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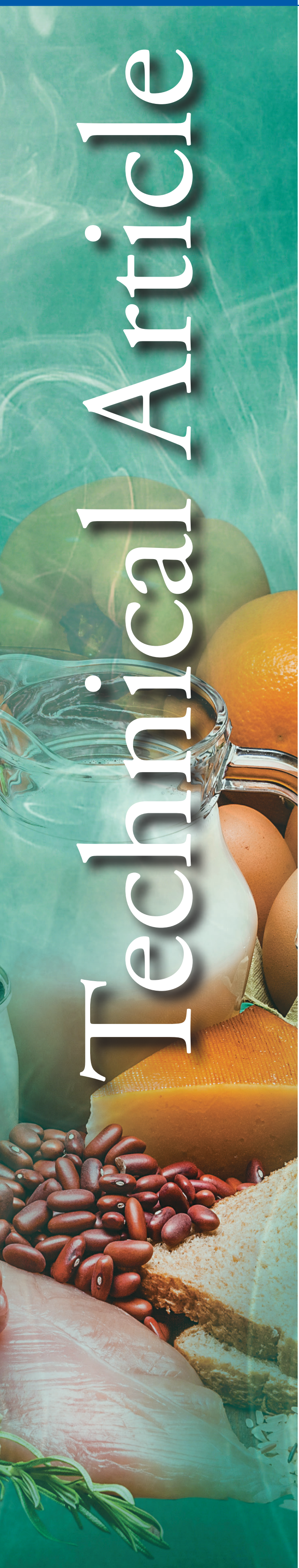
Food and Beverage



Evaluating Microbial Retention Performance in Sterile Air and Gas Filters for the Food and Beverage Industry

Overview

Sterilizing filtration of air and gas is widely used in food and beverage manufacturing applications, to ensure process and brand protection and consumer safety. Its purpose is to remove microorganisms from the air or gases that directly contact food and beverage products or equipment surfaces that are exposed to these products. The goal is to prevent microbial contamination by undesirable bacteria, yeast and molds, which could lead to diminished production yields, food product quality deterioration or spoilage, and in the worst case, food safety hazards.

The typical gases used in food and beverage applications are air, nitrogen and carbon dioxide. In certain fermentation applications for food ingredient manufacturing, hot air or oxygen-enriched air may be used.

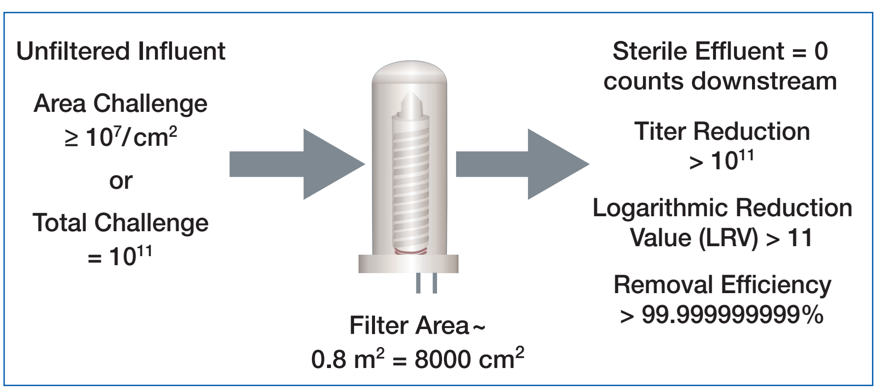
There are different solutions available for sterilizing filtration of air and gas, along with sometimes confusing information about choosing one technology over another. This article will focus narrowly on understanding retention performance of sterilizing-grade cartridge air filters. The goal is to assist the user in navigating the concepts related to validation, including microbial and particle retention validation, and liquid and aerosol challenge. An overview about available cartridge filter types and general application notes are provided.

Definition of Sterilizing Air Filtration

A sterilizing-grade cartridge air filter is defined as one which reliably and reproducibly removes a minimum challenge of 10^7 colony-forming units (cfu) of *Brevundimonas diminuta (B. diminuta)*/ cm^2 of effective filtration area, yielding sterile effluent or the absence of viable microorganisms in the filtered air [1,2]. A microbially validated filter according to this definition will successfully sterilize an air or gas stream if it is used according to the filter manufacturer instructions.

Figure 1 illustrates the concepts of challenge level, titer reduction, logarithmic reduction, and removal efficiency; the last three terms are simply different mathematical ways of expressing the same effect, namely the degree of microbial retention achieved by the filter. For a 10-inch filter cartridge of approximately 0.8 m^2 (8.6 ft^2) effective filtration area, the minimum required area challenge of $10^7/cm^2$, according to the definition for sterilizing-grade air filters, would equate to a total challenge level of 8×10^{10} cfu of challenge organisms/10-inch cartridge. (In practice, a slightly higher total challenge level of 10^{11} cfu in the unfiltered influent is often chosen to meet the minimum area challenge requirement.)

Figure 1: Schematic illustrating common terms in microbial validation of sterilizing-grade air filters



Calculating the ratio of the influent total challenge load (= 10^{11}) to the effluent load (= 0), the effect delivered by the filter is expressed as a titer reduction of >10^{11}; in the case of sterile effluent it is not possible to divide by zero, so the effluent count is assigned to be ‘1’ and the titer reduction shown as >10^{11}. This figure can also be expressed as a logarithmic reduction value (LRV) of >11, or a removal efficiency of >99.999999999%.

The FDA's *Guidance for Industry*[1] states that the microorganism *B. diminuta* (ATCC 19146), when properly grown, harvested and used, is the common standard challenge microorganism for this work, because of its small size.

Sterilizing-grade cartridge air filters are commonly referred to as 0.2 or 0.22 micron (µm) “rated” filters. This designation does not reflect the actual pore sizes of the filters, as pore sizes within the filter are never identical to each other, they vary from smaller to larger than the stated pore size, and the pores are not spherical in shape. Additionally, size exclusion due to pore size is only one of several mechanisms that take place during air filtration[2]. Rather, the pore size designation refers roughly to the size of the model bacteria that filters are validated to remove. In this case, a *B. diminuta* bacterium is a rod-shaped microorganism that measures approximately 0.3-0.4 µm x 0.6-1 µm. (By comparison, an average yeast cell is 4-12 µm in length, with varying diameters; mold spores range from 3-40 µm.)

Validation of Microbial Removal

Microbial retention is the single most important performance attribute of sterilizing-grade air filters. Other key attributes are discussed in “*Attributes of Sterilizing-Grade Air and Gas Cartridge Filters*[3].”

To demonstrate the filter's microbial retention capability, extensive validation work is carried out by filter manufacturers in a laboratory setting, verifying that when the sterilizing-grade test filters are challenged with the defined concentration of the model microorganisms, they will provide sterile effluent. Microbial challenge testing is carried out first on test filters, then on many production filters from different lots, under conditions that represent normal and worst-case production conditions. Due to the mechanisms of air filtration[2], it is important to note that filter retention performance does not only depend on contaminant size or type, but also air velocity and humidity.

There are two main, different types of microbial challenge validation: liquid bacterial challenge and aerosol bacterial challenge. These methods differ in that the first demonstrates a filter's microbial retention and removal efficiency performance from a *liquid* suspension inoculated with the challenge microorganism (*i.e.*, challenge fluid is a liquid); whereas the second demonstrates the same from *air* (*i.e.*, challenge fluid is air).

A detailed description about an air filter's performance under liquid or aerosol challenge conditions and the test work involved is found in “*Liquid and Aerosol Bacterial Challenge in Sterile Air Filter Validation*[4].”

Both these types of validation demonstrate the filter's ability to sterilize air according to the definition; however, the tests are run at very different conditions that differentiate whether the filters will sterilize the air at worst-case, process upset conditions. Liquid bacterial challenge is the more stringent validation method, and a liquid challenge claim in a sterilizing-grade air filter will ensure the lowest possible risk to compromising sterility.

On the other hand, an aerosol challenge claim describes filter retention performance in its most common application, namely in a dry air process. Filter performance under these conditions assumes low risk for process upset situations. In such situations, even hydrophobic filters on compressed air or gas streams may allow moisture through. Examples are failure of upstream air dryers or improper drainage of steam condensate, which can cause pressure surges which overcome the bubble point of a filter, or hydrophilic spots (wetted pores) on the filters due to exposure to solvent chemicals and oils in compressed air, or splashing CIP fluids from tanks which reduce the surface tension of moisture in the air. Should any moisture pass the filter, aerosol-challenged filters would not maintain sterility in the filtered air, while liquid-challenged filters would.

In critical sterilizing air and gas filtration applications, it is always preferable from a microbial retention perspective to use liquid-challenged filters.

Membrane and Depth Filters as Sterilizing-Grade Air Filters

In the food and beverage industry, there are both membrane and depth filter options offered as sterilizing-grade filters. Both types can satisfy the definition for sterilizing-grade filters, based on the defined microbial validation requirements. However, the key difference in retention performance between them is that membrane filters can uniquely be validated by liquid bacterial challenge, whereas depth filters can only be validated by aerosol bacterial challenge. This is due to the basic differences in their media structure and materials of construction.

Membrane cartridge air filters exhibit an extremely fine pore structure made from cast or stretched media, typically of naturally hydrophobic PTFE material, with very narrow pore size distribution (Figure 2). The media has some limited thickness, typically between 40-150 µm. As contaminants pass through this media, they are retained due to a combination of filtration effects that take place within the fine pore structure of the media.

Depth cartridge air filters exhibit a comparatively more open pore structure, as their media construction consists of fibrous materials, typically borosilicate microfibers, impregnated with PTFE or other hydrophobic material (Figure 3). Depth filters, as their name implies, feature much greater media 'depth' or thickness than membrane filters, *e.g.*, 1000-2000 µm. Contaminants navigate a tortuous path through this media, and are retained by a combination of filtration effects within the media thickness. Depth filters may exhibit media flexing and unloading under varying pressure conditions. Higher quality products feature fixed pore construction, which avoids this phenomenon.

Figure 2: PTFE Membrane Media

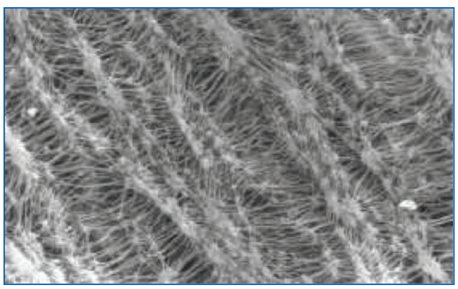


Figure 2: PTFE Membrane Media

In summary, membrane filters have a narrow pore size distribution resulting in a tighter configuration than depth filters. This explains why sterilizing-grade membrane air filters are uniquely capable of passing liquid bacterial challenge validation, and thus are the preferred choice for critical sterilizing air and gas filtration applications. The trade-off for this lowest risk retention performance by membrane filters is air flow: depth filter cartridges exhibit higher air flow rates than membrane filter cartridges. In high velocity, low supply pressure air applications, using depth filters may result in more compact sizing installations, although it must be noted that as application flow rates increase, the filter housing design can become a larger influence on sizing than the filters themselves.

Microbial *versus* Particle Removal

There are key differences between microbial and particle removal validation. Microorganisms and particles are not interchangeable as contaminants, and particles cannot be used as stand-ins for microorganisms in validation work. However, in addition to microbial validation, some filter manufacturers validate sterilizing-grade cartridge air filters for particle removal, but this is typically only for apparent comparison purposes to claims made by competing manufacturers. Users must distinguish between microbial removal and particle removal claims.

Particle removal validation is more relevant to filters designed solely for particle removal, such as cartridge air prefilters.

Microbial retention testing is highly sensitive, as it analyzes the entire test filter effluent stream (whether the challenge fluid is liquid or gas), and can therefore detect even a very small number of microbial cells that may have penetrated the filter, by incubating the effluent for microbial growth. On the other hand, aerosol particle removal tests display less sensitivity. In certain air filtration products, particle counters are used to sample a slip stream of the effluent air, not the total air amount, to count particles in the filter effluent.

Particle removal-based filter retention performance in cartridge filters is typically expressed in terms of a given particle removal rating at a given efficiency of removal. Using an example of a 1 µm filter:

- A 1 µm particle-rated filter with a removal efficiency of 99.98 % (TR = 104) would remove 1 µm or larger particles at a rate of 4999 out of 5000 challenge particles (99.98%). This is a very tight, highly efficient particle-removal filter.
- A 1 µm particle-rated filter with a removal efficiency of 90% (TR = 102) would remove 1 µm or larger particles at a rate of 4500 out of 5000 challenge particles (90%). This is a nominal particle-removal filter.

By contrast, microbially-rated filter retention performance in sterilizing-grade filters is expressed as a titer reduction of > 1011, or a 99.999999999% removal efficiency. It is apparent that there are limits to the sensitivity of the mentioned particle-removal test methods.

Documentation to Support Air Filter Retention Performance Claims

The extensive validation work that filter manufacturers conduct to develop and publish sterilizing-grade air filter retention performance claims on a data sheet is documented in a validation guide or a technical performance document. Understanding this documentation, terminology and methods in microbial validation enables the user to critically evaluate published claims and forms a clear basis for filter selection.

Focusing not only on published titer reduction or removal efficiency, but also considering microbial challenge level, type of challenge, and test conditions applied during filter validation is a way for end users to discern which filters will suit their need.

Verification of Filter Retention Performance in Operation

Microbial validation involves a destructive test. This is why a non-destructive test must be employed, to verify that commercially available filters and filters in operation at end user facilities exhibit expected retention performance. Such a non-destructive test is known as the filter integrity test. Integrity test pass/fail values must be correlated with the bacterial removal performance proven during validation test work.

Integrity testing is typically carried out by filter manufacturers as a quality release criterion prior to shipment. In addition, filter manufacturers recommend that it be carried out by the end user upon filter installation before operation, and at the end of each production batch. Filter damage can go unseen, and only integrity testing provides true performance verification.

Application Notes

Sterilizing-grade air cartridges are always an excellent choice from a retention performance perspective, due to their stringent microbial validation. Liquid-challenged membrane cartridge air filters are always preferred for critical applications, to reduce risk (Figure 4).

Figure 4: Pall Emflon® sterilizing-grade membrane air filters are available in different configurations and sizes to suit various application needs.

Sterilizing-grade cartridge air filters are commonly applied in tank venting applications, where they provide a sterile barrier to the surrounding environment. They prevent transfer of microorganisms from the outside air into storage and buffer tank contents; in some cases, it is also important to prevent microorganisms from the tank contents escaping to the outside.

Sterilization of compressed air and gas for a wide variety of uses is another common application type for cartridge air filters. However, in some cases, sizing cartridge filter assemblies may limit their use. Cartridge installations are sized based on type of gas, supply pressure, supply temperature and gas flow rate. Sizing increases as flow rates increase and supply pressures decrease, which necessitates going from single-round to multi-round filter housing assemblies of varying sizes. In certain applications such as high flow rate, very low supply pressure blower air, sizing a cartridge assembly may become costly and users may choose to turn to other technologies. It is extremely important to ensure that process safety is never compromised, and that users are equipped to ask critical questions when making their selections.

References

[1] Food and Drug Administration. *Guidance for Industry – Sterile Drug Products Produced by Aseptic Processing – Current Good Manufacturing Practice*; CDER, CBER, ORA: Rockville, MD, September 2004. Accessed at https://www.fda.gov/downloads/Drugs/Guidances/ucm070342.pdf.

[2] Parenteral Drug Association (PDA). *Sterilizing Filtration of Gases*; PDA Technical Report No. 40 (TR 40); *PDA J. Pharm. Sci. Technol.* 2005, 58 (No. S-1).

[3] Pall Corporation. *Attributes of Sterilizing-Grade Air and Gas Filters*. 2020.

[4] Pall Corporation. *Liquid and Aerosol Bacterial Challenge in Sterile Air Filter Validation*. 2020.

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