SPECTRUM

Validation Guide

PPPES Filter Cartridges

Contents

Part 1. Introduction.....01-02

Part 2. Studies on Removal Efficiency.....03-04
1. Bacteria Retention..... 03
2. Integrity Test..... 04

Part 3. Validation of Physical Characteristics.....05-07
1. Resistance to Steam Sterilization 05
2. Water Flow/ Differential Pressure Measurements..... 06
3. Resistance to Differential Pressure 07

Part 4. Extractables Testing..... 08

Part 5. Biological Safety Testing.....09-10

Part1. Introduction

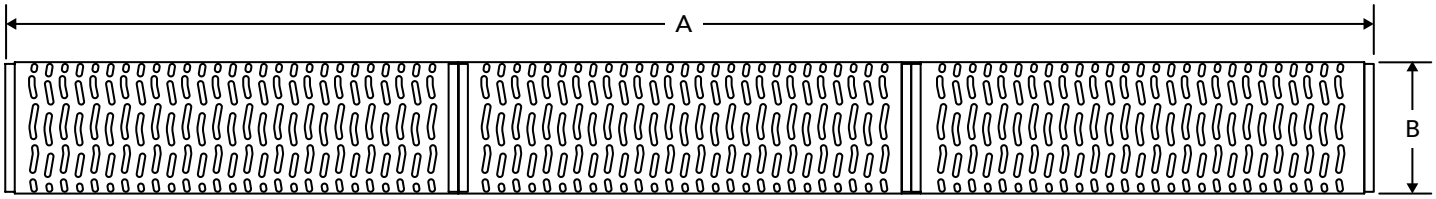
This report contains validation data applicable to the SPECTRUM PPPES filter cartridge. The product are constructed of imported hydrophilic asymmetric PES membrane, imported non-woven fabrics, and silk netting as support and then pleated. The cage, PP Core, and end cap are thermally welded with media without using any glue. All cartridges are manufactured and assembled in a clean room environment. 100% of the cartridges are integrity tested and flushed with EDI pure water. It is suitable for filtering weak acid/ alkali based liquid and ultra pure water.
Validation data contains: Bacterial Challenge, Extractables and Biological Safety. All of the validation tests abide by ISO 9001 quality system standards.

This report is designed to assist the filter user in meeting the validation requirements of regulatory authorities within the Food & Beverage industry.

Manufactured using German engineered and produced high quality polyethersulfone media, the SPECTRUM PPPES provides assured and certified absolute bacteria retention characteristics. Lot coded and 100% individually tested, the high surface area media contains no adhesives or binders, with low extractable content offering consistent final product quality. Meeting industry standard requirements, the cartridges are WRAS approved, FDA Title 21 Compliant and meet USP Class VI-121°C Plastics.

Please contact SPECTRUM if a more detailed description is required.

Code	Micron	Length	End-cap	Seal
PPP	0.1, 0.2, 0.45, 1, 3, 5, 10, 20, 30, 50, 100	4⅞	AA, CG	S, E, V
		93/4,	AA	
		10, 20, 30, 40	CG, EG, EH, FG, FH, MG, MH, QG, ZH	
	0.1, 0.2, 0.45, 1, 5, 10, 20	93/4BB, 20BB	-	-
	1, 5, 10	5 (Junior)	120	S



	Dimension (Nominal) (mm)											Packaging	
	A										B		
Length (")	AA	CG	EG	EH	FG	FH	MG	MH	QG	ZH		Box Qty	Box Weight (kg)
9¾	248	-	-	-	-	-	-	-	-	-	70	9	4
10	-	241	270	310	270	310	270	310	270	310	70	9	4
20	508	506	520	560	520	560	520	560	520	560	70	9	7
30	750	-	770	810	770	810	770	810	770	810	70	9	10
40	1000	-	1020	1060	1020	1060	1020	1060	1020	1060	70	9	14

End-Caps

Pleated Cartridge Configurations

Where product codes indicate an optional end-cap is available, a choice can be made from the following styles. End-cap variations are made to suit housing designs and application requirements, which dictate the reliability and integrity of the seal, along with the ease of cartridge change out.

AA

Double Open Ended

Open-end gaskets, for use with housings containing a knife edge seal mechanism.

CG

213 with Closed Recess

Single internal O-ring, seals onto housings that have a spigot.

EG / MG

222/224 with Closed Recess

Double external O-rings seal into female housing receiver with a closed, recessed end, which is for housings with spigots.

EH / MH

222/224 with Fin Adaptor

Double external O-rings seal into female housing receiver whilst the Fin locates into housing plate holes to maintain vertical orientation.

FG

226 with Closed Recess

Bayonet type tabs lock into female housing receiver whilst the recessed end locates into housings with spigots.

FH

226 with Fin Adaptor

Bayonet type tabs lock into female housing receiver whilst the Fin locates into housing plate holes to maintain vertical orientation.

Stainless Steel Encapsulated End-Caps

QG

222 with Closed Recess

Suitable for high temperature housings, the QG configuration is suitable for repeated sterilisation and offers one of the best seals possible with its double O-ring fitting and stainless steel insert.

ZH

226 with Fin Adaptor

Suitable for multi-round high temperature housings, the ZH configuration provides the most positive seal with double O-rings and twin locking tabs. The encapsulated stainless steel insert makes the Z fitting suitable for repeated sterilisation.

Part 2. Studies on Removal Efficiency

1. Bacterial Retention

The FDA guidelines on Sterile Products Produced by Aseptic Processing (1987) state, "A sterilising filter is one which, when challenged with the micro-organism *Pseudomonas diminuta (P. diminuta*), at a minimum concentration of 107 organisms per cm^2 of filter surface, will produce a sterile effluent".

In order to meet the requirements of this guideline, liquid challenge tests using *Brevundimonas diminuta* (ATCC 19146) were performed with SPECTRUM PPPES filter cartridges using a minimum of 1x107 colony forming units (CFU)/cm^2 of effective filtration area.

The correlation between microbial retention and a non-destructive integrity test is also an important aspect of the validation of sterilizing grade filters. 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". The integrity tests used during this validation study were the Forward flow and Bubble Point tests.

Table (1) Bacterial Retention Test Results

Filter Serial Number	Challenge Concentration (cfu/cm^2)	Number of Organisms in Filtrate
170111289	1.6×10^{11}	0
170211102	1.6×10^{11}	0
170121291	1.6×10^{11}	0
170301041	1.6×10^{11}	0
170202313	1.6×10^{11}	0
170511512	1.6×10^{11}	0
170111295	1.6×10^{11}	0
170420870	1.6×10^{11}	0

2. Integrity Test

The Forward Flow Integrity Test

In the Forward Flow test, a filter is wet with a suitable test liquid and a pre-determined gas pressure is applied to the upstream side of the filter assembly. After a stabilisation period, the gas flow through the wet membrane can be measured manually on the downstream side or on the upstream side, using sensitive flow measurement equipment such as the integrity test devices.

The Bubble Point Integrity Test

In the Bubble Point test, a filter is wetted with a suitable test liquid. After a stabilisation period, increasing the gas pressure to the upstream side of the filter assembly, using sensitive flow measurement equipment such as the integrity test devices to test the change point of the gas flow rate.

Table (2) Integrity Test Results

Wetting Liquid	DI Water
Test Gas	Air
Test Pressure	276 0mbar (40 psi)
Temperature	20°C ± 2°C
Maximum allowable Forward Flow limit	25 mL/min
Minimum allowable Bubble Point limit	3320 mbar (48psi)

Filter Serial Number	Forward Flow (ml/min)	Bubble Point (mbar)
170411011	18.2	3800
170402541	17.3	3950
170201630	20.5	3600
170320260	24.2	3550
170511434	23.1	3550
170420401	18.5	4000
170105111	20.1	4100
170211025	23.2	3950

Part 3. Validation of Physical Characteristics

1.1. Resistance to Steam Sterilisation

During the tests, typical production filters (10inch, 0.65m^2) installed in a stainless steel housing were steamed in place using saturated condensate-free steam

In each series of tests the following was performed:

Steam pressure and flow were held constant during the sterilisation period test filter cartridges were forward flow integrity tested at appropriate intervals
After each steam in place cycle the filters were cooled by passing dry compressed air trough the test filter.
During this study, filters were steamed using high initial differential pressures (1000 mbar (14.5 psig)) at 121°C (249.8°F). The tests were performed in 30 minute cycles in the forward (out to in) direction. These tests were performed in order to simulate steam conditions where transient high differential pressures (>300 mbar (4.3 psig)) may occur during the steam sterilisation cycle. At appropriate intervals, the filters were Forward Flow integrity tested and the results are shown in Table (3).
All filters passed the Forward Flow integrity test (2760mbar, DI water) after exposure to 30 minutes steam cycles 10 times.

Table (3) Effect of High initial Differential Pressures on Forward Flow Values

Filter Serial Number	Forward Flow (ml/min) after the following Number of 30 minutes Steam Cycles							
	0	1	2	3	5	7	9	10
170311171	24.0	18.5	23.2	18.3	23.7	24.4	21.8	15.1
170412124	23.2	24.7	21.2	15.7	16.7	18.2	15.2	24.9
170523333	20.9	24.1	21.3	15.2	21.5	16.7	16.0	20.9
170501231	23.0	23.1	22.4	21.0	16.6	20.3	16.2	23.7

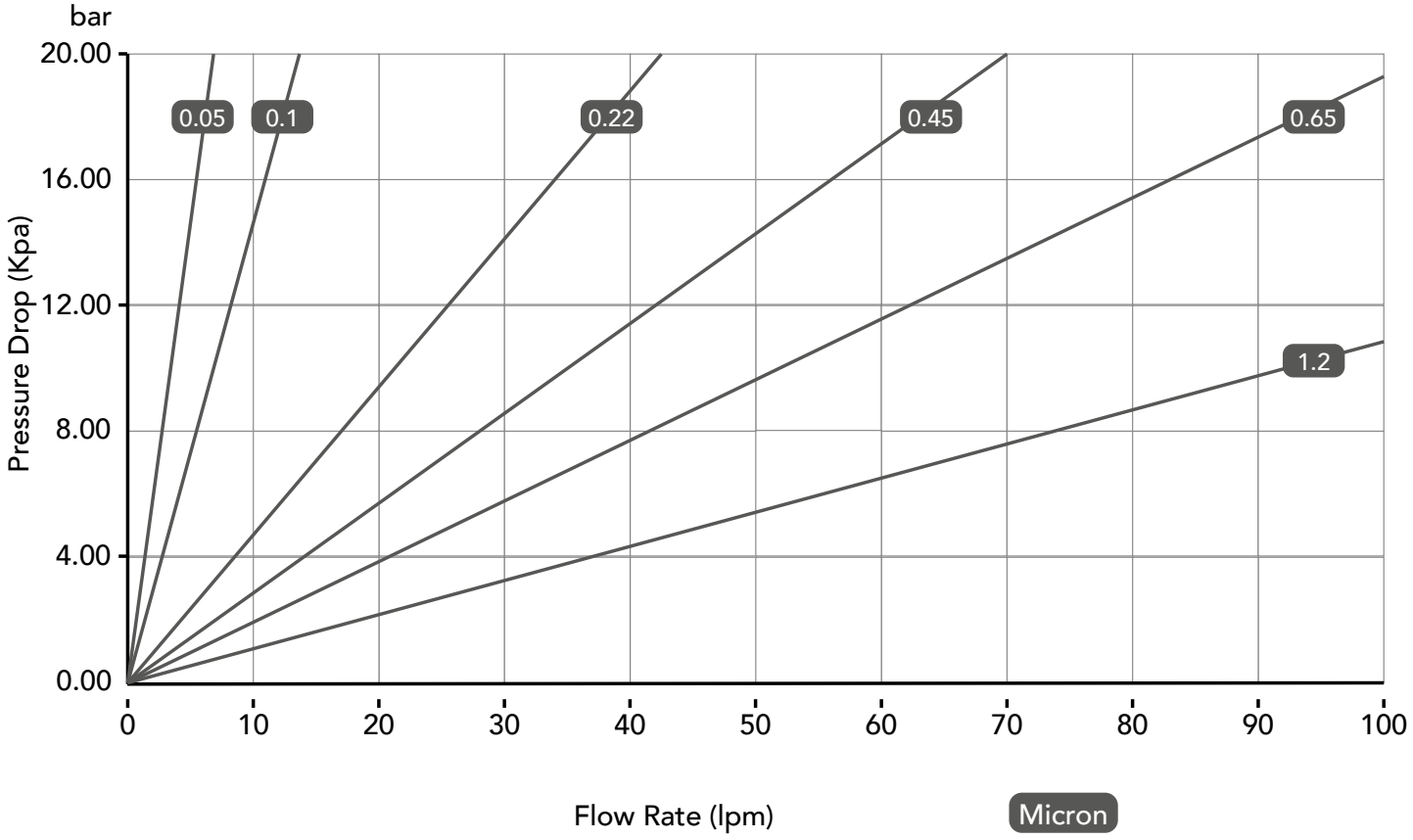
Wetting by DI water before steam sterilising, Limit value: 25mL/min

2.2. Water Flow/ Differential Pressure Measurements

The water flow measurements through typical filters (10 inch, 0.65m^2) at differential pressure are shown in figure (1), the water flow rates at 16Kpa(2.3psig) differential pressure for SPECTRUM PPPES (0.22µm) filter cartridges were found to range between 30-40L/min. This data can be used to form the basis of sizing filter systems using SPECTRUM PPPES(0.22µm) cartridges.

Note: The differential pressures quoted are for liquids with a viscosity of 1cP. Differential pressures for liquids at other viscosities can be estimated by multiplying the differential pressure by the viscosity in cP. To obtain the total pressure drop of a complete filter assembly the housing pressure drop must be added.

Figure (1) Flow Rate / Pressure Drop



3. Resistance to Differential Pressure

The tests were performed on standard production filters (10 inch, 0.65m^2). Test filters were installed in a stainless steel housing and flushed with DI water at differential temperature/ Pressure for 2 hours, Test the integrity of the filters.
The Results of integrity (Forward Flow, 2760mbar, wetting by DI water) at differential Temperature Pressure are shown in Table (4)

Table (3) Effect of High initial Differential Pressures on Forward Flow Values

Temp FF (ml/min) ΔP (psig)	0 mbar	1000 mbar	2000 mbar	2400 mbar	3000 mbar	4000 mbar
Forward 21°C	21.3	22.1	24.6	20.6	22.6	24.0
	20.4	19.8	20.1	21.9	24.1	22.7
Forward 80°C	22.1	23.0	24.0	24.5	N/A	N/A
	22.2	22.1	23.8	24.9	N/A	N/A

Safety Limit value: 25ml/min

The data presented in this section support the following conclusions:

Maximum Forward ΔP at 21°C ≤ 4000mbar (58psig)
Maximum Forward ΔP at 80°C ≤2400mbar (34psig)
Please contact SPECTRUM for further details.

Part 4. Extractables Testing

Preparation of Filter Samples

Extractables tests were performed on typical production filter cartridges (10inch, 0.65m^2), which had been autoclaved in order to maximise the quantity of any extractable material present. The filters were wrapped in aluminium foil and autoclaved for half an hour at 121°C (250°F), using a slow exhaust cycle. Visible droplets of water remaining on the filter elements were allowed to evaporate at room temperature before the extraction was performed.

Extraction Procedure

Dynamic extraction tests were performed. The test filters were immersed in 1500ml of extraction fluid in a clean measuring cylinder. Use Ultrapure water flush the filters for 24 hours.

After the extraction, 1000mL of the extraction liquid was evaporated and the non-volatile extractables were determined gravimetrically.

Table (5) Non-volatile Extractables using Typical (10") SPECTRUM PPPES (0.22µm) Cartridge

Extraction Fluid	Filter Serial Number	Residue
Ultrapure Water	170112150	11.0 mg
	170313298	10.1 mg
	170720751	13.5 mg
Ethanol	170119091	31.8 mg
	170311410	33.1 mg
	170511721	32.0 mg

Part 5. Biological Safety Testing

1. Introduction

The purpose of these tests was to evaluate the biological suitability of the materials of construction of the SPECTRUM PPPES (0.22µm) filter cartridges. The materials of construction of the SPECTRUM PPPES (0.22µm) filter cartridges are as follows:

Filter membrane medium :	PES membrane
Support :	Polypropylene
Core / Cage / Endcap:	Polypropylene PES membrane

2. Summary of methods

The tests were performed in accordance with the Biological Reactivity Tests in vivo for Class VI Plastics (121°C) as described in the current United States Pharmacopoeia. The tests were conducted NAMSA Laboratories.

The testing procedures described in the USP include:

- Injection of extracts of plastic materials
- Implantation of the solid material into animal tissue

The four extracting media listed in the USP simulate parenteral solutions and body fluids. These include:

- Sodium Chloride Injection
- 1 in 20 solution of alcohol in sodium chloride injection
- Polyethylene Glycol 400
- Vegetable Oil (Sesame or cotton seed oil)

The USP states that extracts may be prepared at one of three standard conditions: 50°C (122°F) for 72 hours, 70°C (158°F) for 24 hours, or 121°C (250°F) for 1 hour. The most stringent condition not resulting in physical changes in the plastic is recommended, therefore the filters were extracted at 121°C (250°F).

Acute systemic injection tests
An Acute systemic injection test was performed to evaluate the potential of a single injection of an extract to produce systemic toxicity. Sodium Chloride injection and 1 in 20 solution of alcohol in sodium chloride injection were injected intravenously. Vegetable oil extract and Poly-ethylene Glycol 400 extract were injected intraperitoneally.

Intracutanous tests
An intracutaneous test was performed to evaluate the potential of a single injection of an extract to produce tissue irritation. All four of the extracts listed above were used for these tests.

Implantation tests
Implantation tests were also performed, in order to subject the materials of construction to the most stringent conditions included in the USP. Each of the components of the SPECTRUM PPPES (0.22µm) filter cartridges was implanted separately.

3. Conclusions
SPECTRUM PPPES (0.22µm) filter cartridges meet the requirements of the USP for Class VI (121°C) Plastics).