mdi Membrane Technologies, Inc.

STERILE FILTRATION

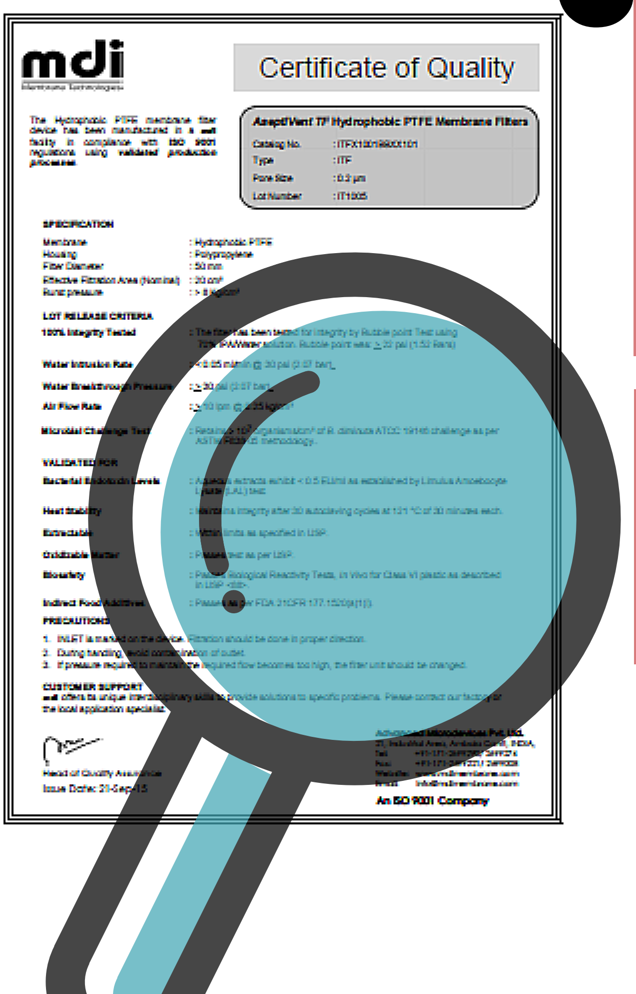
In Compounding Pharmacies

Compounding pharmacies face a number of challenges due to the diversity of products they handle, batch size variation, and any number of other unavoidable variables within their operations. While we cannot claim expertise in every part of the process, we can offer support at one very important point: terminal sterilization of the final product.

Know your filter and know your supplier.

As a filter manufacturer, mdi understands the importance of choosing the right product for final sterilization. A good indicator of quality when it comes to sterilizing grade filters is the provision of a certificate of quality or assurance (COQ/COA). A complete COQ or COA will not only include specifications regarding microbial challenge testing and integrity testing, but also a host of important information concerning validation.

Take a closer look at that COQ.


mdi

Certificate of Quality

The Hydrophobic PTFE membrane filter device has been manufactured in a well facility in compliance with ISO 9001 regulations using validated production processes.

AseptiVent TF Hydrophobic PTFE Membrane Filters

Catalog No.	: ITFX10018800X101
Type	: ITF
Pore Size	: 0.2 µm
Lot Number	: IT1005

SPECIFICATION

Membrane	: Hydrophobic PTFE
Housing	: Polypropylene
Filter Diameter	: 50 mm
Effective Filtration Area (Nominal)	: 20 cm²
Burst pressure	: > 8 kg/cm²

LOT RELEASE CRITERIA

100% Integrity Tested	: The filter has been tested for integrity by Bubble point Test using 70% IPA/Water solution. Bubble point was ≥ 22 psi (1.52 Bars)
Water Intrusion Rate	
Water Breakthrough Pressure	
Air Flow Rate	
Microbial Challenge Test	

VALIDATED FOR

Bacterial Endotoxin Levels	
Heat stability	
Extractable	: Within limits as specified in USP.
Oxidizable Matter	: Passes test as per USP.
Biosafety	: Passes Biological Reactivity Tests, In Vivo for Class VI plastic as described in USP <88>.
Indirect Food Additives	

PRECAUTIONS

1. INLET is marked on the device. Filtration should be done in proper direction.
2. During handling, avoid contamination of outlet.
3. If pressure required to maintain the required flow becomes too high, the filter unit should be changed.

CUSTOMER SUPPORT

Head of Quality Assurance

Issue Date: 21-Sep-15

An ISO 9001 Company

"... The filter has been tested for integrity by Bubble Point Test using 70% IPA/Water solution. Bubble point was > 22 psi (1.52 bar)..."

"...Passes Biological Reactivity Tests, In Vivo for Class VI plastics as described in USP <88>..."

But that's not all...

Microbial Challenge Testing

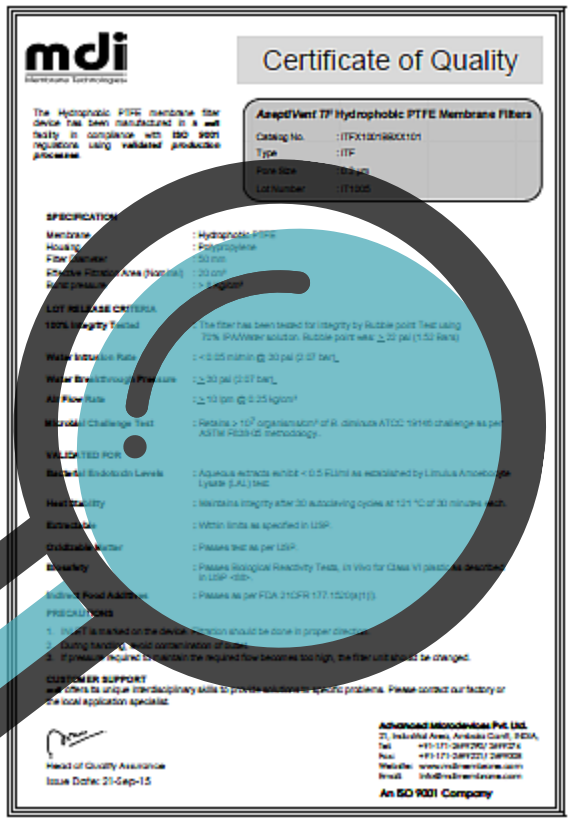
A sterilizing grade filter must be validated for bacterial retention as per compendia requirements for each manufactured lot. This type of challenge testing should follow the methodologies set forth by ASTM F838-05. [1]

"Membranes that are documented to retain 100% of a culture of 107 microorganisms of a strain of Brevundimonas (Pseudomonas) diminuta per square centimeter of membrane surface under a pressure of not less than 30 psi (2.0 bar)."[2]

- USP <797>

"Classically, a sterilizing-grade filter has been defined as a filter that will retain 107 cfu (colony forming unit) of Brevundimonas diminuta* (B. diminuta) ATCC® 19146™/cm2 of effective filter surface area under process conditions."[3]

– PDA Technical Report 26



"Microbial Challenge Test: Retains > 10^7 organisms/cm^2 of B. diminuta ATCC 19146 challenge as per ASTM F838-05 methodology."

What about integrity testing and validation?

Integrity Testing and Validation

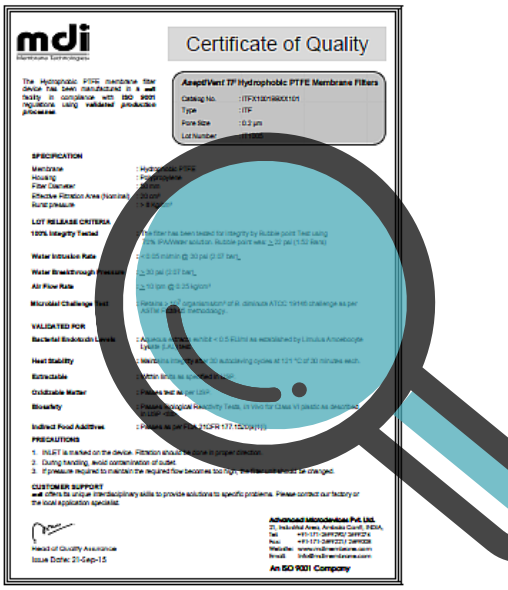
Each individual filter should allow the user to conduct non-destructive, post use Integrity testing. The Integrity test values are defined by the filter manufacturer and are correlated to the pore size rating of the filter based on the actual bacterial retention testing the manufacturer has done.

Specifications regarding validation will also be present including information about bacterial endotoxin levels, extractables, and biosafety.

FDA 21 CFR 210.3(b)(6) tells us that

> "Nonfiber releasing filter means any filter, which after appropriate pretreatment such as washing or flushing, will not release fibers into the component or drug product that is being filtered."

> "Fiber Release: Complies with FDA 21CFR210.3(b)(6)"



Making this information readily available is important for ensuring that our customers are confident in our stringent production procedures. With products that are sterilized by filtration, choice of filter is obviously of the utmost importance. A customer should never be afraid to put their filter manufacturer to the test. Ask questions. Know your filter. Know your supplier.

1. ASTM F838-05, Standard Test Method for Determining Bacterial Retention of Membrane Filters Utilized for Liquid Filtration, ASTM International, West Conshohocken, PA, 2005, www.astm.org
2. Chapter <797> Pharmaceutical Compounding—Sterile Preparations. In: United States Pharmacopeia, 31st rev./National Formulary, 26th ed. Rockville, MD: United States Pharmacopeial Convention; 2009.
3. Technical Report No. 26 Sterilizing Filtration of Liquids. (2008). PDA Journal of Pharmaceutical Science and Technology, 62, 7.