

THE ULTIMATE CHALLENGE:

High-temperature filter for depyrogenation tunnels & ovens.

By Michael Feldtmann



INFLUENCE OF ENDOTOXINS ON BIOLOGICAL APPLICATIONS

Endotoxins strongly influence transfection of DNA into primary cells and sensitive cultured cells, and increased endotoxin levels lead to sharply reduced transfection efficiencies. Furthermore, it is extremely important to use endotoxin-free plasmid DNA for gene therapy applications, since endotoxins cause fever, endotoxic shock syndrome, and activation of the complement cascade in animals and humans. Endotoxins also interfere with in vitro transfection into immune cells such as macrophages and B cells by causing nonspecific activation of immune responses. These responses include the induced synthesis of immune mediators such as IL-1 and prostaglandin. It is important to make sure that plastic ware, media, sera, and plasmid DNA are free of LPS contamination to avoid misinterpretation of experimental results.

WHY HEPA FILTRATION IS NEEDED

In tunnel sterilization systems and depyrogenation tunnels, three important system components have to function optimally to satisfy safety and hygiene standards: the heater elements, the conveyor belt speed and belt recorder, and the HEPA filters. The last are highly important because they ensure cleanroom-quality air and eliminate particles that can contaminate the product and impact production yields.

In the depyrogenation tunnels used in pharmaceutical aseptic filling, these high temperature filters are installed directly over the conveyor belt where vials, ampoules or cartridges are transported. The HT filters are specially made to protect these ultraclean processes and have to meet the most stringent requirements and standards. They are designed to maintain integrity and rated performance values at extremely high temperatures.

PROBLEMS ASSOCIATED WITH HT FILTERS

The offering on the market are a growing selection of HT filters for depyrogenation tunnels, but certain filter products do not perform optimally for the application. Some HT filters will release particulate contamination during the high temperature aseptic filling process.

This impacts output and quality negatively and results in expensive downtime and filter changes. Another major problem for the user has always been the installation of new HT filters. This often needs initial tempering where organic components such as the HEPA media binder are “burned off” before the filters are conditioned for operation. Depending on the equipment and filter choice, this process typically takes many hours or even a few days.

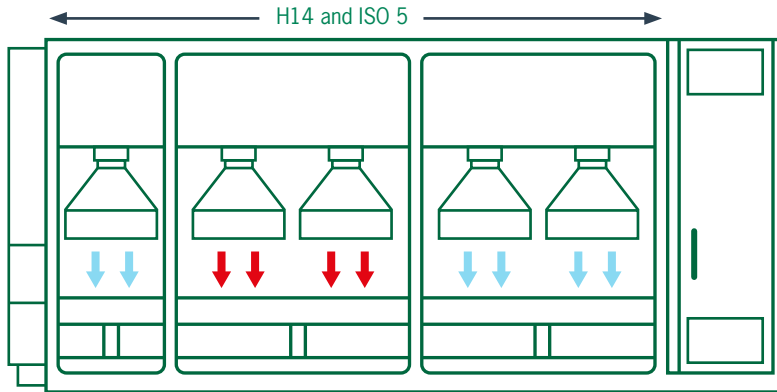
INDUSTRY DEMANDS

HT filter users have expressed four critical needs for cleanroom quality air:

- Ensure the maintenance of ISO Class 5 even when temperature is changing
- Extend HT filter product life time
- Reduce the installation and preparation time and eliminate the cleaning effort
- Reduce process downtime.

End users' ultimate goal is to maximize the production yield of processes creating their highest value products. With that in mind the trend is going towards new filter solutions with highly reduced emissions and with no requirement for tempering or cleaning. Future performance requirements for HT filter are to meet the highest compliance standards for providing a consistent Grade A manufacturing environment and boosts process yields for tunnels used in the life science industry. The ISO 5 requirement in the operating area is key and therefore the design innovations have to be questioned for filter pack, media and construction. A filter to be installed and integrated into processes up to 350°C without any tempering or cleaning. Reducing start-up and operating costs for the depyrogenation tunnel is key.

Consequently, any pharmaceutical-grade filter should have the same efficiency as the H14-grade filters in the other depyrogenation tunnel hot zones, exceeding former HT filter limitations of H13 efficiency.



TESTING FOR INTEGRITY AND PERFORMANCE

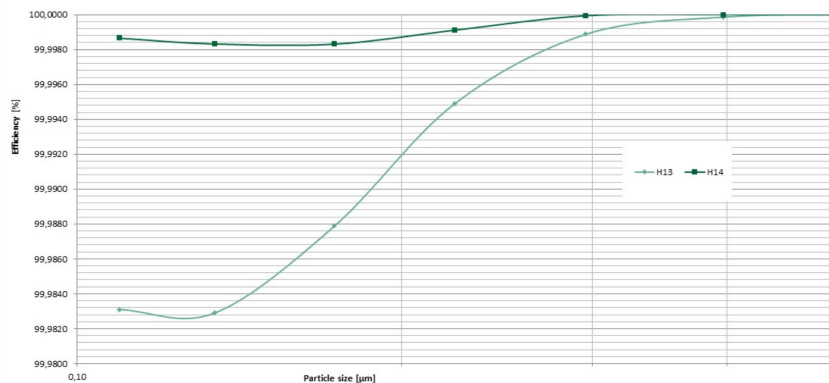
Due to their crucial function and role, all high temperature HEPA filters are factory tested prior to delivery and installation. The manufacturer has to conduct full EN1822 / ISO29463 tests on every filter in a highly controlled clean environment, documenting all test results in accordance with the ISO 9001-2000 quality system.

Enhancing the sampling capability upstream of the filter scanning systems with special dilution equipment is mandatory to measure these high filtration efficiencies. The entire filter face, including the media to frame interface, should be scanned by a specially shaped isokinetic probe traversing in an overlapping pattern and at an appropriate speed to uncover the presence of any leaks. Each Filter should carry an individual scan test report (according to EN1822 or DIN 29643) certifying 100% leak free performance. The individual scan test report which is supplied with every filter is basis for a secured process compliance at user site.

Di-Ethyl-Hexyl-Sebacate (DEHS), an aerosol liquid used to challenge cleanroom filters during scanning, is released upstream of the filters in a particle size of 0.12 to 0.17 microns to test unit leakage.

The efficiency of HT filters is determined according to EN 1822, the European standard for determining the efficiency of Efficiency Particulate Air (EPA), High Efficiency Particulate Air (HEPA) and Ultra Low Penetration Air (ULPA) filters. This standard determines the ability of the filters to collect and remove the Most Penetrating Particle Size (MPPS).

When comparing the particulate removal capabilities of the H13 and H14 filters the benefits of the higher filter class are obvious. (See Figure X the 10X increase in particle efficiency at MPPS resulting from the substitution of an H14 filter for an H13 unit).



The present depyrogeneration tunnel market needs reliable HT filters of H14 efficiency for safe and secure of high-temperature production processes. ISO Class 5 cleanroom conditions are required throughout the depyrogeneration tunnel. It is therefore extremely important that the HT filters do not emit particles during the process, even when temperature changes.

A future design should match benefits including:

- Quality performance throughout all production phases
- No organic components for “plug-and-play” installation without tempering and cleaning requirements
- Ultra low emissions and high efficiency to achieve maintenance of < ISO 5 in hot and cool zones of the tunnel, even when temperatures vary.
- 350°C working temperature; (Short-term peak temperatures to 400°C.)
- To achieve an extended life time a sealed, airtight filter pack in a reinforced frame could be a solution.
- Filter element free of bisphenol A, phthalates and formaldehyde.
- A reliable H14 filter quality also for the Hot Zone .
- High reliability: leak-free, consistent performance after a large number of cycles (>150-200 cycles).
- With the endurance of temperature fluxes up to +5°C per minute the process requirements of ISO class 5 to be maintained.

An important requirement is no “pre-baking” before production. The filter should be ready to operate immediately after installation and not emitting any fumes, eliminating the need to maintain an elevated temperature during the suspension of production or when the depyrogeneration tunnel is not in operation, saving energy.

New developments show excellent results when using a resin with geopolymer type reaction (PSDS) This sealant has been specially formulated to be consistent with the other components of the filter. These polymers have similar properties as inorganic polymers

This geopolymer contains no dangerous solvents, does not burn, and does not outgas toxic fumes. Like a refractory, it is resistant to chemical attack and erosion. This type of reaction allows the geopolymer resin to withstand a temperatures up to 600°C. This specially designed, patented geopolymer matrix has a dimensional stability for temperatures exceeding 450°C and will not shrink, or leak. No protection grid is needed.

A new construction should include the newest material developments, specifically stainless steel materials to reduce elongation at higher temperature, ensuring dimensional stability. The stainless-steel separators for the deep pleats also minimize the risk of particle emission during depyrogeneration and the sterilization processes.

CERTIFIED PERFORMANCE AND MATERIALS

The described applications require strict compliance with safety, traceability and control. Tested and developed according to precise specifications, filters for all filtration stages should be manufactured with materials that will not contaminate delicate production processes.

Reliability for manufacturers that cannot afford to take risks. The products should be specially designed for life science industries requiring filters to be resistant to decontamination agents, and free of any harmful chemical components.

All filters should be compliant with FDA, REACH, EC1935:2004, VDI6022 and ISO 846 raw-material specifications. Letters of conformance should accompany every filter to meet product compliance requirements.



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Michael Feldtmann is the Product Manager for Camfil, the world leader in air filtration solutions and filter production. His responsibility covers the Product Management of the Clean Process in Europe, which includes all airfilter products with very high Efficiency and the associated housing systems. He is working in the air filtration business for over 30 years, responsible for different product portfolios. His profession is Industrial Engineer, Dual Study in cooperation with the Drägerwerk AG in Lübeck. As the german expert in the ISO TC 142 WG 4 (HEPA and ULPA Filter) he is belonging to the german and the international standardisation process for High Airfiltration purposes. As part of his job he has worked over several years with all types of High Temperature Hepa filter and the needs from the industry.

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