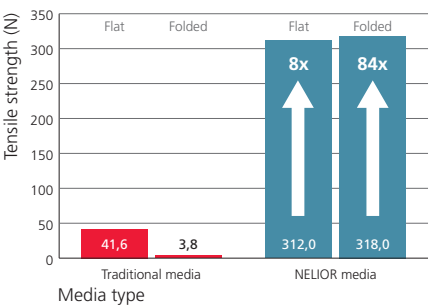
Whereas most of today’s life cycle cost programs solely focus on energy savings, AAF’s NELIOR Life Cycle Valuation (LCV) approach also recognizes indirect cost effects from situations in which clean process conditions fail.

The environmental and monetary savings potential is calculated following a risk management approach. The results are summarized in a clear customer report.

NELIOR Life Cycle Valuation program



Superior mechanical strength



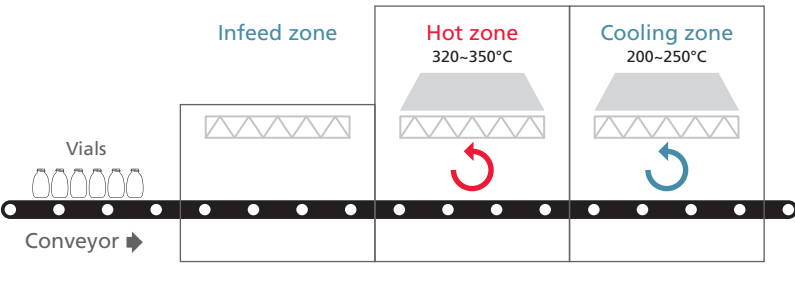
High temperature filtration

To prevent micro-organisms and endotoxins from affecting the final product, dry heat sterilization or depyrogenation of the washed glassware has to be performed. This process requires the air to pass through a reliable HEPA filtration system during high temperature operation. The right conditions for sterile filling and closing of parenterals in the next stage can then be ensured.

Dry heat sterilization and depyrogenation

The sterilization or depyrogenation of vials typically follows a three-step approach: pre-heating, heating and cooling. Especially the heating process, taking place in the 'hot zone', poses high demands on the quality of HEPA filters. At temperatures going up to 350 °C, ISO 5 / GMP A conditions are to be guaranteed for sterility of the containers leaving the dry heat tunnel.

Schematic representation of a sterilization tunnel

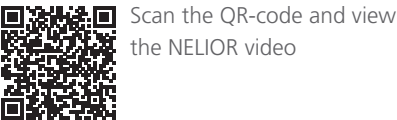


Considerations for hot zone

- ✓ Select air filter with long term durability of construction
- ✓ Select air filter with proven performance on efficiency during operation
- ✓ Select air filter with economic temperature change rates

Consistent air filtration performance

The removal of pyrogens and endotoxins by dry heat is a function of time and temperature. The longer the exposure at high temperature, and the more often heating and cooling cycles are to be performed, the more it comes down to a consistently performing HEPA filter. Particle shedding is a concern to be mitigated at all times. Before putting the dry heat tunnel into service, newly installed HEPA filters require a 'burn-in' period following the installation instructions of the equipment manufacturer.



Scan the QR-code and view the NELIOR video



Scan the QR-code and read the article in the European Journal of Parenteral & Pharmaceutical Sciences (EJPPS)



AstroCel® I HTP

AAF's AstroCel I HTP HEPA filter is designed to provide an excellent protection of dry heat processes. The filter complies to the stringent FDA / GMP guidelines so that high output quality can be realized, but with reduced downtime risk. The AstroCel I HTP proofs to be the right answer to the challenges faced in the hot zones of dry heat sterilization and depyrogenation tunnels.

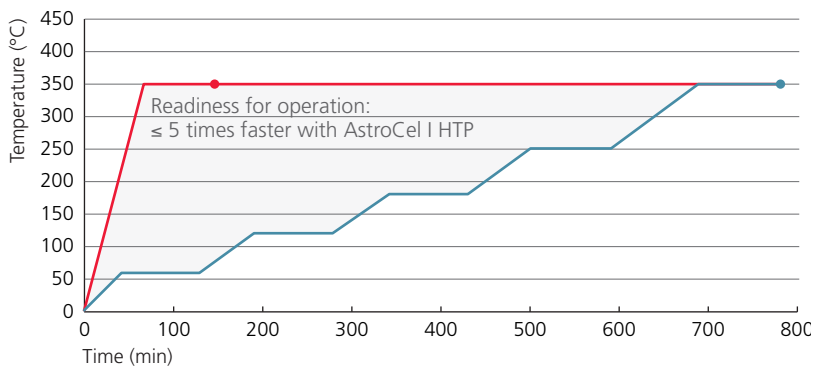
Speedy temperature control

An efficiency of $\geq 99,99\%$ at $0,3\text{ }\mu\text{m}$ and $\geq 99,95\%$ at MPPS is obtained at a nominal airflow rate of $2100\text{ m}^3/\text{h}$. The AstroCel I HTP therewith provides for a speedy temperature control up to $350\text{ }^\circ\text{C}$. Compared to other high temperature filters, requiring tempering, time for burn-in can be significantly reduced. This means that operational readiness is improved.



AstroCel I HTP high temperature HEPA filter

Beneficial temperature profile during burn-in

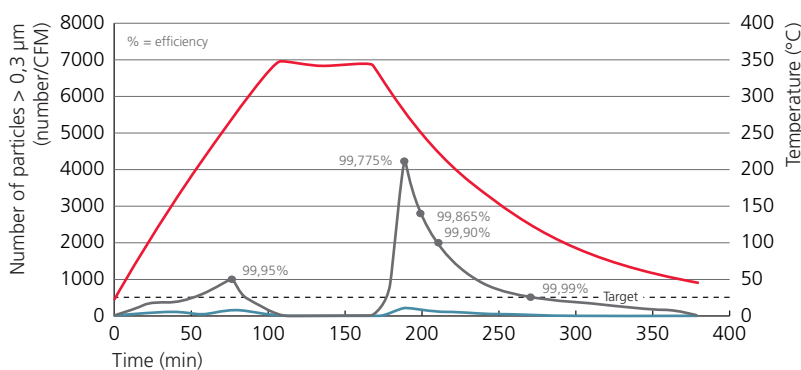


AstroCel I HTP with stainless steel separators and fibreglass sealant
Comparison filter with aluminium separators and ceramic sealant

Reliable high temperature operation

The robust all stainless steel construction results in minimized particle shedding during heating and cooling cycles due to no differences in material expansion coefficients. The elastic fibreglass media sealant is not prone to integrity breaches from stress cracks, which can occur with ceramic sealants. Multiple heat-cycles have confirmed a reliable and consistent operation.

Excellent efficiency during heating and cooling



Scan the QR-code and view the webinar

Temperature
AstroCel I HTP with stainless steel separators and fibreglass sealant
Comparison filter with aluminium separators and ceramic sealant

We understand that the way we treat our air filters impacts how you can assure human health and safety.



The shown burn-in cycles are based on values recommended by air filter manufacturers. The actual burn-in procedure should always follow the instructions of the equipment manufacturer and may therefore result in different values.

Air filtration glossary

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

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

Airflow
Distribution of air passing through a filter element per unit of time. Airflow rate is usually expressed in m³/h or m³/s.

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.

Efficiency
Removal of the number of 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 m/s.

Filter class
Indication of the air filtration performance measured according to test procedures compliant to EN779:2012 or EN1822:2009.

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 in filter class H13 or H14 according to EN1822:2009 based on MPPS efficiency.

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 savings during the installation period.

Mechanical strength
Indication of the elastic or inelastic behaviour 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 fibres, 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.

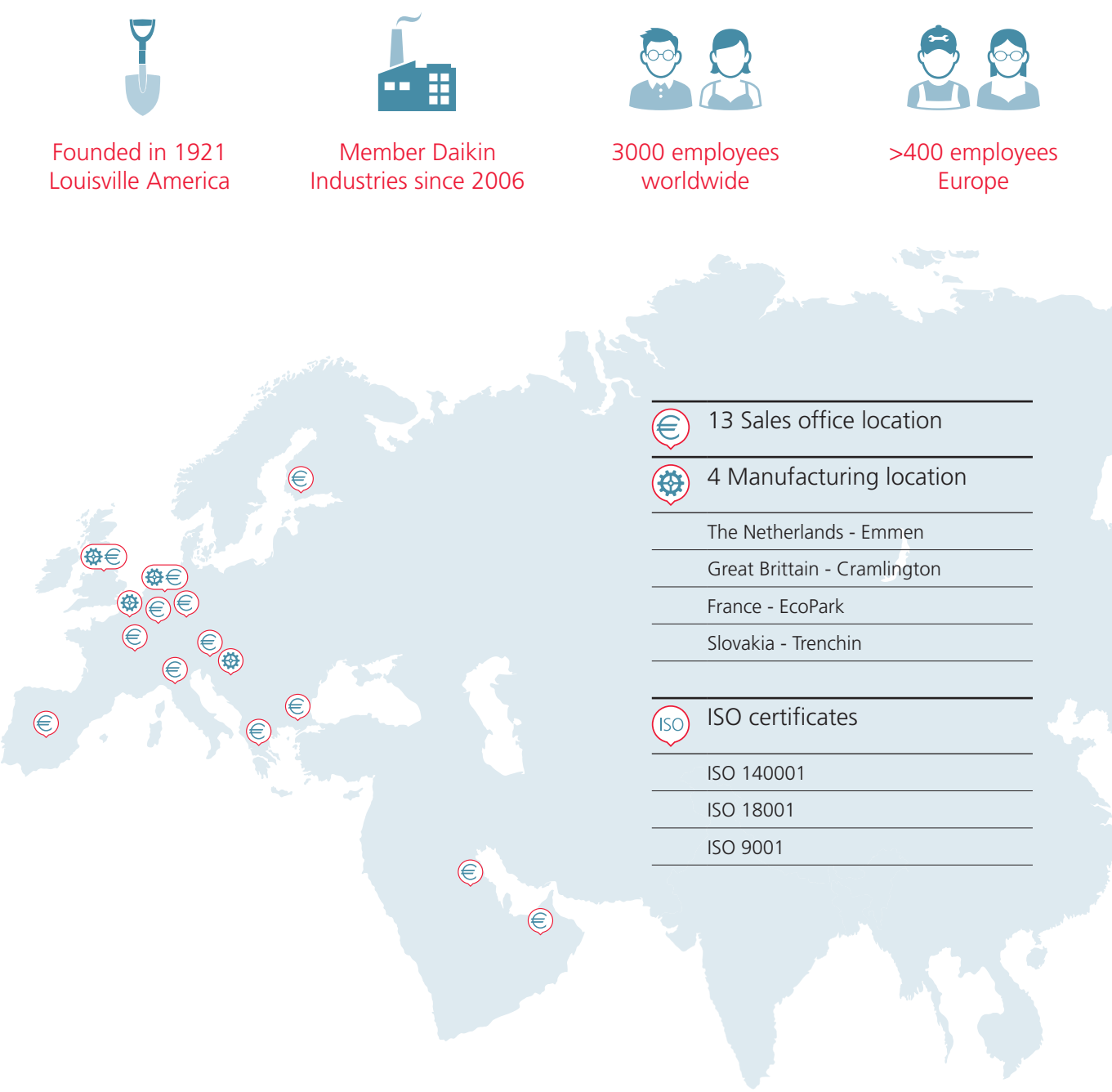
Pre-filter
Air filter installed for removal of larger particles from the passing air to protect the higher efficiency air filters in the next stage.

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 in filter classes U15 to U17 according to EN1822:2009 based on MPPS efficiency.

AAF at a glance in 2015



AAF sales office contact details					
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Finland	+358 10 2290 700	Italy	+39 031 35 25 311	UAE	+971 4 339 7688
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