

Bacteria and Virus Retention in Air by Microporous Membranes

The key to using filters effectively is to understand the characteristics of hydrophobic membranes.

Mary Boomus

There are many different types of filter media, including membrane filters, depth media, carbon filters, screens, molecular-weight-cutoff media, affinity materials, and hydrophilic and hydrophobic membranes. These filter media are used in separations technology, the processes in which unlike materials are separated. Some are used to filter liquids, while others are used to filter gases.

Filter media classified as microporous membranes are typically rated for liquid filtration, although they may be used for air or gas filtration (see Table I). It is important to understand the intended application of a filter because its bacteria- or virus-retention efficiency rating is much different in air than it is in liquid. A filter must be effective enough to produce the results that are required, but not so efficient that it restricts flow or plugs prematurely.

Membrane Pore-Size Validation

Standard Tests. Standard tests are performed to validate the pore size of filter membranes. For instance, 0.2- μm membranes are tested by challenging them with *Brevundimonas diminuta*, which is slightly larger than 0.2 μm (see Table II). At slightly more than 10^7 organisms per square centimeter of effective filtration area, the membrane must retain all organisms. Further, membranes with pore sizes of 0.45 μm are often tested with *Serratia marcescens*. *S. marcescens* are about 0.5 μm in diameter, so the filter should retain 100% of the organisms.

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Standardized tests are conducted specifically for liquid application filter media. The inherent flaw in such validation is that the bacteria-retention test is destructive. The membrane is contaminated and has no further use after the test is completed.

Therefore, it is sometimes necessary to perform a non-destructive test to verify the pore size of the membrane. Such a test should correlate to the pore size. It should also be suitable for in situ use and, of course, cannot contaminate the membrane. A bubble-point test is repeatable, is not harmful to the filter media, and can be correlated with pore size.

Bubble-Point Tests. The bubble point of a membrane is the pressure at which air can be forced through a wetted membrane. This test can be performed in water, isopropyl alcohol, pharmaceuticals, and other liquids. The test liquid should wet the membrane (fill the pores of the membrane) and be similar to those actually used with the filter. It is important that the test liquid be compatible with the filter media; otherwise, the test could fail.

In the pharmaceutical market, for example, sterile filtration is sometimes the last step of the manufacturing process before the pharmaceutical is packaged. This is particularly true for pharmaceuticals sensitive to heat, radiation, or other sterilization methods. After the final filtration procedure, a bubble-point test is performed using the pharmaceutical that was filtered. The test confirms the integrity of the filter. It is typically performed in situ. (It may be performed before pharmaceutical filtration but is usually done post-filtration to reduce the chance of contamination.)

FILTER MEDIA	TYPE	CHARACTERISTICS	TYPICAL USE
PTFE (polytetrafluoroethylene)	Microporous membrane	Highly hydrophobic. Compatible with most solvents. Autoclavable. Withstands high temperatures.	Filtration of solvents and gases. Transducer protectors, suction filters, hydrophobic vents.
PES (polyethersulfone)	Microporous membrane	Hydrophilic. Typically has good flow rates. Non-protein binding.	IV filters, syringe filters, cartridges, capsules, pharmaceutical filtration.
PVDF (polyvinylidene fluoride)	Microporous membrane	Naturally hydrophobic.	Vents, solvent filters, Western blot.
Modified acrylic on nylon substrate (Versapor)	Microporous membrane	Can be hydrophilic or hydrophobic.	Hydrophobic: Vents, transducer protectors, pipette protection. Hydrophilic: Filter for aqueous solutions and some solvents. Not as chemically compatible as PTFE.
Glass microfiber	Depth media	Can be hydrophobic at very low pressures. Sometimes laminated for strength and nonsloughing.	Air filtration, vents, laparoscopic smoke elimination, respiratory filters, good prefilter for microporous membranes.
Nonwoven polyolefins	Depth media	Hydrophobic at low pressure.	Support or protection for microporous membranes, air filtration, can enhance hydrophobicity of other materials.
Nonwoven polyester	Depth media	Hydrophilic.	Air filtration, particulate filter, support or protection for microporous membranes.

Table I. Some of the many different types of filter media.

Another bubble-point testing application would be for an IV filter. It is impractical to perform testing on every product to be assembled into sets. But random samples can be pulled and testing can be done on these samples as a destructive test. Actually, this test can be done with 0.2 µm of filtered water. The procedure is the same as with pharmaceutical testing.

First, the product is wet out with the water (or pharmaceutical). The downstream side of the filter must be placed so that a steady stream of bubbles coming through the filter is visible. The test media should flow through the sample from the inlet side to the outlet side. Attaching a clear tube to the downstream side of the housing can help testers see the bubbles. Alternatively, attaching a tube to the downstream side and then immersing the tube into a reservoir of water so that the bubbles are visible as they exit the tube can also work. An air source is attached upstream of the filter, along with a regulator and a pressure gauge to verify the pressure being applied to the filter. As the air pressure slowly increases, the outlet tube should be watched. A steady stream of bubbles issuing from the outlet of the filter indicates that the bubble point has been

reached. If testing an IV filter, for example, this test will determine that the membrane has not been damaged during the manufacturing process and will confirm the integrity of the housing seal.

The bubble point is related to the ability of the filter to retain bacteria. A series of tests can determine what the bubble point of the membrane should be in a pharmaceutical or in plain water. The filter manufacturer or the user can determine this relationship, as the tests are quite easy.

If a product fails the bubble-point test, that failure does not necessarily mean the product is not sterile, but it does mean that more tests need to be performed. Unfortunately, sterility tests for finding bacteria can take a week or more and can be very inconvenient.

PORE SIZE	CHALLENGE ORGANISM
0.1 µm	<i>Acholeplasma laidlawii</i>
0.2 µm	<i>Brevundimonas diminuta</i>
0.45 µm	<i>Serratia marcescens</i>
0.8 µm	<i>Lactobacillus spp.</i>
1.2 µm	<i>Candida albicans</i>

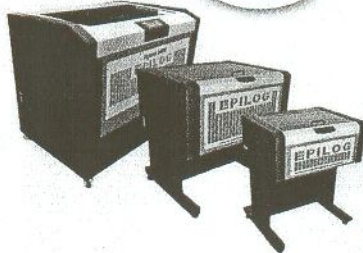
Table II. Challenge organisms that are used to verify membrane pore size.

Hydrophilic and Hydrophobic Efficiency Ratings

The ability of membranes to retain bacteria and viruses in air is much greater than their retention capability in liquids.¹⁻⁴ However, OEM users of air vents and such isolation products as transducer protectors and other hydrophobic products are still confused about the topic.

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FILTER MEDIA >>

Because membrane pore-size nomenclature is typically related to hydrophilic membranes (so called for their affinity to water), manufacturers are not familiar with the ability of membranes to retain bacteria and viruses in air. Most membranes are inherently hydrophobic (that is, they tend to repel water) unless a surfactant (wetting agent) is added to the formulation either when the material is manufactured or as a posttreatment. The surfactant makes these materials hydrophilic.

However, in some cases it may be desirable to make the membrane more resistant to moisture. An agent such as silicone, silane gas, or a fluorocarbon can render the membranes even more hydrophobic. Polytetrafluoroethylene (PTFE) is highly hydrophobic and is not usually treated to make it more so.

It is not necessary to use a hydrophobic membrane for filtration of dry air. But most membranes are treated with a hydrophobic agent if they are to be used for air filtration, such

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as in venting applications. After the treatment, the filters can be used in several ways. They isolate a reservoir of aqueous fluid from the environment to keep the fluid sterile. Or, they isolate the environment from an aqueous fluid that incorporates pathogens. The filters can keep the aqueous fluid where it is, so it will not leak out of the reservoir or go through the system to contaminate the downstream equipment. Keep in mind that membranes are not one-way check valves; the membrane allows air or gas to pass back and forth between one area and the other.

Water-Breakthrough Testing. Because hydrophobic membranes are used in numerous applications, it is important to know how to test them and to understand how they work. The membranes cannot be tested by a simple bubble-point test in water because water will not wet out the membrane. (These membranes inherently repel water while allowing air to pass.)

However, there is a standard test for finding pore size that is simple to perform. It is called a water-breakthrough test (WBT) or water-intrusion test. This test determines the pressure at which water can be forced through the membrane. Although the test result correlates to the pore size of the membrane, it does not indicate the membrane's ability to retain bacteria, particles, or viruses. Also, the WBT refers only to the pore-size rating of the membrane

in liquid and to the ability of the material to stop aqueous fluids.

On the upstream side of the membrane or device, an aqueous fluid (typically water) is introduced to the membrane at increasing pressures. If this test is done off-line, or for testing purposes only, the device or membrane will be discarded after the test. Colored fluid is better to use because it is easier to see when it passes through the membrane. Years ago when I was involved in developing this test, I used green, red, and blue food coloring. Standard green food coloring can be seen the best. When the tester begins to see water coming through the membrane, this indicates that either the water-breakthrough pressure has been reached or there is a large pore in the device. The higher the pressure, the tighter the membrane (the smaller the pores). This is also true for the bubble-point test—the higher the bubble point, the smaller the pores are in the membrane.

The WBT test will also enable users to see flaws in a device, such as a lack of seal integrity or damage to the membrane that may have occurred during the manufacturing process.

Bacterial and Viral Retention Capabilities

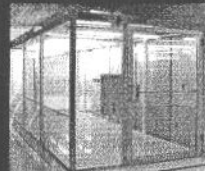
The confusion about retention capabilities of air-filtration membranes stems from the fact that pore size is rated in liquid. The retention characteristics of membranes in air are totally different than those achieved when they are tested in liquids. Actually, the same membranes that are hydrophobic in water become hydrophilic in air.

In air or gas, the efficiency of membranes is about 10 times better than it is in liquids.³ Laws of impaction and

The confusion about retention capabilities of air-filtration membranes stems from the fact that pore size is rated in liquid. The retention characteristics of membranes are different in air than in liquids.

adsorption play a strong role when filtering gases. This means that a 1.2- μm liquid-rated filter is equivalent to about 0.12 μm in air, which can be considered sterilizing grade.⁴ Electrostatic charges in the membrane also contribute to retention in air. The charges attract particles and organisms to the surfaces of the membrane and to the walls of the pores, thus making the product even more efficient. Also, while liquid filtration enables the stream of liquid to carry the particles, bacteria, or viruses through the membrane, this does not happen in air.² And, in air, there is the principle of Brownian motion.⁵ The principle states that particles do not travel in a straight path, but have a zigzagging movement, which makes them more easily retained by membranes.

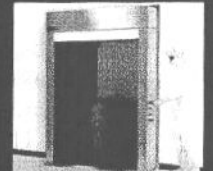
As just mentioned, it has been proven that membranes with liquid ratings are about 10 times more efficient in



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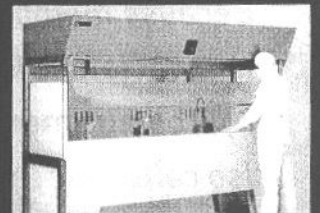
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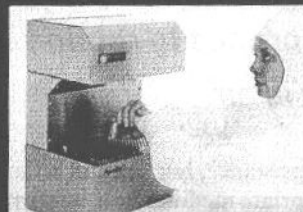
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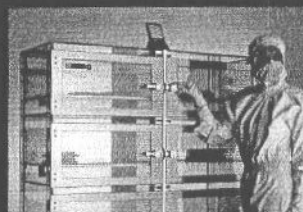
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removing bacteria or viruses in air. Thus, a 0.2- μm liquid-rated membrane will perform in air at the rate of a membrane that would be rated at 0.02 μm if it were rated in air.¹

Although it is well known that IV filters incorporate 0.02–0.03- μm PTFE membrane as vents, the filter characteristics should not be considered part of the bacterial or viral retention characteristics for all applications. The vent membrane is used only for its water-breakthrough characteristics when it is used with a total parenteral nutrition (TPN) solution that includes vitamins. The vitamins incorporate surfactants so that the body will more readily adsorb them. Surfactants lower the surface tension of the solution. When the surface tension of a liquid goes down, the solution can wet out a hydrophobic membrane more easily. A small-pore PTFE membrane is typically used for vents so that they will not wet out over time.

Choosing the Right Filter Media

With the characteristics of hydrophobic filter media retention in mind, it is important to choose the largest pore size available that will give the required results from a device. The reason is a simple one: a larger pore size exhibits

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higher flow rates and less resistance, but can still retain bacteria. To choose the appropriate medium, it is important to consider the following:

- The pressure at which the system will be used.
- The flow rate required.
- The effective filtration area that can be used (i.e., how large the device can be).
- What the solution is. (Keep in mind that, as the pore size increases, the hydrophobicity decreases.)

Hydrophobic Depth Media. Unlike microporous membranes, depth media do not have a set pore structure. Depth media are created by depositing many layers of fibers on a web, and then bonding them together with an adhesive of some type. The mechanism of filtration is labyrinthine. Some of these materials are supported to reduce the slough-

MEMBRANES	DEPTH MEDIA
Absolute retention rating	Nominal retention rating
Lower flow rate	Higher flow rate
High hydrophobicity	Low hydrophobicity
More expensive	Less expensive
More difficult to assemble into device	Less difficult to assemble into device
Can be used as prefilter	Can also be used as prefilter

Table III. Attributes of membranes and depth media compared.

ing of glass or other base materials, while others are not. Although membranes also work as a labyrinth, they do not have the thickness that is present with depth media.

There are several advantages and disadvantages to using depth media in devices (see Table III). To start with the former, depth media are rated in air. Another benefit of using depth media is that the flow rate is much greater than that of microporous membranes; they have less ΔP , or resistance. Also, they will not plug as fast because they have greater depth for capturing particles within the matrix.

Manufacturers should understand, however, that depth media are not absolute filters. Rather, they are nominal materials. The nominal rating is a clear disadvantage. Defined as retaining a percentage of particles of a given size—such as 99.97% of particles sized 0.3 μm and larger—nominal filters do not guarantee absolute retention. These types of media are also much less hydrophobic and less consistent. It is also important to remember that if liquid passes through the filter media, pathogens will as well.²

Conclusion

Bacterial and viral retention is a complex topic. Manufacturers and users need to understand the properties of filter membranes, the implications of pore size, and the limits of each type of filter test. A thorough knowledge of filtration can help manufacturers get the best filter for their application.

The best thing to do when designing filter media is to evaluate what is required of a product ahead of time, and then make a decision about what materials should be used. Membrane manufacturers can often provide the necessary expertise to find the best solution.

References

1. FK Port and IA Bernstein, "Hepatitis Risk from Hemodialysis Pressure Monitors," from *Proceedings of the Third Meeting of ISAO*, supplement to *Artificial Organs* 5 (1981): 638–641.
2. ME Vincent and JC Glorioso, "Evaluation of Vacuum/Suction Safety Devices in Preventing Transmission of Human Virus Pathogens," *American Clinical Laboratory* 8, no. 1 (1989): 26–29.
3. WP Olson, L Vanden Houten, and JE Ellis, "Sterile Vent Filter Function Test," *Journal of Parenteral Science and Technology* 35, no. 2 (1981): 35–36.
4. J Marshall and J Mansfield, "Incorporating Microporous Membranes into Medical Devices," *Medical Device Technology* (June 2004).
5. P Blossie, "Sterile Filtration of Gases," *ISPE NW Region* (June 1, 2005). ■