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The ultimate challenge: High-temperature filter for depyrogenation tunnels and ovens

How industry trends can lead to new concepts and ideas for High temperature Filtration.

Michael Feldtmann
CAMFIL

In the life science industry, hot air up to 350 °C is utilized in static ovens and depyrogenation tunnels to sterilize glass vials, ampoules, and cartridges before they are aseptically filled. The hot air for this process is typically filtered through special high-temperature HEPA filters (HT filters) before it is distributed in a unidirectional airflow through the tunnel.

To avoid product contamination, cleanroom quality air is needed throughout the tunnel. These air filters are therefore of the highest particle collecting efficiency and HT filters of H13 grade are typically used today to filter the air for the hot zone (ISO 5 in the working area acc. to ISO 14644). The choice of the right HT filters is critical to ensure consistent and optimum product safety, as well as maximum production quality and uptime.

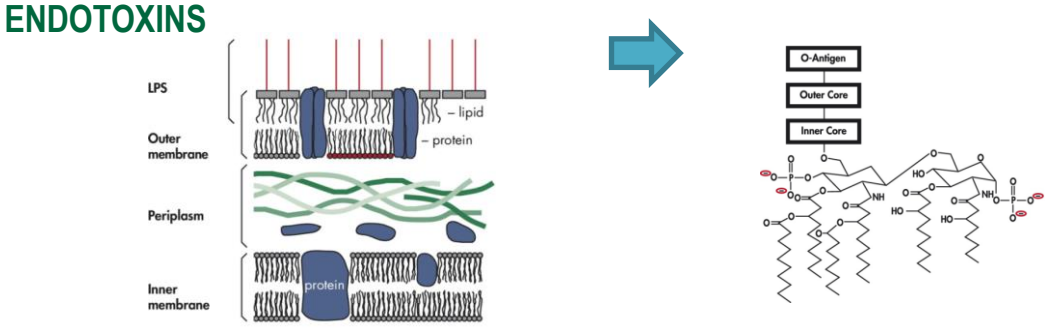
The same applies to OEM suppliers of depyrogenation tunnels, who also need effective air filters to guarantee the reliable function and performance of their specialized equipment.

Sterilization and depyrogenation processes

Manufacturers in the life science industry, such as pharmaceutical companies, use both sterilization and depyrogenation techniques to ensure product quality and safety. Each process has a specific purpose:

- Sterilization renders products free of microorganisms, including bacterial endospores. Sterilization eliminates all forms of life and biological agents. Common methods are the use of high temperatures or intense radiation.

- Depyrogenation removes or inactivates bacterial endotoxin based on a “D-value” – the time required to kill 90% of the exposed microorganisms at a given temperature. The D-value is also used to assess microbial thermal resistance and analyze the thermal death time.



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 processing, 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 wide 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 itself.

This impacts output and quality negatively and results in expensive downtime and filter changes. The particle emission source is often the sealant or other materials used in the filter's construction, which can mechanically interact during periods of rapid temperature change.

Industry demands

HT filter customers 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 HT filter installation, preparation, and cleaning time to eliminate the cleaning & preset afterwards and reduce the preparation time for production
- 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 clearly going towards new filter solution with highly reduced emissions and with no requirement for tempering or cleaning.

A future design and construction for such filter is 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 to be the key and further on this 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.

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

Testing for integrity and performance

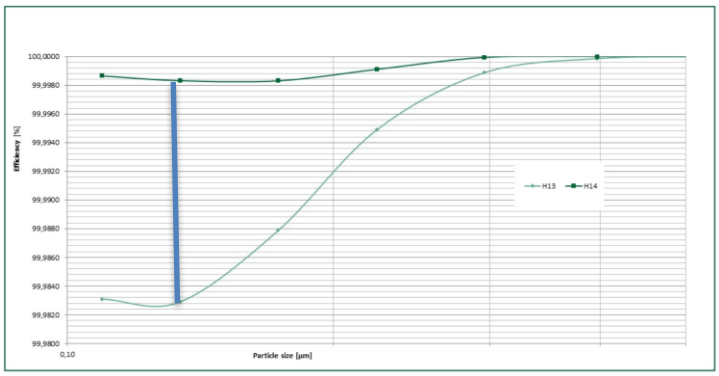
Due to the crucial function and role of these filters, all filters are factory tested prior to delivery and installation. The measurements conducts leak-tests on every high-temperature filter in a highly controlled clean environment, documenting all test results in accordance with the ISO 9001-2000 quality system.

To enhance the sampling capability upstream of the filter scanning systems with special dilution equipment are 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 certifying 100% leak free performance. The individual Scan Test report which is supplied with all Filter are basis for a secured process on customer base.

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 the unit’s leak.

The efficiency of HT filters is determined according to EN 1882, 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, termed MPPS.

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



The present depyrogenation tunnel market needs reliable HT filters of H14 efficiency for safety and security of high-temperature production processes. ISO Class 5 cleanroom conditions are required throughout the depyrogenation tunnel. It is therefore extremely important that the HT filters do not emit particles during tempering and temperature changes. They must also remain leak-free during normal operation at steady temperature.

A future design should match benefits including:

- Quality performance throughout all production phases
- To achieve a fast production set up the filter need not to be tempered or prebaked before use, so particulate emissions is reduced.
- To achieve maintenance of < ISO 5 in hot and cool zones of the tunnel, even when temperatures vary, ultra-low emissions should be enabled.
- 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 media 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.

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

New development show excellent results when the using for example a resin having a 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 has properties similar to plastics, but contains no dangerous solvents, does not burn, and does not outgas toxic fumes. Like a stone, 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 depyrogenation and the sterilization processes.

Certified performance and materials

A need for such applications are complying with strict requirements for 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 against decontamination agents, and for food and beverage industries needing components that are certified for food contact. The materials in the filters also have to be inert against microbial growth, but at the same time, they must be free of any harmful chemical components.

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