# Clean air in the Pharmaceutical Industry

Optimizing process performance for protecting human health

AAF INTERNATIONAL

# Application solutions guide

# Clean air in the pharmaceutical industry

## 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.

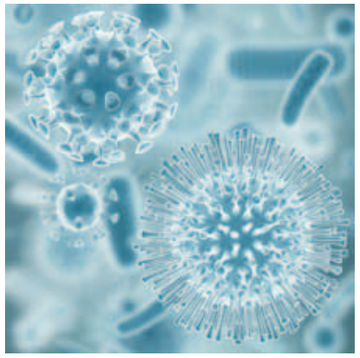
AAF quality statement

**Erik Geertsema**
Test Engineer,
AAF International B.V.

*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

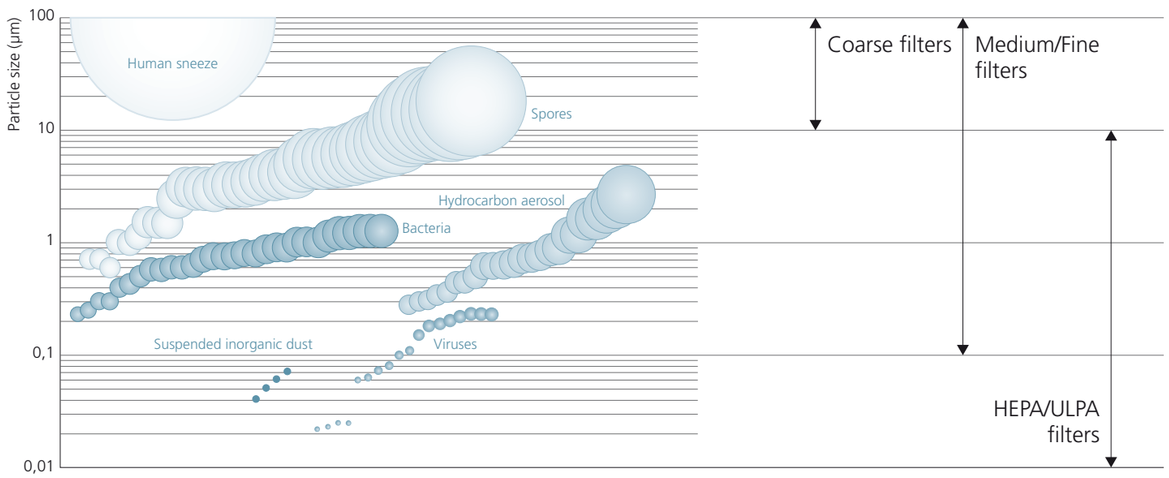
Everything that could come into direct contact with a medicinal product is a potential risk for causing contamination. Limiting exposure to airborne contaminants is critical as they can result in health and safety issues. Preventive measures and detailed quality management procedures are described in 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. Figure 1 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.

Figure 1: Typical size range of airborne contaminants






# 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 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 (table 1). 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.

Table 1: 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 | $50 \le A_m < 65$ | - | - |
| | G2 | 250 | $65 \le A_m < 80$ | - | - |
| | G3 | 250 | $80 \le A_m < 90$ | - | - |
| | G4 | 250 | $90 \le A_m$ | - | - |
| Medium | M5 | 450 | - | $40 \le E_m < 60$ | - |
| | M6 | 450 | - | $60 \le E_m < 80$ | - |
| Fine | F7 | 450 | - | $80 \le E_m < 90$ | 35 |
| | F8 | 450 | - | $90 \le E_m < 95$ | 55 |
| | F9 | 450 | - | $95 \le E_m$ | 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.

### 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


### 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)

Table 2: Air filter classification according to EN1822:2009

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

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) as visualized in table 2.

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 by well-trained AAF personnel before shipment to the customer.

HEPA and ULPA filters with fibreglass media are leak tested by using a DEHS liquid aerosol, whereas for its NELIOR membrane based air filters AAF applies an inert PSL solid 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

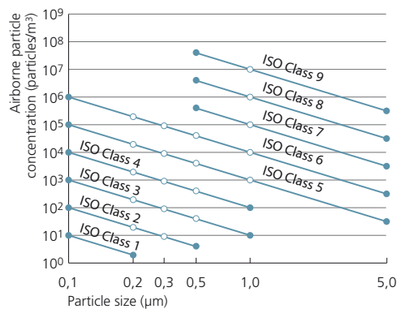
Pharmaceutical cleanrooms and clean air devices are classified according to ISO 14644-1. The level of airborne particulate cleanliness, applicable to a clean area, is expressed in terms of an ISO class *N*. The ISO class represents maximum allowable concentrations for considered particle sizes, ranging from 0,1 µm up to 5,0 µm. 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 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 (table 3). 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.

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.

Table 3: 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 |

| 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 |



Table 4: Monitoring microbial contamination according to EU GMP Annex 1

| | Recommended limits for microbial contamination (average values) | | | |
|---|---|---|---|---|
| Grade | 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 (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 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.

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<br>Preparation of materials and products (non-sterile filtering)<br>Handling and filling of aseptically prepared products |
| B | - | Background area for grade A zones |
| C | Filling of products for sterilization (usual risk profile)<br>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 (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 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

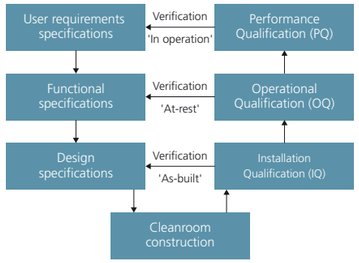
- Absence of any visual damage to filter media, gasket and frame
- Successful in-situ test result with confirmed filter integrity
- Actual initial resistance performance consistent with specification

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 fibre shedding that could cause contamination

Figure 3: Cleanroom validation procedure, derived from ISO 14644-4






## 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 ($m^2$) | : 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 ($m^2$) | : 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

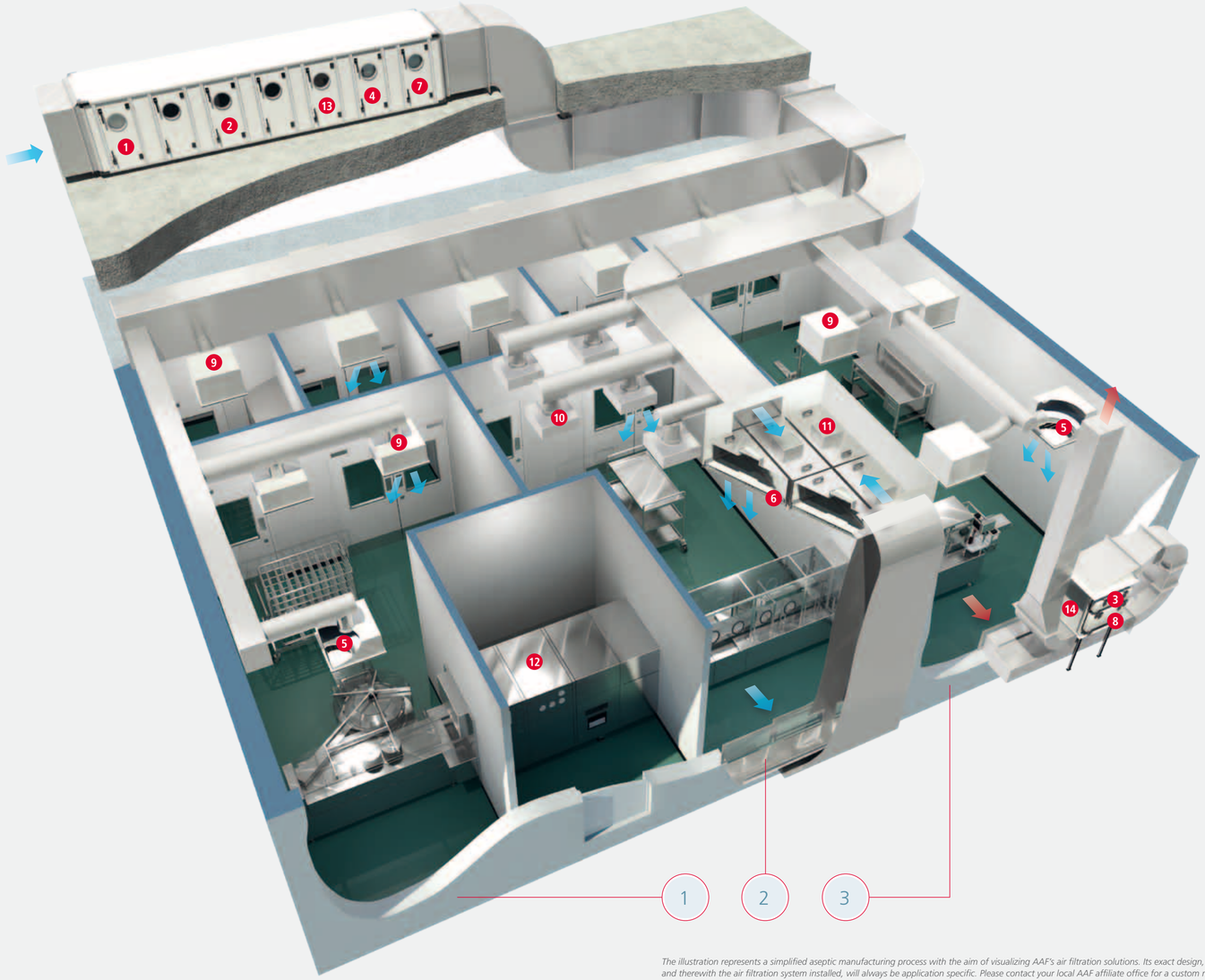
### Checking and packaging

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 ($m^2$) | : 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 custom made solution.*

# AAF air filtration solutions

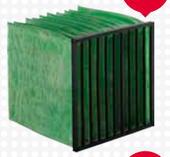
## 1 DriPak® GX

NEW

Low resistance fibreglass pocket filter in a new tapered design for guaranteed efficiency performance

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
- Header: metal or plastic
- Temperature limit: 70 °C
- Energy efficiency class: A



## 2 DriPak® NX

NEW

Highly efficient synthetic pocket filter in a new tapered design with low resistance and long lifetime

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

Configuration and performance:
- Filter class EN779/EN1822: F7 + F9
- Media: extended surface synthetic
- Header: metal or plastic
- Temperature limit: 70 °C
- Energy efficiency class: A

## 3 VariPak®

Low resistance mini-pleat filter and ultrafine fibreglass media packs available in various frame executions

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

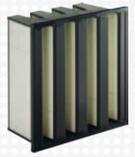
Configuration and performance:
- Filter class EN779/EN1822: M6 - F9
- Media: fibreglass
- Filter frame: extruded aluminium or MDF
- Temperature limit: 70 °C

## 4 VariCel® VXL

High capacity filter in a robust V-shaped configuration with a light weight and fully incinerable HIPS 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: HIPS
- Temperature limit: 70 °C
- Energy efficiency class: A



## 5 AstroCel® II

High efficiency and rigid mini-pleat filter individually factory tested for guaranteed filtration performance

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

Configuration and performance:
- Filter class EN779/EN1822: H14 - U17
- Media: fibreglass
- Filter frame: anodized extruded aluminium
- Seal: dry, fluid or knife
- Temperature limit: 70 °C



## 6 VITCAcel®

NEW

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

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

Configuration and performance:
- Filter class EN779/EN1822: H14 - U16
- Media: NELIOR membrane
- Filter frame: anodized extruded aluminium
- Seal: dry, fluid or knife
- Temperature limit: 70 °C

## 7 AstroCel® III

High efficiency filter in a V-shaped configuration with optimized fibreglass media packs for handling 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: metal
- Temperature limit: 70 °C

## 8 MEGAcel® III

NEW

High capacity filter in a V-shaped configuration for handling high airflow rates at an extremely low resistance

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

Configuration and performance:
- Filter class EN779/EN1822: H13 - U15
- Media: NELIOR membrane
- Filter frame: steel or ABS plastic
- 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-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 light weight 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 cleanrooms

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®

## 12 AstroCel® I HTP

NEW

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

Configuration and performance:
- Efficiency: ≥ 99,97% for 0,3 µm particles
- Media: fibreglass
- Filter frame: stainless steel with support bars
- Sealant: 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: M6
- Media: synthetic with activated carbon
- Filter frame: HIPS
- Relative humidity limit: 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 4/11 and may differ per filter class.*

# NELIOR Filtration Technology

AAF's VITCAcel® and MEGAcel® III filters feature NELIOR Filtration Technology; the latest advancement in high-end air filtration, exclusively developed and marketed by AAF. HEPA filters with NELIOR Filtration Technology give 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 fibres with nanometer-scale diameters. It provides for an 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 a high resistance to any potential damage, for example due to errors in handling or installation. In daily practice this means that filter media failure risk is limited and that fibre shedding, which could increase contamination risk when entering the airstream, is eliminated.

With AAF's 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 or visit: nelior.com.

## The value areas:

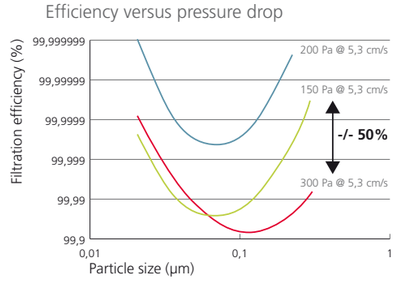
**Consistent Air Quality**
Providing a reliably high air quality to optimize contamination control and meet the stringent conditions in clean environments

**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: Superior performance of NELIOR media




Scan the QR-code and view the NELIOR video

Winner of the annual cleanliness technology award by Fraunhofer IPA

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."*

# High temperature HEPA solution

To prevent harmful Endotoxins from affecting 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. AAF's new AstroCel® I HTP high temperature HEPA filter is designed to provide an excellent protection of this critical sterilization process.

## Reliable high temperature operation

In continuous service, the AstroCel® I HTP offers a maximum temperature resistance of 350 °C, with a peak of 400 °C for one hour. Its robust structure out of stainless steel 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 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 AstroCel® I HTP therewith offers a unique combination of high temperature operation and superior durability, optimizing process results and limiting unscheduled downtimes.

AAF's new AstroCel® I HTP high temperature HEPA filter

## 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 2100 m3/h. 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 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, AAF's AstroCel® I HTP provides the right solution for ensuring that the strict air cleanliness conditions are met.



# 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.

### Airflow
Distribution of air passing through a filter element per unit of time. Airflow rate is usually expressed in $m^3/h$ 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 micron (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.

### 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.

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Manufacturing location
Sales office and manufacturing location

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