Hidden Dangers of HEPA Filter Leak Testing: The Risks are Hidden. The Consequences are Not.

History of Leak Testing

From the 1960s to mid-1980s, dioctylphthalate (DOP) was used in concentrations of 80 mg/m^3 (μg/L) as an aerosol challenge for leak testing HEPA filters.[1] In the 1980s, the design of aerosol photometers progressed to incorporate solid state electronics, which helped these photometers become more sensitive instruments to identify filter leaks.

With the implementation of these more sensitive and stable units, the recommendation for DOP aerosol challenge concentrations was reduced to 10 mg DOP/m^3 of air.[2]

The early 1990s brought a change to the challenge material, due to DOP being labeled as a potential carcinogen. Emery 3004 polyalphaolefin (PAO) was recognized as a non-hazardous replacement and has now become the industry standard.[3]

FDA regulations require regular testing, but how often testing procedures are utilized beyond those requirements depends on the quality of the filters and how they are used. HEPA filter integrity has to be maintained to ensure aseptic conditions. Leak testing should therefore be performed at installation to detect integrity breaches around the sealing gaskets, through the frames, or through various points on the filter media. Thereafter, leak tests should be performed at suitable time intervals for HEPA filters in the aseptic processing facility.

The FDA requires testing to be performed twice a year for aseptic processing rooms, although additional testing may be appropriate when air quality is found to be unacceptable. There can be other reasons for additional testing, such as facility renovations, or as part of an investigation into a media fill or drug product sterility failure. But extra testing due to the use of lower quality filters incurs the additional cost of more filters being certified, increasing time, money and potential damage.

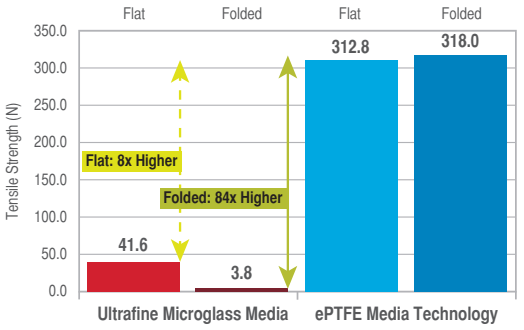
Overcertification In Non-Critical Environments

Excess certification can cause many problems for environments, some more obvious than others:

- Additional costs for certification services
- Consumes valuable time during shutdowns
- Increases exposure to damage
- Premature gel liquefaction and leakage
- Media degradation

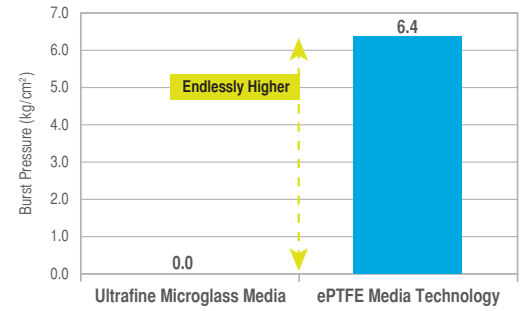
But there are steps that can be taken. While FDA Testing Guidance requires critical room leak testing twice a year, non-critical rooms require the testing only once a year. However, many companies still test twice a year, due to using fragile microglass media. There are risks associated with this, though.

Tensile Strength



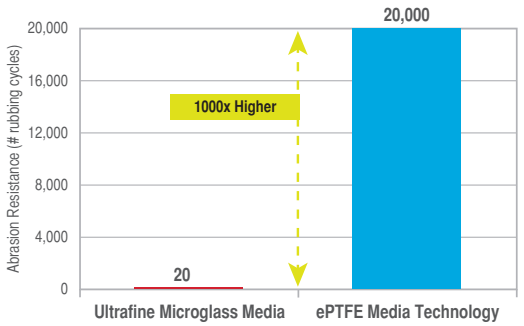
Results based on Test Standard DIN EN 29073-3.

Burst Pressure - Flat



Results based on Test Standard DIN EN 13938-2.

Abrasion Resistance - Flat



Results based on Test Standard DIN EN 12947-2.

Overexposure to PAO

One of these risks is Gel Degradation. It has been documented that PAOs can affect the stability of this gel. In fact, at least four Fortune 500 companies have recently reported problems with gel degradation, the liquefaction of the substance used to install and seal the filters. The integrity of the gel and the effectiveness of the filter seal are therefore compromised. Leaking issues caused by gel degradation are even more devastating than simple damage to the filter. When the gel itself becomes liquefied and drops to the floor of a cleanroom, the cleanroom is no longer sterile. This presents a major risk. Gel liquefaction also initiates an unplanned shutdown with enormous financial ramifications. These contamination failures bring about production losses and premature changeouts—and with them, potentially millions of dollars in damages and profits.

Reducing Your Risk

Effectively managing the risks and costs associated with successful operation requires utilizing HEPA filters with dramatically higher tensile strength that are highly resistant to chemical degradation, thereby eliminating premature leaking and failure. The only HEPA filter media with these properties is polytetrafluoroethylene (ePTFE). Utilizing ePTFE can increase time between testing, allowing for annual certification, which results in lower labor costs and reduces your risk to gel liquefaction contamination and early changeouts.

The strength of the HEPA filter material is critical to the success of a pharmaceutical environment. In fact, there is no more important component of a cleanroom. Depending on the carrier substrate, the strength of ePTFE filters is up to 100 times stronger than microglass. This creates a filtration media that does not fail under standard operating procedures, cleaning, installing, or testing, and provides a durability to mitigate almost all risks of contamination from airflow. The filter will not shed, tear, puncture, or sustain pleat tip separation.

The costs associated with failed media can be staggering:

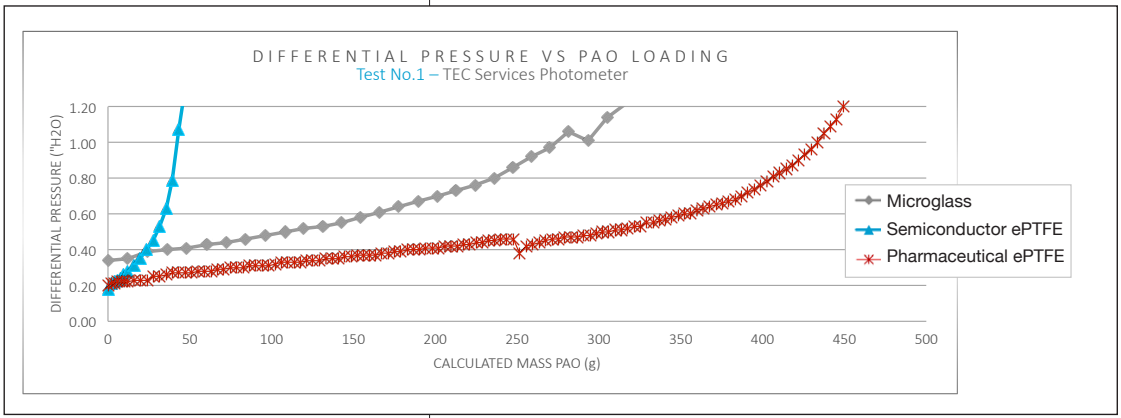
- Complete loss of production for unspecified periods
- Costly FDA 483 citations, warning letters, and consent decrees
- Expensive follow-up qualifications/validations
- Catastrophic recalls

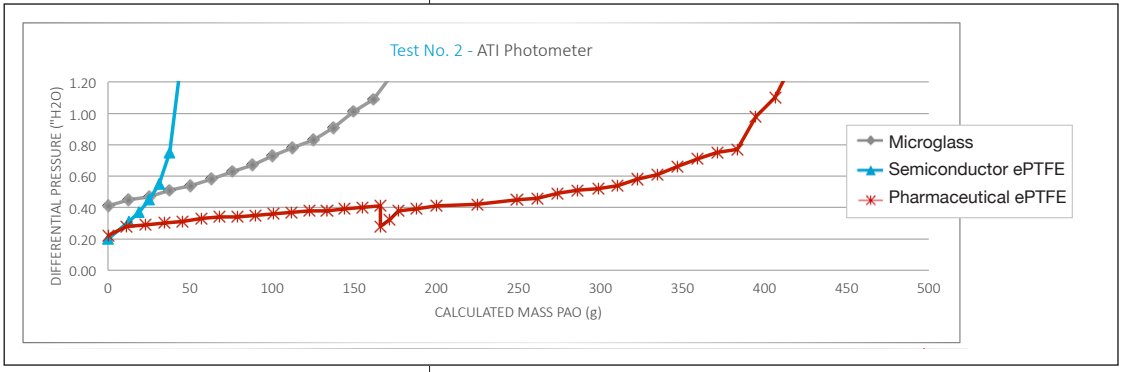
ePTFE and Pharma

The benefits of ePTFE filters, including the significant reduction in energy cost, enhanced chemical tolerance, and increased durability, have long been known in critical semiconductor applications.[4] However, until recently, this technology was not available for use in pharmaceutical environments.

But now there is an ePTFE media that is specifically designed to retain at least equivalent amounts of PAO aerosol with a pressure drop that is equivalent or lower than that of microglass. This new dual-layer ePTFE Technology allows for the in-depth capture of progressively smaller solid particles.

In fact, independent laboratory studies have shown that ePTFE filters possess a far superior PAO holding capacity over traditional microglass HEPA media, as seen in the results below.





Filter failures pose a significant cost to pharmaceutical manufacturers that produce product in a GxP critical environment. The ability to widely use ePTFE filters in pharmaceutical applications provides extraordinary benefits, as well as avoiding the setbacks that almost certainly will lead to disastrous repercussions in money, risk, and time.

You can't afford not to investigate ePTFE filters:

- Increase in cleanroom uptime
- Lower production loss and labor costs
- Increase in time between certifications
- Significant energy savings

Attention to these critical factors will lead to more than operational efficiency and risk mitigation—it will lead to a more viable commercial enterprise.

Challenges and Opportunities Concerning Testing: Looking Back and Planning Ahead

If business can learn anything from history, it is that the past is prologue. What we have seen before is likely to be seen again. And what we have seen is change.

Cleanroom testing has always been an integral, if expensive and sometimes dangerous, component of the pharmaceutical industry. It has also come with its own set of concerns, including DOP's cancer worries, and the more recent considerations of gel and media degradation. Decisions must be made to continually improve. In fact, the idea of using microglass HEPA filters as part of a standard operating procedure may very well become obsolete in the pharmaceutical industry in the near future.

Standard operating procedures and necessary change will always be, to a degree, in conflict. What was useful yesterday, even what is chosen as a solution today, will quickly become an obstacle on the road to progress and innovation. But vigilance and an openness to "what's next" will ensure the industry its best chance of continued growth and success.

References

1. Hale, Dean, "HEPA Filter Gel Seal Failure Study and Conclusions," 2006 CETA Presentation.
2. Mil Standard 286, 1956 Department of Defense Test Method Standard.
3. FDA Guidance for Industry Sterile Drug Products Produced by Aseptic Processing Current Good Manufacturing Practice, September 2004.
4. Galken, Ned, and Abhishek Saxena, "Air Filtration Applications for Membranes," AFS Web site.

Acknowledgements:

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