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VALIDATION GUIDE

BY MS VALIDATION SERVICE CENTER

Sterilizing-grade Hydrophilic Polyvinylidene Fluoride Pleated Filter Cartridges

KPL 0.20µm/0.20µm+0.2µm



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1 Introduction

The data contained in this guide applies to KPL series 0.20μm/ 0.20μm+ 0.20μm hydrophilic polyvinylidene fluoride (Abbreviated as PVDF) filter cartridges manufactured by Membrane Solutions LLC (Abbreviated as MS).

Validation data includes: liquid bacteria challenge test, bacteria challenge test after multiple sterilization, integrity test, pure water flow rate-differential pressure test, heat and pressure resistance test, extractable level in model solvents, etc.

The purpose of this report is to assist users in completing the validation and confirmation procedures required by the regulations.

*0.20μm and 0.22μm are both descriptions of membrane pore size. The difference between the two names comes from the industry's habitual title of the sterile filter membrane. In practice, they are the same and will be referred to as 0.20μm in the following sections.

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2 Technical Parameters

2.1 Technical Parameters of KPL 0.20μm Filter Cartridge

Size		5"	10"	20"	30"	40"
Bacteria Retention Efficiency		*Brevundimonas diminuta*（ATCC 19146） Interception＞ 10^7CFU/cm^2				
Bubble Point (Pure Water) @ 25°C		≥340 kPa				
Diffusion Flow (Pure Water) @ 25°C		≤7.5 mL/min @270 kPa	≤15.0 mL/min @270 kPa	≤30.0 mL/min @270 kPa	≤45.0 mL/min @270 kPa	≤60.0 mL/min @270 kPa
Pure Water Flow Rate[1] @ 25°C		≥3.3 L/min	≥6.6 L/min	≥13.2L/min	≥19.8 L/min	≥26.4L/min
Max.Forward Differential Pressure		520 kPa at 25°C 450 kPa at 40°C 360 kPa at 60°C 270 kPa at 80°C 250 kPa at 90°C				
Max.Reverse Differential Pressure		210 kPa at 25°C 200 kPa at 40°C 180 kPa at 60°C 160 kPa at 80°C 150 kPa at 90°C				
Autoclaving		124 ° C, 30 minutes, 30times； 134 ° C, 20 minutes, 30 times				
SIP		124 ° C, 30 minutes, 30times； 134 ° C, 20 minutes, 30 times				
Materials	Filter Membrane	PVDF				
	Support	PP				
	Cage and Adaptor	PP				
	Adaptor Reinforcing Ring[2]	Stainless Steel				
	O-ring	Choose according to the situation				
Bacteria Endotoxin Release		The bacteria endotoxin content of flushing water is less than 0.25 EU/mL The bacteria endotoxin release level of the filter cartridge in non heat source water is less than 0.25 EU/mL				
Biocompatibility		All raw materials comply with the provisions of USP<88> for Class VI-121 ° C Plastic				

1 The pressure drop of pure water flow rate is 10kPa.

2 When selecting a reinforced adaptor for the product, it includes a reinforcing ring.

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2.2 Technical Parameters of KPL 0.20μm+0.20μm Filter Cartridge

Size		5"	10"	20"	30"	
Bacteria Retention Efficiency		*Brevundimonas diminuta*（ATCC 19146） Interception＞ 10^7CFU/cm^2				
Bubble Point (Pure Water) @ 25°C		≥340 kPa				
Diffusion Flow (Pure Water) @ 25°C		≤5.5 mL/min @270 kPa	≤11.0 mL/min @270 kPa	≤22.0 mL/min @270 kPa	≤33.0 mL/min @270 kPa	≤44.0 mL/min @270 kPa
Pure Water Flow Rate[1] @ 25°C		≥1.8 L/min	≥3.6 L/min	≥7.2L/min	≥10.8 L/min	≥14.4L/min
Max.Forward Differential Pressure		520 kPa at 25°C 450 kPa at 40°C 360 kPa at 60°C 270 kPa at 80°C 250 kPa at 90°C				
Max.Reverse Differential Pressure		210 kPa at 25°C 200 kPa at 40°C 180 kPa at 60°C 160 kPa at 80°C 150 kPa at 90°C				
Autoclaving		124 ° C, 30 minutes, 30times； 134 ° C, 20 minutes, 30 times				
SIP		124 ° C, 30 minutes, 30times； 134 ° C, 20 minutes, 30 times				
Materials	Filter Membrane	PVDF				
	Support	PP				
	Cage and Adaptor	PP				
	Adaptor Reinforcing Ring[2]	Stainless Steel				
	O-ring	Choose according to the situation				
Bacteria Endotoxin Release		The bacteria endotoxin content of flushing water is less than 0.25 EU/mL The bacteria endotoxin release level of the filter cartridge in non heat source water is less than 0.25 EU/mL				
Biocompatibility		All raw materials comply with the provisions of USP<88> for Class VI-121 ° C Plastic				

1 The pressure drop of pure water flow rate is 10kPa.

2 When selecting a reinforced adaptor for the product, it includes a reinforcing ring.

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3 Ordering Information*

3.1 Ordering Information of KPL Filter Cartridge

	Length	Pore Size	Adaptor	Sealing	Core
CRPVDFL	005=5" 010=10" 020=20" 030=30" 040=40"	020=0.20μm X20=0.20μm+0.20μm	0=DOE 1=222/Flat with SS insert 2=222/Flat 3=222/Fin 4=222/Fin with SS insert 5=226/Fin with SS insert 6=226/Fin 7=226/Flat 8=226/Flat with SS inser	S=Silicone E=EPDM N=NBR F=Fluorine Rubber	Blank=PP R=GF Reinforced PP S=316L Stainless Steel

* This information is a guide to the part number structure and possible options. For applications requiring autoclaving and sterilization, MS recommends the use of adaptor with SS insert to ensure filter sealing after cooling, If products that require autoclaving and sterilization use EPDM sealing rings and require customization. For availability of specific options and housing details, please contact MS.

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4 Microbial Retention Efficiency

4.1 Integrity Test

Bubble Point

This method is mainly based on the capillary model. In this model, the structure of the filter membrane is considered to be filled with microporous flow channels, which form many "capillaries". After the microfiltration membrane is completely wetted by the wetting liquid, the liquid is retained inside the membrane under the function of surface tension. If the liquid wants to be squeezed out of the membrane, an additional gas pressure is required. The minimum pressure required to overcome surface tension and completely extrude the liquid in the membrane pore is the bubble point pressure of the filter membrane, which is also the bubble point of the filter membrane.

Diffusion Flow/Forward Flow

This method is mainly based on the dissolution/diffusion model. After the filter membrane is completely wetted by the wetting liquid, if there is compressed gas on the upstream of the filter and the pressure value of the compressed gas is lower than the bubble point pressure, the gas concentration on the side of compressed gas will be higher than that on the other side, and the gas molecules in the high-pressure side will dissolve in the wetting liquid and diffuse to the atmospheric side. And a slow outflow of gas will be observed if a pipe is connected to the downstream. The gas flow on the low-pressure side is called diffusion flow, and the integrity test method by detecting diffusion flow is called diffusion flow test.

Pressure Hold/Pressure Decay

This method is also based on the dissolution/diffusion model. Strictly speaking, the data of this method cannot be correlated with the data of the bacteria retention test. However, when the operating conditions are determined, the pressure hold/pressure decay limits can be calculated based on the diffusion flow/forward flow test data.

4.2 Liquid Bacteria Challenge Test

4.2.1 Summary of Test Methods

The "FDA Guidelines for the Sterile Drug Industry" (1987 Edition) stipulates: "a filter which, when challenged with the microorganism Pseudomonas diminuta [nowcalled: *Brevundimonas diminuta*], at a minimum concentration of 10^7 organisms per cm^2 of filter surface, will produce a sterile effluent." The "FDA Guidelines for the Sterile Drug Industry" (2004 Edition) stipulates: "Sterilizing grade filter- A filter that, when appropriately validated, will remove all microorganisms from a fluid stream, producing a sterile effluent."

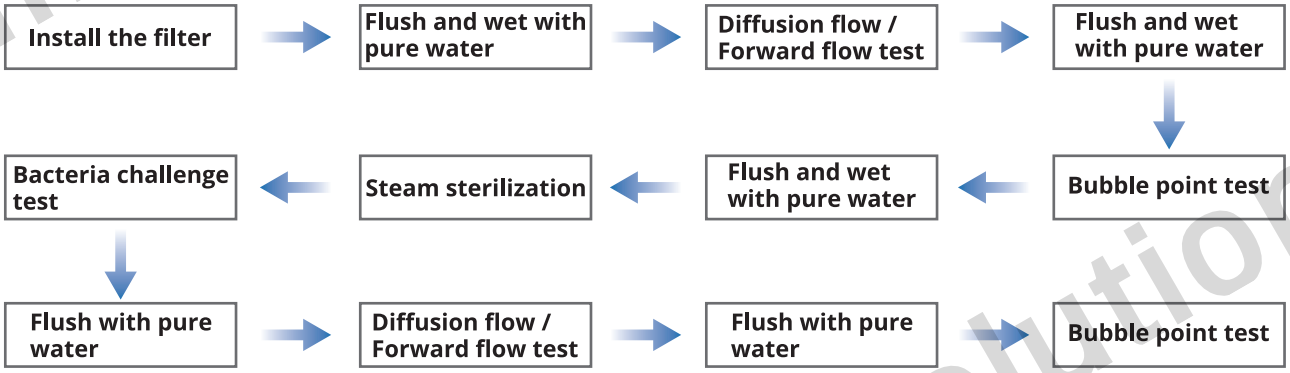
To meet the above requirements, the liquid challenge test uses Brevundimonas diminuta (ATCC 19146) to test 0.2μm hydrophilic PVDF filter cartridge, and the challenge quantity is greater than 10^7CFU/cm^2.

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The correlation between the bacteria retention efficiency test data and the non-destructive integrity test data of the sterilizing-grade filter cartridge is also an important aspect of the validation guide.The FDA guideline further states, “After a filtration process is properly validated for a given product, process and filter, it is important to assure that identical filter replacements (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”. "PDA No. 26 Technical Report" stipulates: "It generally is regarded as a CGMP requirement that filters or filter systems routinely be integrity tested both prior to and after use."

The purpose of this chapter's testing is to use Brevundimonas diminuta (ATCC 19146) bacterial suspension to perform water-based bacteria challenge testing on the 0.2μm hydrophilic PVDF filter cartridge. Associate the integrity test data of the filter with the bacteria challenge results, and determine the integrity limit of the sterilizing-grade filter.

The bacteria challenge test was conducted according to ASTM F838-15, and the testing steps are as follows:



Select KPL 0.2μm filter cartridges and KPL 0.2μm+0.2μm filter cartridges with a series of integrity data, and see Table (1) for specific models. This section considers that the packaging process of the filter membrane has the most significant impact on the bacteria retention performance of the filter in production. Therefore, all sizes of independent packaging components should be tested, while components further processed by independent packaging components do not require repeated validation.

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Table (1) Samples for Bacteria Challenge Testing*

Type	Art.No.	Size	Adaptor	Removal Ratings	EFA
Filter Cartridge	CRPVDFL0100205S	10 inch	226/Fin with SS insert	0.20 μm	0.65 m^2
	CRPVDFL010X205S	10 inch	226/Fin with SS insert	0.20 μm+0.2μm	0.55 m^2

* Due to the fact that the 20 inch filter cartridge and the 30 inch filter cartridge can be considered as further processed from the 10 inch filter cartridge, this section only validates the 5 inch and 10 inch filter cartridges.

Due to the fact that the adaptor form of the filter cartridge does not affect the bacteria retention performance of the filter, only a single adaptor will be validated in this section of the test.

Install the filter cartridge sample in the testing device shown in Figure (1), conduct diffusion flow/forward flow and bubble point tests in turn, and sterilize it at 121℃ (250° F) for 30 minutes. Then conduct a bacteria challenge test and an integrity test again after the challenge test.

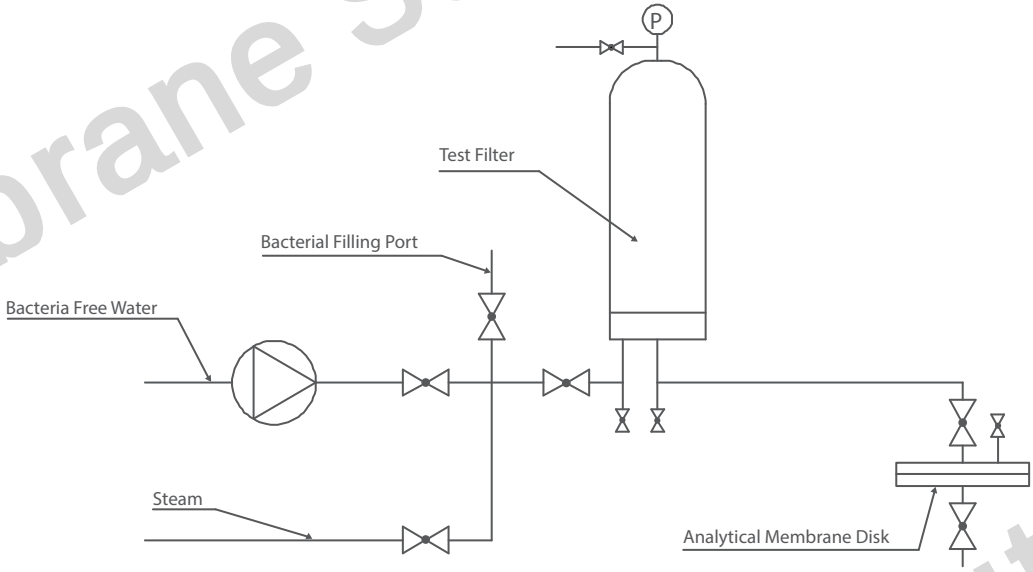


Figure (1) Liquid Bacteria Challenge Apparatus

During the bacteria challenge test, all the filtrate from the tested filter cartridge is passed through an analytical membrane disk located downstream of the tested filter cartridge, with an analytical membrane pore size of 0.45μm PES membrane. Attach the analytical membrane to TSA medium and culture it upside down at a suitable temperature. After 72 hours, check whether there are colonies on the analytical membrane disk.

The titer reduction value (T_R) of each filter cartridge can be calculated by the following formula:

$$T_R = \frac{\textbf{Total number of bacteria in filtrate to be filtered}}{\textbf{CFU on the analytical membrane}}$$

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When there are no colonies on the downstream analysis membrane, T_R can be expressed as:

$$T_R > \textbf{Total number of bacteria in filtrate to be filtered} (\text{eg.} > 7.4\times10^{10})$$

The logarithmic reduction value (LRV) of filter cartridge can be calculated by the following formula:

$$\textbf{LRV}=\log_{10}\frac{\textbf{Total number of bacteria in filtrate to be filtered}}{\textbf{CFU on the analytical membrane}}$$

When there are no colonies on the downstream analysis membrane, LRV can be expressed as:

$$\textbf{LRV}>\log_{10}\textbf{Total number of bacteria in filtrate to be filtered}$$

4.2.2 Test Results

Table (2) shows the integrity values and *B.diminuta* retention data of the CRPVDFL0100205S filter cartridge. From Table (2), it can be seen that among the 18 filter cartridges from 3 batches, the sample of diffusion flow ≤ 17.9mL/min, under the challenge of *B.diminuta* in quantity> 8.74×10^{10} CFU, the filtrates of all samples are sterile; the sample of bubble point ≥ 307.3kPa, under the challenge of *B.diminuta* in quantity> 8.74×10^{10} CFU, the filtrates of all samples are sterile.

Table (2) Correlation Between the Integrity of 10 inch KPL 0.2μm Pleated Filter Cartridge and *B.diminuta* Retention Efficiency

Serial Number	Initial diffusion flow* mL/min	Initial bubble point** kPa	Challenge quantity CFU	Filtrate colony CFU	T_R	LRV
137960BD080	8.3	377.3	9.26×10^{10}	0	> 9.26×10^{10}	> 10.97
140146BD045	8.6	454.0	9.18×10^{10}	0	> 9.18×10^{10}	> 10.96
140146BD076	8.7	380.9	9.45×10^{10}	0	> 9.45×10^{10}	> 10.98
140146BD062	9.4	378.1	1.04×10^{11}	0	> 1.04×10^{11}	> 11.01
137960BD010	10.1	371.6	9.75×10^{10}	0	> 9.75×10^{10}	> 10.99
140146BD029	10.7	385.7	1.10×10^{11}	0	> 1.10×10^{11}	> 11.04
137960BD079	11.0	467.2	9.77×10^{10}	0	> 9.77×10^{10}	> 10.99
145891BD033	11.9	421.2	9.51×10^{10}	0	> 9.51×10^{10}	> 10.98
145891BD040	12.6	318.5	9.23×10^{10}	0	> 9.23×10^{10}	> 10.97
137960BD034	12.9	310.9	9.12×10^{10}	0	> 9.12×10^{10}	> 10.96
140146BD086	12.9	425.3	8.74×10^{10}	0	> 8.74×10^{10}	> 10.94
137960BD066	13.3	423.3	8.83×10^{10}	0	> 8.83×10^{10}	> 10.95
145891BD061	13.8	307.3	1.10×10^{11}	0	>1.10×10^{11}	> 11.04
145891BD089	16.1	361.1	1.01×10^{11}	0	> 1.01×10^{11}	> 11.00
140146BD027	16.3	324.8	9.59×10^{10}	0	> 9.59×10^{10}	> 10.98
137960BD003	16.3	438.0	9.79×10^{10}	0	> 9.79×10^{10}	> 10.99
145891BD057	17.8	362.7	9.62×10^{10}	0	> 9.62×10^{10}	> 10.98
145891BD007	17.9	339.0	1.02×10^{11}	0	> 1.02×10^{11}	> 11.01

*The test pressure is 270 kPa, and the wetting liquid is pure water
**The wetting liquid is pure water

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Table (3) shows the integrity values and *B.diminuta* retention data of the CRPVDFL010X205S filter cartridge. From Table (3), it can be seen that among the 18 filter cartridges from 3 batches, the sample of diffusion flow ≤ 15.5mL/min, under the challenge of *B.diminuta* in quantity> 1.11×10^{11} CFU, the filtrates of all samples are sterile; the

Table (3) Correlation Between the Integrity of 10 inch KPL 0.2μm+0.2μm Pleated Filter Cartridge and *B.diminuta* Retention Efficiency

Serial Number	Initial diffusion flow*	Initial bubble point**	Challenge quantity	Filtrate colony	T_R	LRV
	mL/min	kPa	CFU	CFU		
113566DD054	4.9	480.8	1.20×10^{11}	0	$> 1.20\times10^{11}$	> 11.08
93255BD056	5.0	498.4	1.14×10^{11}	0	$> 1.14\times10^{11}$	> 11.06
113566DD059	5.2	394.2	1.11×10^{11}	0	$> 1.11\times10^{11}$	> 11.05
93255BD013	5.3	474.8	1.34×10^{11}	0	$> 1.34\times10^{11}$	> 11.13
134248BD080	6.3	477.4	1.34×10^{11}	0	$> 1.34\times10^{11}$	> 11.13
93255BD016	7.1	460.0	1.15×10^{11}	0	$> 1.15\times10^{11}$	> 11.06
93255BD065	7.2	373.0	1.14×10^{11}	0	$> 1.14\times10^{11}$	> 11.06
134248BD061	8.1	415.2	1.30×10^{11}	0	$> 1.30\times10^{11}$	> 11.11
134248BD035	9.6	335.2	1.30×10^{11}	0	$> 1.30\times10^{11}$	> 11.11
113566DD076	10.3	347.5	1.17×10^{11}	0	$> 1.17\times10^{11}$	> 11.07
93255BD071	11.5	498.6	1.17×10^{11}	0	$> 1.17\times10^{11}$	> 11.07
113566DD011	11.6	303.9	1.25×10^{11}	0	$> 1.25\times10^{11}$	> 11.1
113566DD005	11.7	369.0	1.13×10^{11}	0	$> 1.13\times10^{11}$	> 11.05
134248BD023	11.9	327.7	1.32×10^{11}	0	$> 1.32\times10^{11}$	> 11.12
134248BD015	12.4	444.2	1.14×10^{11}	0	$> 1.14\times10^{11}$	> 11.06
134248BD055	13.1	373.6	1.12×10^{11}	0	$> 1.12\times10^{11}$	> 11.05
93255BD034	15.1	349.7	1.19×10^{11}	0	$> 1.19\times10^{11}$	> 11.08
113566DD088	15.5	324.9	1.11×10^{11}	0	$> 1.11\times10^{11}$	> 11.05

*The test pressure is 270 kPa, and the wetting liquid is pure water

**The wetting liquid is pure water

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4.2.3 Conclusions

According to the results of the validation test in this chapter, it is easy to see that both diffusion flow/forward flow and bubble point are suitable non-destructive integrity testing methods for KPL 0.2μm hydrophilic PVDF filter cartridge and KPL 0.2μm+0.2μm hydrophilic PVDF filter cartridge. According to the test results, and considering the possible influence of filtration area on integrity and reasonable security boundary limits, the parameters of integrity test are as follows:

Table (4) Integrity Test Conditions

Wetting Liquid	Deionized water
Test Gas	Compressed Air
Test Ambient Temperature	25±2 ℃

Table(5) Limit Value of Diffusion Flow for KPL Filter Cartridge

Removal Ratings	Test Pressure	Limit Value of Diffusion Flow*				
		5 inch	10 inch	20 inch	30 inch	40 inch*
	kPa	mL/min	mL/min	mL/min	mL/min	mL/min
0.2 μm	270	7.5	15	30	45	60
0.2 μm+0.2 μm	270	5.5	11	22	33	44

*As the diffusion flow is proportional to the filtration area, the diffusion flow limit values for larger or smaller components are calculated from the validated diffusion flow limit values of the components

Table(6) Limit Value of Bubble Point for KPL Filter Cartridge

Removal Ratings	Bubble Point Limits**
	kPa
0.2 μm	340
0.2 μm+0.2 μm	340

** Due to the insensitivity of the bubble point of the component to the filtration area, the bubble point limit values of components of different sizes directly refer to the limits of similar components that have been validated.。

The limit value for pressure holding test can be calculated based on the quantity of product used and diffusion flow. If you need to know the calculation method for pressure holding test limit value, please contact us.

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4.3 Bacteria Challenge Testing after Repeated Sterilization

4.3.1 Summary of Test Methods

To validate that the filter cartridges and capsule filters can still achieve the expected bacteria retention effect after multiple moist heat sterilization. In this section, bacteria challenge test will be conducted on filter cartridges and capsule filters that have undergone multiple moist heat sterilization.

The testing method and testing device are the same as described in section 4.2. Challenge the KPL 0.2μm filter cartridge and KPL 0.2μm+0.2μm filter cartridge after multiple moist heat sterilization as shown in Table (7) using Brevundimonas diminuta (ATCC 19146) water-based bacterial suspension, with a challenge amount per unit effective filtration area >10^7 CFU.The samples used for bacteria challenge test were sourced from the tested filter cartridges in section 4.2.

Table (7) Moist Heat Sterilization Conditions and Sample Models of KPL Filter Cartridge

Type	Models	Removal Ratings	Sterilization Method	Sterilization Parameters
Filter Cartridge	CRPVDFL0100205S	0.2 μm	SIP A	Sterilization temperature: 124 ± 2 ° C, Sterilization time: 30 ± 1 minute, Sterilization frequency: 150 times.
	CRPVDFL0100205S	0.2 μm	SIP B	Sterilization temperature: 134 ± 2 ° C, Sterilization time: 20 ± 1 minute, Sterilization frequency: 150 times.
Filter Cartridger	CRPVDFL010X205S	0.2 μm+0.2 μm	SIP A	Sterilization temperature: 124 ± 2 ° C, Sterilization time: 30 ± 1 minute, Sterilization frequency: 150 times.
	CRPVDFL010X205S	0.2 μm+0.2 μm	SIP B	Sterilization temperature: 134 ± 2 ° C, Sterilization time: 20 ± 1 minute, Sterilization frequency: 150 times.

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4.3.2 Test Results

Table (8) and Table (9) show the bacteria challenge results of KPL 0.2μm filter cartridge and KPL 0.2μm+0.2μm filter cartridge after multiple moist heat sterilization.

Table (8) Bacteria Challenge Results of KPL 0.2μm Filter Cartridge

Sterilization Conditions	Models	Serial Number	Diffusion Flow before Challenge	Challenge Quantity	Filtrate Colony	T_R	LRV
			ml/min	CFU	CFU		
SIP A	CRPVDFD0100205S	145891BD049	9.3	9.52×10^{10}	0	$> 9.52\times10^{10}$	> 10.98
		137960BD039	12.6	9.21×10^{10}	0	$> 9.21\times10^{10}$	> 10.96
SIP B	CRPVDFL010X205S	140146BD066	10.6	9.33×10^{10}	0	$> 9.33\times10^{10}$	> 10.97
		137960BD062	12.3	9.47×10^{10}	0	$> 9.47\times10^{10}$	> 10.98

Table (9) Bacteria Challenge Results of KPL 0.2μm+0.2μm Filter Cartridge

Sterilization Conditions	Models	Serial Number	Diffusion Flow before Challenge	Challenge Quantity	Filtrate Colony	T_R	LRV
			ml/min	CFU	CFU		
Autoclaving A	CRPVDFD0100205S	113566DD031	8.8	9.68×10^{10}	0	$> 9.68\times10^{10}$	> 10.98
		134248BD009	10.2	9.10×10^{10}	0	$> 9.10\times10^{10}$	> 10.96
Autoclaving C	CRPVDFL010X205S	113566DD097	8.2	9.27×10^{10}	0	$> 9.27\times10^{10}$	> 10.97
		134248BD096	7.3	9.45×10^{10}	0	$> 9.45\times10^{10}$	> 10.98

4.3.3 Conclusions

From the test results, it can be seen that after multiple moist heat sterilization, the integrity of KPL 0.2μm filter cartridge and KPL 0.2μm+0.2μm filter cartridge still holds a correlation with the bacteria challenge results. The retention effect of the filter cartridge on the corresponding bacterial species meets the expectations and relevant regulatory requirements.

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5 Studies on Physical Characteristics

5.1 Pure Water Flow Rate-Differential Pressure

5.1.1 Summary of Test Methods

The purpose of this section is to determine the flow-differential pressure relationship of KPL 0.2μm filter cartridge and KPL 0.2μm+0.2μm filter cartridge when filtering pure water at room temperature. To avoid the impact of product interfaces, the filter cartridge used in the test uses a 226/fin lined with stainless steel adaptor. The specific sample models are shown in Table (10). Due to their similar structure, the flow-differential pressure relationship of other size filter cartridges in pure water filtration is converted using data from 10 inch filter cartridges.

Table (10) Samples for Pure Water Flow Rate-Differential Pressure Test*

Art.No.	Size	Removal Ratings	Adaptor	Serial Number
CRPVDFL0100205S	10 inches	0.2 μm	226/Fin with SS insert	145891BD004
				145891BD014
				140146BD033
				140146BD068
				137960BD018
				137960BD045
CRPVDFL010X205S	10 inches	0.2 μm+ 0.2 μm	226/Fin with SS insert	113566DD032
				113566DD085
				93255BD041
				93255BD084
				134248BD064
				134248BD082

*Some samples may be used for testing other than cleanliness testing after undergoing pure water flow rate-differential pressure testing.

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The filter cartridge is installed in the testing device shown in Figure (2). Before starting the test, flush the filter cartridge with deionized water to fully wet it. The flushing and testing water flow directions of the filter cartridge are both outward in and inward out, while the flushing and testing water flow directions of the capsule filter are both upward in and downward out.

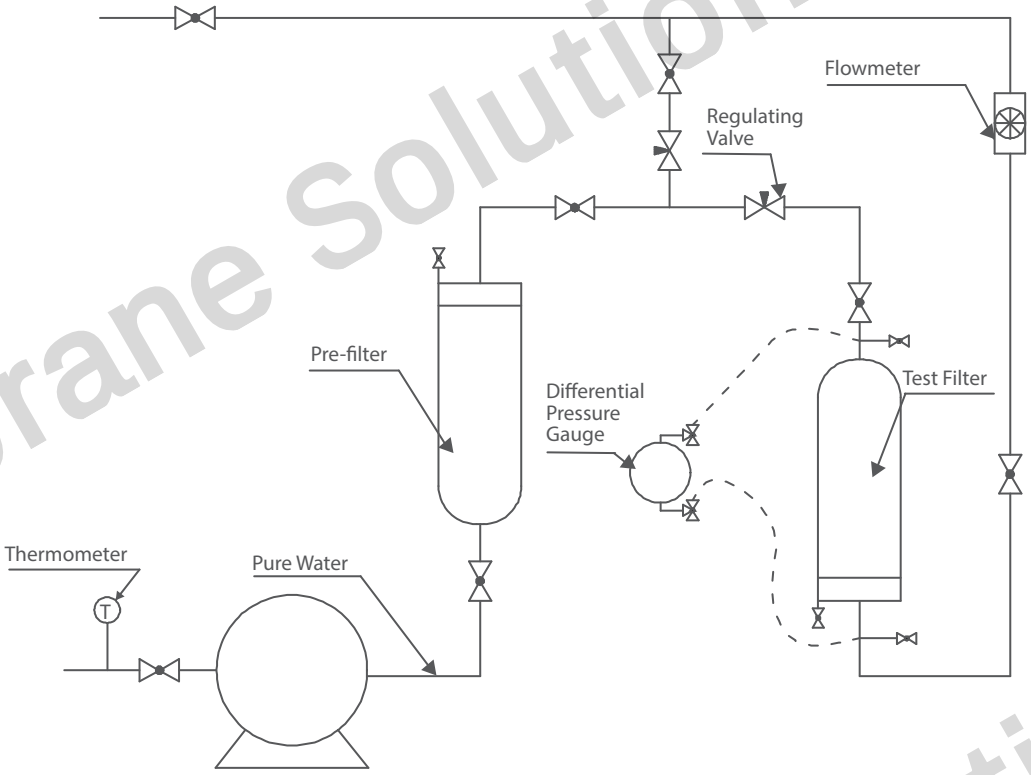


Figure (2) Pure Water Flow Rate Test Apparatus

During the testing process, the pure water flow rate in the pipeline is controlled by adjusting the inlet valve. After the flow rate and differential pressure readings stabilize, record flow rate, differential pressure and temperature data. Then test and record flow rate, differential pressure and temperature data of testing system in the same way. After converting all differential pressure data to standard values at 25 ° C/77 ° F, deduct the system flow rate-differential pressure data as blank.

5.1.2 Test Results

Calculate the average value of the flow rate-differential pressure of tested filter cartridge, and draw a flow rate-differential pressure diagram, as shown in Figure (3) and Figure (4). These data can be used as the basis for calculating the flow rate of KPL 0.2μm filter cartridge and KPL 0.2μm+0.2μm filter cartridge with different sizes in other fluids.

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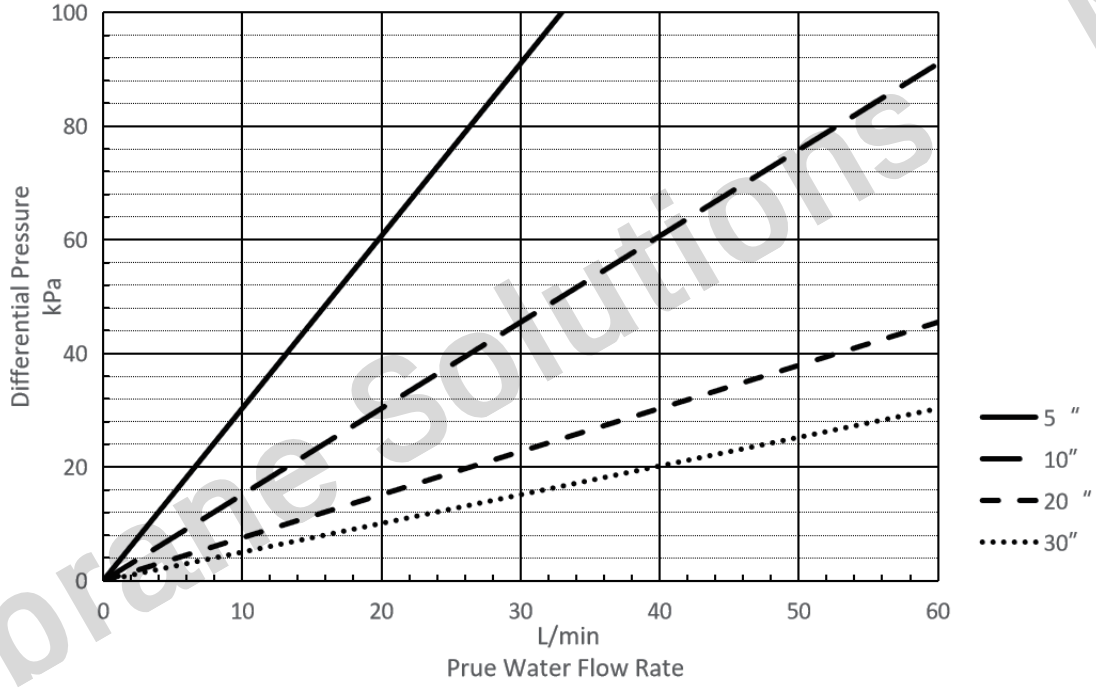


Figure (3) Pure Water Flow Rate-Differential Pressure for 5-30 inch KPL 0.2µm Filter Cartridge*

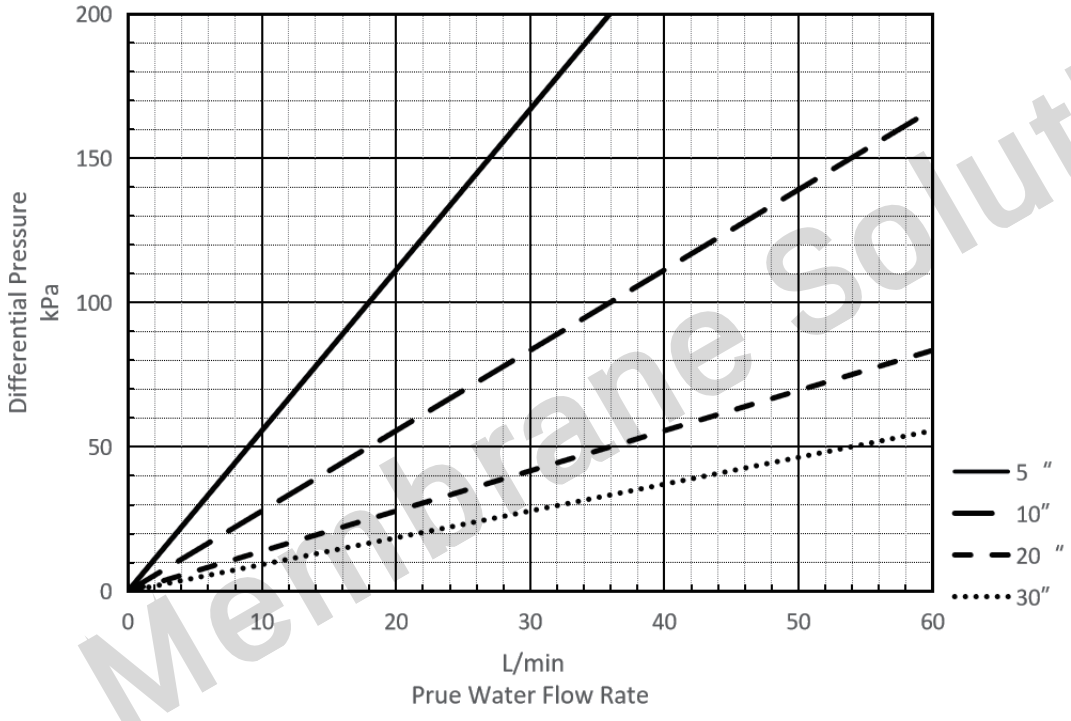


Figure (4) Pure Water Flow Rate-Differential Pressure for 5-30 inch KPL 0.2µm+ 0.2µm Filter Cartridge*

*The above differential pressure is suitable for liquids with 1 cp viscosity. The differential pressure of the filter cartridge in other viscosity fluids or temperatures can be estimated by multiplying the above values by the actual viscosity. To obtain the total differential pressure of the complete filter, must add the differential pressure of the housing.

5.2 Resistance to High Temperature and Moist Heat Sterilization

5.2.1 Summary of Test Methods

The purpose of this section is to determine the effect of high temperature and moist heat sterilization (124℃ and 134℃) on the integrity of KPL 0.2μm filter cartridge and KPL 0.2μm+0.2μm filter cartridge. Moist heat sterilization generally includes offline high-pressure steam sterilization and SIP. During the SIP process, the filter cartridge needs to withstand differential pressure, so the risk of filter cartridge failure is higher than that of offline high-pressure steam sterilization.

The filter cartridges used in this test are CRPVDFL0100205S and CRPVDFL010X205S. After thoroughly flushing and wetting the filter cartridges with deionized water, install them in the testing device shown in Figure (5) and introduce saturated steam for SIP. The test adopts a forward steam sterilization method, with a single sterilization time of 30 minutes (124 ℃) and 20 minutes (134 ℃). Control the differential pressure between the front and rear ends of the filter cartridge in steam sterilization at a relatively high level (30kPa and 15kPa respectively). After reaching the sterilization time, cool at room temperature for 1 hour and conduct integrity testing every 5 SIP tests.

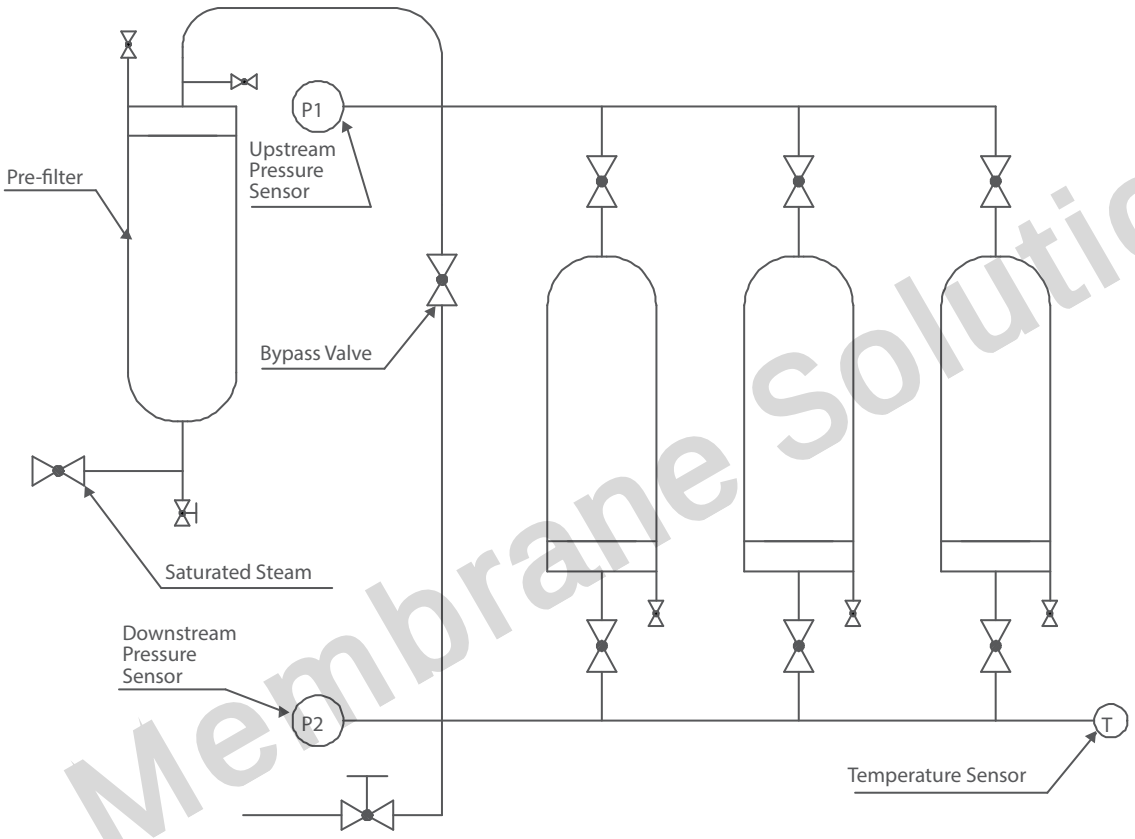


Figure (5) Steam Sterilization Resistance Testing Device

Membrane Solutions

5.2.2 Test Results

The diffusion flow of KPL 0.2μm hydrophilic PVDF filter cartridge samples after 150 cycles of SIP at 124 ° C for 30 minutes meets the corresponding limit value, and the results are shown in Table (11).

Table (11) The Influence of 124℃ SIP on Diffusion Flow/Forward Flow of KPL 0.2μm Filter Cartridges

Models	Removal Ratings	Serial Number	Initial	30 Cycles	50 Cycles	100 Cycles	150 Cycles
			mL/min	mL/min	mL/min	mL/min	mL/min
CRPVDFL0100205S	0.20 μm	145891BD049*	6.9	6.2	9.6	8.8	9.3
		140146BD073	9.1	8.5	9.1	9.9	10.2
		140146BD091	11.5	11.7	13.6	11.9	10.7
		137960BD013	10.5	10.4	9.0	10.8	11.4
		137960BD039*	9.1	8.8	7.3	9.3	12.6

The test pressure in the diffusion flow test is 270 kPa.

*The samples were selected for bacteria challenge testing, and the specific test results are shown in Chapter 4.3.

The diffusion flow of KPL 0.2μm hydrophilic PVDF filter cartridge samples after 150 cycles of SIP at 134 ° C for 20 minutes meets the corresponding limit value, and the results are shown in Table (12).

Table (12) The Influence of 134℃ SIP on Diffusion Flow/Forward Flow of KPL 0.2μm Filter Cartridges

Models	Removal Ratings	Serial Number	Initial	30 Cycles	50 Cycles	100 Cycles	150 Cycles
			mL/min	mL/min	mL/min	mL/min	mL/min
CRPVDFL0100205S	0.20 μm	145891BD091	7.6	6.8	7.5	6.9	8.6
		145891BD099	8.9	8.9	8.3	7.7	9.9
		140146BD066*	8.4	7.4	7.0	8.4	10.6
		140146BD098*	8.1	8.2	10.3	7.8	9.8
		137960BD062	12.5	12.0	11.1	13.7	12.3

The test pressure in the diffusion flow test is 270 kPa.

*The samples were selected for bacteria challenge testing, and the specific test results are shown in Chapter 4.3.

Membrane Solutions

The diffusion flow of KPL 0.2μm+ 0.2μm hydrophilic PVDF filter cartridge samples after 150 cycles of SIP at 124 ° C for 30 minutes meets the corresponding limit value, and the results are shown in Table (13).

Table (13) The Influence of 124℃ SIP on Diffusion Flow/Forward Flow of KPL 0.2μm+0.2μm Filter Cartridges

Models	Removal Ratings	Serial Number	Initial	30 Cycles	50 Cycles	100 Cycles	150 Cycles
			mL/min	mL/min	mL/min	mL/min	mL/min
CRPVDFL010X205S	0.20 μm+0.20 μm	113566DD031*	6.8	6.8	7.6	5.9	8.8
		113566DD096	7.9	7.3	6.3	7.2	6.8
		93255BD059	6.1	6.3	5.4	8.1	7.1
		93255BD076	10.5	9.6	8.8	10.1	8.5
		134248BD009*	9.2	10.0	8.6	9.4	10.2

The test pressure in the diffusion flow test is 270 kPa.

*The samples were selected for bacteria challenge testing, and the specific test results are shown in Chapter 4.3.

The diffusion flow of KPL0.2μm+ 0.2μm hydrophilic PVDF filter cartridge samples after 150 cycles of SIP at 134 ° C for 20 minutes meets the corresponding limit value, and the results are shown in Table (14).

Table (14) The Influence of 134℃ SIP on Diffusion Flow/Forward Flow of KPL0.2μm+0.2μm Filter Cartridges

Models	Removal Ratings	Serial Number	Initial	30 Cycles	50 Cycles	100 Cycles	150 Cycles
			mL/min	mL/min	mL/min	mL/min	mL/min
CRPVDFL010X205S	0.20 μm+0.20 μm	113566DD072	7.4	7.5	10.5	7.9	8.2
		113566DD097*	7.3	7.0	8.1	7.1	8.2
		93255BD040	6.1	5.6	6.1	4.9	6.4
		134248BD077	5.8	5.9	5.5	6.8	6.1
		134248BD096*	5.7	7.9	5.1	6.7	7.3

The test pressure in the diffusion flow test is 270 kPa.

*The samples were selected for bacteria challenge testing, and the specific test results are shown in Chapter 4.3.

After the test, samples with significant fluctuations in diffusion flow were selected for bacteria challenge testing. The results are shown in 4.3.

Membrane Solutions

5.2.3 Conclusions

After 150 cycles of steam sterilization at 124 °C and 150 cycles of steam sterilization at 134 °C of 10 inch KPL 0.2μm filter cartridge and KPL 0.2μm+0.2μm filter cartridge, the diffusion flow of all samples met the release standards. Based on the risk analysis of the filter structure and production process, the risk of failure of the 10 inch filter cartridge during testing is not lower than that of other size filters, so it can represent the 5-40 inch filter cartridge. Due to the stricter environmental stress in terms of temperature change rate, high temperature, and differential pressure compared to offline sterilization, SIP can be used instead of offline high-pressure steam sterilization.

Due to significant differences between actual usage conditions and laboratory testing conditions, after adding a reasonable safety factor to the number of testing cycles, the following conclusions can be drawn:

Table (15) Number of Moist Heat Sterilization Resistance Times for KPL 0.2μm filter cartridge and KPL 0.2μm+0.2μm filter cartridge

Temperature	Time	Number of Cycles
124°C	30 minutes	30 cycles
134°C	20 minutes	30 cycles

Membrane Solutions

5.3 Resistance to Differential Pressure

5.3.1 Summary of Test Methods

The purpose of this section is to determine the effect of continuous forward/reverse differential pressure on the integrity of KPL 0.2μm filter cartridge and KPL 0.2μm+0.2μm filter cartridge at different temperatures.

In this testing process, the environmental stress is temperature and differential pressure. Therefore, the KPL 0.2μm filter cartridge with item number CRPVDFL0100205S was used as the test sample, which can cover the KPL 0.2μm+0.2μm filter cartridge of the same size from a risk perspective. At the same time, from the analysis of the force structure, the crushing risk of the 10 inch filter cartridge is higher than that of the 5 inch filter cartridge and equivalent to the 20-40 inch filter cartridge.

Install the filter cartridge to be tested in the testing device as shown in figure (6) and fully flush and wet the filter cartridge with pure water after the water temperature rises to the test temperature. Adjust the flow rate to 15L/min and after the flow rate stabilizes, add an inert blockage to the pipeline to be tested to increase the differential pressure of the filter cartridge. At the same time, adjust the valve to maintain the flow rate unchanged.

In the forward test, flush with deionized water for 1 hour each according to the pressure and temperature of test condition 1 to condition 5 listed in Table (16). In the reverse test, flush with deionized water for 1 hour each according to the pressure and temperature of test condition 6 to condition 10 listed in Table (16). After the test is completed, wait for the filter cartridge to cool to room temperature before testing the diffusion flow of the filter cartridge.

Table (16) Test Conditions of Resistance to Differential Pressure

Direction of compression	Condition	Temperature	Differential Pressure	Time
Forward (from outside to inside)	Condition 1	25±2°C	≥ 520 kPa	1 h
	Condition 2	40±3°C	≥ 450 kPa	1 h
	Condition 3	60±3°C	≥ 360 kPa	1 h
	Condition 4	80±3°C	≥ 270 kPa	1 h
	Condition 5	90±3°C	≥ 250 kPa	1 h
Reverse (from inside to outside)	Condition 6	25±2°C	≥ 210 kPa	1 h
	Condition 7	40±3°C	≥ 200 kPa	1 h
	Condition 8	60±3°C	≥ 180 kPa	1 h
	Condition 9	80±3°C	≥ 160 kPa	1 h
	Condition 10	90±3°C	≥ 150 kPa	1 h

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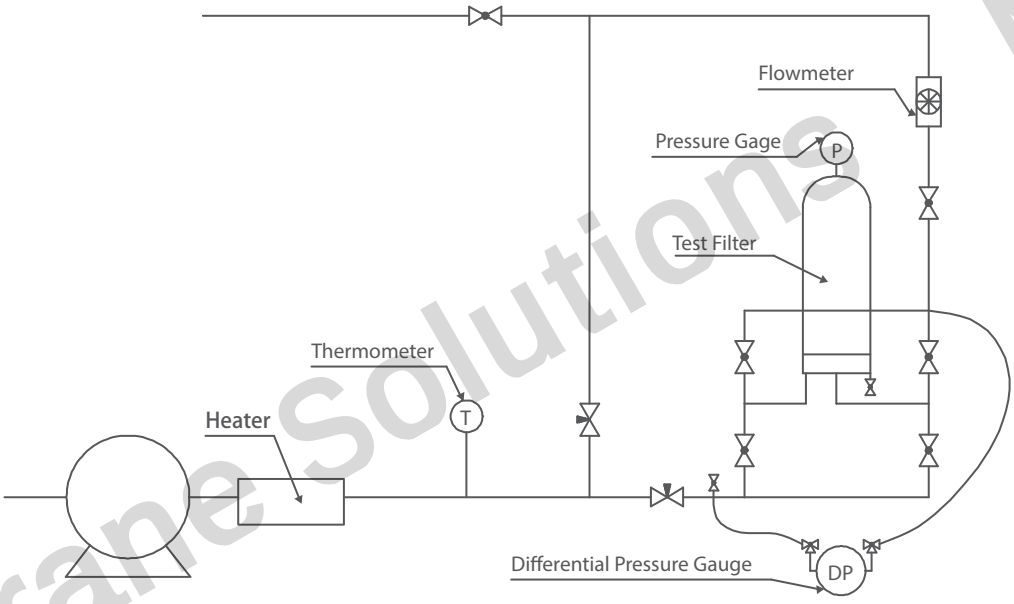


Figure (6) Testing Device of Differential Pressure Resistance

5.3.2 Test Results

Three KPL 0.2μm filter cartridges are sequentially flushed with pure water from condition 1 to condition 5 in a forward direction, while three KPL 0.2μm filter cartridges are sequentially flushed in a reverse direction from condition 6 to condition 10. The diffusion flow values before and after the test are shown in Table (17), and the integrity of all filter cartridges meets the relevant limits.

Table (17) Test Results of Forward/Reverse Differential Pressure Resistance

Models	Removal Ratings	Testing Direction	Serial Number	Diffusion Flow before Testing	Diffusion Flow after Testing
				mL/min	mL/min
CRPVDFL0100205S	0.20 μm	Forward	145891BD029	11.5	12.3
			145891BD054	7.9	10.2
			140146BD085	8.8	7.9
			137960BD024	9.4	8.7
			137960BD088	10.2	10.8
			145891BD095	11.0	12.5
		Reverse	140146BD071	8.4	10.2
			140146BD089	6.9	7.8
			137960BD044	12.0	11.8
			137960BD096	13.2	10.5

The test pressure in the diffusion flow test is 270 kPa..

Membrane Solutions

5.3.3 Conclusions

Based on risk analysis, the 10 inch filter cartridge in the samples validated in this section can represent 5-40 inch filter cartridges. Therefore, it can be proven that the forward and reverse pressure resistance of KPL 0.2μm filter cartridge and KPL 0.2μm+0.2μm filter cartridge comply with the following table.

Table (18) Forward and Reverse Pressure Resistance of KPL Filter Cartridge

Temperature	KPL 0.2μm Filter Cartridge		KPL 0.2μm+0.2μm Filter Cartridge	
	Forward	Reverse	Forward	Reverse
25°C	520 kPa	210 kPa	520 kPa	210 kPa
40°C	450 kPa	200 kPa	450 kPa	200 kPa
60°C	360 kPa	180 kPa	360 kPa	180 kPa
80°C	270 kPa	160 kPa	270 kPa	160 kPa
90°C	250 kPa	150 kPa	250 kPa	150 kPa

Membrane Solutions

6 Cleanliness Test

6.1 Non-Volatile Residue (NVR)

6.1.1 Summary of Test Methods

The purpose of this section of testing is to determine the total mass of non volatile residues removed from KPL 0.2μm filter cartridge and KPL 0.2μm+0.2μm filter cartridge in deionized water, acidic water, alkaline water, 50% ethanol (v/v), and 95% ethanol (v/v) at 40 ° C. These 5 extracting solutions represent actual potential contact solutions with different pH and polarity, and the test temperature is slightly higher than the normal contact temperature. The specific test conditions are shown in Table (19).

Table (19) Extraction Conditions

Type	Components	pH	Temperature	Temperature	Notes
Pure water	Deionized water	7±0.2	40±2°C	24 hours	-
Acid water	Hydrochloric acid, deionized water	3±0.2	40±2°C	24 hours	-
Alkaline water	Ammonia water, deionized water	10±0.2	40±2°C	24 hours	-
50% ethanol	Ethanol, deionized water	-	40±2°C	24 hours	v/v
95% ethanol	Ethanol, deionized water	-	40±2°C	24 hours	v/v

All samples in the test have KPL 0.2μm+0.2μm filter cartridges with the model CRPVDFL010X205S, and the sealing ring of this model of sample is silicone rubber. Due to the fact that the majority of extractable substances in the filter cartridge come from the filter membrane, the KPL 0.2μm+0.2μm dissolution level using a double-layer hydrophilic PVDF membrane will be higher than that of the same size KPL 0.2μm filter cartridge.

Before testing, soak all samples in no more than 200mL of pure water for 1 hour, and remove the wetting liquid from the wetted samples. Wrap the sample in aluminum foil and place it in a steam sterilizer, and heat treat at 121 ° C/250 ° F for 30 minutes to maximize the extractables. Before extraction, the sample is placed in a room temperature environment until the surface water droplets completely evaporate.

After installing the filter cartridge into the 316L stainless steel filter, add 1.2L of extracting solution and place it in a 40 ° C air bath shaker until the extraction is complete. After extraction, take 0.2-0.5 L of extracting solution and evaporate it to dryness. Weigh the residue and calculate the total mass of non-volatile residue (NVR) in all extracting solutions. Collect the residue and identify it using FITR.

Membrane Solutions

6.1.2 NVR Test Results

TThe extraction experimental results of filter cartridges are shown in Table (20) to Table (24). The NVR in the extracting solution of the product has a strong correlation with the filtration area of the filter and the extracting solvents.

Table (20) NVR of Samples Extracted with Pure Water

Art.No.	Removal Ratings	Serial Number	NVR	Average NVR
CRPVDFL010X205S	0.2 μm+0.2 μm	113566DD027	11.5 mg	10.0 mg
		93255BD029	8.8 mg	
		134248BD045	9.7 mg	

Table (21) NVR of Samples Extracted with Acid Solution

Art.No.	Removal Ratings	Serial Number	NVR	Average NVR
CRPVDFL010X205S	0.2 μm+0.2 μm	113566DD077	19.5 mg	20.7 mg
		93255BD023	13.2 mg	
		134248BD066	29.5 mg	

Table (22) NVR of Samples Extracted with Alkaline Solution

Art.No.	Removal Ratings	Serial Number	NVR	Average NVR
CRPVDFL010X205S	0.2 μm+0.2 μm	113566DD075	18.7 mg	15.3 mg
		93255BD064	12.4 mg	
		134248BD063	14.9 mg	

Table (23) NVR of Samples Extracted with 50% Ethanol

Art.No.	Removal Ratings	Serial Number	NVR	Average NVR
CRPVDFL010X205S	0.2 μm+0.2 μm	113566DD040	120.5 mg	88.9 mg
		93255BD006	78.6 mg	
		134248BD017	67.6 mg	

Table (24) NVR of Samples Extracted with 95% Ethanol

Art.No.	Removal Ratings	Serial Number	NVR	Average NVR
CRPVDFL010X205S	0.2 μm+0.2 μm	113566DD061	100.8 mg	129.0 mg
		93255BD042	138.5 mg	
		134248BD011	147.6 mg	

*This sample is used for FTIR identification, and the identification results are shown in the next chapter. Given that the differences between various types of filter cartridges are limited to aspects such as membrane pore size and filtration area, while the material and cleaning process are completely consistent, the latter has a crucial impact on the extractable types. Therefore, during the selection process, the result with the highest extractable level can be selected as the calibration sample.

Membrane Solutions

6.1.3 FTIR Test Results

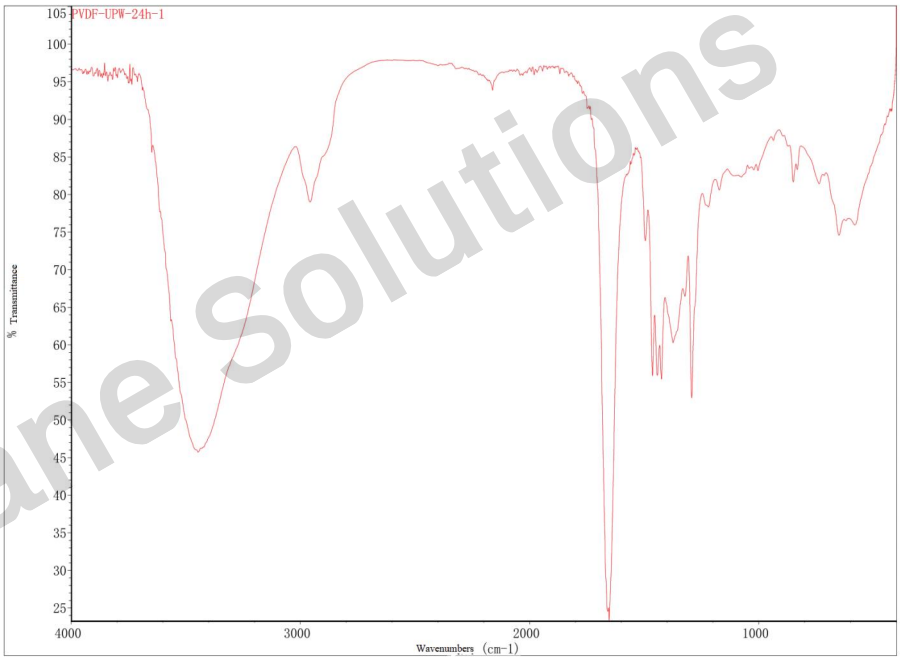


Figure (7) FTIR Spectra of NVR of KPL Series Filter Cartridges in Pure Water

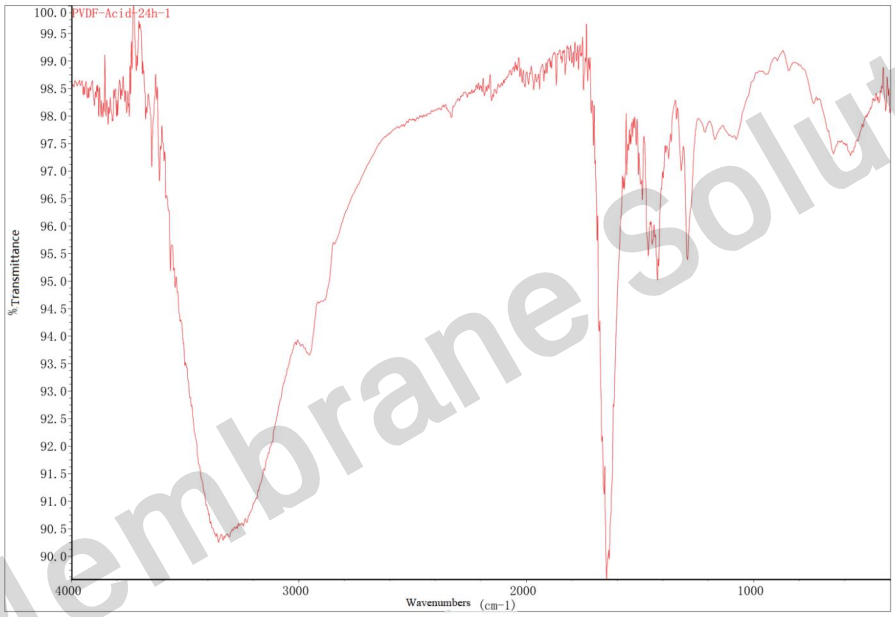


Figure (8) FTIR Spectra of NVR of KPL Series Filter Cartridges in Acid Water

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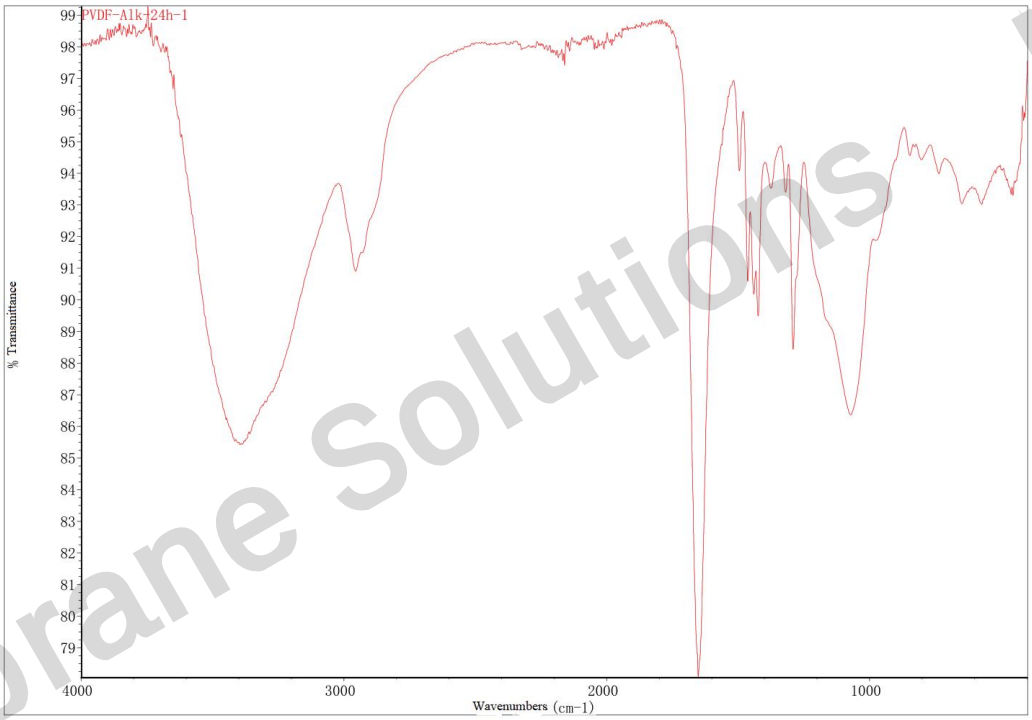


Figure (9) FTIR Spectra of NVR of KPL Series Filter Cartridges in Alkaline Water

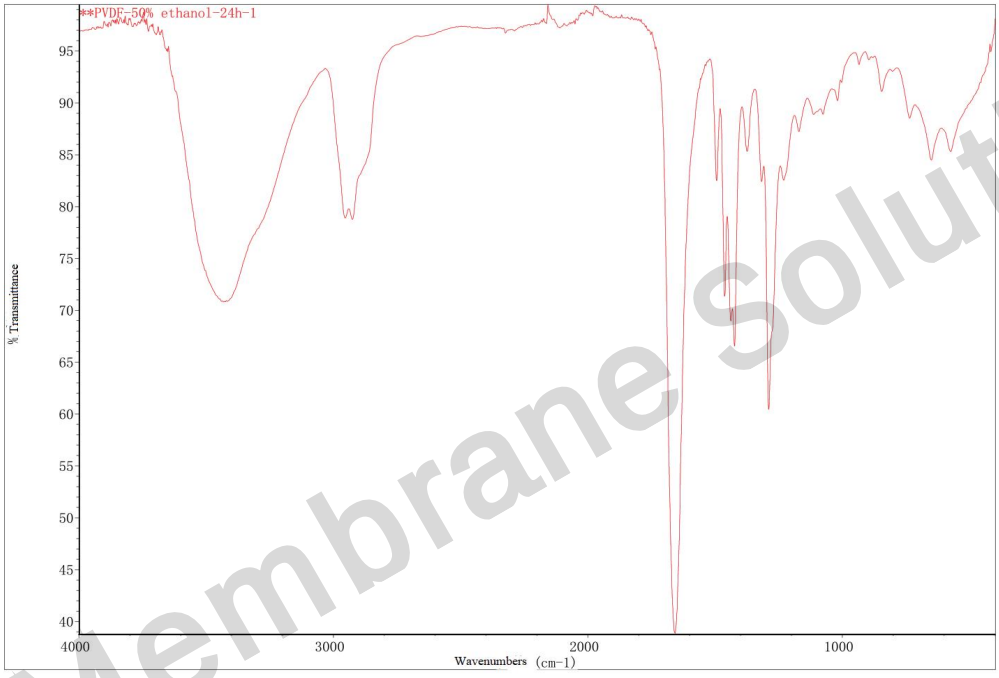


Figure (10) FTIR Spectra of NVR of KPL Series Filter Cartridges in 50% Ethanol

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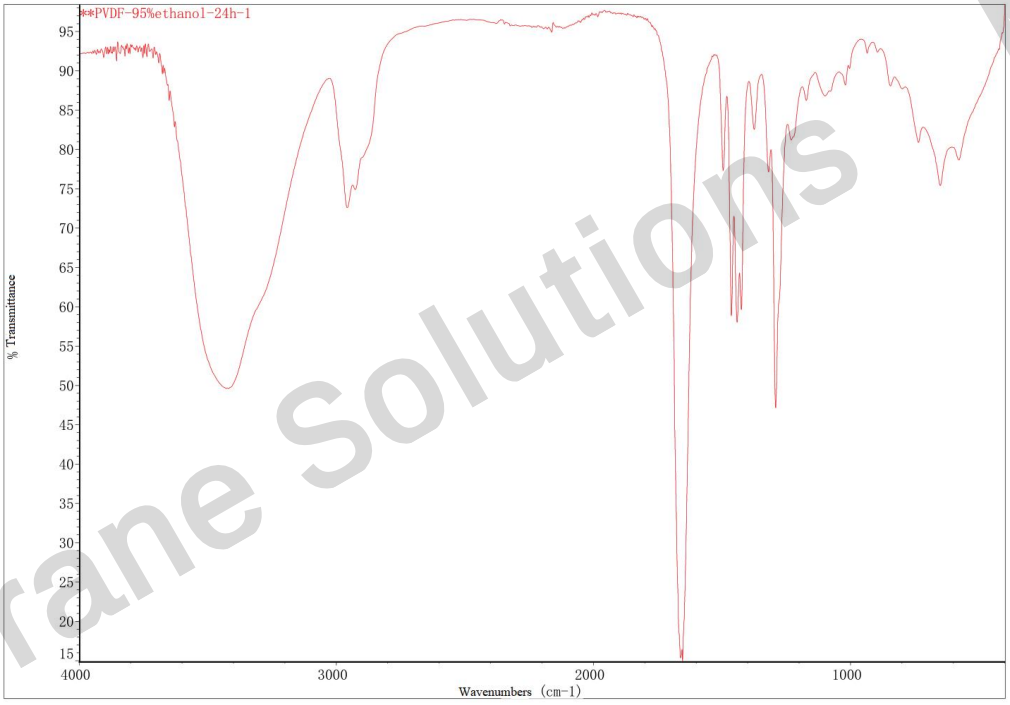


Figure (11) FTIR Spectra of NVR of KPL Series Filter Cartridges in 95% Ethanol

Membrane Solutions

6.1.4 Conclusions

From the NVR test results, it can be seen that the extraction level of the filter cartridge is influenced by the properties of the extracting solution. In typical model solution extraction tests, a 10" KPL 0.2μm+0.2μm filter cartridge with an effective filtration area of 0.55m^2 (actual membrane usage of 1.1m^2) has a lower extractable level. Qualitative analysis of the extraction residue using FTIR revealed that the main extractable component of the filter cartridge in all extraction solvents was PVP. PVP is one of the main raw materials for hydrophilic PVDF membranes, so it can be inferred that the extractable material comes from the filter membrane itself.

PVP (Polyvinylpyrrolidone), CAS No. 9003-39-8, chemical formula: (C6H9NO) n, also known as Povidone-iodine, Povidone, English nicknames K-30, PVP-K, etc., is a commonly used pore-forming agent. PVP is a kind of synthetic water-soluble polymer compounds widely used in industries such as industry, medicine, food, cosmetics, etc. According to relevant experimental analysis, PVP is not recognized as a genotoxic carcinogen. The carcinogenicity data of PVP is limited, and studies on the carcinogenicity of polyvinylpyrrolidone compounds with molecular weights of 20000, 22000, 50000, and 300000g/mol have shown that subcutaneous or intraperitoneal injection in animals did not induce tumors. Based on its negative genotoxicity and extensive medical application, PVP is not considered a genotoxic carcinogen.

The extractable levels of KPL 0.2μm filter cartridge and KPL 0.2μm+0.2μm filter cartridge are affected by different conditions during actual use, such as exposure time, temperature, pH, solution concentration, liquid polarity, etc. Therefore, it is recommended to evaluate the extractable level of the filter cartridge under actual working conditions based on the operating conditions used.

Membrane Solutions

6.2 Fiber Shedding and Release of Insoluble Particles

6.2.1 Summary of Test Methods

The purpose of this section of testing is to determine the downstream fiber shedding and insoluble particle shedding levels of KPL 0.2μm filter cartridge and KPL 0.2μm+0.2μm filter cartridge after being washed with deionized water at a constant flow rate. Due to the inability of insoluble particles and fibers to pass through a PVDF membrane with a pore size of 0.2μm, it can be inferred that the possible detachment of insoluble particles and fibers on the filter cartridge comes from the backflow surface of the filter membrane, downstream support layer, and other downstream accessories in the filter cartridge, and the likelihood of detachment is proportional to the filtration area. Therefore, based on the level of risk considerations, in this test, the KPL 0.2μm filter cartridge with model PVDFL0100205S was selected to represent other models and sizes of filter cartridges.

Before testing, soak and wet all filter cartridge samples in no more than 200mL of pure water for 1 hour, and remove the wetting solution from the wetted samples. Wrap the sample in aluminum foil and place it in a steam sterilization pot. Heat treatment at 121 ° C/250 ° F for 30 minutes. After sterilization, continue to wrap the sample in aluminum foil and place it in an open ultra clean workbench until it cools to room temperature. The flushing conditions and sampling conditions before sampling are shown in Table (25).

Table (25) Flushing Conditions for Filter Cartridge

Models	Removal Ratings	Flushing Flow Rate	Flushing Volume	Sampling Flow Rate
CRPVDFL0100205S	0.20μm	1 L/min	5 L	0.5 L/min

Filter cartridge sampling: Slowly load the sample into the testing device shown in Figure (12). After ensuring the cleanliness of the testing system, switch to the pipeline containing the filter to be tested. Open the water pump and adjust the valve to slowly fill the filter with pure water at a lower flow rate. After the water is discharged from the filter exhaust valve, open the downstream valve and adjust the flow rate to 1 L/min. After the flushing water reaches 5L, adjust the flow rate to 0.5 L/min. Take 3 consecutive samples, 1L each time.

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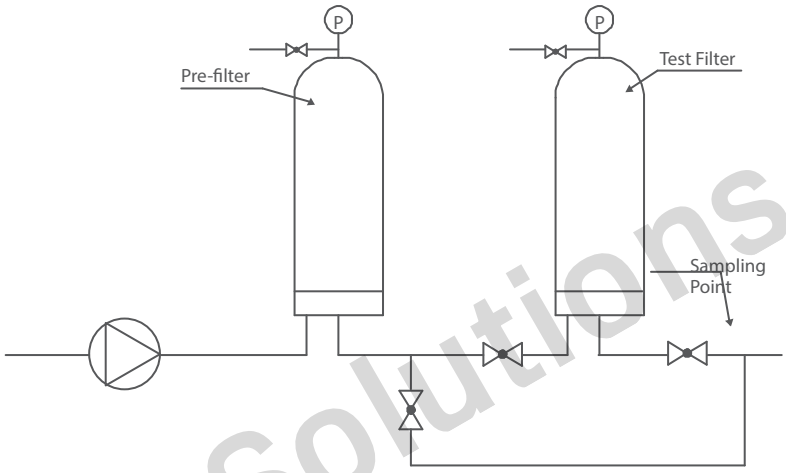


Figure (12) Fiber Shedding and Insoluble Particle Release Testing Apparatus

Fiber shedding: In the ultra clean workbench, filter the water samples with 0.8μm and φ47mm black grid membrane. Observe and count fibers that meet the definition of CFR21 210.3 intercepted on the grid membrane under an 80x microscope.

Insoluble particles: In the ultra clean workbench, use a particle counter (photoresist method) to sample and test, with each injection of 10mL. When the particle size >25μm in water sample and particles <3 particles/mL, particle size >10 μm and particles <25 particles/mL, the test passes.

Membrane Solutions

6.2.2 Test Results

The results of fiber shedding of all samples are shown in table (26). No shedding fibers were observed in the filtrates of 6L, 7L, and 8L, meeting the requirements of relevant regulations.

Table (26) Sample Fiber Shedding Level

Models		Removal Ratings	Serial Number	Fiber Shedding Quantity		
				6L	7L	8L
Filter Cartridge	CRPVDFL0100205S	0.20 μm	145891BD044	0	0	0
			140146BD083	0	0	0
			137960BD076	0	0	0

The release situation of insoluble particles in the sample is shown in Table (27). In the filtrates of 6L, 7L, and 8L, the particle count of ≥ 25μm and ≥10μm meets the requirements of relevant regulations.

Table (27) Release Levels of Insoluble Particles

Models		Removal Ratings	Serial Number	Fiber Shedding Quantity		
				6L	7L	8L
Filter Cartridge	CRPVDFL0100205S	0.20 μm	145891BD062	Pass	Pass	Pass
			140146BD018	Pass	Pass	Pass
			137960BD074	Pass	Pass	Pass

The release situation of insoluble particles in the sample is shown in Table (27). In the filtrates of 6L, 7L, and 8L, the particle count of ≥ 25μm and ≥10μm meets the requirements of relevant regulations.

Membrane Solutions

6.2.3 Conclusions

In daily use, after flushing as shown in Table (28), the product will not produce fiber shedding or insoluble particle release.

Table (28) Flushing Conditions

Models	length	Flow Rate	Time	Volume
KPL0.2μm Filter Cartridge KPL0.2μm+0.2μm Filter Cartridge	5"	≥ 0.6 L	≥ 5 minutes	≥ 3 L
	10"	≥ 1 L	≥ 5 minutes	≥ 5 L
	20"	≥ 2 L	≥ 5 minutes	≥ 10 L
	30"	≥ 3 L	≥ 5 minutes	≥ 15 L

Membrane Solutions

7 Biological Safety

7.1 Bacterial Endotoxin

7.1.1 Summary of Test Methods

The purpose of this test is to evaluate the bacterial endotoxin release levels of KPL 0.2μm filter cartridge and KPL 0.2 μm+0.2μm filter cartridge in pure water. The extraction method for bacterial endotoxin testing is the same as described in section 6.1.

After soaking the filter cartridge for 1 hour, use a pipette equipped with a non heat source gun to take 2mL of soaking solution from the extracting solution and transfer it into a 5mL non heat source test tube. The LAL method is used for testing, with a sensitivity of 0.25EU/mL of horseshoe crab reagent used to test the sample, and the positive and negative controls of the sample are reasonably set.

7.1.2 Test Results

The test results are shown in Table (29). The extracting solutions of all samples were negative in the LAL test. Representative extracting solution samples were selected to produce positive control for the test sample, and the set positive and negative control groups were normal.

Table (29) Bacterial Endotoxin Test Results

Models		Removal Ratings	Serial Number	Endotoxin Level	Result
Filter Cartridge	CRPVDFL0100205S	0.20 μm	145891BD013	< 0.25 EU/mL	Negative
			145891BD069	< 0.25 EU/mL	Negative
			140146BD087	< 0.25 EU/mL	Negative
			137960BD016	< 0.25 EU/mL	Negative
			137960BD064	< 0.25 EU/mL	Negative
Filter Cartridge	CRPVDFL010X205S	0.20 μm+0.20 μm	113566DD047	< 0.25 EU/mL	Negative
			113566DD079	< 0.25 EU/mL	Negative
			93255BD044	< 0.25 EU/mL	Negative
			134248BD043	< 0.25 EU/mL	Negative
			134248BD094*	< 0.25 EU/mL	Negative
Positive Sample	CRPVDFL010X205S	0.20 μm+0.20 μm	-	> 0.25 EU/mL	Positive
Positive Control			PC 1#	> 0.25 EU/mL	Positive
			PC 2#	> 0.25 EU/mL	Positive
Negative Control			NC 1#	< 0.25 EU/mL	Negative
			NC 2#	< 0.25 EU/mLL	Negative

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7.1.3 Conclusions

The KPL 0.2μm filter cartridge and KPL 0.2μm+0.2μm filter cartridge are all flushed with pure water (endotoxin <0.25 EU/mL) before leaving the factory, and enter the drying process on the same day. Therefore, the KPL 0.2μm filter cartridge and KPL 0.2μm+0.2μm filter cartridge have lower levels of bacterial endotoxin release in pure water.

7.2 Biocompatibility

The purpose of this section is to evaluate the biocompatibility of raw materials used in KPL filter cartridge. The materials used in KPL 0.2μm filter cartridge and KPL 0.2μm+0.2μm filter cartridge are as follows:

Table (30) Materials of KPL 0.2μm Filter Cartridge

Composition	Material	FDA 21CFR
Filter Medium	Polyvinylidene Fluoride	177.2510
Support/Drainage	Polypropylene	177.1520
Cage/End Cap/Adaptor	Polypropylene	177.1520
Sealing	Silicone	177.1210

Table (31) Materials of KPL 0.2μm+0.2μm Filter Cartridge

Composition	Material	FDA 21CFR
Pre-filtration Medium/ Filtration Medium	Polyvinylidene Fluoride	177.2510
Support/Drainage	Polypropylene	177.1520
Cage/End Cap/Adaptor	Polypropylene	177.1520
Sealing	Silicone	177.1210

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All the above materials meet the requirements of USP <87> and USP <88> Class VI-121 ° C Plastic. The tests are conducted in accordance with the Biological Reactivity Tests (in vivo) for Class VI Plastics (121 °C) as described in the current United States Pharmacopeia.

The testing procedures described in the USP include:

- Injection of extractables of plastic materials
- Implantation of plastic solid material

Four extracting solutions are listed in the USP that simulate parenteral fluids and body fluids, including:

- Sodium chloride injection
- 1:20 ethanol and sodium chloride injection
- Polyethylene glycol 400
- Vegetable oil (sesame oil or cottonseed oil)

The USP stipulates that the extractables can be prepared under the following three standard conditions: 50 °C (122 °F) for 72 hours, 70 °C (158 °F) for 24 hours, and 121 °C (250 °F) for 1 hour. It is recommended to choose the strictest condition not resulting in physical changes to the plastic. Therefore, the filter is extracted at 121°C/250°F, and the following tests are conducted:

- Acute Systemic Toxicity Test in Mice
- Rabbit Intradermal Stimulation Test
- Rabbit muscle implantation Test

The test results showed that all raw materials of the KPL 0.2μm filter cartridge and KPL 0.2μm+0.2μm filter cartridge showed no toxicity in the above tests, indicating that the filter cartridge meets the requirements of USP Class VI-121 ° C.

If you need a relevant test report, please contact us.

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Membrane Solutions

Address: 4530 B STREET NW #A, AUBURN WA 98001, USA

Phone: 001-866-528-4572

Email: info@membrane-solutions.com

Web: www.membrane-solutions.com

Membrane Solutions