ULTRAFILTER
THE FILTRATION MANUFACTURER
Kronsbein ultrafilter ®

PF-PVDF

Filter Cartridges | Validation Guide

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PF-PVDF

CONTENT

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VALIDATION GUIDE

INTRODUCTION

This Validation Guide provides information of Ultrafilter PF-PVDF series filters, including test methods, performance, and specifications related to the pharmaceutical manufacturing process. This guide is designed as a reference for end user to validate Ultrafilter PF-PVDF series filters to meet requirements of regulatory authorities within the pharmaceutical industry.

Ultrafilter PF-PVDF series filters contain 0.1 µm, 0.20 µm, 0.45 µm, 0.65 µm, or 1.0 µm hydrophilic polyvinylidene fluoride (PVDF) membrane, which are designed for different filtration processes in pharmaceutical applications.

Quality Assurance

Ultrafilter GmbH establishes and continuously maintains the company's quality assurance system in accordance with the requirements of ISO 9001:2015 quality management system. All the products are manufactured under strict quality system to ensure stable and reliable quality.

Raw Material Control

Ultrafilter GmbH has established a rigorous supplier selection and periodic evaluation system. The core materials are selected from internationally renowned raw material suppliers and manage the suppliers hierarchically. The injection molding pellets, support layers, O-rings and other materials or components are inspected according to the company's internal control standards to ensure the quality of raw materials is stable and reliable.

Environment Management

The entire manufacturing process of the Ultrafilter filter from raw material storage to product packaging is completed in the ISO Class 8 clean area, which ensures the cleanliness of the product and prevents pollution. The air purification system is confirmed and maintained regularly to ensure that the cleanliness of environment continuously meets the requirements of ISO Class 8. The suspended particles, sedimentation bacteria, temperature, humidity and differential pressure are monitored periodically to provide for a highly controlled clean environment.

Lot Release and Traceability

The sterilizing grade Ultrafilter filter requires 100% integrity testing before delivery. The test methods include bubble point, diffusion flow and water intrusion. The specific test method can be found in the integrity test section of the quality certificate.

The product lot number and serial number of Ultrafilter filter are engraved on the cartridge cage. Customers can also find the corresponding product lot number in the product label and quality certificate. The product can be traced from the whole process of raw materials, equipment, manufacturing process through the lot number and serial number.

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PF-PVDF

PRODUCT SPECIFICATIONS

CATALOGUE NUMBERS DESCRIPTION					
PF-PVDF					
	PORE SIZE	**FILTER LENGTH**	**CARTRIDGE ADAPTER TYPE**	**SEAL MATERIAL**	**PHARMA GRADE**
	10 = 0.1 µm	05 = 5"	2 = Code 2	A = EPDM	-V
	20 = 0.2 µm	10 = 10"	3 = Code 3	B = Silicone	
	45 = 0.45 µm	20 = 20"	7 = Code 7	G = Fluoroelastomer	
	65 = 0.65 µm	30 = 30"	8 = Code 8		
	10 = 1.0 µm	40 = 40"	MF = DOE		
			UF = UF		

Example Part Number:	**Filter-Type**	**Pore size**	**Filter Lenght**	**Connection Type**	**Sealing**	**Pharma Grade**
	PF-PVDF	45	30	7	-B	-V

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SPECIFICATIONS

FILTER	PF-PVDF 0.1 µm	PF-PVDF 0.2 µm
LENGTH	254.0 MM (10 INCH)	
DIAMETER	69.0 MM (2.7 INCH)	
MATERIALS OF CONSTRUCTION		
FILTER MEMBRANE	HYDROPHILIC POLYVINYLIDENE FLUORIDE (PVDF)	
SUPPORTS	POLYPROPYLENE	
CORE, CAGE, END CAPS	POLYPROPYLENE	
ADAPTER INTERNAL SUPPORT	STAINLESS STEEL 316L, PBT	
O-RINGS	SILICONE, EPDM, FLUOROELASTOMER	
PORE SIZE	0.1 µm	0.2 µm
EFFECTIVE FILTRATION AREA	0.58 M2 (6.2 FT2)	
MAXIMUM OPERATING PRESSURE	6.9 BAR (100 PSI) AT 25 °C 4.0 BAR (58 PSI) AT 60°C 2.4 BAR (35 PSI) AT 80 °C	
MAXIMUM DIFFERENTIAL PRESSURE		
FORWARD	6.9 BAR (100 PSI) AT 25 °C 4.0 BAR (58 PSI) AT 60 °C 2.4 BAR (35 PSI) AT 80 °C	
REVERSE	3.0 BAR (44 PSI) AT 25 °C 1.0 BAR (15 PSI) AT 80 °C	
WATER BUBBLE POINT AT 20 °C	≥ 1.6 BAR (23 PSI) IN 60% IPA 40% WATER, AIR	≥ 3.2 BAR (46 PSI) IN WATER, AIR
AIR DIFFUSION AT 20 °C	≤ 30 ML/MIN AT 3.86 BAR (56 PSI), WATER WETTED	3.0 BAR (44 PSI) AT 25 °C
BACTERIAL RETENTION	RETENTION OF 107 CFU/CM2 BREVUNDIMONAS DIMINUTA (ATCC® 19146) ACCORDING TO ASTM F838.	
STERILIZATION		
STEAM IN PLACE	CAN BE STEAM STERILIZED FOR 30 MINUTES AT 135 °C IN FORWARD DIRECTION (< 0.3 BAR, 5 PSI) WITH 100 CYCLES AND IN REVERSE DIRECTION (< 0.1 BAR, 1.5 PSI) WITH 50 CYCLES.	
AUTOCLAVE	CAN BE AUTOCLAVED 400 CYCLES FOR 30 MINUTES AT 130 °C.	
TOC / CONDUCTIVITY AT 25 °C	AUTOCLAVED FILTER EFFLUENT MEETS THE USP <643> FOR TOTAL ORGANIC CARBON AND USP <645> FOR WATER CONDUCTIVITY PER WFI REQUIREMENTS AFTER A UPW FLUSH OF 30 L.	
PARTICLE SHEDDING	AUTOCLAVED FILTER EFFLUENT MEETS THE REQUIREMENTS IN USP <788> FOR LARGE VOLUME PARENTERALS.	
NON-FIBER RELEASING	COMPONENT MATERIALS MEET THE CRITERIA FOR A "NON-FIBER-RELEASING FILTER" AS DEFINED IN 21 CFR 210.3 (B) (6).	
BACTERIAL ENDOTOXIN	AQUEOUS EXTRACTION OF AUTOCLAVED FILTER CONTAINS < 0.25 EU/ML AS DETERMINED BY LIMULUS AMEBOCYTE LYSATE (LAL), USP <85>.	
USP <87> CYTOTOXICITY	MEET THE REQUIREMENT OF USP <87> IN VITRO BIOLOGICAL REACTIVITY TEST.	
USP <88> BIOLOGICAL REACTIVITY	MEET THE CRITERIA OF THE USP <88> BIOLOGICAL REACTIVITY TEST FOR CLASS VI-121 °C PLASTICS.	
INDIRECT FOOD ADDITIVE	ALL COMPONENT MATERIALS MEET THE FDA INDIRECT FOOD ADDITIVE REQUIREMENTS CITED IN 21 CFR 177–182.	
QUALITY ASSURANCE	THESE PRODUCTS ARE MANUFACTURED IN A FACILITY WHICH ADHERES TO ISO 9001:2015 PRACTICES.	

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PF-PVDF

SPECIFICATIONS			
FILTER	**PF-PVDF 0.45 µm**	**PF-PVDF 0.65 µm**	**PF-PVDF 1.0 µm**
LENGTH	254.0 MM (10 INCH)		
DIAMETER	69.0 MM (2.7 INCH)		
MATERIALS OF CONSTRUCTION			
FILTER MEMBRANE	HYDROPHILIC POLYVINYLIDENE FLUORIDE (PVDF)		
SUPPORTS	POLYPROPYLENE		
CORE, CAGE, END CAPS	POLYPROPYLENE		
ADAPTER INTERNAL SUPPORT	STAINLESS STEEL 316L, PBT		
O-RINGS	SILICONE, EPDM, FLUOROELASTOMER		
PORE SIZE	0.1 µm	0.2 µm	1.0 µm
EFFECTIVE FILTRATION AREA	0.58 M2 (6.2 FT2)		
MAXIMUM OPERATING PRESSURE	6.9 BAR (100 PSI) AT 25 °C 4.0 BAR (58 PSI) AT 60°C 2.4 BAR (35 PSI) AT 80 °C		
MAXIMUM DIFFERENTIAL PRESSURE			
FORWARD	6.9 BAR (100 PSI) AT 25 °C 4.0 BAR (58 PSI) AT 60 °C 2.4 BAR (35 PSI) AT 80 °C		
REVERSE	3.0 BAR (44 PSI) AT 25 °C 1.0 BAR (15 PSI) AT 80 °C		
WATER BUBBLE POINT AT 20 °C	≥ 1.2 BAR (17 PSI), AIR	≥ 1.0 BAR (15 PSI), AIR	≥ 0.4 BAR (6 PSI), AIR
AIR DIFFUSION AT 20 °C	≤ 30 ML/MIN AT 3.86 BAR (56 PSI), WATER WETTED	3.0 BAR (44 PSI) AT 25 °C	
BACTERIAL RETENTION	RETENTION OF 107 CFU/CM2 BREVUNDIMONAS DIMINUTA (ATCC® 19146) ACCORDING TO ASTM F838.		
STERILIZATION			
STEAM IN PLACE	CAN BE STEAM STERILIZED FOR 30 MINUTES AT 135 °C IN FORWARD DIRECTION (< 0.3 BAR, 5 PSI) WITH 100 CYCLES AND IN REVERSE DIRECTION (< 0.1 BAR, 1.5 PSI) WITH 50 CYCLES.		
AUTOCLAVE	CAN BE AUTOCLAVED 400 CYCLES FOR 30 MINUTES AT 130 °C.		
TOC / CONDUCTIVITY AT 25 °C	AUTOCLAVED FILTER EFFLUENT MEETS THE USP <643> FOR TOTAL ORGANIC CARBON AND USP <645> FOR WATER CONDUCTIVITY PER WFI REQUIREMENTS AFTER A UPW FLUSH OF 30 L.		
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QUALITY ASSURANCE	THESE PRODUCTS ARE MANUFACTURED IN A FACILITY WHICH ADHERES TO ISO 9001:2015 PRACTICES.		

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1. Verification and Validation

Bacteria Challenge Test and Correlation with Non-Destructive Integrity Test

The USP < 1229.4 > defines "A sterilizing-grade filter is one that is capable of retaining a minimum 1×107 cfu of B. diminuta (ATCC® 19146) per square centimeter of effective filter area when tested in accordance with ASTM® F838-05 (2013), Standard Test Method for Determining Bacterial Retention of Membrane Filters Utilized for Liquid Filtration."

A liquid bacteria challenge test (BCT) was performed to confirm that Ultrafilter PF-PVDF 0.2 µm cartridge filter can completely retain a minimum concentration of 107 cfu/cm2 (EFA) Brevundimonas diminuta (ATCC® 19146) and meet the criteria for sterilizing grade performance as defined in ASTM methodology.

Since the bacteria challenge test is a destructive method, it must be correlated with a non-destructive integrity test. The FDA guideline states, "After a filtration process is properly validated for a given product, process and filter, it is important to assure that identical filter replacement (membrane or cartridge) used in production runs will perform in the same manner. One way of achieving this is to correlate filter performance data with filter integrity testing data. Normally, integrity testing of the filter is performed after the filter unit is assembled and sterilized prior to use. More importantly, however, such testing should be conducted after the filter is used in order to detect any filter leaks or perforations that may have occurred during the filtration."

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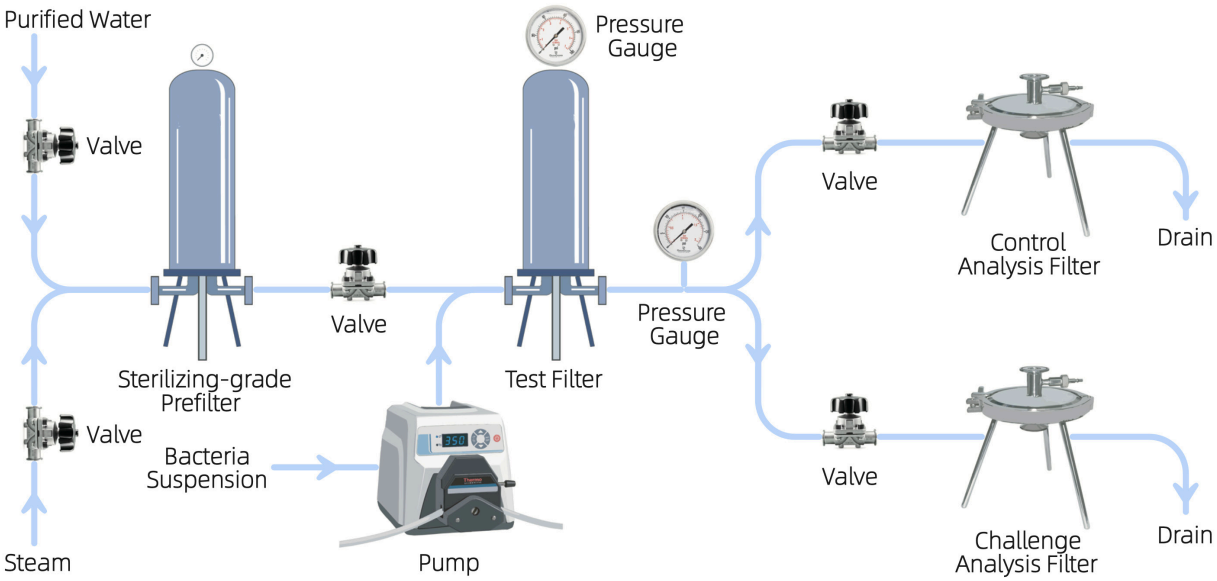
PF-PVDF

Summary of Method

Ultrafilter PF-PVDF 0.2 µm cartridge filters were wetted with water and steamed at 135 °C for 30 minutes prior to testing. The cartridge filters were subjected to integrity test and then challenged with Brevundi- monas diminuta (ATCC® 19146) of the challenge level over 1×107 cfu/cm2 (EFA) in accordance with ASTM F838 at a pressure of 2 bar.

After the bacteria challenge test, the control analysis filter and challenge analysis filters are incubated on Tryptic Soy Agar (TSA) plates at 30 °C to determine if there are any challenge bacteria passing through the tested filter. The analysis is conducted according to ASTM methodology.

Bacterial Challenge Test Schematic



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Results

LOT NUMBER	DIFFUSION @ 2.8 BAR (ML/MIN)	CHALLENGE LEVEL (CFU/UNIT)	FILTRATE STERILITY	LRV/CM²
XM10318210	10.1	1.13×10^{11}	Sterile	7.29
XM12128604	11.6	1.07×10^{11}	Sterile	7.27
XM12028408	12.7	1.74×10^{11}	Sterile	7.48
XCL9017630	12.8	1.90×10^{11}	Sterile	7.52
XM12128604	13.0	1.07×10^{11}	Sterile	7.27
XM11348314	13.2	1.13×10^{11}	Sterile	7.29
XM11148323	13.4	1.86×10^{11}	Sterile	7.51
XM12218309	13.8	7.51×10^{11}	Sterile	7.11
XM11138531	14.3	1.07×10^{11}	Sterile	7.27
XM10348119	14.5	1.74×10^{11}	Sterile	7.48
XCD1017322	14.5	9.35×10^{11}	Sterile	7.21
XM12028408	14.7	1.90×10^{11}	Sterile	7.52
XM10348119	15.3	7.74×10^{11}	Sterile	7.13
XMO2117829	15.3	1.86×10^{11}	Sterile	7.51
XM10338305	15.7	1.02×10^{11}	Sterile	7.25
XM07148524	15.9	6.90×10^{11}	Sterile	7.08
XCB7017105	16.8	1.90×10^{11}	Sterile	7.52
XMO3247A24	17.3	1.02×10^{11}	Sterile	7.25
XCK9017818	17.8	1.86×10^{11}	Sterile	7.51
XM12518619	18.1	1.74×10^{11}	Sterile	7.48
XM10348119	18.8	9.35×10^{11}	Sterile	7.21
XM10328206	18.9	7.33×10^{11}	Sterile	7.10
XM02337920	19.2	6.90×10^{11}	Sterile	7.08
XM09028225	19.7	7.74×10^{11}	Sterile	7.13
XM09028225	20.3	8.17×10^{11}	Sterile	7.15
XM09028225	20.9	7.74×10^{11}	Sterile	7.13
XCL6017704	21.1	1.02×10^{11}	Sterile	7.25
XM11348314	21.8	7.51×10^{11}	Sterile	7.11
XM21128306	22.7	8.17×10^{11}	Sterile	7.15
XCB7017105	23.2	7.51×10^{11}	Sterile	7.11
XCK9017818	23.6	7.33×10^{11}	Sterile	7.10
XCM1017818	23.9	9.35×10^{11}	Non sterile	<7
XCL9017630	24.4	7.33×10^{11}	Non sterile	<7
XMO3017C20	25.3	1.13×10^{11}	Non sterile	<7
XCD3017322	25.7	6.90×10^{11}	Sterile	7.08
XM10348119	26.2	8.17×10^{11}	Non sterile	<7

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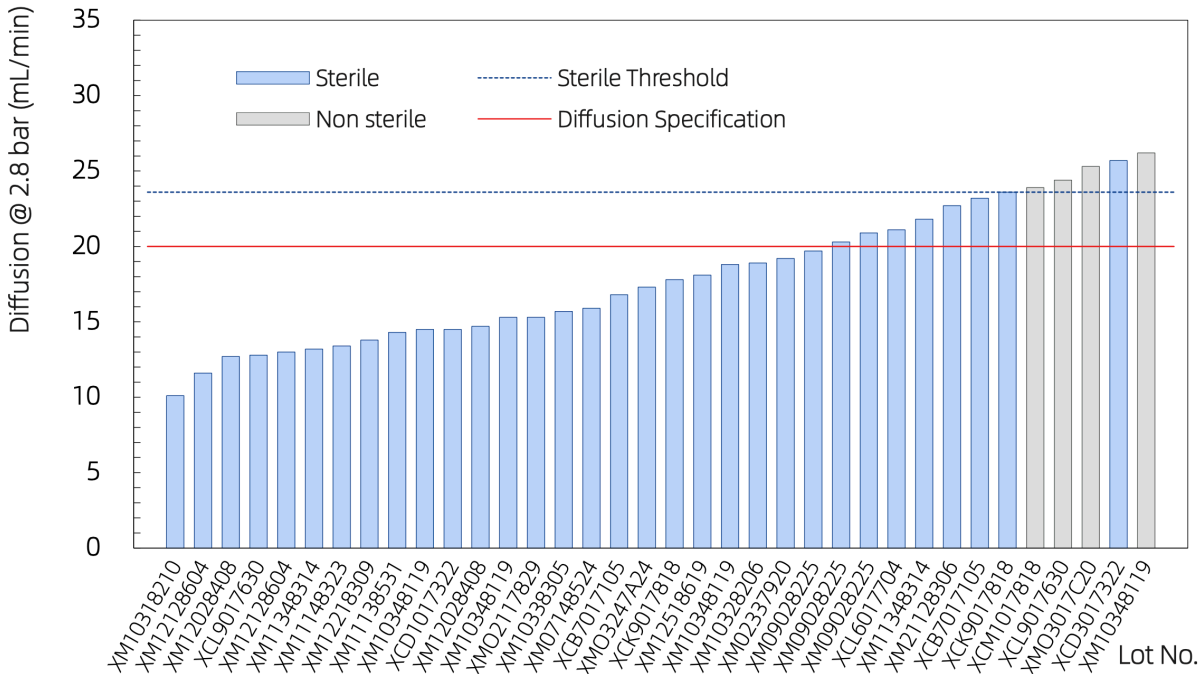
Conclusion

Correlation of the ASTM Bacteria Challenge Tests with Non-Destructive Integrity Test



According to the results of the bacterial challenge test, Ultrafilter PF-PVDF 0.2 µm cartridge filters can completely retain a minimum concentration of 107 cfu/cm2 Brevundimonas diminuta (ATCC® 19146) with a sterile filtrate when the diffusion of tested filter is less than 23.6 mL/min at a test pressure of 2.8 bar. Taking into account the safety factor, the integrity specification for Ultrafilter PF-PVDF 0.2 µm cartridge filter is set to:

Air Diffusion ⩽ 20 mL/min at 2.8 bar (40 psi) in water at 20 °C.
Bubble point ⩾ 3.2 bar (46 psi) in water at 20 °C.

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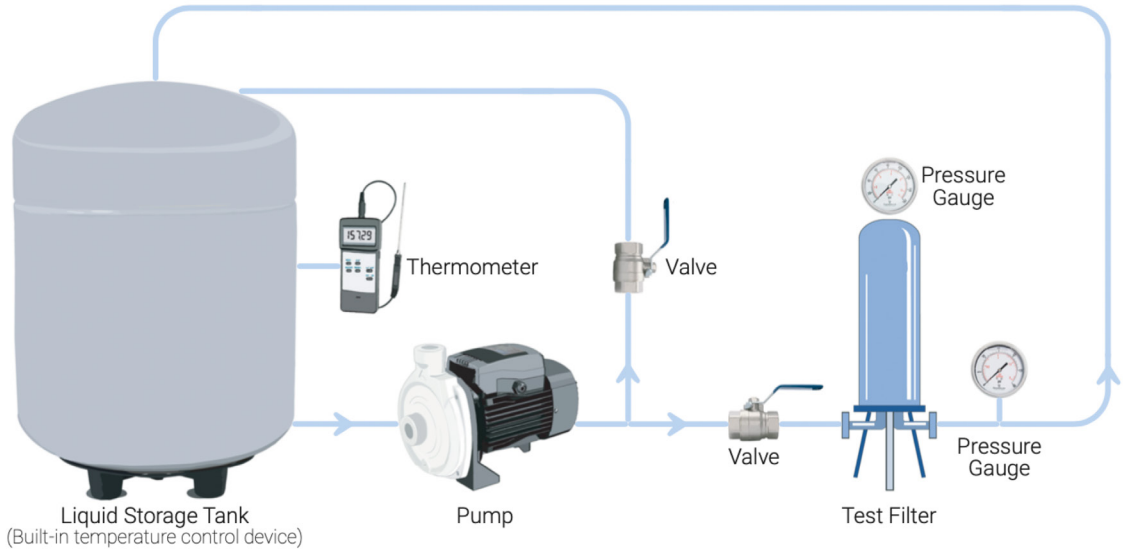
2. Hydraulic Stress

The maximum operating pressure and maximum differential pressure of the filter element at a specific temperature depend on its pressure resistance. The hydraulic stress test is to confirm the pressure resistance of the filter at a specific temperature under the worst-case simulated conditions.

The mechanical and structural features of the filter determine the high risk of reverse-use of the filter causing structural damage. It is not recommended to use the filter in reverse direction in the actual production process. The reverse test conditions in this validation test are only the worst-case simulation of the instantaneous reverse pressure difference that may occur in the actual production process, and cannot be used as the basis for the reverse use of the filter.

Hydraulic Stress Test Schematic



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Hydraulic Stress Test at 25 °C

Summary of Method

Ultrafilter PF-PVDF series cartridge filters were wetted with water and steamed at 135 °C for 30 minutes. Ultrafilter PF-PVDF capsule filters with PVDF 0.2 µm membrane were wetted with water and autoclaved at 130 °C for 30 minutes prior to testing. The filters were wetted with water and integrity tested.

Ultrafilter PF-PVDF series cartridge filters were plugged with test dust to increase the differential pressure across the upstream and downstream of the filter. A hydraulic stress of 6.9 bar was applied to the filters at 25 °C for 30 minutes in the forward direction with 10 cycles. Then a differential pressure of 3.0 bar was applied to the filters at 25 °C for 10 minutes in the reverse direction with 3 cycles.

Ultrafilter PF-PVDF capsule filters with PVDF 0.2 µm membrane were plugged with test dust to increase the differential pressure across the upstream and downstream of the filter. A hydraulic stress of 5.5 bar was applied to the filters at 25 °C for 30 minutes in the forward direction with 6 cycles. Then a differential pressure of 2.1 bar was applied to the filters at 25 °C for 10 minutes in the reverse direction with 3 cycles.
The filter integrity test was carried out to find any changes in the process of the hydraulic stress tests.

Ultrafilter PF-PVDF 0.1 µm Cartridge Filter

LOT NUMBER	PRIOR TO HYDRAULIC STRESS		POST HYDRAULIC STRESS	
	BUBBLE POINT (BAR)	DIFFUSION @ 3.86 BAR(ML/MIN)	BUBBLE POINT (BAR)	DIFFUSION @ 3.86 BAR (ML/MIN)
XM0E048B02	2.040	14.9	2.024	15.1
XAU38412	2.087	15.1	2.021	14.9
XM0E138A10	2.157	17.3	2.173	16.7

Ultrafilter PF-PVDF 0.2 µm Series Filter

LOT NUMBER	PRIOR TO HYDRAULIC STRESS		POST HYDRAULIC STRESS	
	BUBBLE POINT (BAR)	DIFFUSION @ 3.86 BAR(ML/MIN)	BUBBLE POINT (BAR)	DIFFUSION @ 3.86 BAR (ML/MIN)
Ultrafilter PF-PVDF 0.2 µm cartridge filter				
XM0E048B02	2.040	14.9	2.024	15.1
XAU38412	2.087	15.1	2.021	14.9
XM0E138A10	2.157	17.3	2.173	16.7
Ultrafilter PF-PVDF capsule filter with PVDF 0.2 µm membrane				
XM12228316	3.884	6.9	3.754	7.3
XM12248327	4.277	5.1	4.540	5.2
XM03027B10	3.906	6.4	3.928	6.6

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Ultrafilter PF-PVDF 0.45 µm, 0.65 µm and 1.0 µm Cartridge

LOT NUMBER	BUBBLE POINT (BAR)	
	PRIOR TO HYDRAULIC STRESS	POST HYDRAULIC STRESS
Ultrafilter PF-PVDF 0.45 µm cartridge filter		
XM06038504	2.024	2.049
XM0L018413	1.903	1.887
XM0L028511	1.911	1.962
Ultrafilter PF-PVDF 0.65 µm cartridge filter		
XM0M139322	1.513	1.537
XC0P139322	1.552	1.533
XM0M119322	1.533	1.575
Ultrafilter PF-PVDF 1.0 µm cartridge filter		
XC12017502	1.019	1.009
XAIM2017C27	0.900	0.885
XAIM3047C27	0.946	0.974

Conclusion

Ultrafilter PF-PVD series cartridge filters maintain integrity after a series of hydraulic stress tests at 25 °C described above.

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Hydraulic Stress Test at 60 °C

Summary of Method

Ultrafilter PF-PVDF series cartridge filters were wetted with water and steamed at 135 °C for 30 minutes prior to testing. The filters were wetted with water and integrity tested.

The filters were plugged with test dust to increase the differential pressure across the upstream and downstream of the filter. A hydraulic stress of 4.0 bar was applied to the filters at 60 °C for 30 minutes in the forward direction with 6 cycles.

The filter integrity test was carried out to find any changes during the hydraulic stress tests

Ultrafilter PF-PVDF 0.1 µm Cartridge Filter

LOT NUMBER	PRIOR TO HYDRAULIC STRESS		POST HYDRAULIC STRESS	
	BUBBLE POINT (BAR)	DIFFUSION @ 3.86 BAR(ML/MIN)	BUBBLE POINT (BAR)	DIFFUSION @ 3.86 BAR (ML/MIN)
XM0E048B02	2.022	14.4	2.045	14.1
XAU38412	2.226	15.9	2.179	15.6
XM0E138A10	2.361	17.4	2.280	17.0

Ultrafilter PF-PVDF 0.2 µm Cartridge Filter

LOT NUMBER	PRIOR TO HYDRAULIC STRESS		POST HYDRAULIC STRESS	
	BUBBLE POINT (BAR)	DIFFUSION @ 3.86 BAR(ML/MIN)	BUBBLE POINT (BAR)	DIFFUSION @ 3.86 BAR (ML/MIN)
XM11138524	4.085	10.6	3.997	10.4
XM11138531	3.770	13.9	3.621	14.3
XM12128604	3.660	14.4	3.765	14.9

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Ultrafilter PF-PVDF 0.45 µm, 0.65 µm and 1.0 µm Cartridge

LOT NUMBER	BUBBLE POINT (BAR)	
	PRIOR TO HYDRAULIC STRESS	POST HYDRAULIC STRESS
Ultrafilter PF-PVDF 0.45 µm cartridge filter		
XM06038504	2.128	2.070
XM0L018413	2.024	2.051
XM0L028511	1.955	1.909
Ultrafilter PF-PVDF 0.65 µm cartridge filter		
XM0M139322	1.519	1.516
XC0P139322	1.503	1.543
XM0M119322	1.530	1.472
Ultrafilter PF-PVDF 1.0 µm cartridge filter		
XC12017502	1.091	1.083
XAIM2017C27	0.933	0.923
XAIM3047C27	0.860	0.836

Conclusion

Ultrafilter PF-PVD series cartridge filters maintain integrity after a series of hydraulic stress tests at 60 °C described above.

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Hydraulic Stress Test at 80 °C

Summary of Method

Ultrafilter PF-PVDF series cartridge filters were wetted with water and steamed at 135 °C for 30 minutes. Ultrafilter PF-PVDF capsule filters with PVDF 0.2 µm membrane were wetted with water and autoclaved at 130 °C for 30 minutes prior to testing. The filters were wetted with water and integrity tested.

Ultrafilter PF-PVDF series cartridge filters were plugged with test dust to increase the differential pressure across the upstream and downstream of the filter. A hydraulic stress of 2.4 bar was applied to the filters at 80 °C for 30 minutes in the forward direction with 4 cycles. Then a differential pressure of 1.0 bar was applied to the filters at 80 °C for 10 minutes in the reverse direction with 3 cycles.

Ultrafilter PF-PVDF capsule filters with PVDF 0.2 µm membrane were plugged with test dust to increase the differential pressure across the upstream and downstream of the filter. A hydraulic stress of 1.0 bar was applied to the filters at 80 °C for 10 minutes in the forward direction with 6 cycles.

The filter integrity test was carried out to find any changes in the process of the hydraulic stress tests.

Ultrafilter PF-PVDF 0.1 µm Cartridge Filter

LOT NUMBER	PRIOR TO HYDRAULIC STRESS		POST HYDRAULIC STRESS	
	BUBBLE POINT (BAR)	DIFFUSION @ 3.86 BAR(ML/MIN)	BUBBLE POINT (BAR)	DIFFUSION @ 3.86 BAR (ML/MIN)
XM0E048B02	2.186	15.2	2.141	15.7
XAU38412	2.270	15.5	2.302	15.1
XM0E138A10	2.191	16.7	2.257	16.0

Ultrafilter PF-PVDF 0.2 µm Cartridge Filter

LOT NUMBER	PRIOR TO HYDRAULIC STRESS		POST HYDRAULIC STRESS	
	BUBBLE POINT (BAR)	DIFFUSION @ 3.86 BAR(ML/MIN)	BUBBLE POINT (BAR)	DIFFUSION @ 3.86 BAR (ML/MIN)
Ultrafilter PF-PVDF 0.2 µm cartridge filter				
XM0E048B02	3.966	11.4	4.082	11.6
XAU38412	4.148	10.7	4.097	10.5
XM0E138A10	3.807	13.4	3.700	11.8
Ultrafilter PF-PVDF capsule filter with PVDF 0.2 µm membrane				
XM12228316	3.847	7.1	3.915	7.2
XM12248327	3.801	7.6	3.711	7.5
XM03027B10	4.030	6.8	4.140	7.0

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Ultrafilter PF-PVDF 0.45 µm, 0.65 µm and 1.0 µm Cartridge

LOT NUMBER	BUBBLE POINT (BAR)	
	PRIOR TO HYDRAULIC STRESS	POST HYDRAULIC STRESS
Ultrafilter PF-PVDF 0.45 µm cartridge filter		
XM06038504	2.188	2.239
XM0L018413	2.106	2.024
XM0L028511	1.922	1.875
Ultrafilter PF-PVDF 0.65 µm cartridge filter		
XM0M139322	1.516	1.494
XC0P139322	1.593	1.570
XM0M119322	1.501	1.447
Ultrafilter PF-PVDF 1.0 µm cartridge filter		
XC12017502	0.873	0.851
XAIM2017C27	0.877	0.863
XAIM3047C27	1.004	1.006

Conclusion

Ultrafilter PF-PVD series cartridge filters maintain integrity after a series of hydraulic stress tests at 80 °C described above.

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Hydraulic Stress Test at 135 °C

Summary of Method

Ultrafilter PF-PVDF series cartridge filters were plugged with test dust to increase the differential pressure across the upstream and downstream of the filter, and integrity tested. Then the filters were wetted with water and steamed at 135 °C for 30 minutes with a differential pressure of 0.35 bar.

The filter integrity test was carried out to find any changes during the hydraulic stress tests.

Ultrafilter PF-PVDF 0.1 µm Cartridge Filter

LOT NUMBER	PRIOR TO HYDRAULIC STRESS		POST HYDRAULIC STRESS	
	BUBBLE POINT (BAR)	DIFFUSION @ 3.86 BAR(ML/MIN)	BUBBLE POINT (BAR)	DIFFUSION @ 3.86 BAR (ML/MIN)
XM0E048B02	2.038	15.7	2.082	15.9
XAU38412	2.221	15.8	2.236	15.3
XM0E138A10	2.101	17.6	2.060	17.5

Ultrafilter PF-PVDF 0.2 µm Cartridge Filter

LOT NUMBER	PRIOR TO HYDRAULIC STRESS		POST HYDRAULIC STRESS	
	BUBBLE POINT (BAR)	DIFFUSION @ 3.86 BAR(ML/MIN)	BUBBLE POINT (BAR)	DIFFUSION @ 3.86 BAR (ML/MIN)
XM0E048B02	3.918	10.9	3.952	10.7
XAU38412	3.732	14.2	3.766	14.1
XM0E138A10	3.658	13.7	3.621	13.9

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Ultrafilter PF-PVDF 0.45 µm, 0.65 µm and 1.0 µm Cartridge

LOT NUMBER	BUBBLE POINT (BAR)	
	PRIOR TO HYDRAULIC STRESS	POST HYDRAULIC STRESS
Ultrafilter PF-PVDF 0.45 µm cartridge filter		
XM06038504	1.940	1.944
XM0L018413	2.029	1.987
XM0L028511	2.021	1.997
Ultrafilter PF-PVDF 0.65 µm cartridge filter		
XM0M139322	1.574	1.558
XC0P139322	1.542	1.533
XM0M119322	1.586	1.548
Ultrafilter PF-PVDF 1.0 µm cartridge filter		
XC12017502	1.097	1.070
XAIM2017C27	1.043	1.043
XAIM3047C27	0.800	0.776

Conclusion

Ultrafilter PF-PVD series cartridge filters maintain integrity after a series of hydraulic stress tests at 135 °C described above.

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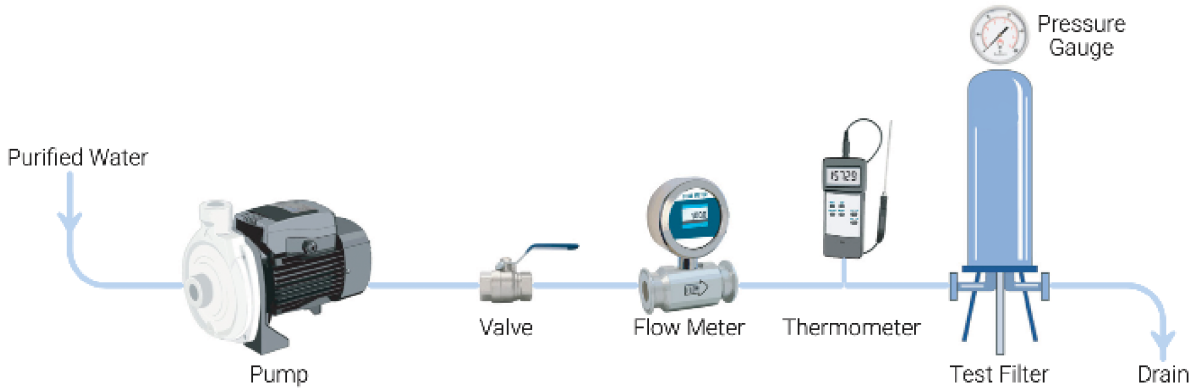
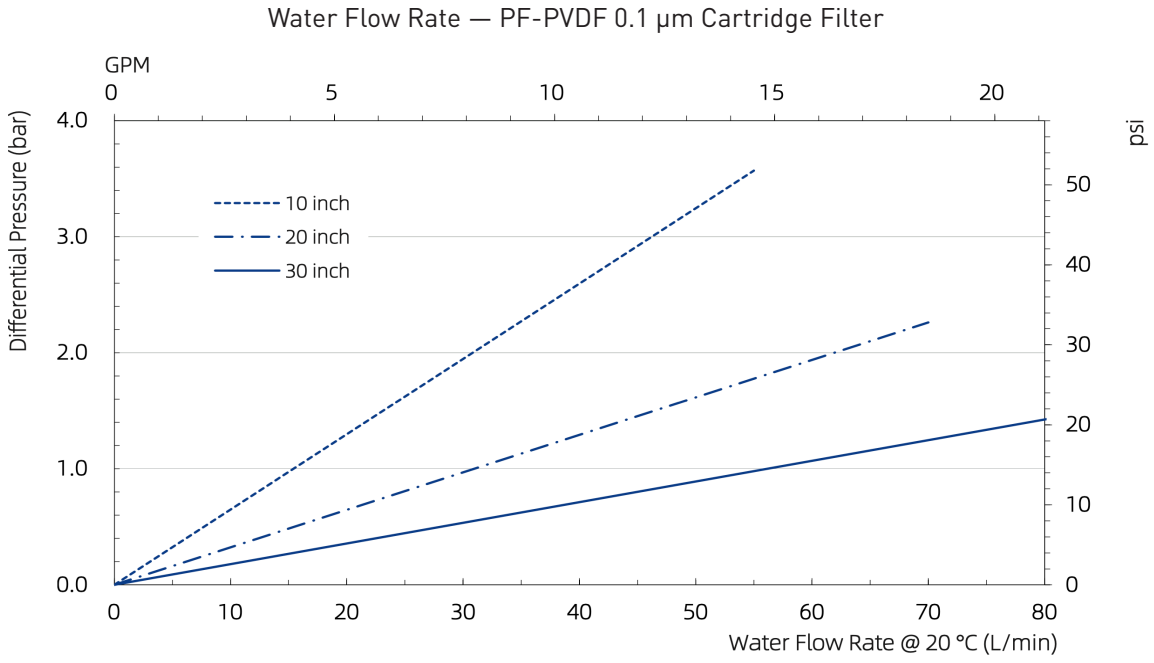
3. Water Flow Rate

Ultrafilter PF-PVDF series cartridge filters were wetted with water and steamed at 135 °C for 30 minutes. Ultrafilter PF-PVDF capsule filters with PVDF 0.2 µm membrane were wetted with water and autoclaved at 130 °C for 30 minutes prior to testing. The filters were wetted with water and integrity tested. The required differential pressure for the test is acquired by adjusting the inlet valve of the filter. After achieving a constant differential pressure, the flow rate and water temperature were recorded. Results of the filters were corrected to a water temperature of 20 °C. The graph was plotted after the pressure drop were measured from the filters at various water flow rates.

Water Flow Rate Test Schematic



Results



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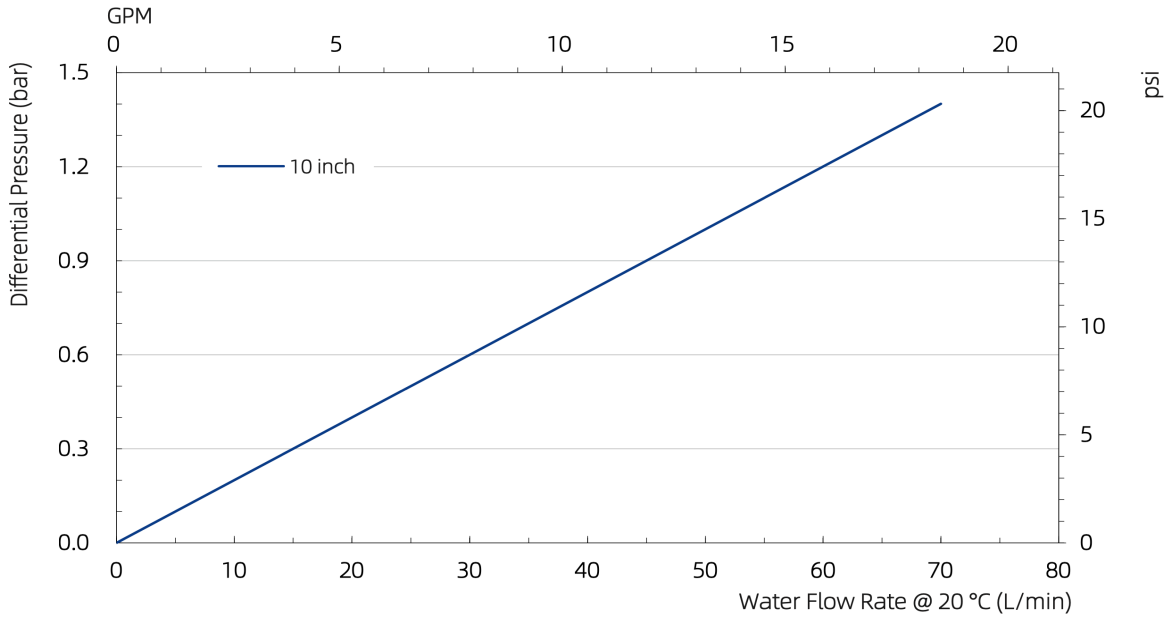
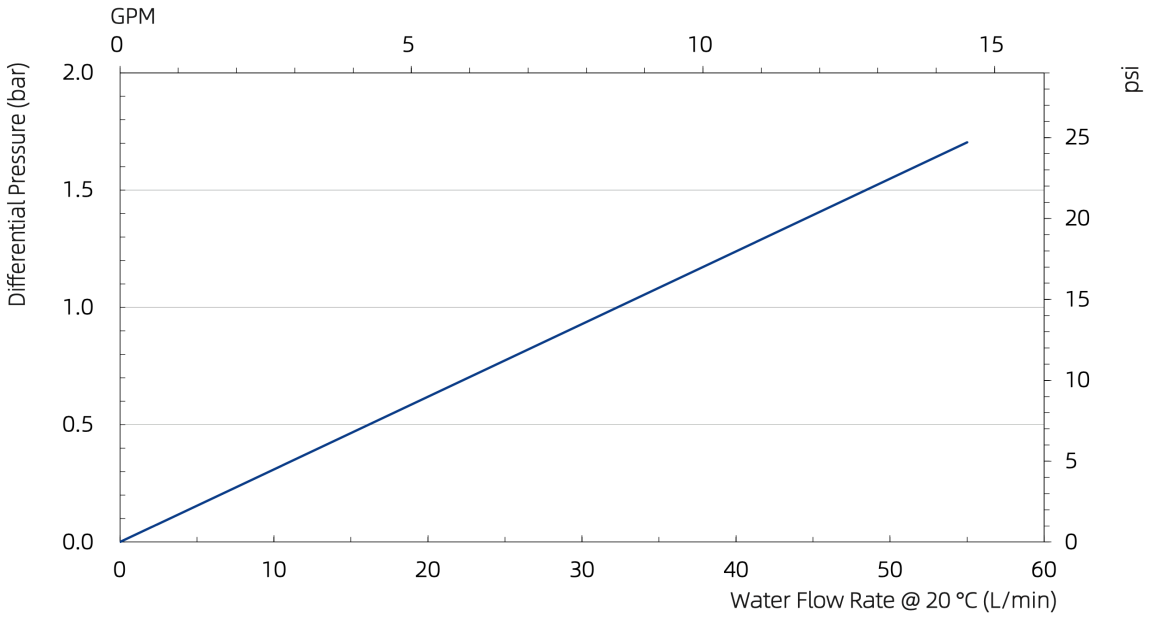
Water Flow Rate — PF-PVDF 0.2 µm Cartridge Filter



Water Flow Rate — PF-PVDF Capsule Filter with PVDF 0.2 µm Membrane



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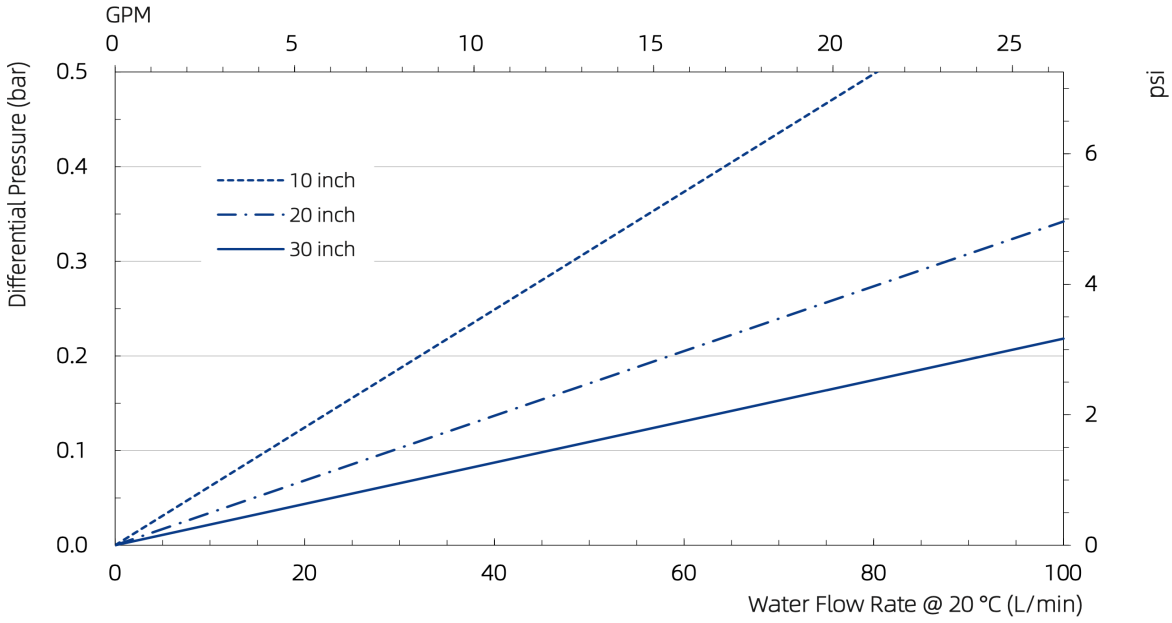
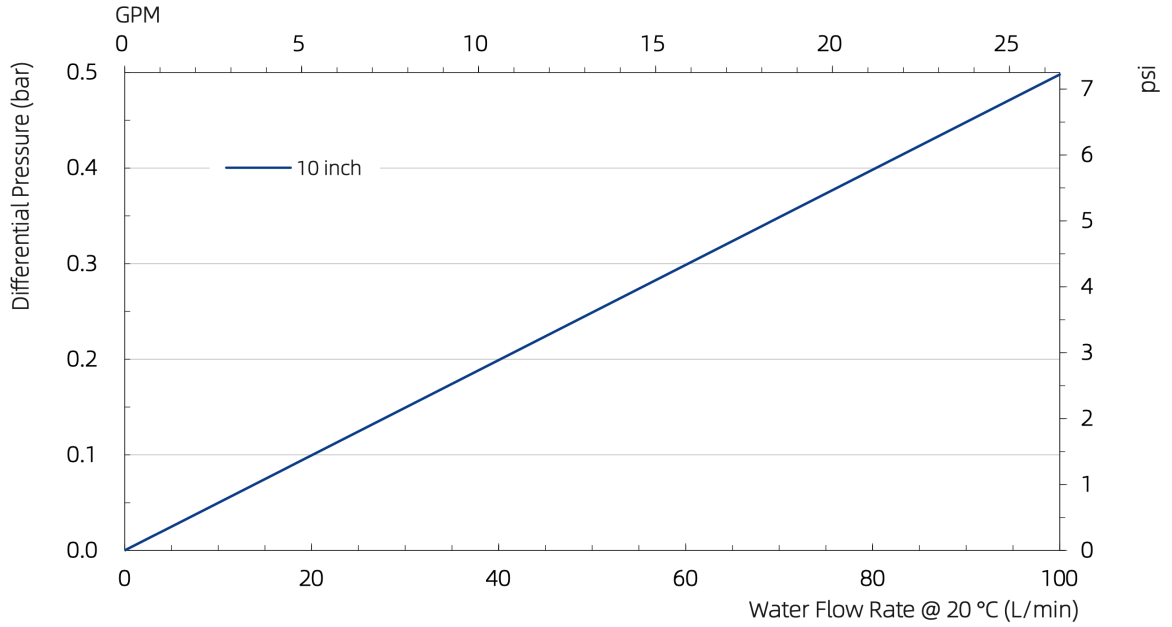
PF-PVDF

Water Flow Rate — PF-PVDF 0.45 µm Cartridge Filter



Water Flow Rate — PF-PVDF Capsule Filter with PVDF 0.65 µm Membrane



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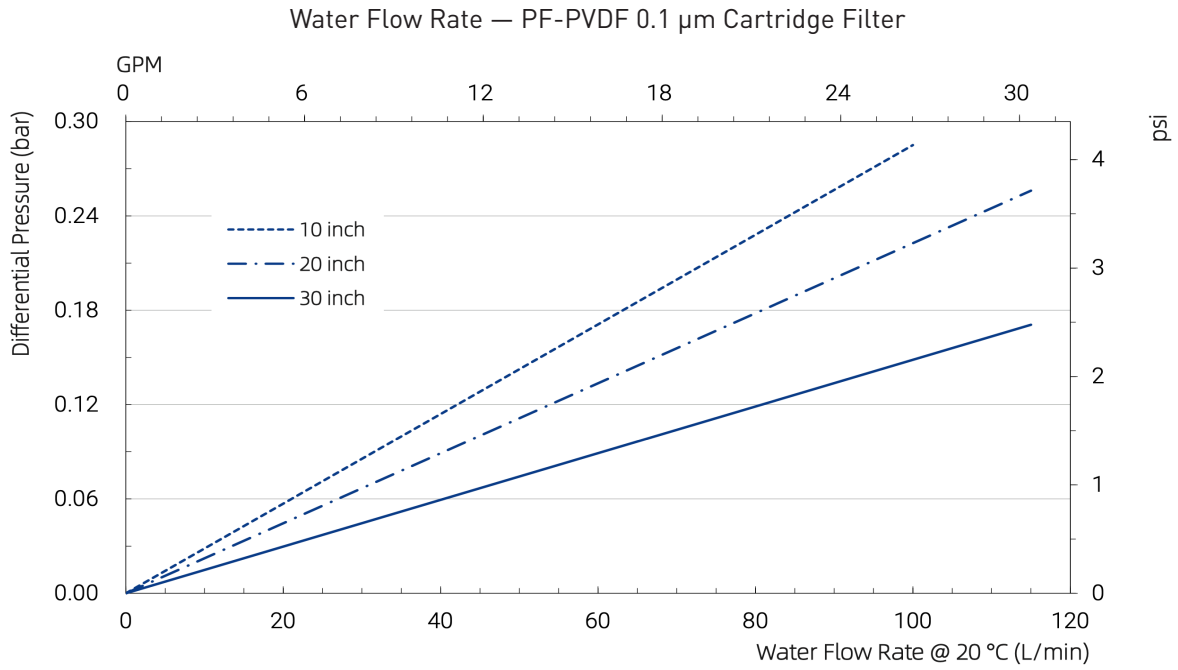

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4. Thermal Resistance

Ultrafilter PF-PVDF series cartridge filters can be either steamed in place (SIP) or autoclaved. Ultrafilter PF-PVDF capsule filters with PVDF 0.2 µm membrane can be autoclaved. Since multiple sterilization cycles may be required in actual use, the influences of the sterilization on the performances of Ultrafilter PF-PVDF series filters were examined. As a result, recommendations and limits for multiple sterilization are given below.

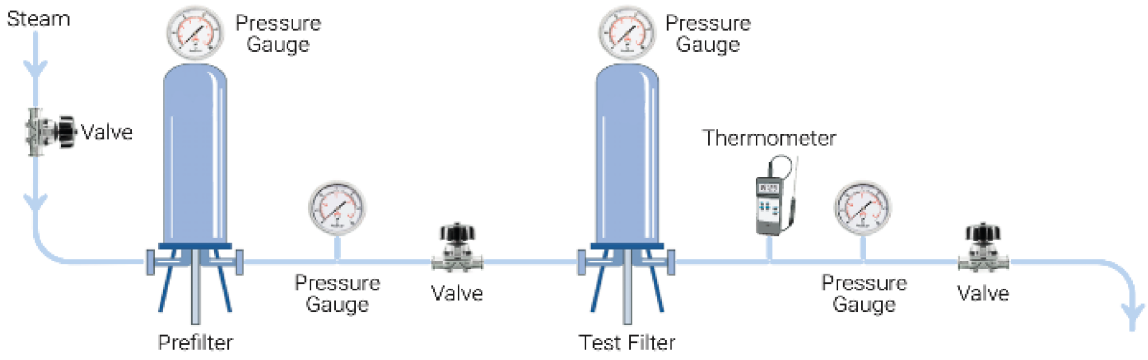
Ultrafilter PF-PVDF series filters were wetted with water and subjected to integrity test prior to testing.

Ultrafilter PF-PVDF cartridge filters were wetted with water and installed in the steam sterilization device in the forward direction. The steam valve and downstream valve were slowly adjusted to increase the temperature to 135 °C as the same time ensuring the differential pressure across the upstream and downstream of the filter less than 0.3 bar. The cartridge filters were steam sterilized at a constant temperature of 135 °C for 30 minutes. After a 30-minute steam sterilization, closed the steam valve and slowly adjusted the downstream valve to release steam pressure. The steam sterilization device was cooled by dry compressed air or natural cooling. Continually monitored the differential pressure across the upstream and downstream of the filter within 0.3 bar during the whole process of temperature rise, sterilization and cooling. The sequence was repeated until the 100 SIP cycles had been achieved for each filter. Ultrafilter PF-PVDF cartridge filters were wetted with water and installed in the steam sterilization device in the reverse direction. The cartridge filters were steam sterilized at 135 °C for 30 minutes with 50 cycles in the reverse direction under the differential pressure less than 0.1 bar.
Ultrafilter PF-PVDF cartridge filters were water wetted and wraped with tinfoil or cleansteam bag. Ultrafilter PF-PVDF series filters were autoclaved at 130 °C for 30 minutes. The cartridge filters were autoclaved 400 cycles at 130 °C for 30 minutes.

Ultrafilter PF-PVDF capsule filters with PVDF 0.2 µm membrane were water wetted and wraped the inlet and outlet of the capsules with tinfoil or cleansteam bag, loosening the vent valve. The capsule filters were autoclaved 50 cycle at 130 °C for 30 minutes.

The filters were validated by integrity test to analyze and evaluate the influences of multiple sterilization.

Schematic of Steam-in-Place



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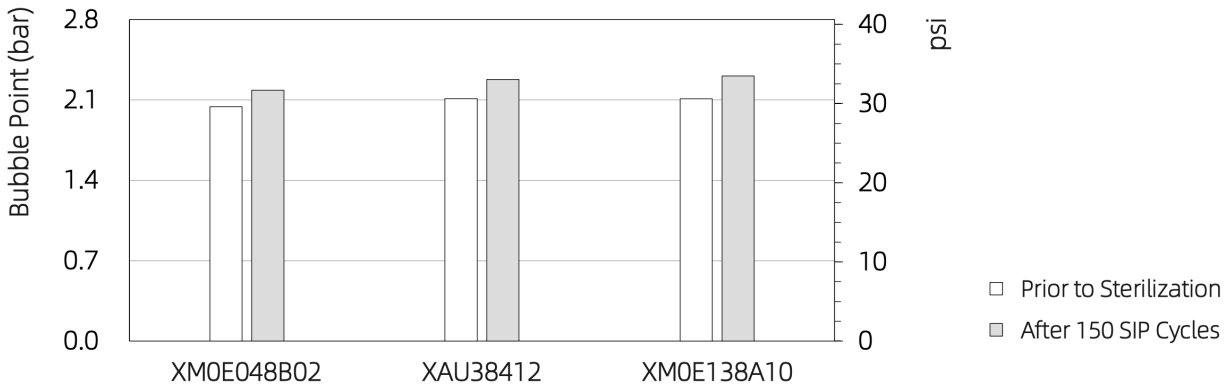
PF-PVDF 0.1 µm Cartridge Filter

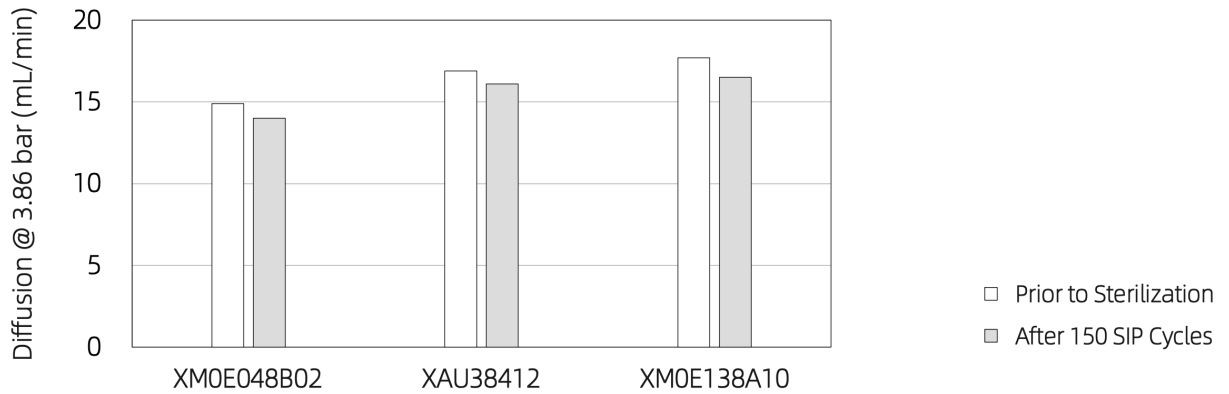
Steam in Place

LOT NUMBER	PRIOR TO STERILIZATION		AFTER 150 SIP CYCLES	
	BUBBLE POINT (BAR)	DIFFUSION @ 3.86 BAR(ML/MIN)	BUBBLE POINT (BAR)	DIFFUSION @ 3.86 BAR (ML/MIN)
XM0E048B02	2.041	14.9	2.185	14.0
XAU38412	2.111	16.9	2.278	16.1
XM0E138A10	2.109	17.7	2.309	16.5

Effect on Bubble Point
PF-PVDF 0.1 µm Cartridge Filter



Effect on Diffusion
PF-PVDF 0.1 µm Cartridge Filter



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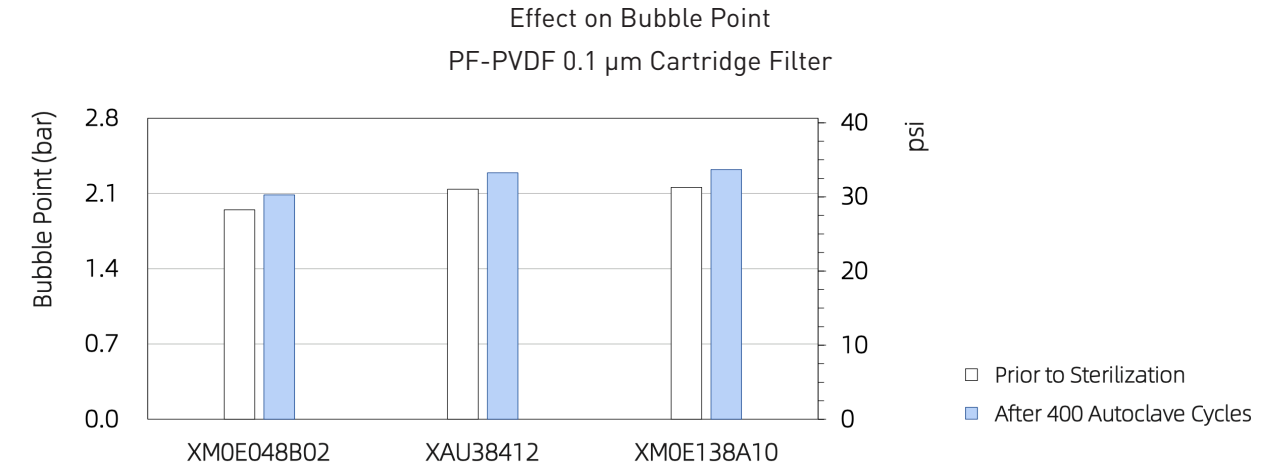
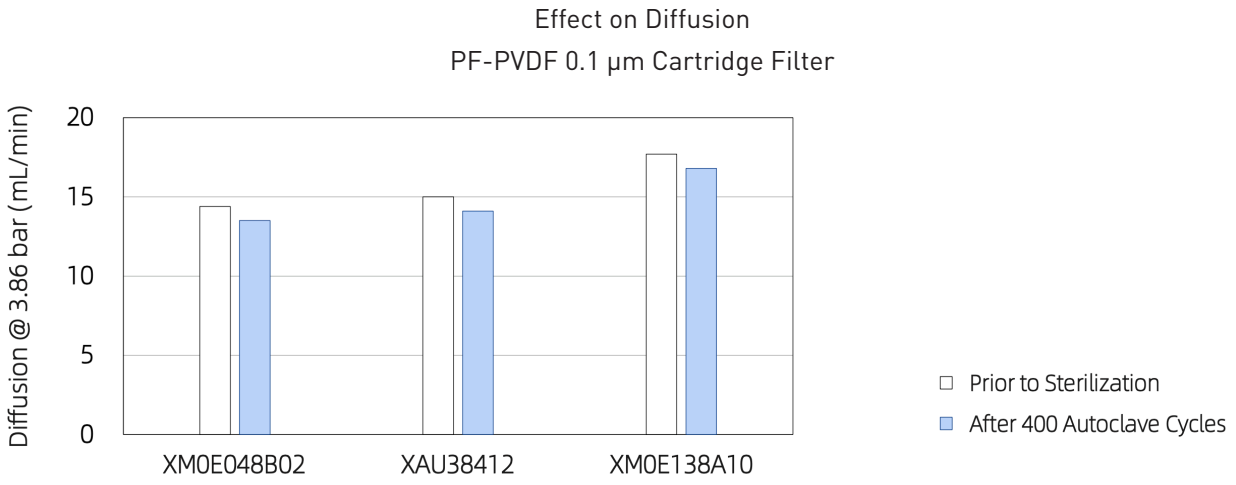
PF-PVDF

Autoclave

LOT NUMBER	PRIOR TO STERILIZATION		AFTER 400 AUTOCLAVE CYCLES	
	BUBBLE POINT (BAR)	DIFFUSION @ 3.86 BAR(ML/MIN)	BUBBLE POINT (BAR)	DIFFUSION @ 3.86 BAR (ML/MIN)
XM0E048B02	1.948	14.4	2.087	13.5
XAU38412	2.140	15.0	2.293	14.1
XM0E138A10	2.157	17.7	2.323	16.8





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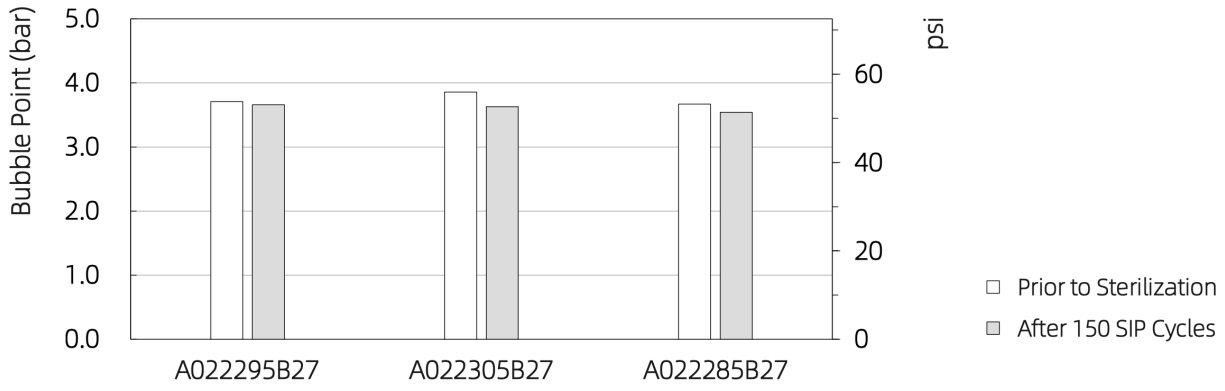
PF-PVDF 0.2 µm Cartridge Filter

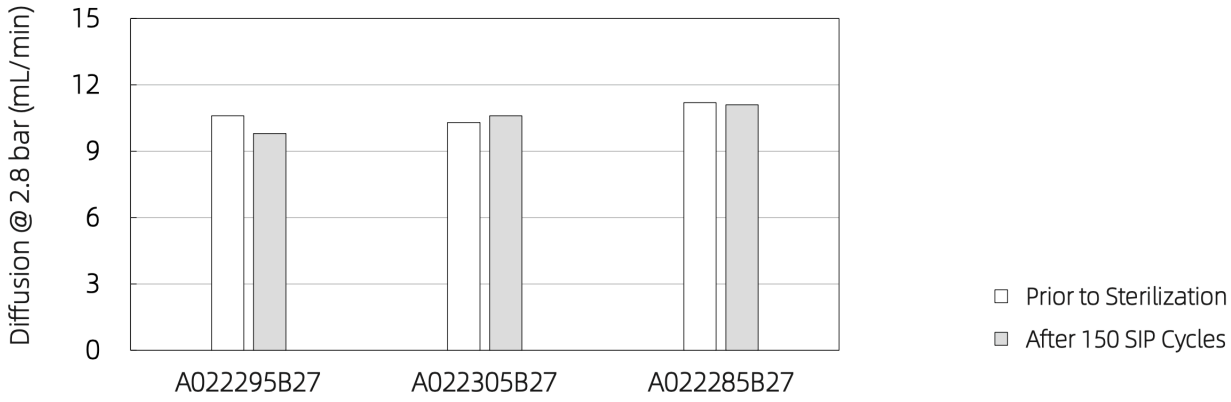
Steam in Place

LOT NUMBER	PRIOR TO STERILIZATION		AFTER 150 SIP CYCLES	
	BUBBLE POINT (BAR)	DIFFUSION @ 2,8 BAR(ML/MIN)	BUBBLE POINT (BAR)	DIFFUSION @ 2.8 BAR (ML/MIN)
A022295B27	3.707	10.6	3.658	9.8
A022305B27	3.856	10.3	3.630	10.6
A022285B27	3.669	11.2	3.541	11.1

Effect on Bubble Point
PF-PVDF 0.2 µm Cartridge Filter



Effect on Diffusion
PF-PVDF 0.2 µm Cartridge Filter



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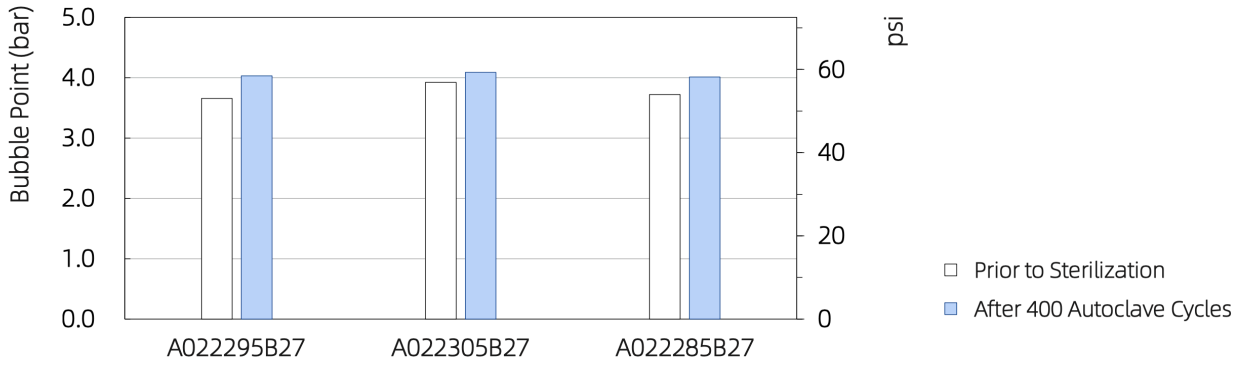
PF-PVDF

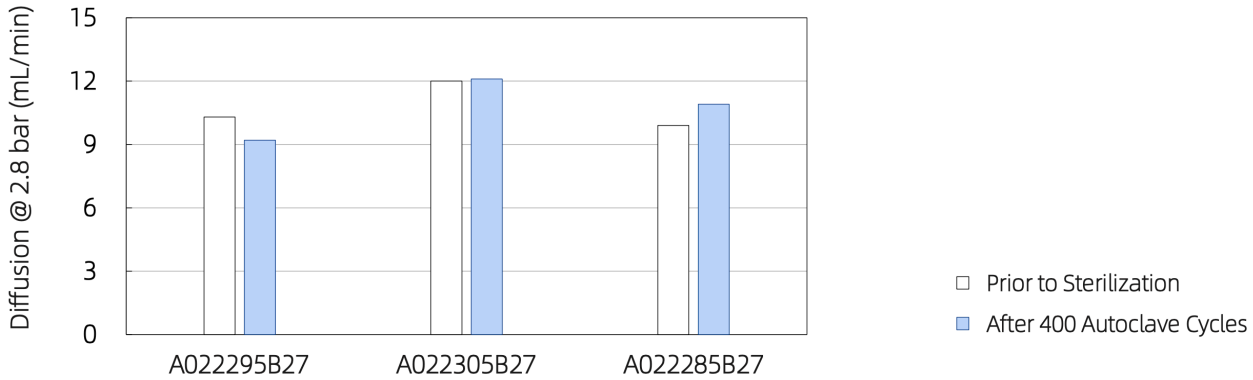
Autoclave

LOT NUMBER	PRIOR TO STERILIZATION		AFTER 400 AUTOCLAVE CYCLES	
	BUBBLE POINT (BAR)	DIFFUSION @ 2.8 BAR(ML/MIN)	BUBBLE POINT (BAR)	DIFFUSION @ 2.8 BAR (ML/MIN)
A022295B27	3.655	10.3	4.032	9.2
A022305B27	3.921	12.0	4.089	12.1
A022285B27	3.722	9.9	4.013	10.9

Effect on Bubble Point
PF-PVDF 0.2 µm Cartridge Filter



Effect on Diffusion
PF-PVDF 0.2 µm Cartridge Filter



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VALIDATION GUIDE

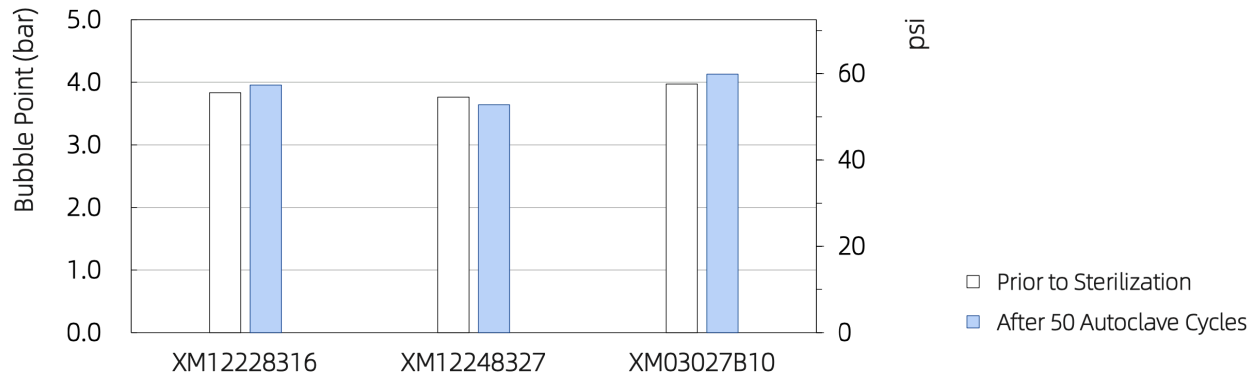
Ultrafilter PF-PVDF capsule filters with PVDF 0.2 µm membrane

Steam in Place

LOT NUMBER	PRIOR TO STERILIZATION		AFTER 150 SIP CYCLES	
	BUBBLE POINT (BAR)	DIFFUSION @ 2,8 BAR(ML/MIN)	BUBBLE POINT (BAR)	DIFFUSION @ 2.8 BAR (ML/MIN)
XM12228316	3.832	6.2	3.954	5.7
XM12248327	3.763	7.4	3.641	7.7
XM03027B10	3.972	5.8	4.128	5.5

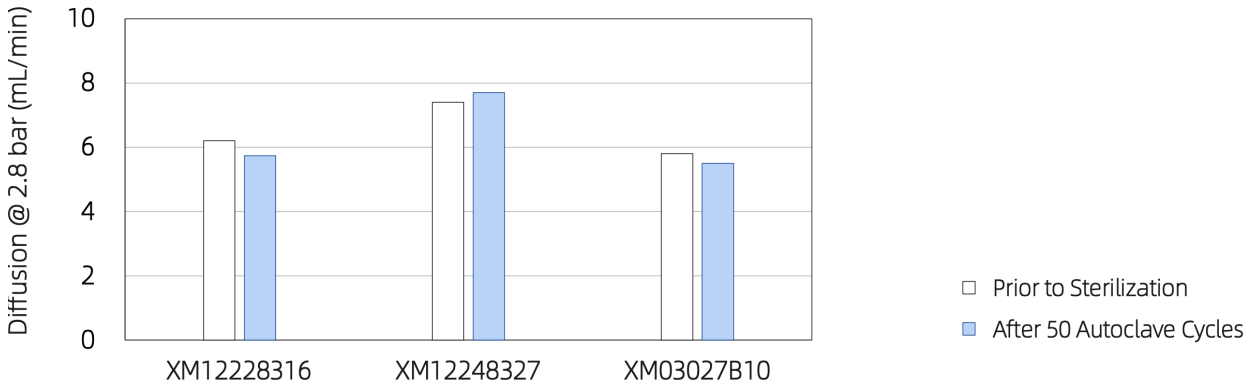
Effect on Bubble Point

Ultrafilter PF-PVDF capsule filters with PVDF 0.2 µm membrane



Effect on Diffusion

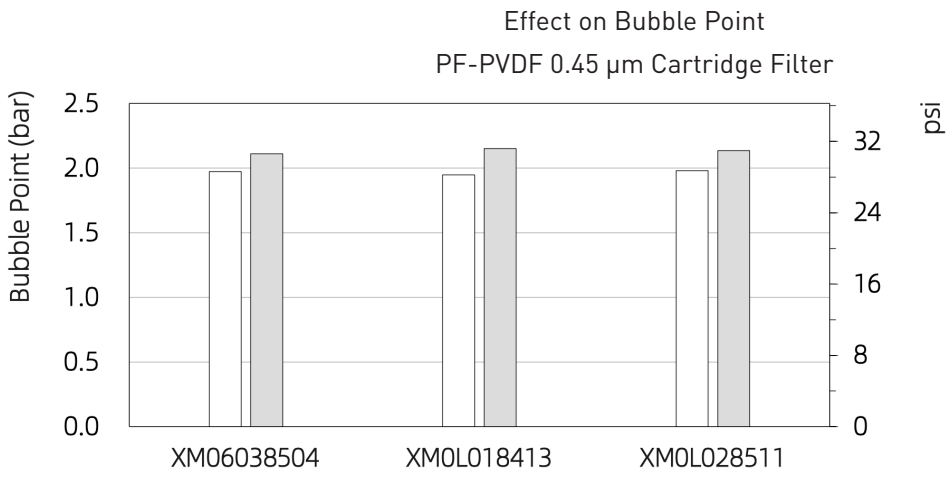
Ultrafilter PF-PVDF capsule filters with PVDF 0.2 µm membrane

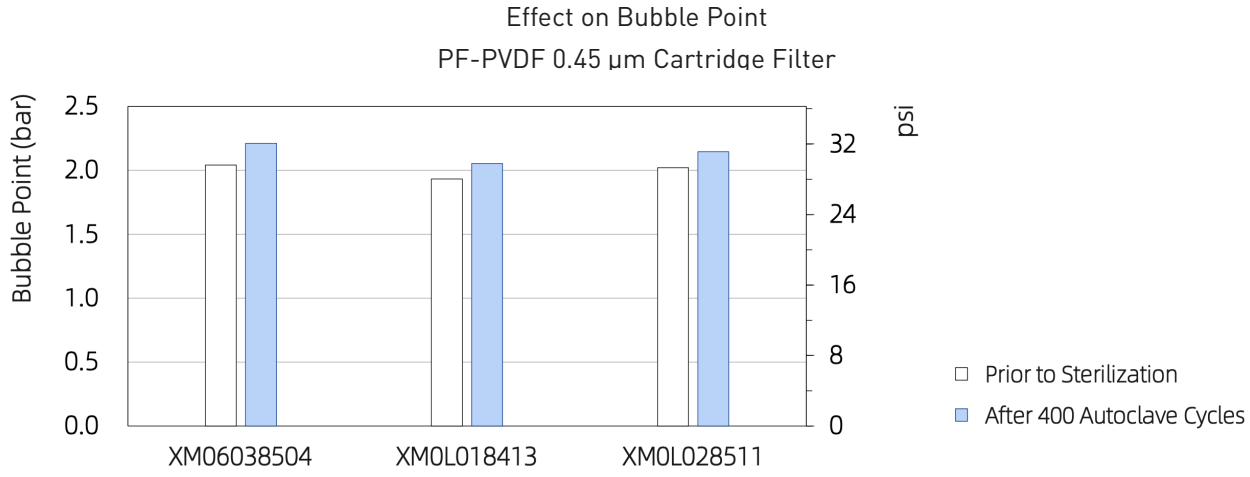


PF-PVDF

PF-PVDF 0.45 µm Cartridge Filter

LOT NUMBER	BUBBLE POINT (BAR)	
	PRIOR TO STERILIZATION	AFTER MULTIPLE STEAM CYCLES
After 150 SIP cycles		
XM06038504	1.974	2.110
XM0L018413	1.947	2.151
XM0L028511	1.980	2.135
After 400 autoclave cycles		
XM06038504	2.041	2.211
XM0L018413	1.932	2.053
XM0L028511	2.021	2.146





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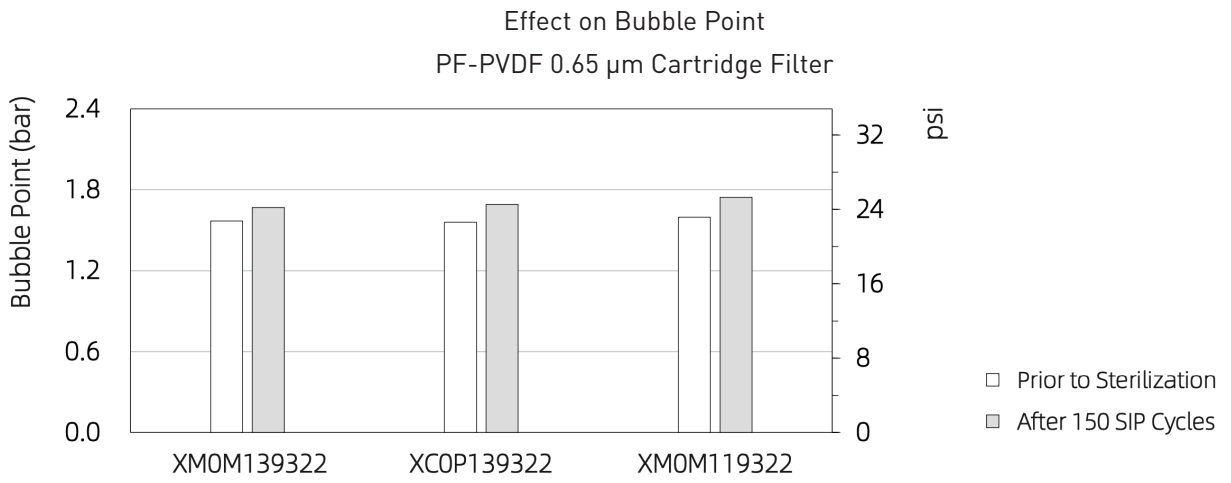
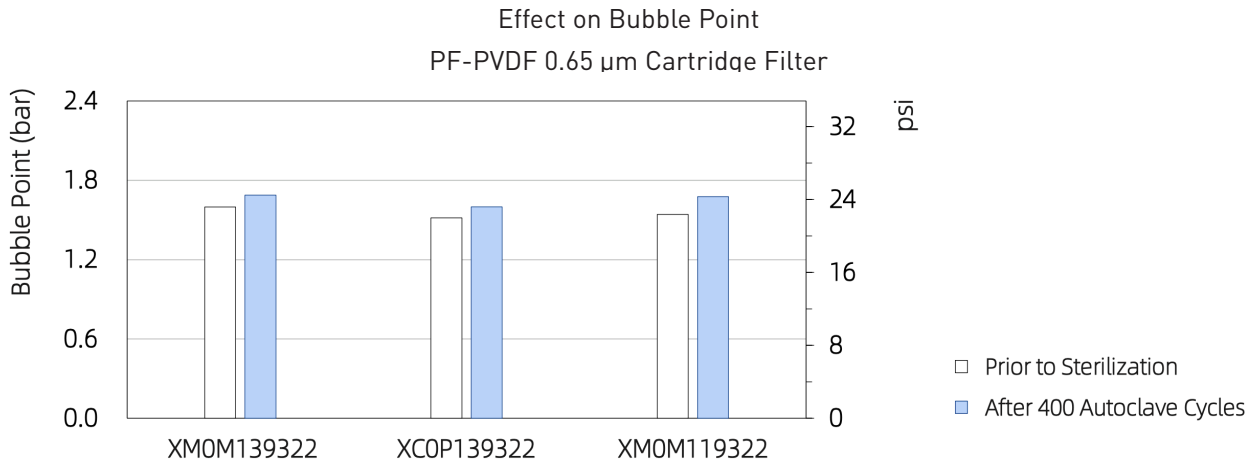
PF-PVDF 0.65 µm Cartridge Filter

LOT NUMBER	BUBBLE POINT (BAR)	
	PRIOR TO STERILIZATION	AFTER MULTIPLE STEAM CYCLES
After 150 SIP cycles		
XM0M139322	1.568	1.669
XC0P139322	1.559	1.692
XM0M119322	1.597	1.744
After 400 autoclave cycles		
XM0M139322	1.599	1.688
XC0P139322	1.516	1.600
XM0M119322	1.543	1.677





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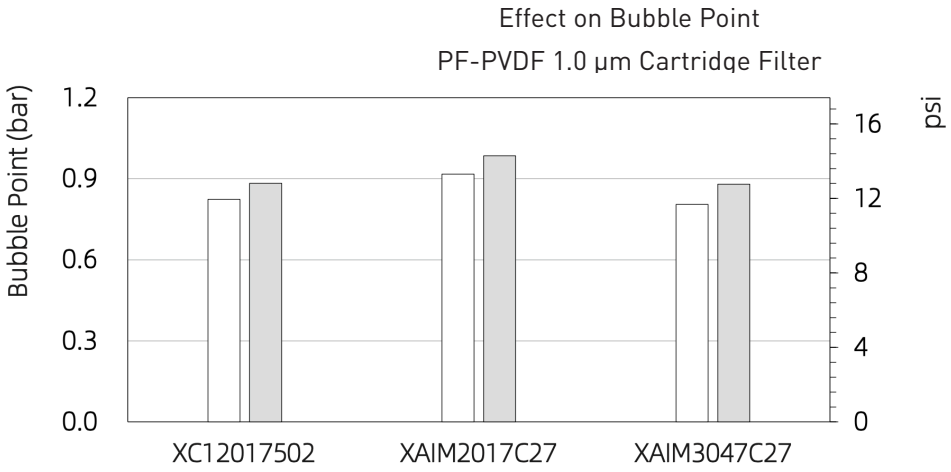
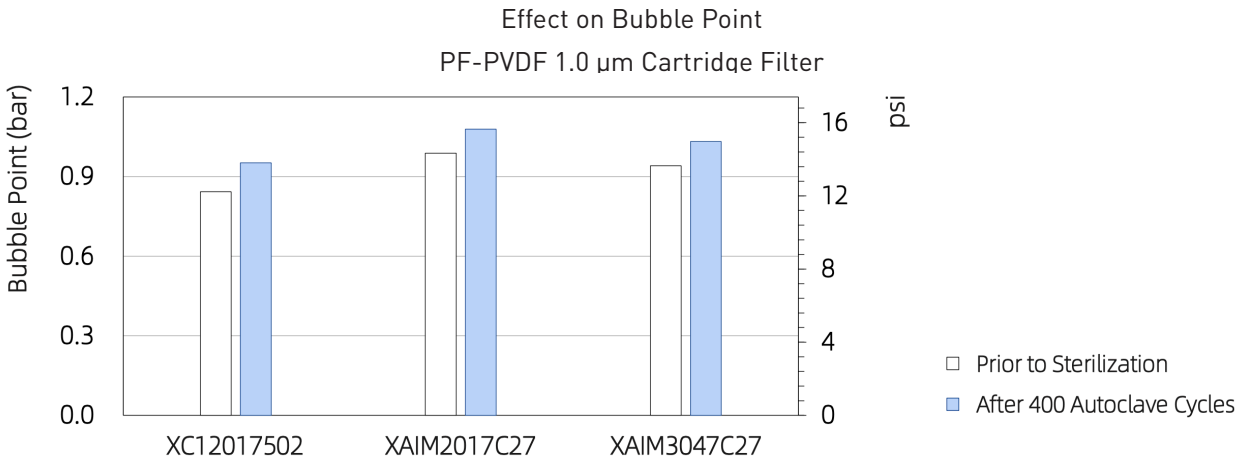
PF-PVDF

PF-PVDF 1.0 µm Cartridge Filter

LOT NUMBER	BUBBLE POINT (BAR)	
	PRIOR TO STERILIZATION	AFTER MULTIPLE STEAM CYCLES
After 150 SIP cycles		
XC12017502	0.824	0.883
XAIM2017C27	0.917	0.985
XAIM3047C27	0.805	0.880
After 400 autoclave cycles		
XC12017502	0.843	0.952
XAIM2017C27	0.988	1.079
XAIM3047C27	0.941	1.032





Conclusion

The results indicate that the integrity of the Ultrafilter PF-PVDF series filters is not affected by the recommended sterilization methods.

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5. Chemical Compatibility

Summary of Method

The evaluation of chemical compatibility for Ultrafilter PF-PVDF series filters was determined using a 48-hour static soak in the test solvent at 25 °C.

SOLVENT	CARTRIDGE ELEMENT	O-RINGS		
		SILICONE	EPDM	FLUOROELASTOMER
Acetic Acid, glacial	R	L	L	N
Acetic Acid, 90%	R	R	-	N
Acetic Acid, 30%	R	R	-	L
Acetic Acid, 10%	R	R	-	L
Hydrochloric Acid, conc. 35%	N	N	N	N
Hydrochloric Acid, 20%	L	N	N	L
Hydrochloric Acid, 3.3%	-	R	N	R
Nitric Acid, conc. 67%	N	N	N	R
Nitric Acid, 27%	N	N	L	R
Sulfuric Acid, conc. 96%	N	N	-	R
Sulfuric Acid, 16%	-	N	-	R
Ammonium Hydroxide, 3N, 5.7%	-	R	-	R
Ammonium Hydroxide, 6N, 11.4%	N	R	-	R
Potassium Hydroxide, 15%	N	N	R	R
Sodium Hydroxide, 3N, 11%	N	L	R	R
Sodium Hydroxide, 22%	N	L	R	R
Amyl Alcohol	R	N	R	R
Benzyl Alcohol	R	L	-	R
Butanol	R	L	R	R
Ethanol	R	L	R	R
Isopropanol	R	L	R	R
Methanol	R	R	R	N
Ethylene Glycol	R	R	-	R
Glycerol	R	R	-	R
Propylene Glycol	R	R	-	R
Ethylether	R	N	-	N
Tetrahydrofuran	N	N	N	N
Tetrahydrofuran, 50% (v-v)	-	-	-	N
Acetone	N	N	R	N
Cyclohexanone	N	N	L	N
Methyl Ethyl Ketone (MEK)	N	N	R	N
Methyl Isobutyl Ketone (MIBK)	N	N	R	N

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PF-PVDF

SOLVENT	CARTRIDGE ELEMENT	O-RINGS		
		SILICONE	EPDM	FLUOROELASTOMER
Amyl Acetate	R	N	R	N
Butyl Acetate	L	N	R	N
Cellusolve Acetate	L	R	-	N
Ethyl Acetate	R	N	R	N
Isopropyl Acetate	R	N	R	N
Methyl Acetate	N	N	R	N
Carbon Tetrachloride	L	N	N	R
Chloroform	L	N	N	R
Ethylene Dichloride	N	-	-	-
Methylene Chloride	N	N	N	N
Tetrachloroethylene	R	-	-	-
Trichloroethane	N	N	N	R
Benzene	L	N	N	R
Toluene	L	N	N	R
Xylene	L	N	N	R
Cottonseed	R	R	-	R
Peanut	R	R	-	R
Formaldehyde, 37%	R	L	R	N
Formaldehyde, 4%	R	R	-	R
Hexan	L	N	-	R
Acetonitrile	L	N	R	N
Dimethyl Formamide (DMF)	N	N	N	N
Dimethyl Sulfoxide (DMSO)	N	-	-	-
Kerosene	R	N	N	R
Pyridine	N	N	N	N
Petroleum Spirits	N	N	N	R
Hydrogen Peroxide	R	R	R	R
Ozone	N	N	L	N
Phenol	N	N	R	R

Legend:
R - Compatible
L - Limited compatibility Incompatible
N - Incompatible
- - No data

Conclusion

The chemical compatibility results under laboratory conditions are for reference only. It is recommended to verify the compatibility of the product with the filter under actual process conditions before use.

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6. Extractables (NVR)

The purpose of this test was to determine the quantity of material that can be extracted from Ultrafilter PF-PVDF 0.2 µm cartridge filter using purified water.

Summary of Method

Ultrafilter PF-PVDF 0.2 µm cartridge filters were autoclaved at 130 °C for 30 minutes prior to testing. The quantity of gravimetric extractables for filters were determined using a 24-hour static soak in purified water at ambient room temperature. Partial extraction solution was evaporated to dryness using a rotary evaporator and then dried to constant weight to evaluate non-volatile residues (NVR). At the same time, using purified water as a blank control for NVR tests.

Results

LOT NUMBER	NVR (MG/10-INCH)
XBR1016B14	8.6
XBR2016B14	8.4
XBT7016B14	21.4

Conclusion

The extractable level of the Ultrafilter PF-PVDF 0.2 µm cartridge filter under laboratory conditions is for reference only. It is recommended to test under actual process conditions.

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7. Total Organic Carbon (TOC) and Conductivity

The extractables in the filter can be reduced by flushing with water. The filter effluent was tested online for conductivity and total organic carbon (TOC) under different flush volumes of ultra-pure water. The recommended pre-flush volume is given when the TOC and conductivity of effluent meet the WFI specification.

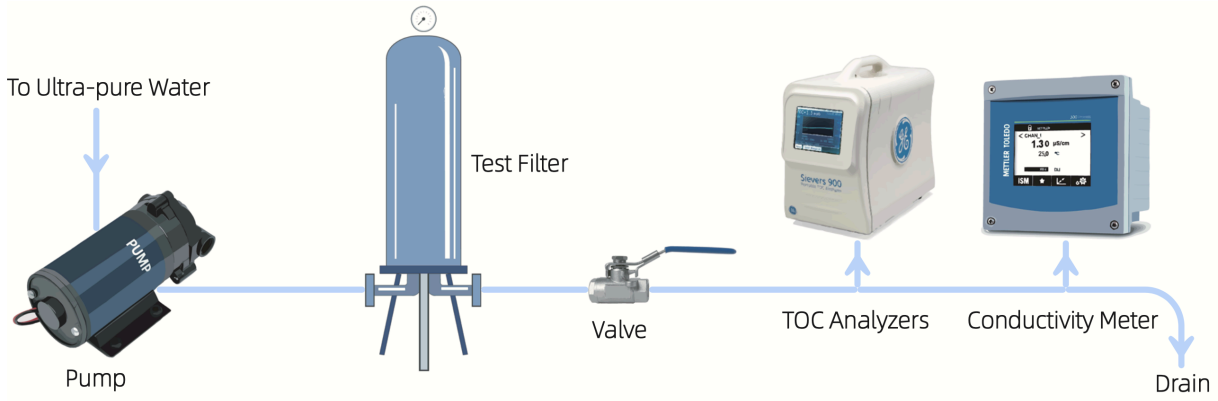
Summary of Method

Ultrafilter PF-PVDF series filters were autoclaved at 130 °C for 30 minutes prior to testing. The filters were flushed with ultra-pure water which meets the WFI specification of TOC less than 500 ppb and conductivity less than 1.3 µS/cm at 25 °C. Ultrafilter PF-PVDF 0.2 µm cartridge filters were flushed at a flow rate of 500 mL/min, Ultrafilter PF-PVDF 0.1 µm, 0.45 µm, 0.65 µm, 1.0 µm cartridge filters were flushed at a flow rate of 1 L/min and 250 mL/min for Ultrafilter PF-PVDF capsule filters with PVDF 0.2 µm membrane. The filter effluent was tested online for conductivity and total organic carbon (TOC).

Depending on the online measurement of conductivity, the maximum conductivity is based on USP <645> Stage 1—Temperature and Conductivity Requirements table.

STAGE 1 — TEMPERATURE AND CONDUCTIVITY REQUIREMENTS			
TEMPERATURE (°C)	CONDUCTIVITY REQUIREMENT (MS/CM)	TEMPERATURE (°C)	CONDUCTIVITY REQUIREMENT (MS/CM)
10	0.9	25	1.3
15	1.0	30	1.4
20	1.1	35	1.5

TOC and Conductivity Test Schematic



Recommended Pre-flush Volume

ULTRAFILTER PF-PVDF	0.1 µm	0.2 µm	0.2 µm capsule	0.45 µm	0.65 µm	1.0 µm
Flush volume (L)	30	30	15	40	60	60

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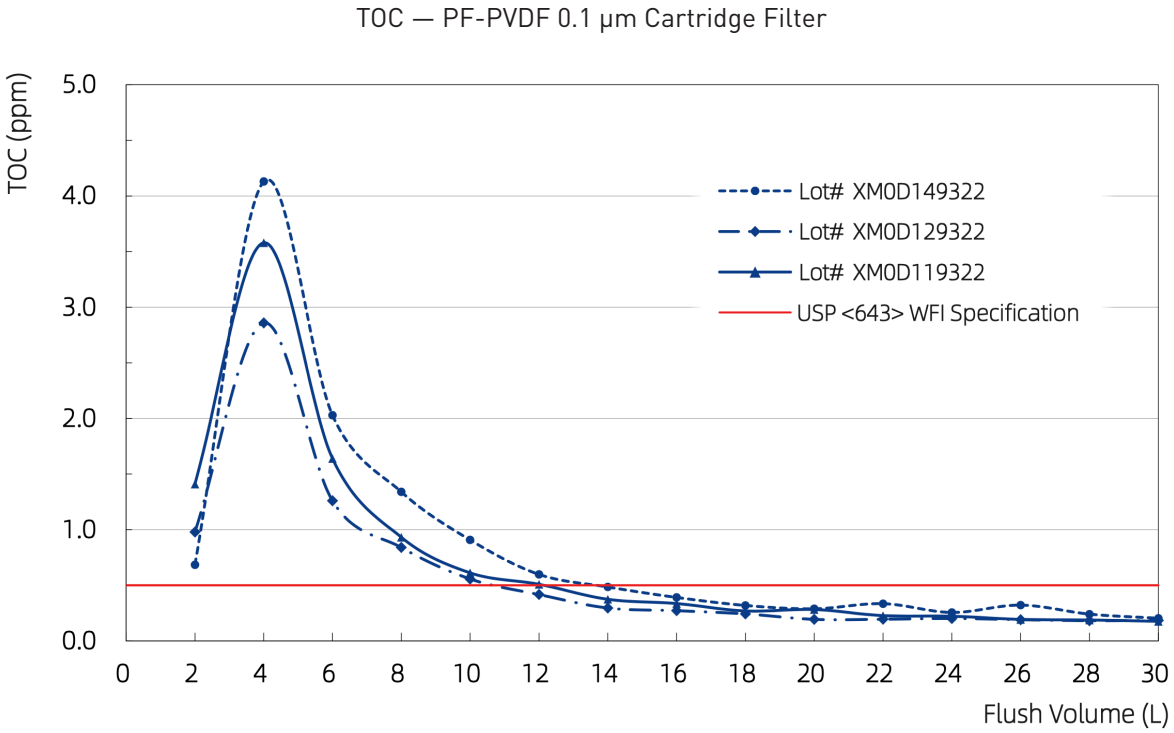
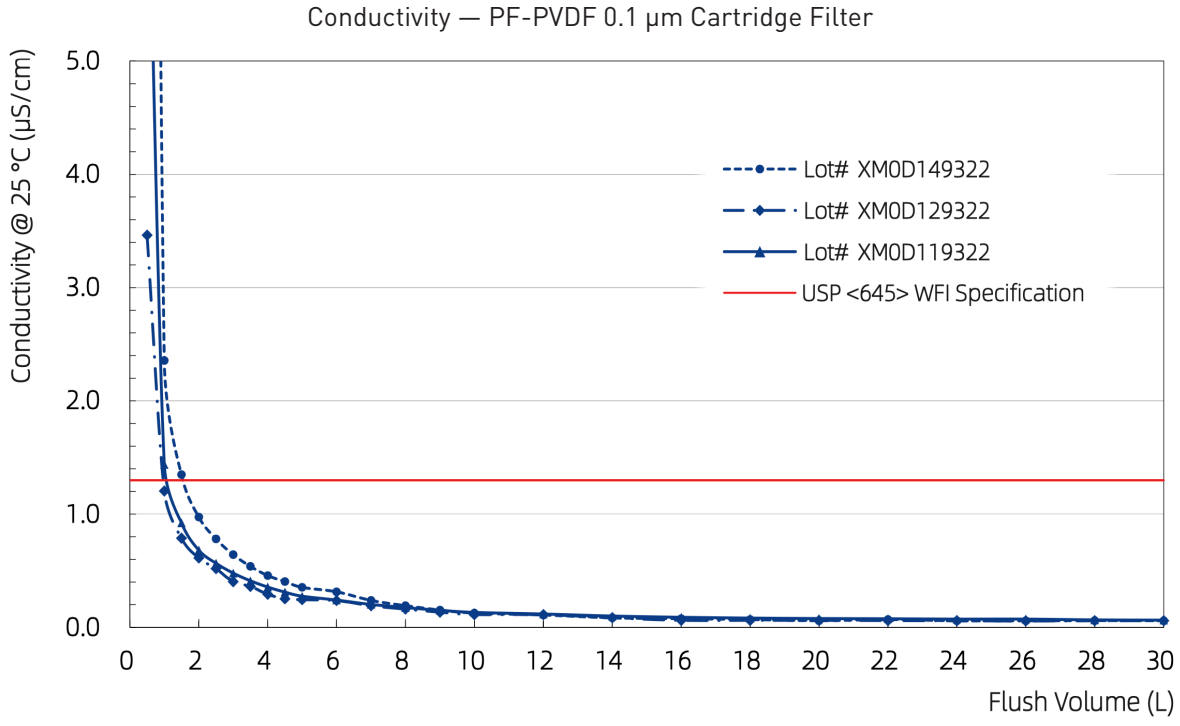
PF-PVDF 0.1 µm Cartridge Filter





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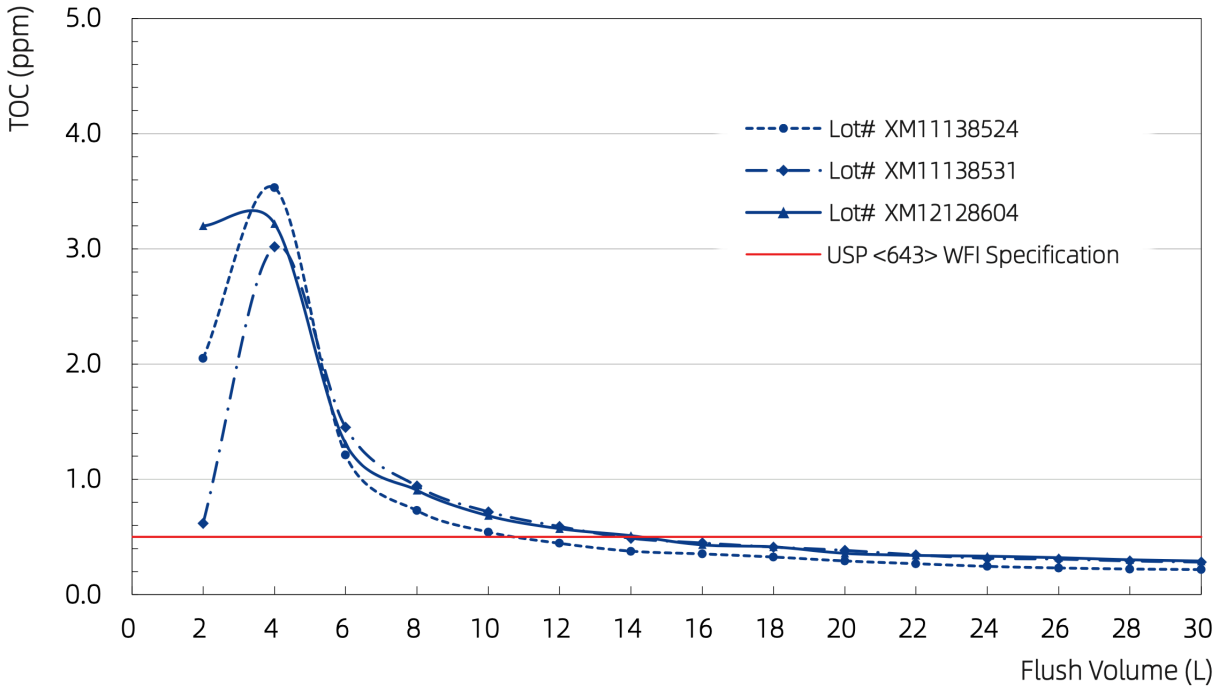
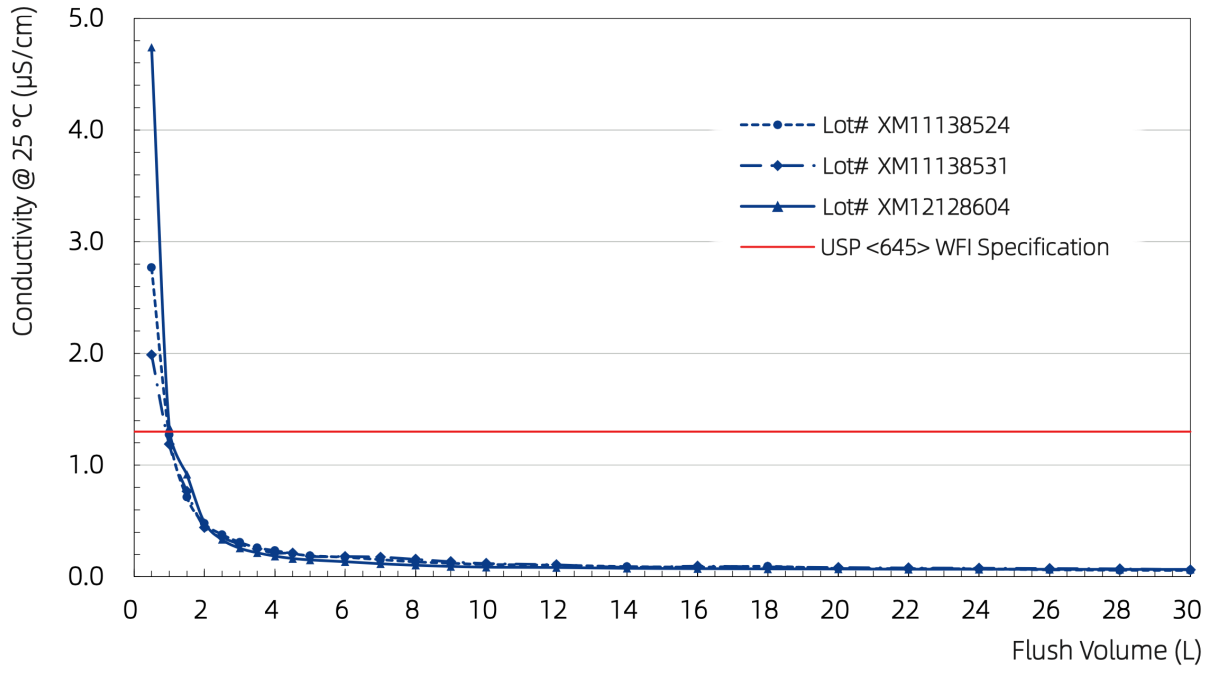
PF-PVDF 0.2 µm Cartridge Filter

TOC — PF-PVDF 0.2 µm Cartridge Filter



Conductivity — PF-PVDF 0.2 µm Cartridge Filter



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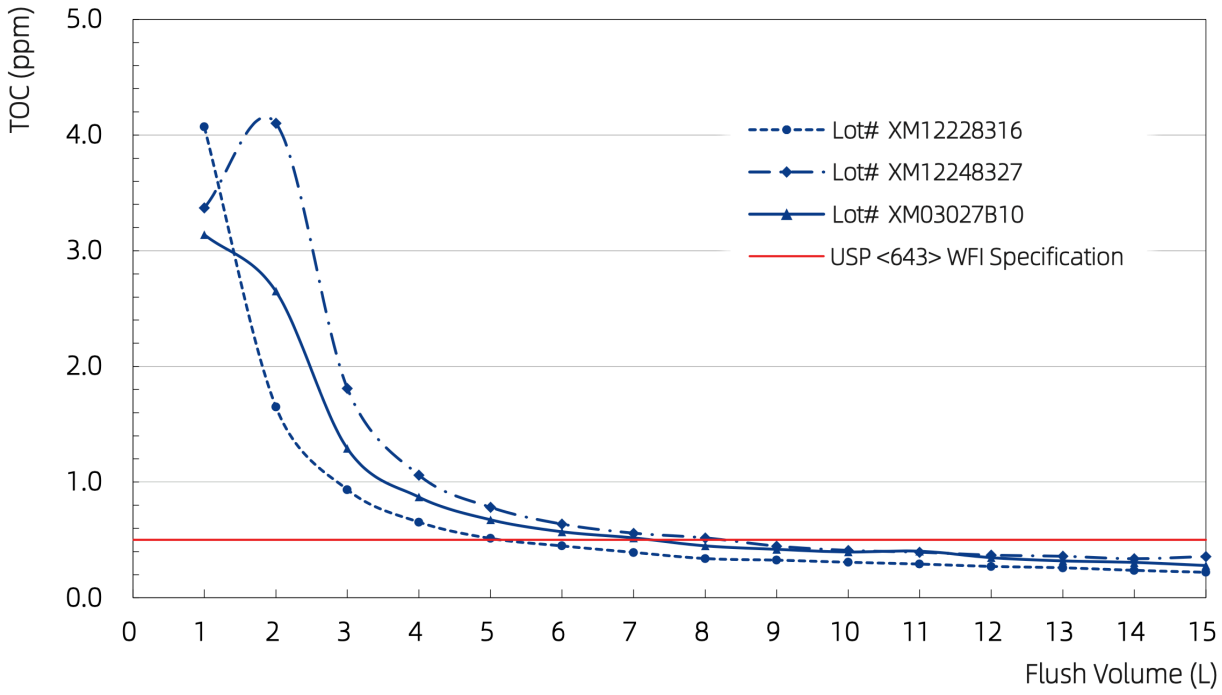
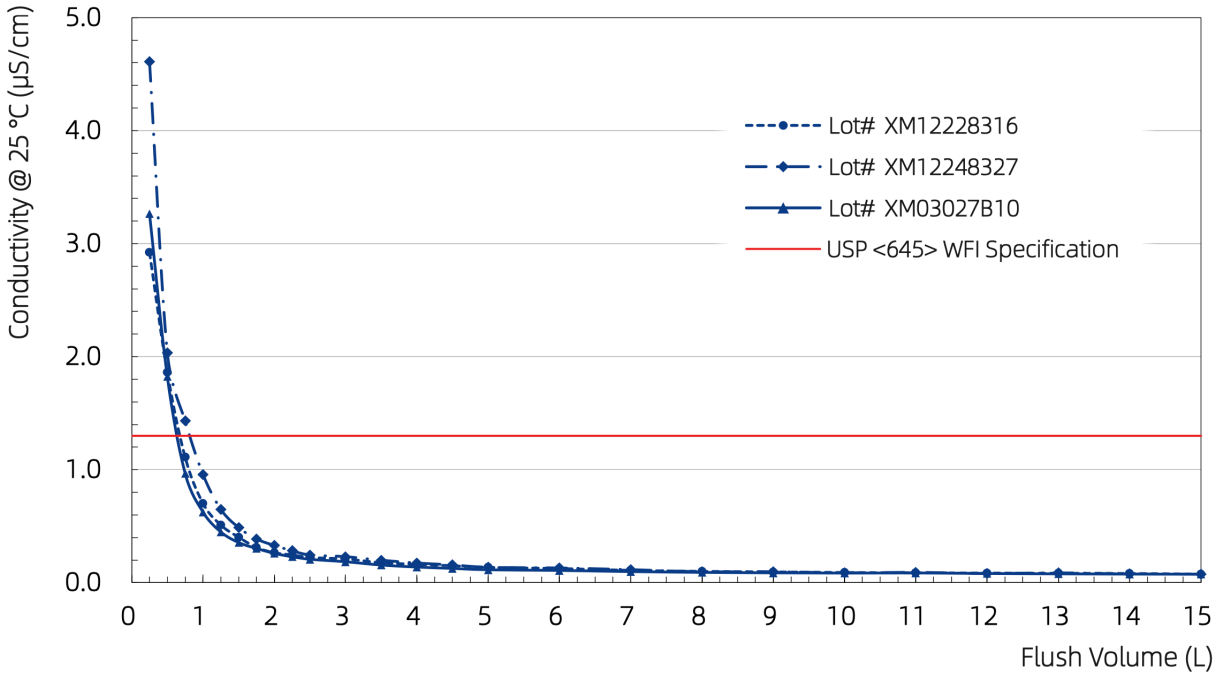
Ultrafilter PF-PVDF capsule filters with PVDF 0.2 µm membrane

TOC — PF-PVDF capsule filters with PVDF 0.2 µm membrane



Conductivity — PF-PVDF capsule filters with PVDF 0.2 µm membrane



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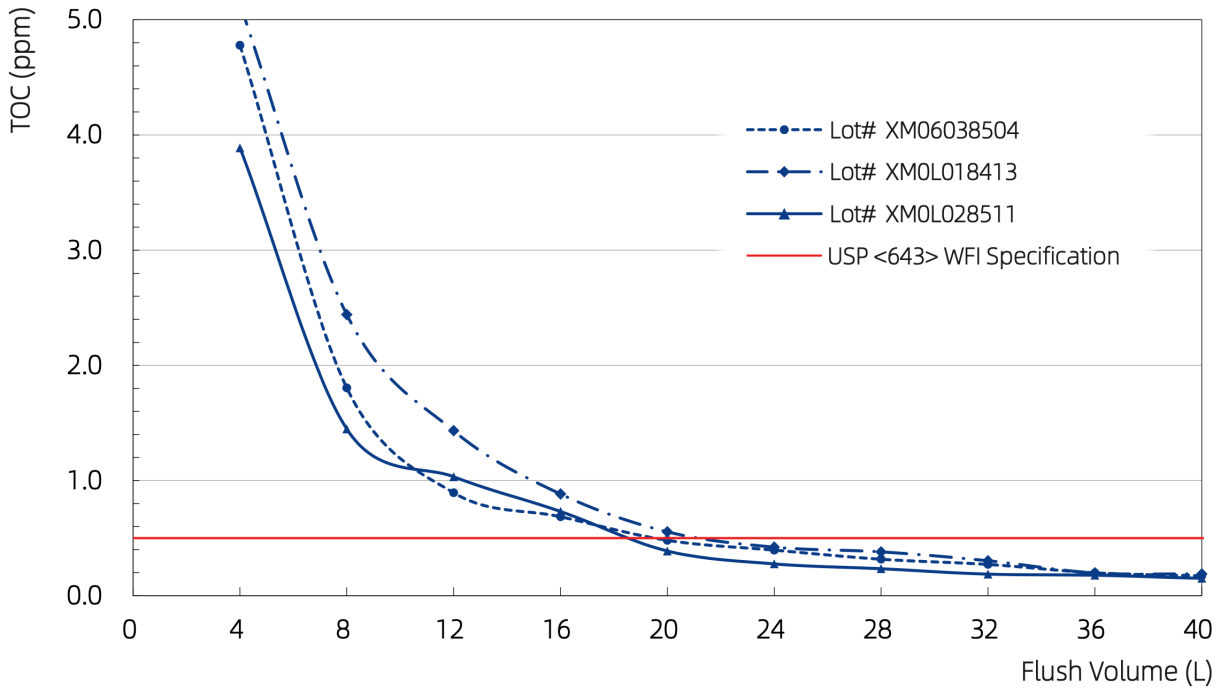
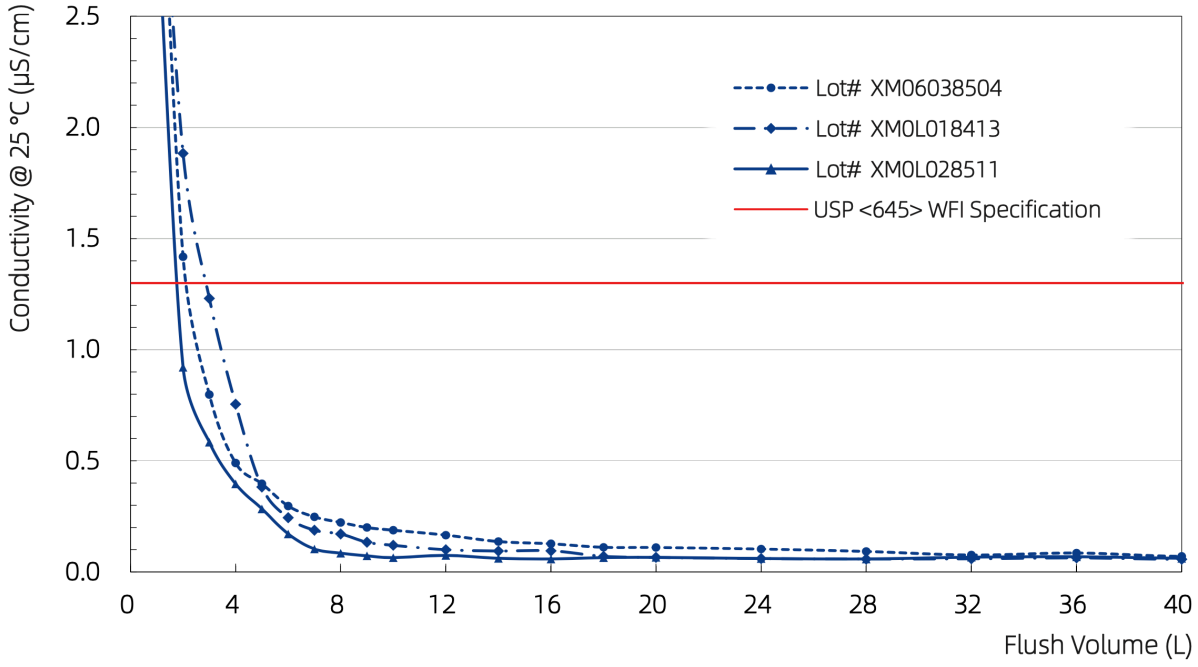
PF-PVDF 0.45 µm Cartridge Filter

TOC — PF-PVDF 0.45 µm Cartridge Filter



Conductivity — PF-PVDF 0.45 µm Cartridge Filter



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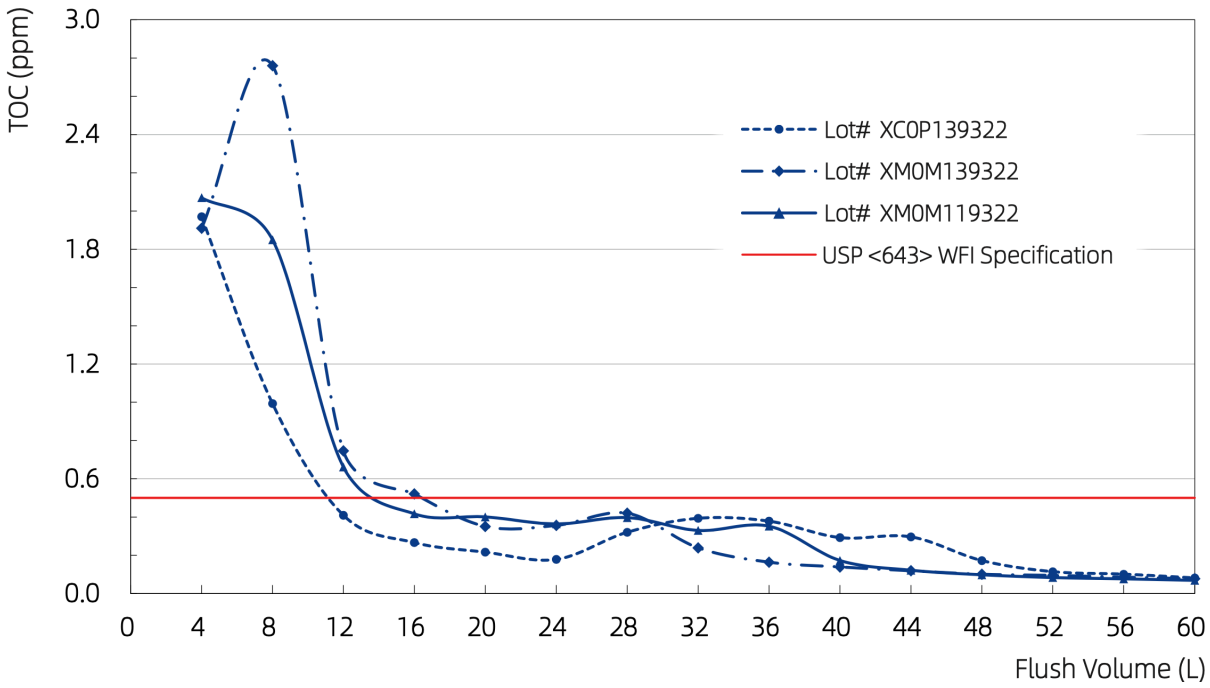
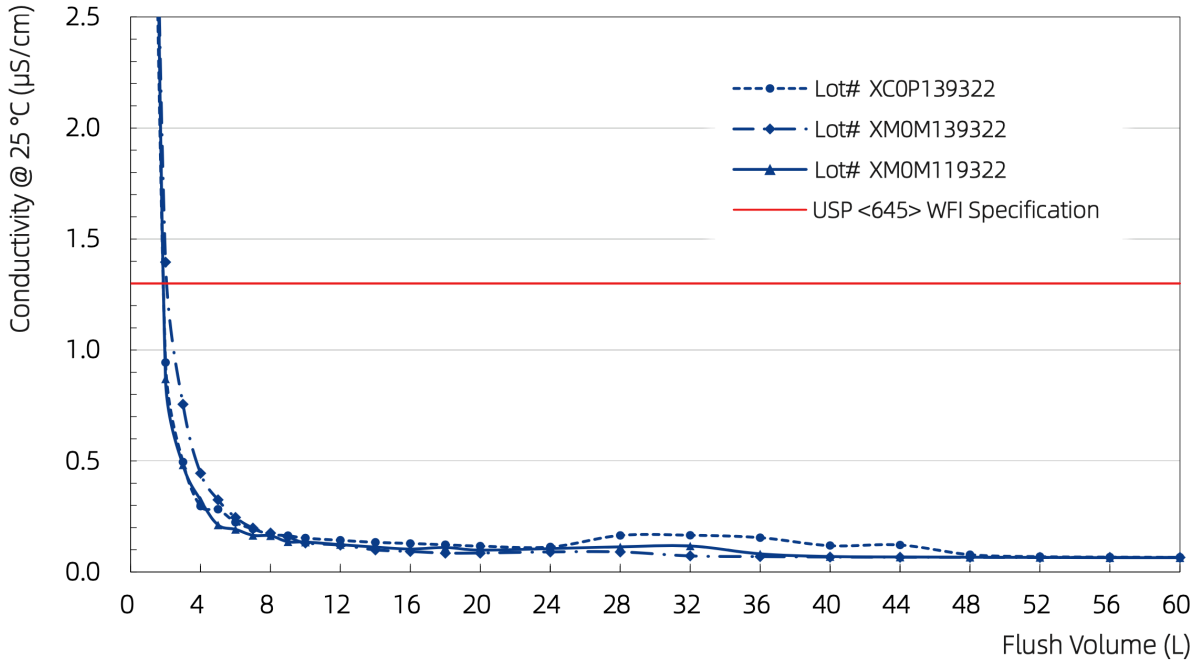
PF-PVDF 0.65 µm Cartridge Filter

TOC — PF-PVDF 0.65 µm Cartridge Filter



Conductivity — PF-PVDF 0.65 µm Cartridge Filter



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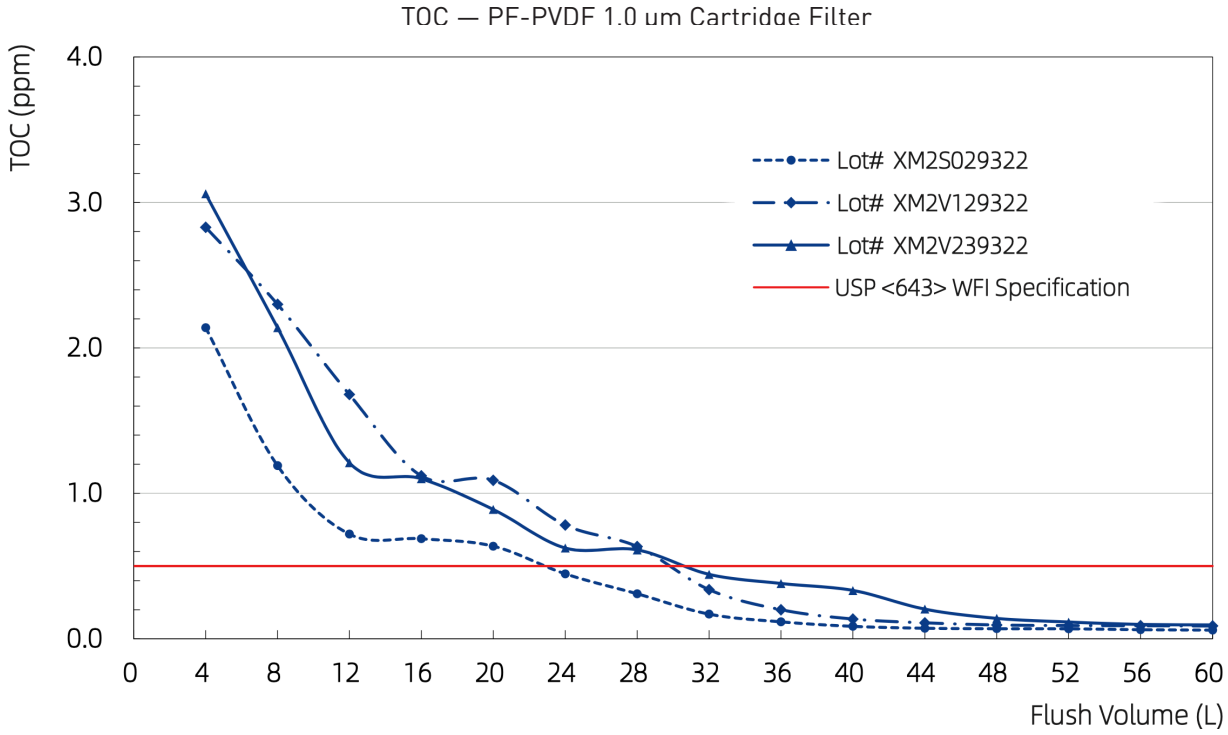
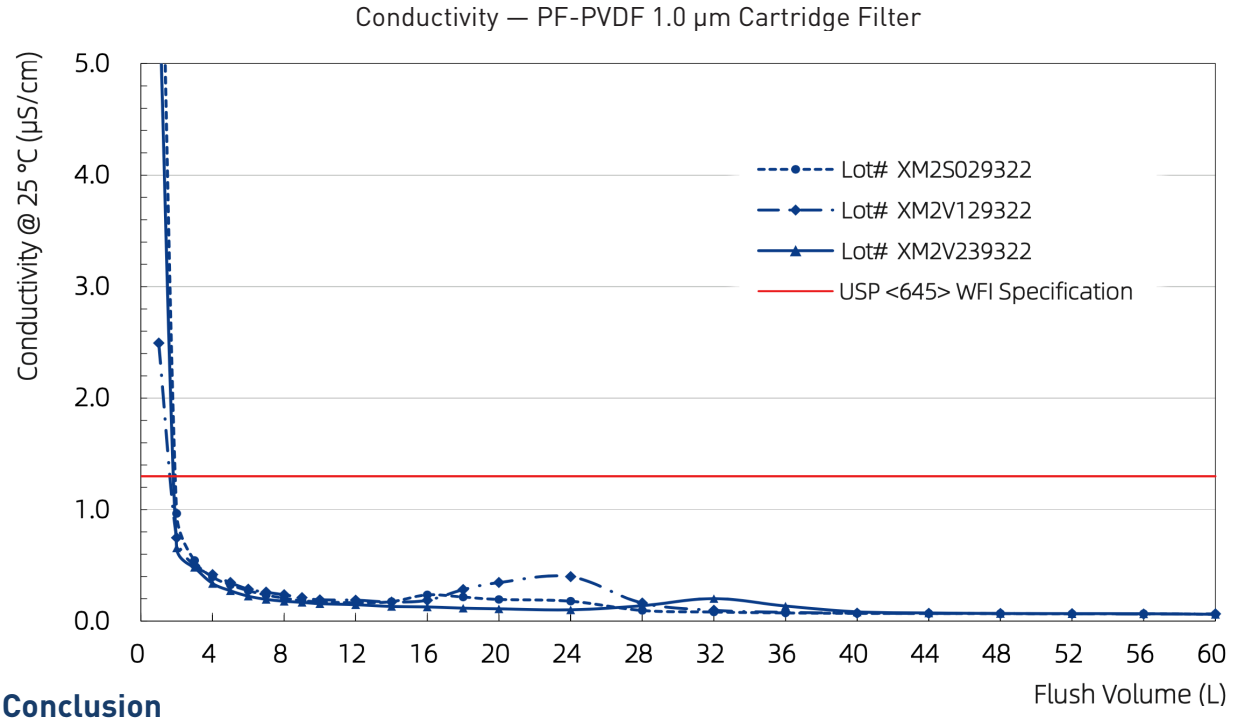
PF-PVDF

PF-PVDF 1.0 µm Cartridge Filter





Conclusion

The effluent of Ultrafilter PF-PVDF filters meets the USP <643> for Total Organic Carbon and USP <645> for Water Conductivity per WFI requirements after a water flush of recommended pre-flush volume.

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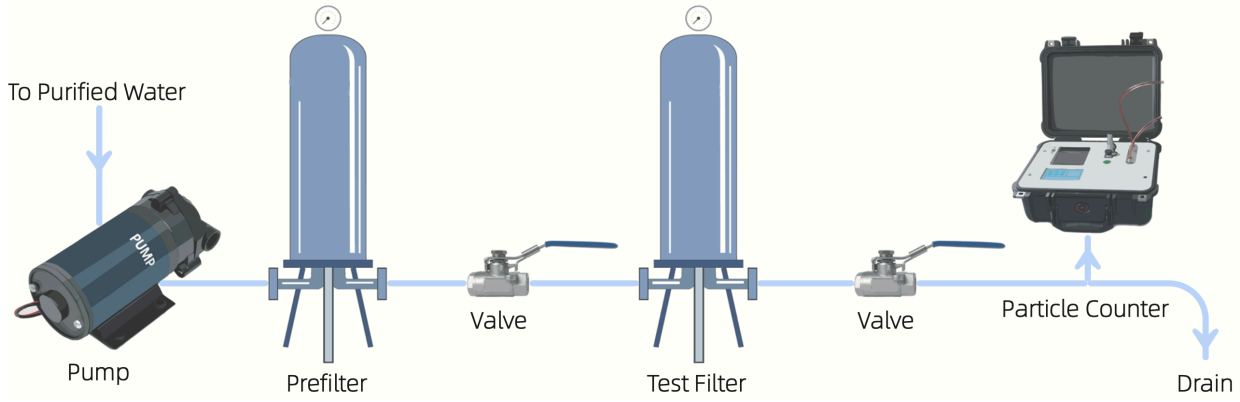
8. Particle Shedding

Summary of Method

Ultrafilter PF-PVDF series filters were autoclaved at 130 °C for 30 minutes prior to testing. The test devices and connected tubing were pre-flushed until the system condition meets the testing requirements. Ultrafilter PF-PVDF series cartridge filters were flushed with prefiltered purified water at a flow rate of 1 L/min for a total of 20 L. Ultrafilter PF-PVDF capsule filters with PVDF 0.2 µm membrane were flushed with prefiltered purified water at a flow rate of 500 mL/min for a total of 10 L. The filter effluent was analyzed by following USP <788> Method 1 (light obscuration particle count test) for particle shedding.

Particle Shedding Test Schematic



Particle Requirements for Large Volume Parenterals in USP <788>

PARTICLE SIZE (µM)	REQUIREMENTS
≥ 10	≤ 25 particles/mL
≥ 25	≤ 3 particles/mL

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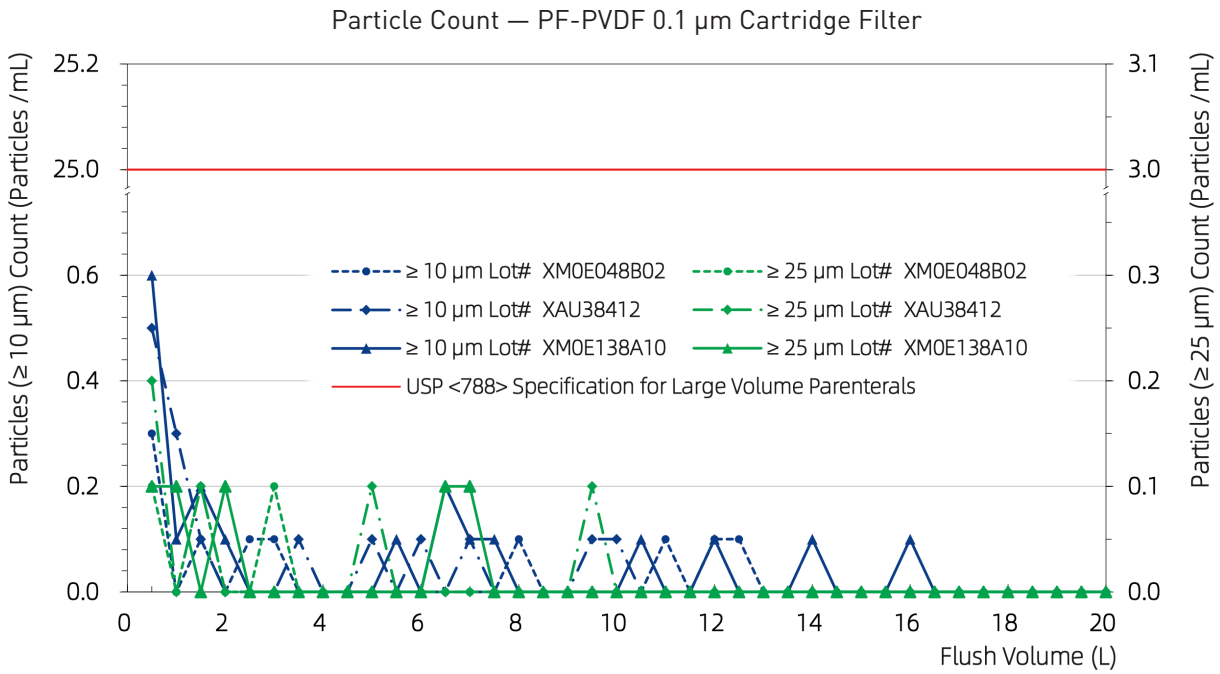
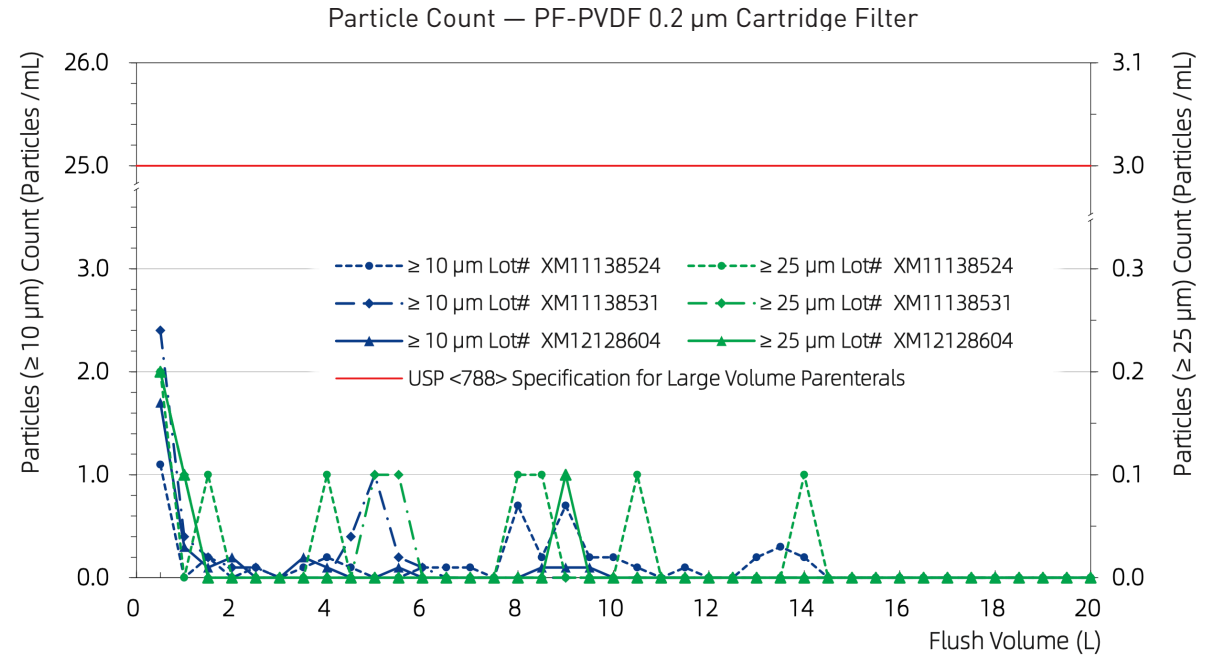
PF-PVDF

PF-PVDF 0.1 µm Cartridge Filter



PF-PVDF 0.2 µm Cartridge Filter



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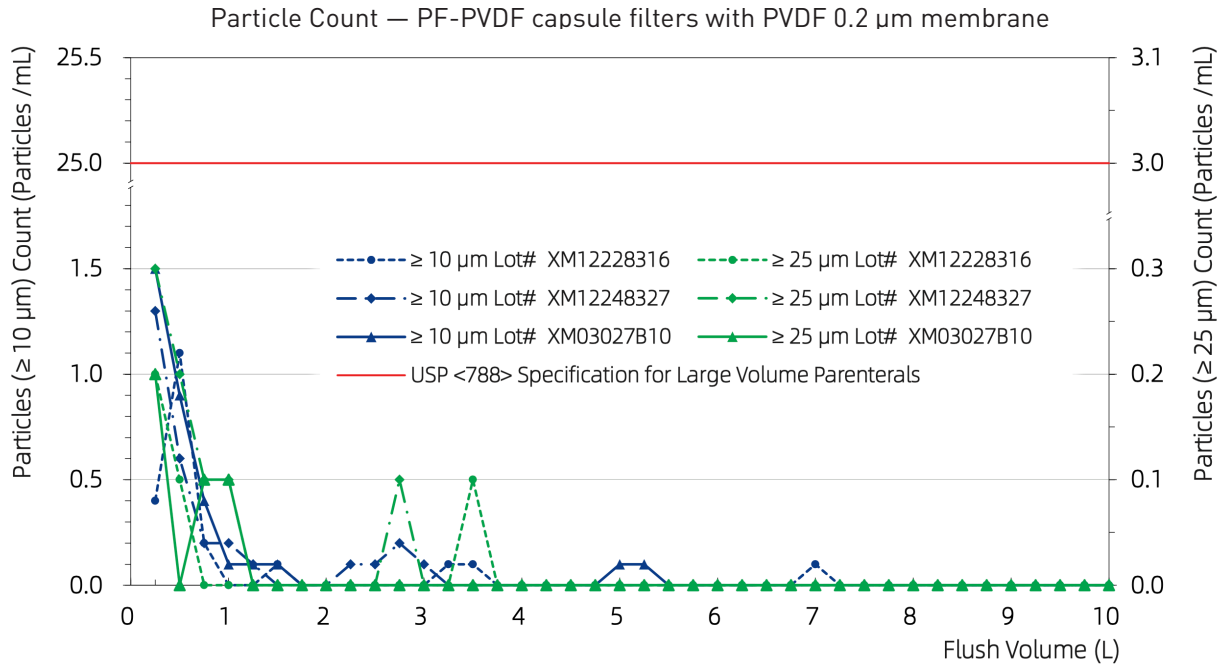
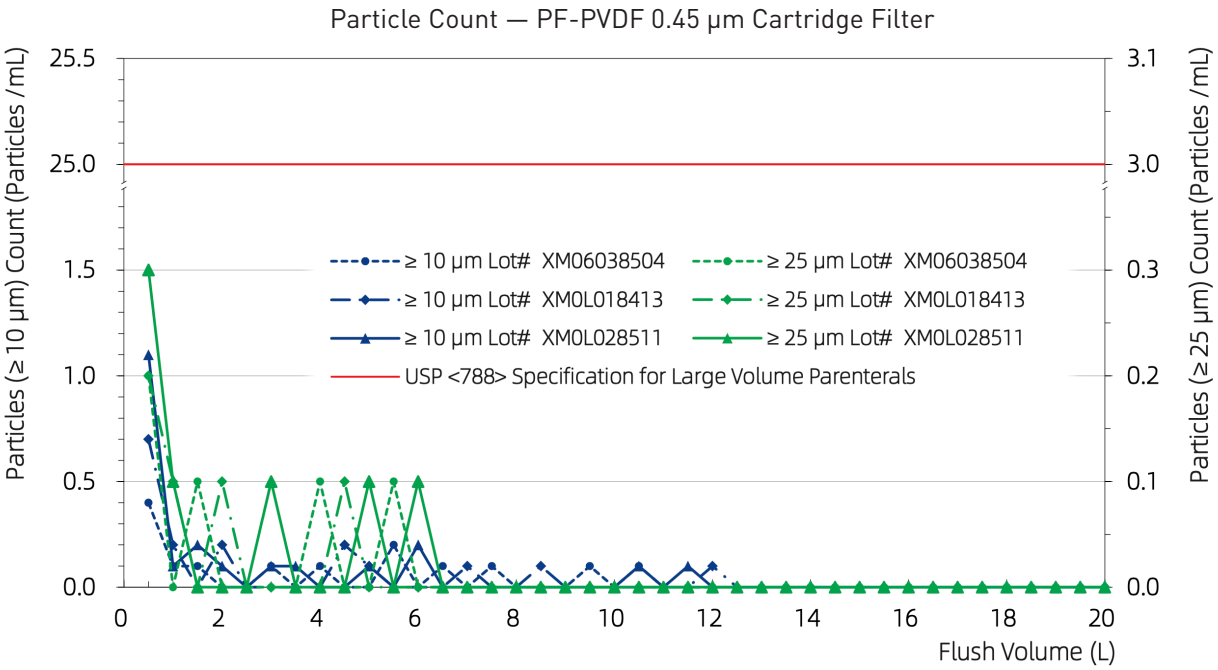
Ultrafilter PF-PVDF capsule filters with PVDF 0.2 µm membrane



PF-PVDF 0.45 µm Cartridge Filter



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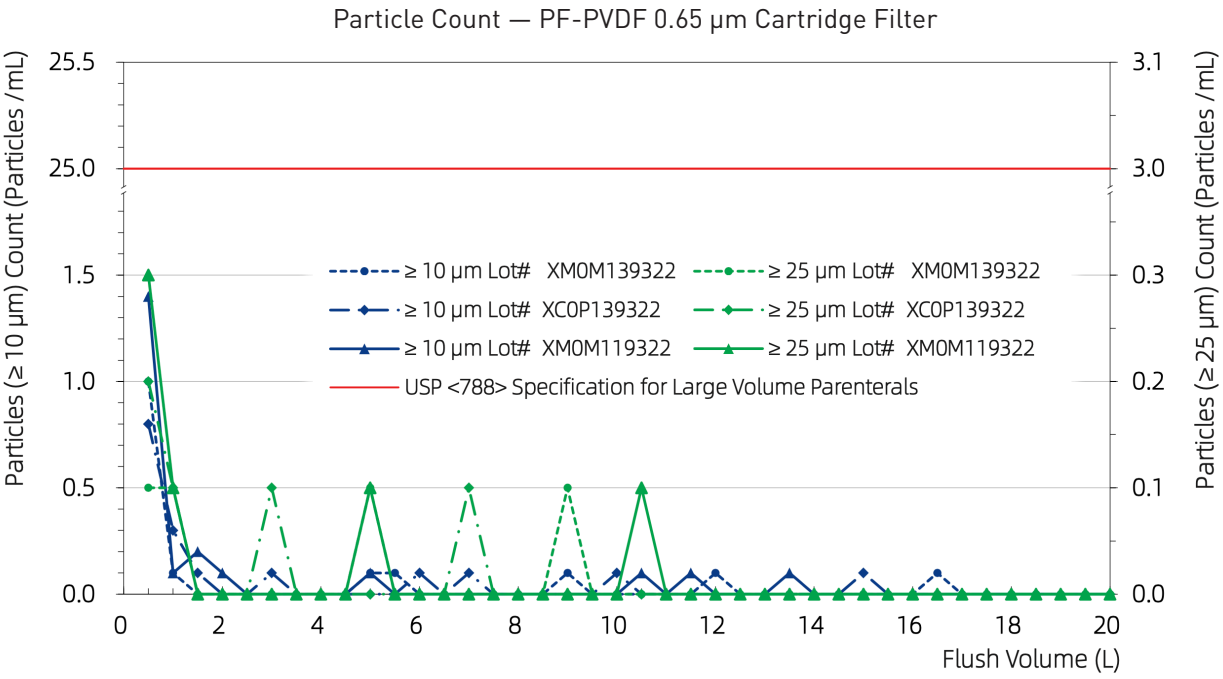
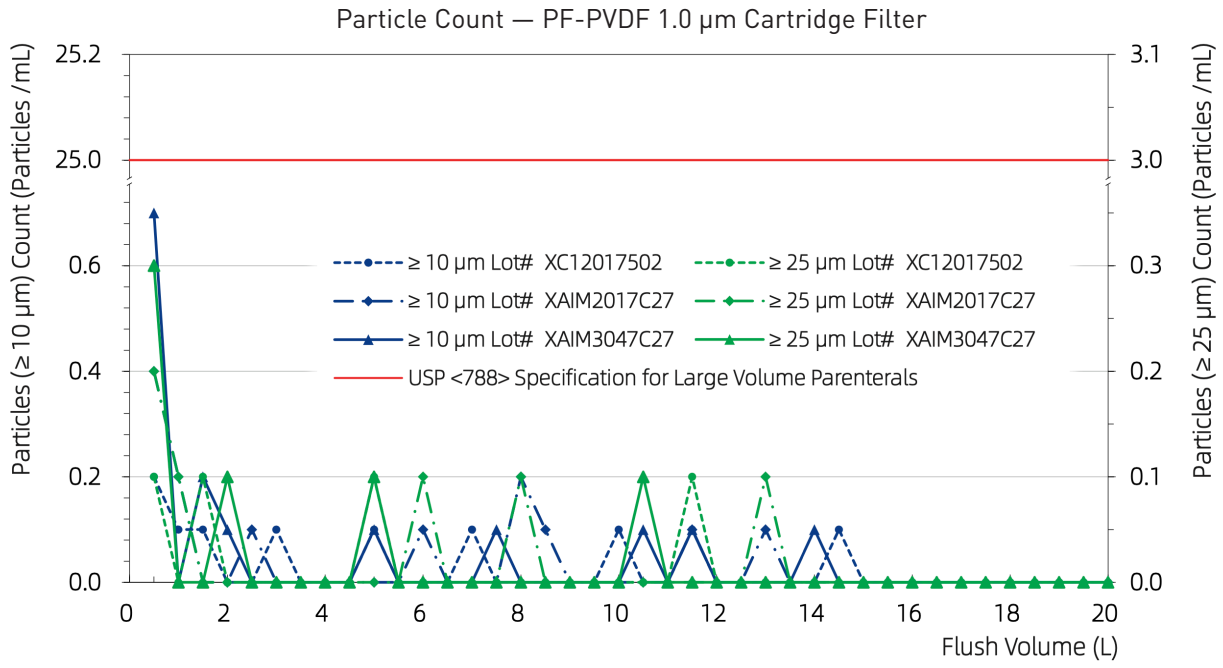
PF-PVDF

PF-PVDF 0.65 µm Cartridge Filter



PF-PVDF 1.0 µm Cartridge Filter



Conclusion

The particle count in effluent of autoclaved Ultrafilter PF-PVDF filters meets the requirements in USP <788> for large volume parenterals.

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9. Non-fiber Releasing

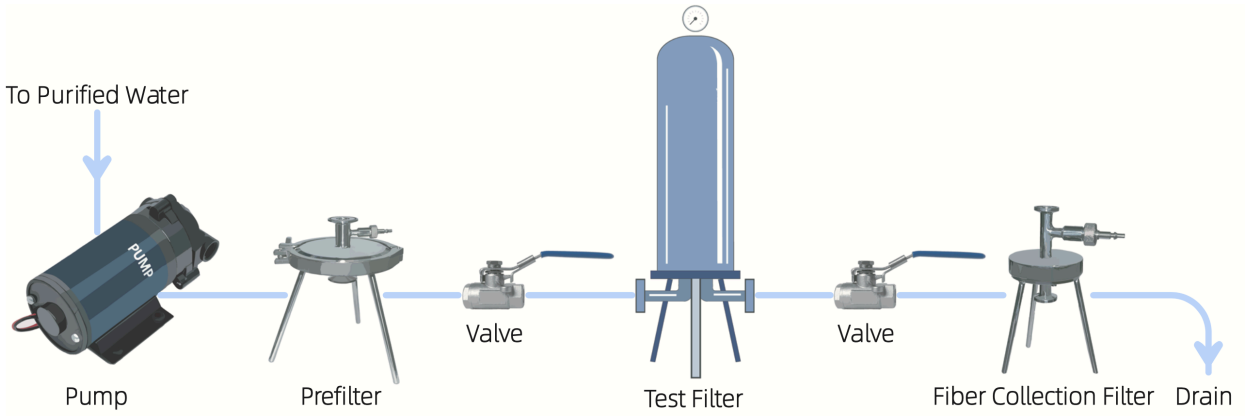
Filters for liquid filtration used in the manufacture, processing, or packaging of injectable drug products intended for human use shall not release fibers into such products that is being filtered.

"Non-fiber Releasing Filter" and "Fiber" are defined in 21 CFR 210.3(b) (6). "Non-fiber-releasing filter means any filter, which after any appropriate pretreatment such as washing or flushing, will not release fibers into the component or drug product that is being filtered." "Fiber means any particulate contami- nant with a length at least three times greater than its width."

Summary of Method

Ultrafilter PF-PVDF series filters were autoclaved at 130 °C for 30 minutes prior to testing. Ultrafilter PF-PVDF series cartridge filters were flushed with prefiltered purified water at a flow rate of 1 L/min for a total of 10 L. Ultrafilter PF-PVDF capsule filters with PVDF 0.2 µm membrane were flushed with prefiltered purified water at a flow rate of 500 mL/min for a total of 5 L. The filter effluent was filtered through 0.8 µm black gridded disc filter to collect any fibers released from the filters. The disc filter was examined under 50x microscope for presence of any fibers.

Non-fiber Releasing Test Schematic



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Results

LOT NUMBER	NUMBER OF FIBERS IN EFFLUENT
Ultrafilter PF-PVDF 0.1 µm Cartridge Filter	
XM0E048B02	0
XAU38412	0
XM0E138A10	0
Ultrafilter PF-PVDF 0.2 µm Cartridge Filter	
XM11138524	0
XM11138531	0
XM12128604	0
Ultrafilter PF-PVDF capsule filters with PVDF 0.2 µm membrane	
XM12228316	0
XM12248327	0
XM03027B10	0
Ultrafilter PF-PVDF 0.45 µm Cartridge Filter	
XM06038504	0
XM0L018413	0
XM0L028511	0
Ultrafilter PF-PVDF 0.65 µm Cartridge Filter	
XM0M139322	0
XC0P139322	0
XM0M119322	0
Ultrafilter PF-PVDF 1.0 µm Cartridge Filter	
XC12017502	0
XAIM2017C27	0
XAIM3047C27	0

Conclusion

Ultrafilter PF-PVDF series filters meet the criteria for a “Non-fiber-releasing filter” as defined in 21 CFR 210.3 (b) (6).

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10. Bacterial Endotoxins Test

Bacterial endotoxins test for Ultrafilter PF-PVDF series filters were performed according to current USP <85> BACTERIAL ENDOTOXINS TEST. The Bacterial Endotoxins Test (BET) is a test to detect or quantify endotoxins from Gram-negative bacteria using amoebocyte lysate from the horseshoe crab (Limulus polyphemus or Tachypleus tridentatus).

Summary of Method

Ultrafilter PF-PVDF series cartridge filters were installed in non-pyrogenic stainless steel housing. Ultrafilter PF-PVDF capsule filters with PVDF 0.2 µm membrane were tested directly. The filters were filled with endotoxin free water (Water for BET) and static soaking for one hour at ambient room temperature. Samples were then taken and evaluated with the Limulus Amebocyte Lysate (LAL) gel clot test with a sensitivity of 0.25 EU/mL (= 0.25 EU/mL).

Preparation of solutions

	SOLUTION	ENDOTOXIN CONCENTRATION / SOLUTION TO WHICH ENDOTOXIN IS ADDED	NUMBER OF REPLICATES
A	Sample solution	None / Sample Solution	2
B	Positive product control	2λ / Sample Solution	2
C	Positive control	2λ / Water for BET	2
D	Negative control	None / Water for BET	2

Prepare Solution A and the positive product control Solution B using Sample solution. The positive control Solutions B and C contain the Standard Endotoxin Solution at a concentration corresponding to twice the labeled lysate sensitivity. The negative control Solution D consists of Water for BET .

Incubate the reaction mixture at 37 ± 1 °C for 60 ± 2 minutes, avoiding vibration. To test the integrity of the gel, take each tube in turn directly from the incubator, and invert it through about 180° in one smooth motion. If a firm gel has formed that remains in place upon inversion, record the result as positive. A result is negative if an intact gel is not formed. The test is considered valid when both replicates of Solutions B and C are positive and those of Solution D are negative. When a negative result is found for both replicates of Solution A, the preparation under test complies with the test. When a positive result is found for both replicates of Solution A , the preparation under test does not comply with the test.

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PF-PVDF

Results

LOT NUMBER	LYSATE SENSITIVITY (EU/ML)	SOLUTION				RESULT (EU/ML)
		A	B	C	D	
Ultrafilter PF-PVDF 0.1 µm Cartridge Filter						
XM0E048B02	0.25	——	++	++	——	< 0.25
XAU38412	0.25	——	++			< 0.25
XM0E138A10	0.25	——	++			< 0.25
Ultrafilter PF-PVDF 0.2 µm Cartridge Filter						
XM11138524	0.25	——	++	++	——	< 0.25
XM11138531	0.25	——	++			< 0.25
XM12128604	0.25	——	++			< 0.25
Ultrafilter PF-PVDF capsule filters with PVDF 0.2 µm membrane						
XM12228316	0.25	——	++	++	——	< 0.25
XM12248327	0.25	——	++			< 0.25
XM03027B10	0.25	——	++			< 0.25
Ultrafilter PF-PVDF 0.45 µm Cartridge Filter						
XM06038504	0.25	——	++	++	——	< 0.25
XM0L018413	0.25	——	++			< 0.25
XM0L028511	0.25	——	++			< 0.25
Ultrafilter PF-PVDF 0.65 µm Cartridge Filter						
XM0M139322	0.25	——	++	++	——	< 0.25
XC0P139322	0.25	——	++			< 0.25
XM0M119322	0.25	——	++			< 0.25
Ultrafilter PF-PVDF 1.0 µm Cartridge Filter						
XC12017502	0.25	——	++	++	——	< 0.25
XAIM2017C27	0.25	——	++			< 0.25
XAIM3047C27	0.25	——	++			< 0.25

Legend:
' + ' —— A firm gel has formed that remains in place upon inversion, Positive.
' — ' —— An intact gel is not formed, Negative.

Conclusion

The aqueous extraction of Ultrafilter PF-PVDF series filters contains < 0.25 EU/mL as determined by Limulus Amebocyte Lysate (LAL), meeting the requirements of USP monographs for Sterile Water for Injection.

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11. USP <87> Biological Reactivity Test, In Vitro

USP <87> Biological Reactivity Test, In Vitro is designed to determine the biological reactivity of mammalian cell cultures following contact with the elastomeric plastics and other polymeric materials with direct or indirect patient contact or of specific extracts prepared from the materials under test.

Conclusion

The component materials of Ultrafilter PF-PVDF series filters meet the requirement of USP <87> Biological Reactivity Test, In Vitro.

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12. USP <88> Class VI Biological Reactivity Test, In Vivo

USP <88> Biological Reactivity Test, In Vivo is designed to determine the biological response of animals to elastomerics, plastics, and other polymeric material with direct or indirect patient contact, or by the injection of specific extracts prepared from the material under test.

USP <88> Class VI Biological Reactivity Tests were performed on all components of Ultrafilter PF-PVDF series filters to estimate the biosafety. The tests were conducted in an accredited, independent laboratory.

Summary of Method

The current USP<88> Class VI-121 °C Plastics tests, including the following tests:

PROCEDURE	ANIMAL	TEST MATERIAL
Systemic Injection Test	Mouse	• Extract of Sample in Sodium Chloride Injection • Extract of Sample in 1 in 20 Solution of Alcohol in Sodium Chloride Injection • Extract of Sample in Polyethylene Glycol 400 • Extract of Sample in Vegetable Oil
Intracutaneous Test	Rabbit or Guinea Pig	
Implantation Test	Rabbit	Implant strips of Sample

Conclusion

The component materials of Ultrafilter PF-PVDF series filters meet the criteria of the USP <88> Biological Reactivity Test for Class VI-121 °C plastics.

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FDA 21 CFR INDIRECT FOOD ADDITIVE

The raw materials used in manufacture Ultrafilter PF-PVDF series cartridge filters were confirmed to be fully compliant with the Federal Food, Drug and Cosmetic Act and applicable food additive regulations.

RESULTS

COMPONENT	MATERIALS	FDA 21 CFR REFERENCE
Membranes	Polyvinylidene fluoride	177.2510
Supports	Polypropylene	177.1520
Core, cage, end caps	Polypropylene	177.1520
Capsule Housing	Polypropylene	177.1520
O-rings	Silicone	177.2600
O-rings	EPDM	177.2600
O-rings	FEP/PFA encapsulated Fluoroelastomer	177.1550

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