GLOBAL FILTER
Filtration Group®

Validated Filtration Solutions to Industry Leaders®

Validation Guide

GBPES-series 0.2, 0.45, & 0.65 Micron Membrane Elements

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I. Technical Specifications

1. Mechanism of Filtration

The retention of particles and microorganisms is achieved by a sieving mechanism through the polyethersulfone filter membrane. The throughput is enhanced by the highly asymmetric pore structure of the polyethersulfone membrane.

2. Pore Size

0.2 µm, 0.45 µm, and 0.65 µm

3. Materials of Construction

All materials meet the FDA requirements as defined in Title 21 Code of Federal Regulations

Upstream Support Layer:
Polypropylene

Filter Membrane:
Polyethersulfone, single layer

Downstream Support:
Polypropylene

Outer Cage:
Polypropylene

Inner Core:
Polypropylene

End Caps and Adapters:
Polypropylene

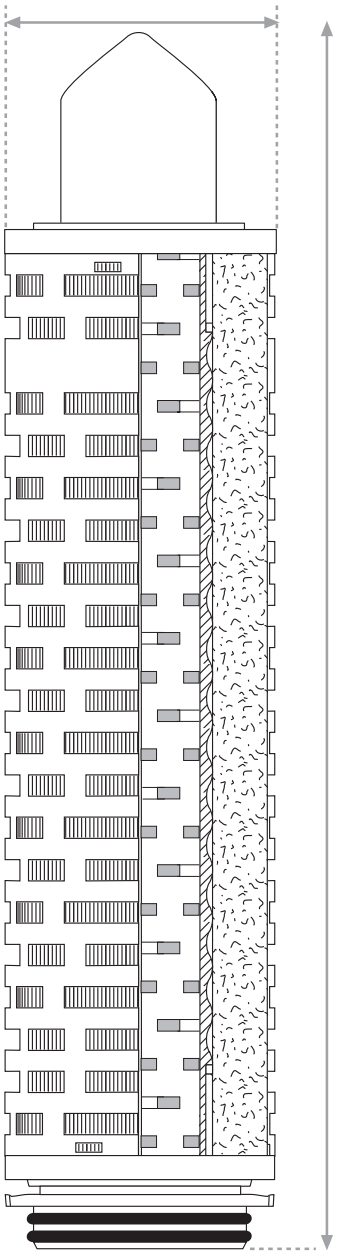
O-Rings|Gaskets:
Silicone

4. Height and Diameter

	Height				
Adapter	**10″**	**20″**	**30″**	**40″**	**Diameter**
Type 3 - 222/Flat	10.76″	20.41″	30.07″	39.72″	2.76″
Type 7 - 226/Fin	12.58″	22.33″	32.09″	41.84″	2.76″

± 0.10” per 10” length

Height measurements include adapter and fin where indicated in the diagram.



5. Maximum Differential Pressure

The maximum allowable differential pressure depends on the temperature at which the pressure is exerted. Maximum allowable differential pressures in the direction of filtration.

Temperature (°C)	20°	80°	121°
Pressure (bar)	5	2	0.5
Pressure (psi)	72.5	29	7.5

6. Wetting the Filters for Integrity Testing

For each 10"|250 mm filter cartridge, rinse the filters in the direction of flow for 5 minutes with a differential pressure of 0.3 bar|4 psi and back pressure 0.5 bar|7 psi in order to assure that the filters have been wetted completely. Generally, filters are wetted with water. In cases where a different wetting medium is used, if the surface tension of the fluid is different from water (> 70 dynes/cm), different integrity test values than indicated on the next page may be required.

7. Sterilization

Autoclaving of wet filter cartridges up to a maximum temperature of 134°C, for 30 minutes

or

In-line steam sterilization of wetted cartridges with a maximum of 2.3 bar|34 psi inlet pressure and 2 bar|29 psi outlet pressure (max. dP= 0.3 bar|5 psi).

8. Sanitization

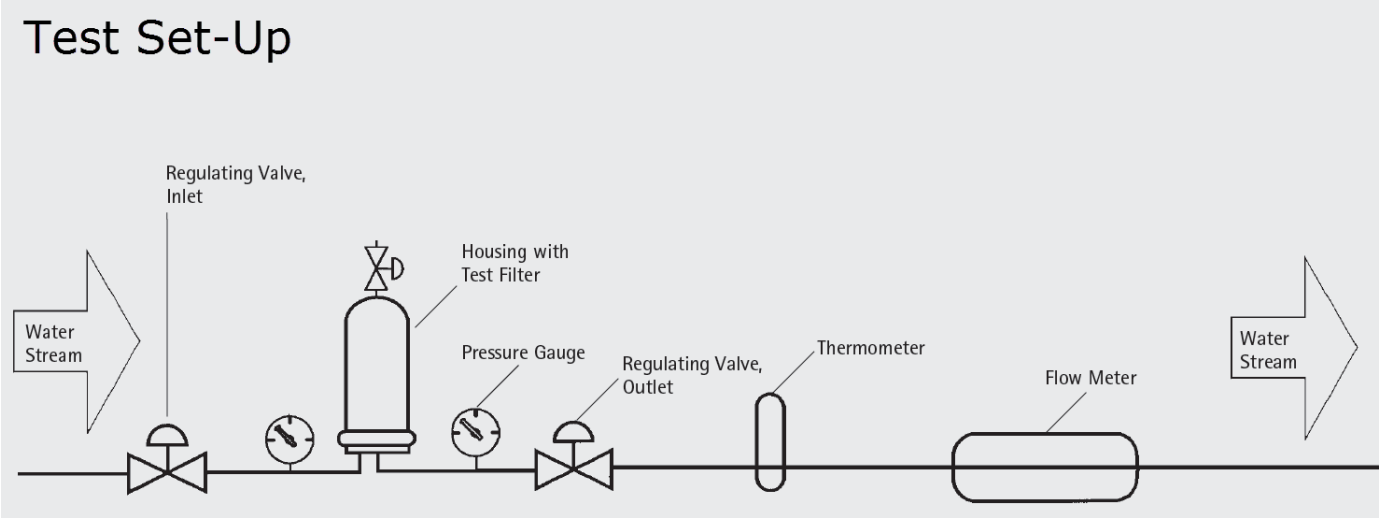
Sanitization with hot water (85°C)

Number of sanitization cycles: at least 100 cycles

9. Integrity Test Limits

Pore Size	Height	Test Pressure (bar|psi)	Max. Diffusion (ml/min)
0.2 µm	10″	2.5|36	21
	20″	2.5|36	42
	30″	2.5|36	63
	40″	2.5|36	84
0.45 µm	10"	1.5|21.8	15
	20″	1.5|21.8	30
	30″	1.5|21.8	45
	40″	1.5|21.8	60
0.65 µm	10"	1.0|14.5	13
	20″	1.0|14.5	26
	30″	1.0|14.5	39
	40″	1.0|14.5	52

II. Flow Rate



Background
Test filter cartridges are placed into a filter housing. The water inlet is opened and the filter housings are completely vented.

The filters are rinsed for approximately 5 minutes at 0.3 bar|4 psi differential pressure to assure complete wetting. The filter cartridges are then integrity tested to assure that only integral filters are tested. The inlet pressure (Pi) is held constant at 2.5 bar|36 psi.

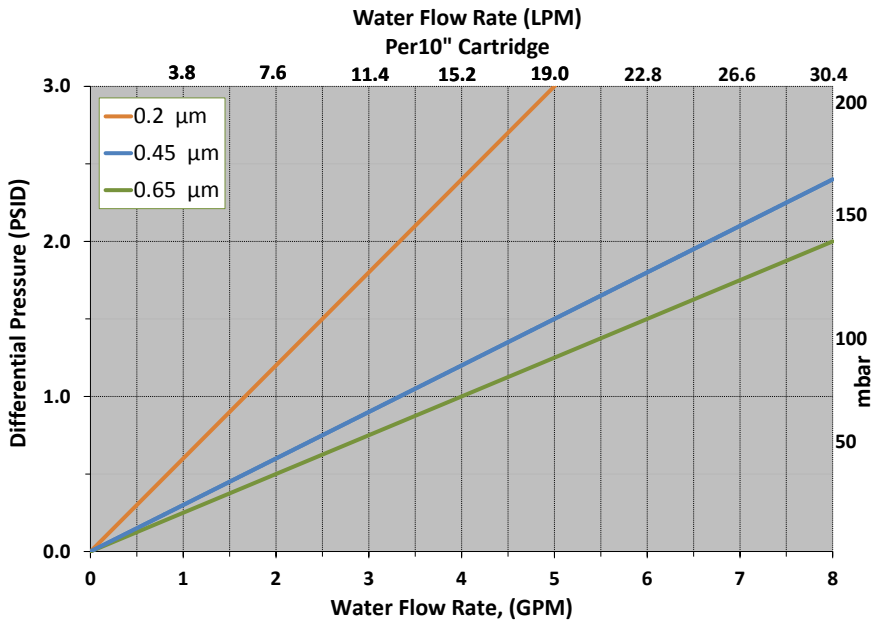
Through the adjustment of valves on the downstream side of the filter housing, the required differential pressure for the test measurements is established. After achieving a constant differential pressure, the flow rate is recorded from the flow meter and the temperature is noted. The flow meter used in this testing was a Fisher & Porter COPA XM Magnetic Inductive Flow Meter Model D10D1465.

Results
The flow rate curves for water through the filter cartridges of the various lengths versus differential pressure are on the following pages.

Note
The flow rate is strongly influenced by the viscosity of the medium being filtered. For this reason, all flow rate measurements are taken at 20°C so that the influence of temperature on viscosity is not a factor.

1. Membrane Filters

Flow Rate vs Pressure Drop



III. Chemical Compatibility

	Filter Cartridges with Optional O-Ring Materials		
	Silicone	**EPDM**	**Viton**
Acids:			
HCL, 30%	■	■	■
HCL, 25%	■	■	■
HNO_3, 10%	■	■	■
HNO_3, 65%	□	□	■
H_2SO_4, conc.	– –	– –	– –
H_2SO_4, 25%	□	■	■
H_3PO_4, 25%	□	■	■
Formic acid, conc.	– –	□	– –
Formic acid, 25%	□	■	□
Acetic acid, conc.	□	■	□
Acetic acid, 25%	– –	■	□
Trichloroacetic acid, 25%	□	■	– –
Trichloroacetic acid, 10%	□	■	– –
Citric acid	■	■	■
Tartaric acid	■	■	■
Lactic acid	■	■	■
Bases:			
Ammonia, 10%	□	■	– –
Ammonia, 30%	– –	■	– –
NaOH, 1 M	□	■	□
NaOH, 2.5 M	– –	■	– –
KOH, 1 M	□	■	□
Solvents:			
Acetone	– –	– –	– –
Cyclohexanone	– –	– –	– –
Methyl ethyl ketone	– –	– –	– –
Methyl isobutyl ketone	– –	□	– –
Diethyl ether	□	□	□
Methanol, 98%	■	■	■
Ethanol, 10 %	■	■	■
Ethanol, 98%	■	■	■
Isopropyl alcohol	■	■	■
n-Propanol	■	■	■
n-Amylalcohol	■	■	□
n-Butanol	■	■	■
Glycerol	■	■	■
Ethylene glycol	■	■	■
Methylene glycol	■	■	■
Dioxane	– –	– –	– –
Tetrahydrofuran	– –	– –	– –
Dimethyl sulfoxide	– –	– –	– –
Dimethylformamide	– –	– –	– –
Triethanolamine	□	□	■
Miscellaneous:			
Aniline	– –	– –	– –
Sodium hypochlorite	□	■	■
Benzyl alcohol	– –	– –	– –
Phenol, 10%	– –	– –	– –
Formalin, 30%	■	■	■
Hexane	□	□	■

Legend

■ = Compatible
□ = Limited compatibility
– – = Not compatible

Specifications

7 days contact time at 20°C

Important

Compatibility is influenced by various factors, such as temperature, concentration, mixture, etc. If necessary, a compatibility test should be performed with the solution to be filtered before the actual filtration run. For further assistance, please contact your Global Filter representative.

Legend

■ = Compatible
□ = Limited compatibility
– – = Not compatible

Specifications

7 days contact time at 20°C

Important

Compatibility is influenced by various factors, such as temperature, concentration, mixture, etc. If necessary, a compatibility test should be performed with the solution to be filtered before the actual filtration run. For further assistance, please contact your Global Filter representative.

	Filter Cartridges with Optional O-Ring Materials		
	Silicone	**EPDM**	**Viton**
Xylene	– –	– –	– –
Toluene	– –	– –	– –
Benzene	– –	– –	– –
Tetralin	– –	– –	– –
Decaline	□	– –	■
Methylene chloride	– –	– –	– –
Chloroform	– –	– –	– –
Carbon tetrachloride	– –	– –	– –
Trichloroethylene	– –	– –	– –
Perchloroethylene	– –	– –	■
Monochlorobenzene	– –	– –	– –
Methyl acetate	– –	– –	– –
Ethyl acetate	– –	– –	– –
Amyl acetate	□	■	– –
Propyl acetate	□	■	– –
Turpentine	□	– –	■
H_2O_2, 0.3%	■	■	■
Ammonium persulfate, 25%	■	■	■
Sodium hypochlorite, 0.3%	■	■	■
Starch solution	■	■	■
Water	■	■	■

IV. Integrity Test Limits

1. Basis for the Determination of Integrity Test Values

Establishing a correlation between bacterial retention of a membrane filter and a non-destructive integrity test is critical in order to ensure filter reliability prior to the filter being used to produce a sterile effluent. The FDA "Guidelines on Sterile Drug Products Produced by Aseptic Processing", June 1987 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. 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 filtration.

Test-Method

Several filter cartridges from numerous production lots were tested according to the Bacteria Challenge Test and DIN 58356, Part 1.

Test Organism

Pore Size 0.2 µm
Brevundimonas diminuta

Pore Size 0.45 µm
Lactobacillus lindneri

Pore Size 0.65 µm
Lactobacillus lindneri

Note

For validation studies of the filter cartridges, a minimum concentration of 1×10^7 microorganisms per cm^2 filtration area was used.

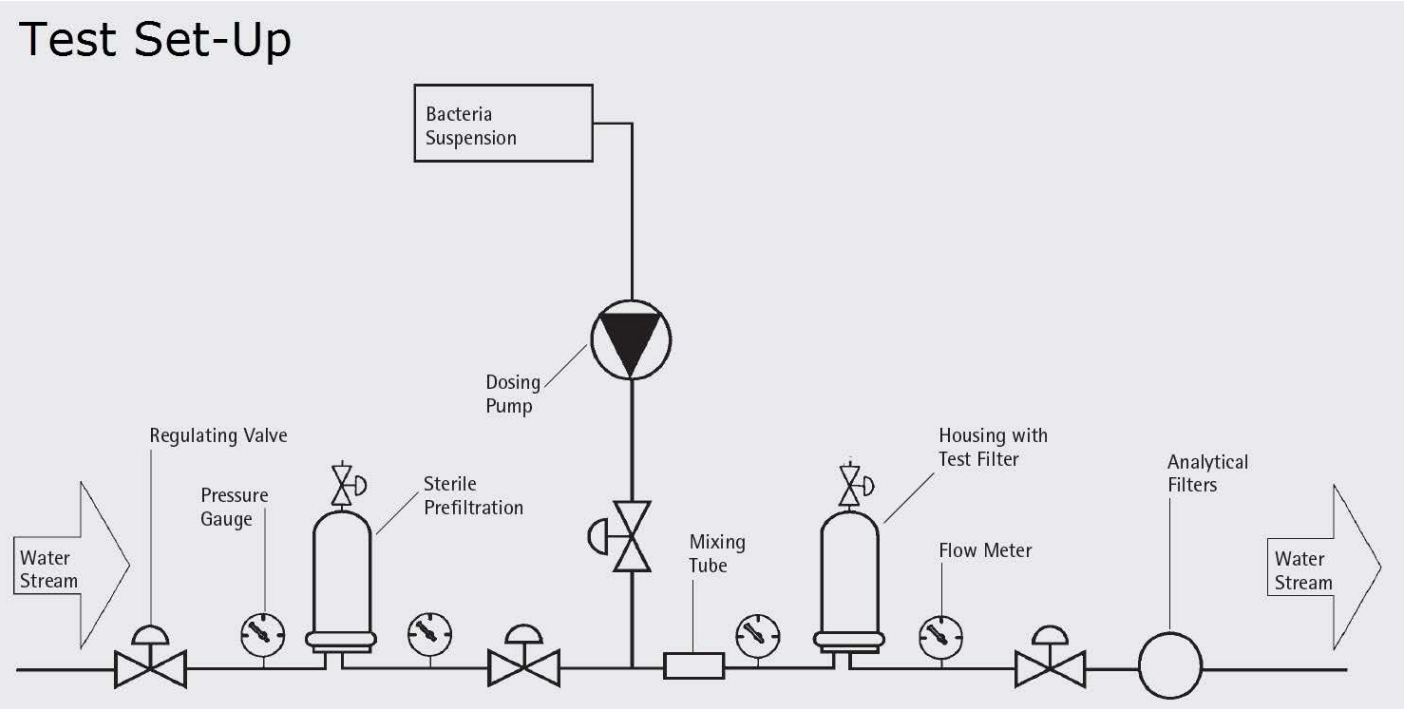
Integrity Test

The filter cartridges were integrity tested by Diffusion and Bubble Point Test methods in order to correlate the results of the destructive Bacteria Challenge Test with these non-destructive integrity tests.

The Diffusion Test and the Bubble-Point-Test are performed utilizing an automated integrity test unit.

The diffusion values are determined at the test pressure. For the determination of the bubble point, air pressure is slowly increased on the upstream side of the filter housing by an integrity tester.

2. HIMA Bacteria Retention Test



Water flow is initiated and the water stream first passes through a sterilizing grade filter cartridge. The purpose of this filter is to remove particles and bacteria to assure the Test Filter is only challenged with the bacterial load.

The bacterial challenge bio-burden that will be introduced to the test filter cartridge is controlled by dosing of the bacterial suspension into the water stream with a peristaltic pump. After the bacterial suspension is added to the water stream, the flow is directed through a mixing tube to ensure that proper mixing of the bacterial suspension has occurred. For the control and monitoring of the differential pressure during the Bacteria Challenge Test, pressure gauges and valves have been installed on the upstream and downstream side of the filter cartridges. The filtrate that passes through the test filter then flows through the analytical filters. After the completion of the Bacteria Challenge Test, these analytical filters can be examined according to the analytical methods described in the HIMA document.

Test Procedure
The filter cartridges are installed and wetted as described in the operating instructions. The filter system is then in-line steam sterilized.

In-line Steam Sterilization Parameter:
121°C, 1 bar|15 psi, for 30 minutes
The time is measured when the outlet of the filtration system has reached the sterilization temperature.

After the steam sterilization, the system is allowed to cool to room temperature. The system is then rinsed with water and the test filter is integrity tested. The water flow is controlled with the valuing of the system and set so that the bacterial suspension can be dosed into the water stream. After the Bacteria Challenge Test, the analytical filters are incubated on agar plates to determine if there was passage of bacteria through the test filter.

3. Diffusion Test Limits

Cartridge 0.2 µm

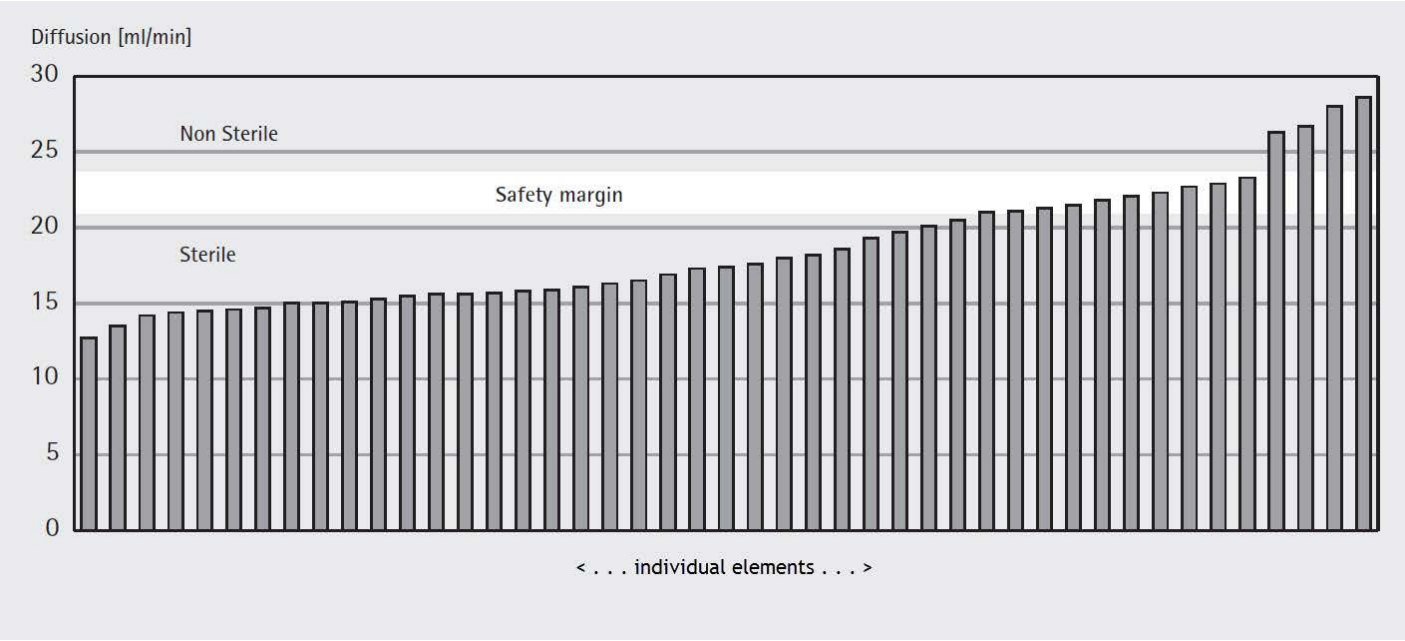
Note
Since most of the filter cartridges tested during the validation studies had low diffusion values and produced sterile filtrate, the following data is a sampling from all filters tested during the validation testing indicating results near the diffusion limits.

Bio-burden inlet values were in excess of $1x10^{10}$ Colony Forming Units.

Test Microorganism:
Brevundimonas diminuta

Lot Number	Diffusion Rate [ml/min.]	LRV
1025-1241	12.7	> 8
1025-1241	13.5	> 8
1025-0941	14.2	> 8
1025-0941	14.4	> 8
1025-1241	14.5	> 8
1025-0941	14.6	> 8
1025-1041	14.7	> 8
1025-0941	15.0	> 8
1025-0941	15.0	> 8
1025-1041	15.1	> 8
1025-0941	15.3	> 8
1025-0941	15.5	> 8
1025-1241	15.6	> 8
1025-1041	15.6	> 8
1025-1241	15.7	> 8
1025-0941	15.8	> 8
1025-0941	15.9	> 8
1025-1041	16.1	> 8
1025-5341	16.3	> 8
1025-1041	16.5	> 8
1025-1241	16.9	> 8
1025-5341	17.3	> 8
1025-1041	17.4	> 8
1025-5341	17.6	> 8
1025-1241	18.0	> 8
1025-5541	18.2	> 8
1025-1241	18.6	> 8
1025-1041	19.3	> 8
1025-5541	19.7	> 8
1025-0941	20.1	> 8
1025-5341	20.5	> 8
1025-5541	21.0	> 8
1025-1241	21.1	> 8
1025-1041	21.3	> 8
1025-1041	21.5	> 8
1025-5541	21.8	> 8
1025-0941	22.1	> 8
1025-5541	22.3	> 8
1025-1241	22.7	> 8
1025-1041	22.9	> 8
1025-5341	23.3	> 8
1025-0941	26.3	> 8
1025-0941	26.7	> 8
1025-0941	28.0	> 8
1025-0941	28.6	> 8

Cartridges (10”|250 mm), 0.2 µm



Cartridge 0.45 µm

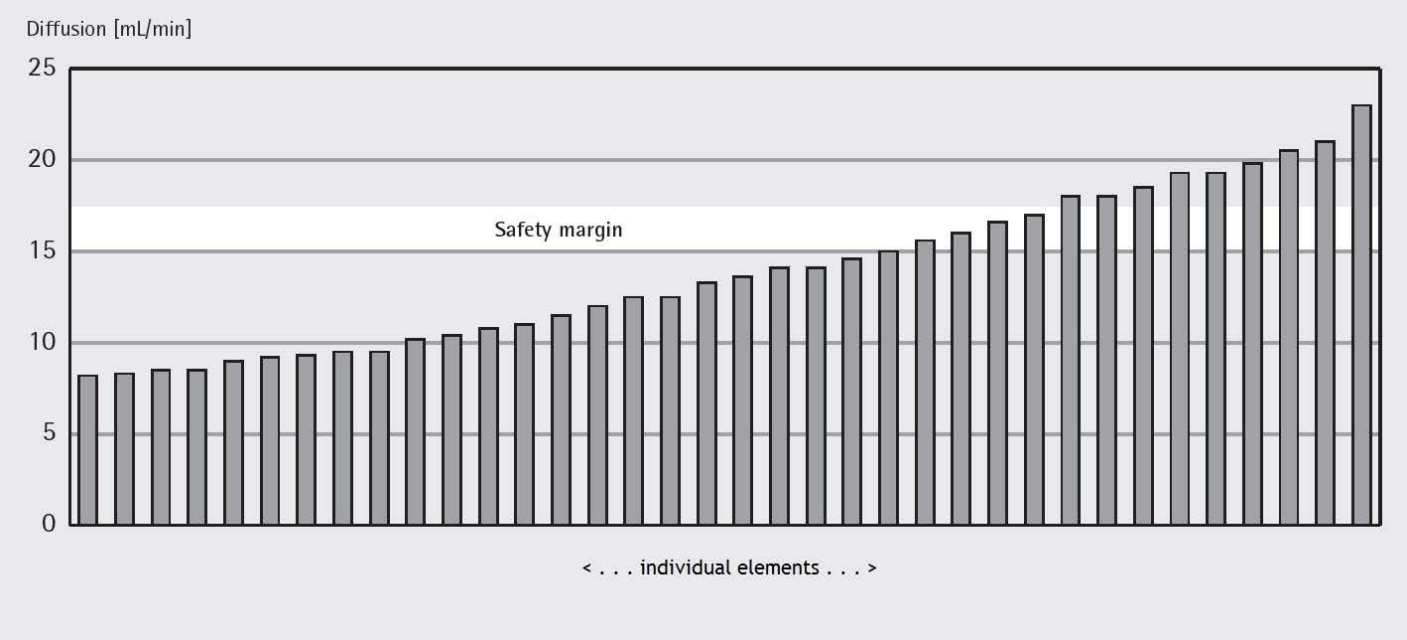
Note
Since most of the filter cartridges tested during the validation studies had low diffusion values and produced sterile filtrate, the following data is a sampling from all filters tested during the validation testing indicating results near the diffusion limits.

Bio-burden inlet values were in excess of $1x10^{10}$ Colony Forming Units.

Test Microorganism:
Lactobacillus lindneri

Lot Number	Diffusion [ml/min]	LRV
1025-2681	< 15	> 8
1025-2581	< 15	> 8
1025-2581	< 15	> 8
1025-2581	< 15	> 8
1025-2681	< 15	> 8
1025-2681	< 15	> 8
1025-5481	< 15	> 8
1025-7641	< 15	> 8
1025-7641	< 15	> 8
1025-7641	< 15	> 8
1025-7641	< 15	> 8
1025-7641	< 15	> 8
1025-7641	< 15	> 8
1025-2581	< 15	> 8
1025-2681	< 15	> 8
1025-2681	< 15	> 8
1025-2681	< 15	> 8
1025-2681	< 15	> 8
1025-2681	< 15	> 8
1025-2681	< 15	> 8
1025-2581	< 15	> 8
1025-2581	< 15	> 8
1025-2581	< 15	> 8
1025-2681	< 15	> 8
1025-2681	< 15	> 8
1025-7641	< 15	> 8
1025-7641	< 15	> 8
1025-7641	< 15	> 8
1025-7641	< 15	> 8
1025-2581	< 15	> 8
1025-6681	< 15	> 8
1025-5481	< 15	> 8
1025-2681	< 15	> 8
1025-2681	< 15	> 8
1025-2681	< 15	> 8
1025-2681	< 15	> 8

Cartridges (10”|250 mm), 0.45 µm



Cartridge 0.65 µm

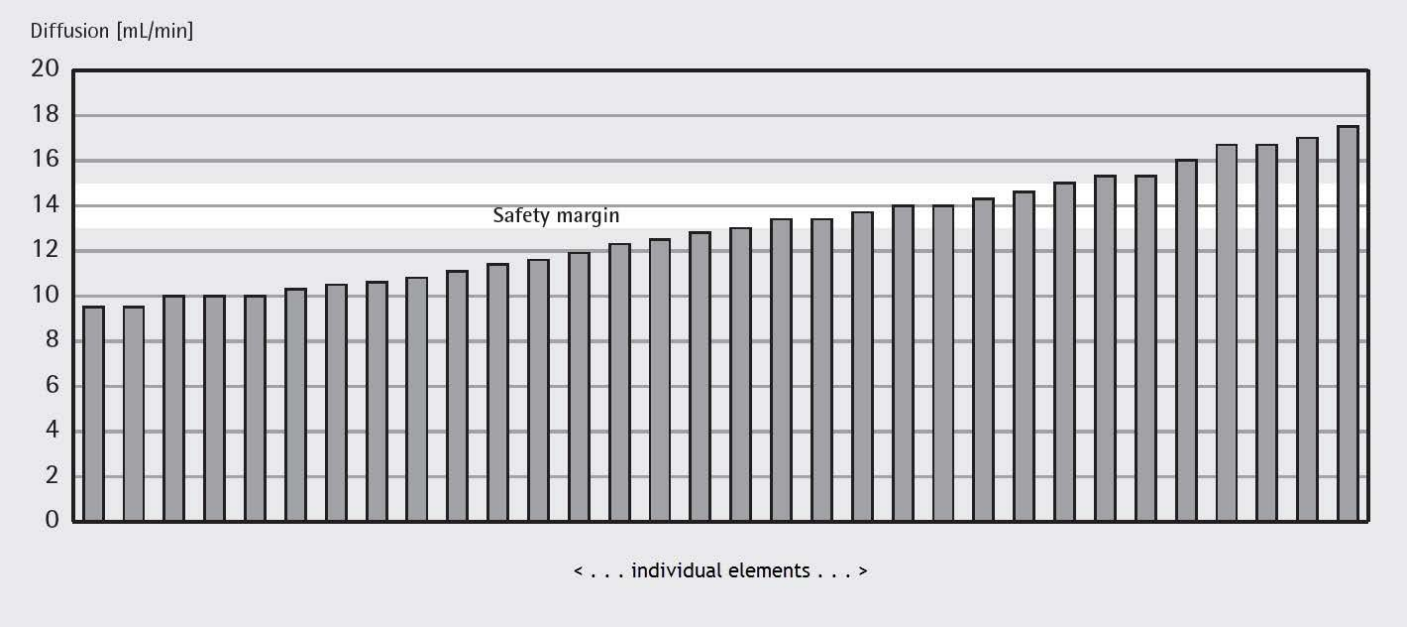
Note
The following data is a sampling from all filters tested during the validation testing indicating results near the diffusion limits.

Bio-burden inlet values were in excess of $1x10^9$ Colony Forming Units.

Test Microorganism:
Lactobacillus lindneri

Lot Number	Diffusion [ml/min]	LRV
1025-4581	< 13	> 8
1025-2941	< 13	> 8
1025-2941	< 13	> 8
1025-2941	< 13	> 8
1025-5041	< 13	> 8
1025-4641	< 13	> 8
1025-4641	< 13	> 8
1025-4641	< 13	> 8
1025-4641	< 13	> 8
1025-4641	< 13	> 8
1025-4641	< 13	> 8
1025-4641	< 13	> 8
1025-5041	< 13	> 8
1025-5041	< 13	> 8
1025-5041	< 13	> 8
1025-5041	< 13	> 8
1025-2941	< 13	> 8
1025-4641	< 13	> 8
1025-2941	< 13	> 8
1025-2941	< 13	> 8
1025-2941	< 13	> 8
1025-2941	< 13	> 8
1025-4641	< 13	> 8
1025-4581	< 13	> 8
1025-4581	< 13	> 8
1025-4641	< 13	> 8
1025-2941	< 13	> 8
1025-2941	< 13	> 8
1025-5041	< 13	> 8
1025-4641	< 13	> 8
1025-4641	< 13	> 8
1025-4641	< 13	> 8
1025-4581	< 13	> 8

Cartridges (10”|250 mm), 0.65 µm



Conclusion
The data shows that filter cartridges that have the specified diffusion rate values always produced a filtrate with LRV >8 of the test organism. For a thoroughly water wetted 10” filter cartridge, the maximum allowable diffusion values are:

Pore Size	Maximum Diffusion Rate	Test Pressure
0.2 µm	21 ml/min	2.5 bar
0.45 µm	15 ml/min	1.5 bar
0.65 µm	13 ml/min	1.0 bar

Tested at 20°C

Note
The diffusion Test results are influenced by the nature of the wetting medium. The diffusion values listed in this validation guide are for filter cartridges wetted with water at 20°C. It should be noted, that a variation of the test conditions such as temperature, wetting liquid or type of gas may require a different integrity test limit related to those mentioned above.

If a different test method is selected, for example an integrity test device that measures the values by monitoring the upstream pressure decay, this test method must be verified to the direct methods described above. The upstream pressure decay test is not only influenced by the diffusion of gas through the wetted filter membranes, but also the upstream volume of the filtration system. Without exact values for the upstream volume of the filtration systems, maximum allowable pressure decay values cannot be calculated for a particular filter system.

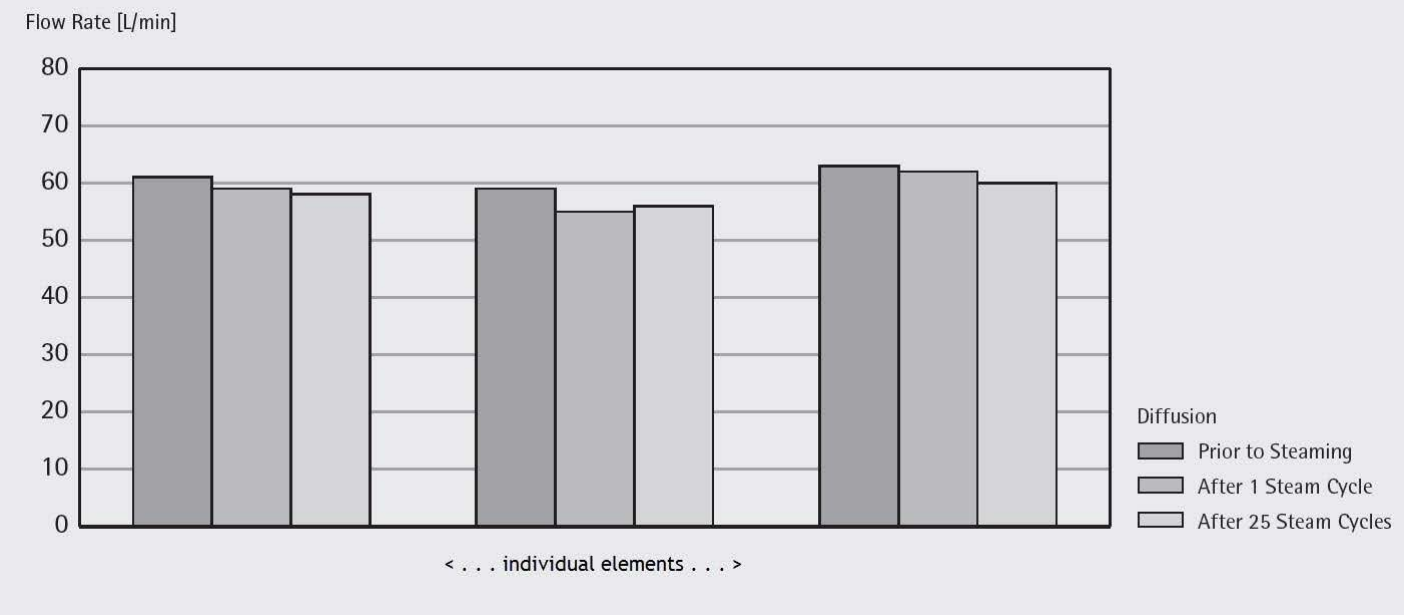
V. Steam Sterilization (Thermal Stability)

1. Effects on Water Flow Rates

Test Procedure
Nine 0.45 µm 10" filter cartridges from three different lot numbers were installed and wetted in standard filter housings. The flow rate was measured at a differential pressure of 0.2 bar. The values are the average of the filters from the production lot.

Values have been normalized for temperature and viscosity.

Lot Number	Flow Rate prior to Steaming [lpm]	Flow Rate after 1 Steam Cycle [lpm]	Flow Rate after 25 Steam Cycles [lpm]
1025-2681	61	59	58
1025-6681	59	55	56
1025-7641	63	62	60



2. Effects on Diffusion Test Values

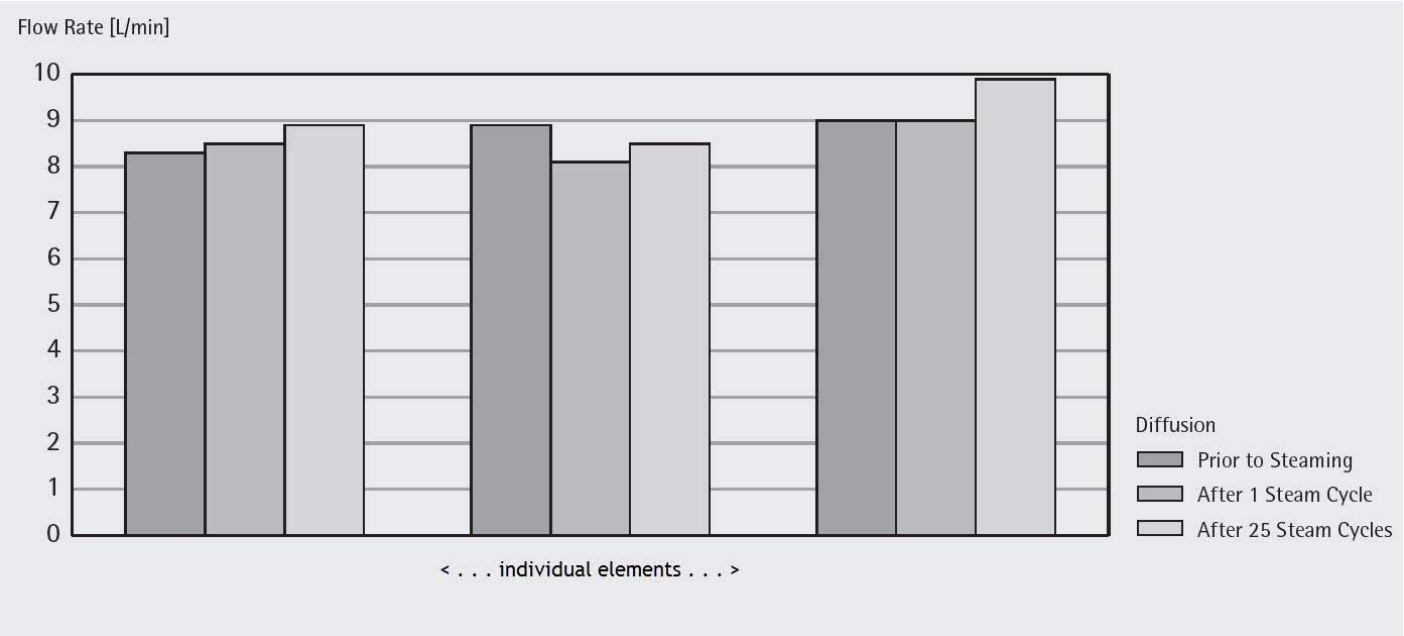
Results

Test Procedure
Filter 0.45 µm 10" filter cartridges were wetted in standard filter housings. A Diffusion Test with the following parameters was conducted utilizing an automated integrity test system:

Test Pressure: 1.5 bar|21.8 psi
Stabilization Time: 5 minutes
Test Time: 5 minutes

The following results are the averages for the filters from the three different production lots tested.

Lot Number	Diffusion prior to Steaming [lpm]	Diffusion after 1 Steam Cycle [lpm]	Diffusion after 25 Steam Cycles [lpm]
1025-2681	8.3	8.5	8.9
1025-6681	8.9	8.1	8.5
1025-7641	9.0	9.0	9.9



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