Biotech

Validation Guide

USTR 3369

Pall 0.45 µm-Rated Filter Cartridges and Filter Capsules with Fluorodyne® II Grade DBL Membrane

Contents

1 Overview

1.1 Introduction

Pall Fluorodyne II grade DBL filters have been designed as bioburden reduction and pre-filtration liquid filters. The removal rating of 0.45 µm is based on challenges with *Serratia marcescens* (ATCC♦ 14756) with typical titer reduction (TR) of > 10^6. The filter cartridges are comprised of two serial layers (0.65/0.45 µm) of Pall hydrophilic polyvinylidene fluoride (PVDF) filter membrane with polypropylene support and drainage materials. The core, cage, and end caps of the filters are all polypropylene. Thermal bonding sealing technology is used throughout the construction. Fluorodyne II grade DBL filters are available as 'P' (pharmaceutical grade) and 'W' (food and beverage) options. As the materials and construction are identical, the data presented in this report apply to both options. Fluorodyne II grade DBL filter 254 mm (10 in.) cartridges are designated as AB1DB(*)7*. In this report (*) denotes the letter 'L' or 'blank' and * denotes 'W' or 'P' + O-ring code.

Fluorodyne II grade DBL filter capsules with an 'S' designation in the part number are supplied pre-sterilized. Following manufacturing, sterilization is achieved by gamma irradiation using a minimum dose of 25 kGy (maximum dose of 50 kGy). These conditions ensure a minimum Sterility Assurance Level (SAL) of 10^{-6}. The sterilization process is validated and works to the principles of the following standards:

- ISO 11137-1:2006 Sterilization of health care products - Radiation - Part 1 – Requirements for development, validation and routine control of a sterilization process for medical devices.
- ISO 11137-2:2013 Sterilization of health care products - Radiation - Part 2 - Establishing the sterilization dose.
- AAMI TIR 33:2005 Sterilization of health care products - Radiation. Substantiation of a selected sterilization dose - Method VDmax.

Fluorodyne II grade DBL filter capsules with a 'G' designation in the part number may be gamma irradiated. The 'G' option products have identical structures to the 'S' option capsules, and both are manufactured using the same gamma-tolerant hardware. The 'G' option product is designed for gamma irradiation with doses up to 50 kGy or can be autoclaved.

This report summarizes the tests conducted to qualify the performance of Fluorodyne II grade DBL filter cartridges and filter capsules under a range of standard test conditions.

The qualification program included:

- Microbial challenge tests
- Resistance to *in situ* steam and autoclave conditions
- Determination of water flow characteristics
- Extractables testing using water
- Biological reactivity tests

The units of pressure quoted in this document are bar or millibar (mbar) and pounds force per square inch (psi). The following formula can be used to convert these units of pressure to Pascals (Pa):

1 bar = 1000 mbar = 1 x 10^5 Pa

1 psi = 6.89476 x 10^3 Pa = 0.069 bar = 69.85 mbar

Configurations of Fluorodyne II grade DBL filter cartridges and filter capsules supported by this validation guide are listed in Table 1.

Table 1.

Configurations of Fluorodyne II grade DBL filter cartridges and filter capsules

Filter Type	Style	Part Number Prefix	Effective Filter Area (m^2)
Pleated membrane filter cartridges, for use in stainless steel filter housings	Junior filter cartridges (MCY style)	MCY4440DBL	0.15
	Sealkleen™ filter cartridges (SLK style)	SLK7002DBL	0.19
	Standard (‘AB-style’) filter cartridges	AB05DBL	0.27
		AB1DBL	0.55
		AB2DBL	1.10
		AB3DBL	1.65
	Kleenpak™ capsules	KA1DBL	0.04
		KA2DBL	0.08
		KA3DBL	0.15
		KA4DBL	0.33
		NP5DBL (AB05)	0.27
		NP6DBL (AB1)	0.55
		NP7DBL (AB2)	1.10
		NP8DBL (AB3)	1.65
Pleated membrane filter elements in polymeric capsule housing	Kleenpak Nova capsules	NT6DBL (AB1)	0.55
		NT7DBL (AB2)	1.10
		NT8DBL (AB3)	1.65

The performance parameters, physical appearance, inlet and outlet adaptor/connection options and part number nomenclature for the above formats of Fluorodyne II grade DBL filters are described in detail in Pall publication USD2562 (datasheet for Fluorodyne II filters).

1.2 Summary of Conclusions

1.2.1 Microbial Challenge Tests

Fluorodyne II grade DBL filter cartridges were tested for bacterial removal of *Serratia marcescens (*ATCC 14756). Fluorodyne II grade DBL filters, part number AB1DB(*)7*, have been shown to provide high bioburden reduction > 10^6 removal for *Serratia marcescens.* Forward Flow integrity test parameters (Table 2) have been set as follows for 254 mm (10 in.) AB-style filter cartridges.

Table 2.

*Forward Flow integrity test parameters for Fluorodyne II grade DBL filter cartridges, part number AB1DB(*)7**

Test Parameters	
Test pressure	1240 mbar (18 psi)
Wetting liquid	Water
Temperature	20 °C ± 5 °C
Test gas	Air
Maximum allowable Forward Flow limit[1]	13.0 mL/min

[1]*During the test, the temperature of the filter assembly should not vary by more than ±1 °C*

Forward Flow integrity test values have also been set for other filter formats incorporating Fluorodyne II grade DBL filter membrane, as shown in Table 3. Typical filters from production were subjected to Forward Flow integrity testing and bacterial challenge tests, demonstrating that the filters that pass the Forward Flow integrity test also provide a bioburden reduction as specified above.

Table 3.

Forward Flow integrity test parameters for other formats of Fluorodyne II grade DBL filter cartridges and capsules

Pall Filter Part Number[1]	Wetting Liquid[2]	Air Test Pressure	Maximum Allowable Forward Flow Limit[3]
KA1DBLP*	Water	1240 mbar (18 psi)	0.95 mL/min
KA2DBLP*	Water	1240 mbar (18 psi)	1.9 mL/min
KA3DBLP*	Water	1240 mbar (18 psi)	4.0 mL/min
KA4DBLP*	Water	1240 mbar (18 psi)	8.0 mL/min
NP5LDBLP*	Water	1240 mbar (18 psi)	6.5 mL/min
N*6DBLP*	Water	1240 mbar (18 psi)	13.0 mL/min
N*7DBLP*	Water	1240 mbar (18 psi)	22.8 mL/min
N*8DBLP*	Water	1240 mbar (18 psi)	31.2 mL/min
MCY4440DBLP	Water	1240 mbar (18 psi)	4.0 mL/min
SLK7002DBLP	Water	1240 mbar (18 psi)	4.0 mL/min
AB05DBL	Water	1240 mbar (18 psi)	6.5 mL/min
AB2DBL	Water	1240 mbar (18 psi)	22.8 mL/min
AB3DBL	Water	1240 mbar (18 psi)	31.2 mL/min

[1] ** denotes "blank", S or G option*
[2]*Temperature: 20 °C ± 5 °C*
[3] *During the test the temperature of the filter assembly should not vary more than ± 1 °C*

1.2.2 Resistance to *In Situ* Steam and Autoclave Conditions

Fluorodyne II grade DBL filters (part number, AB1DB(*)7*) can withstand multiple in-line steam sterilization cycles (Table 4). The data presented in Table 4 of this guide supports the product claims for the *in situ* steaming of Fluorodyne II grade DBL filter cartridges in AB-style.

The physical test conditions for *in situ* steaming of Fluorodyne II grade DBL filters can be considered as worst case for any sterilization process by steam and therefore include autoclave process conditions with the same temperature exposure and cycle times.

Table 4.

Product claims for in situ steaming of Fluorodyne II grade DBL high area AB-style filter cartridges

Steaming Conditions	Maximum Recommended Steam Life Claim[1]
In situ steam cycles at 125 °C	30 x 1-hour cycles
In situ steam cycles at 140 °C	10 x 1-hour cycles

[1]The above claims are supported by data that incorporates a safety margin. The maximum recommended product claim for in situ steaming is 10 x 1-hour cycles at 140 °C, but further data exist for 142 °C (Table 9).

1.2.3 Determination of Water Flow Characteristics

Differential pressure (DP) measurements at set water flow rates have been determined for typical Fluorodyne II grade DBL filter AB-cartridges (part number, AB1DB(*)7*). These data can be used in sizing filter systems employing Fluorodyne II grade DBL filter cartridges (see Section 4 for details).

1.2.4 Extractables Testing using Water

As most of applications for Fluorodyne II filters are with aqueous solutions, the typical amount of non-volatile residue (NVR) extracted from Fluorodyne II grade DBL filters has been determined using water as the extraction fluid. For the 254 mm (10 in.) filter elements tested (part number AB1DB(*)7*), the non-volatile residue measured was < 6 mg per 254 mm (10 in.) filter.

Actual service in pharmaceutical applications will impose different conditions, such as different steaming conditions, exposure times, temperature and liquid types. Evaluation under process conditions is therefore also recommended.

1.2.5 Biological Reactivity Tests on the Material of Construction

All materials used in Fluorodyne II grade DBL filter cartridges and capsules meet the requirements of the Biological Reactivity Tests *(in vivo)*, listed in the current revision of the United States Pharmacopeia (USP) chapter <88> for Class VI-121 °C plastics. The tests included the Systemic Injection test, the Intracutaneous test and the Implantation test.

2 Microbial Challenge Tests

2.1 Introduction

This study determined the microbial removal efficiency of typical Fluorodyne II grade DBL filters from production in liquid challenge tests using *Serratia marcescens (*ATCC 14756).

2.2 Summary of Methods

Typical Fluorodyne II grade DBL filter cartridges, part number AB1DB(*)7*, with an effective filtration area of 0.55 m² (5.9 ft²), from a minimum of three separate manufacturing batches, were subjected to microbial challenge tests using an aqueous suspension of *Serratia marcescens (*ATCC 14756).

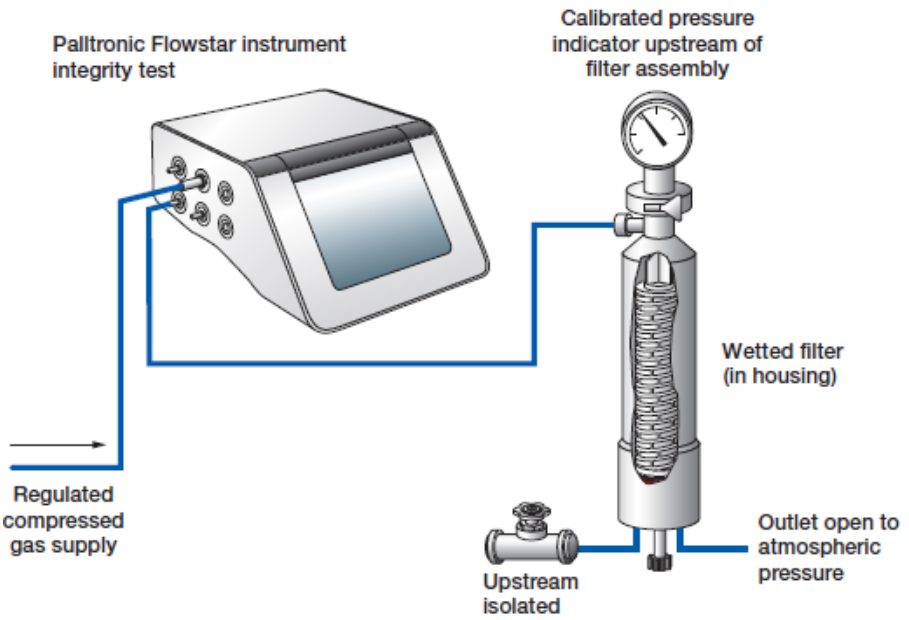
During this test procedure, the filters were integrity tested using the Forward Flow test method, subjected to a microbial challenge test and Forward Flow integrity tested again.

2.2.1 The Forward Flow Integrity Test

In the Forward Flow integrity test, a filter is wetted with an appropriate test liquid, and pre-determined gas pressure is applied to the upstream side of the filter assembly. After a suitable stabilization period, the gas flow through the wetted membrane can be measured on the upstream side, using sensitive flow measurement equipment such as the Palltronic Flowstar filter integrity test instrument (Figure 1).

Figure 1.

The automated integrity test



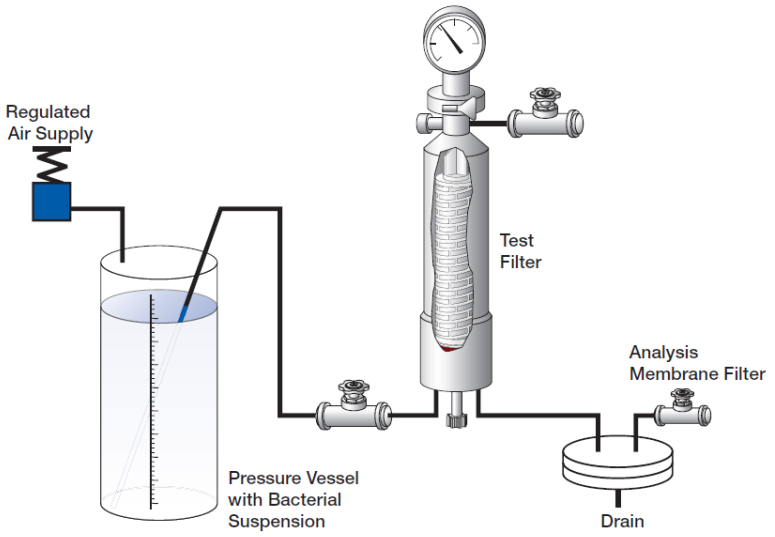
During this study, Fluorodyne II grade DBL filters were installed in an appropriate housing, flushed with deionized (DI) water at a flow rate of 8 L/min for 5 minutes. Forward Flow values were determined using a Palltronic Flowstar integrity test instrument. A test pressure of 1240 mbar (18 psi) was applied and the test gas was compressed air.

2.2.2 The Microbial Challenge Test

Before the challenge tests the filters were installed in an appropriate housing and Forward Flow integrity tested pre-sterilization as described in Section 2.2.1. The filter assemblies were then sterilized in an autoclave at 121 °C for 60 minutes and then aseptically connected to the pre-sterilized challenge apparatus, as shown in Figure 2.

Figure 2.

Microbial challenge apparatus



An aqueous suspension of *Serratia marcescens* was passed through the filter cartridge to achieve a challenge level of > 1 x 10^6 colony forming units (CFU) per cm^2 of effective filtration area.

During the challenge test the entire filter effluent was passed through a 0.2 µm-rated analysis disc on the downstream side of the test filter assembly. The filter disc was incubated on agar. The disc was then examined to determine if any colonies had grown, indicating whether or not bacteria had passed through the test filter during the challenge. The titer reduction (T_R) for each filter (Equation 1) was determined as follows:

Equation 1. *Titer reduction*

$$T_R = \frac{\text{Total number of bacteria influent to the filter}}{\text{Number of colonies recorded on the downstream analysis disc}}$$

When no colonies were detected downstream, the titer reduction was expressed as:

> Total number of bacteria influent to the filter (e.g. **>** 1 x 10^7)

On completion of the challenge test, the filter assemblies were autoclaved and then flushed and Forward Flow integrity tested as described previously.

2.3 Results

The Forward Flow and *Serratia marcescens* removal results are shown in Table 5. The higher of the two Forward Flow values (pre- and post-challenge) are presented and the data are arranged in order of increasing Forward Flow value.

All tested filters provided a titer reduction of > 1 x 10^6 when challenged with *Serratia marcescens*.

Table 5.

*Results of Forward Flow integrity test and Serratia marcescens removal for typical Fluorodyne II grade DBL filter cartridges, part number AB1DB(*)7**

Filter Serial Number	Forward Flow[1] (mL/min)	Titer Reduction (TR)
IA6130180	0.5	5.45×10^{8}
IA6130002	1.0	7.43×10^{8}
IA6130246	1.0	1.19×10^{9}
FR2831/0058	3.4	$> 5.47 \times 10^{11}$
FR2830/0098	3.5	$> 2.16 \times 10^{11}$
FR2830/0123	3.5	1.67×10^{8}
FR2832/0032	3.6	1.12×10^{11}
FR2830/0077	3.6	$> 2.01 \times 10^{11}$
FR2831/0075	3.7	1.84×10^{7}
FR2830/0142	3.7	$> 2.27 \times 10^{11}$
FR2830/0006	3.8	3.60×10^{9}
FR2831/0002	3.8	$> 2.35 \times 10^{11}$
FR2830/0042	3.8	$> 1.12 \times 10^{11}$
FR2831/0033	3.9	1.76×10^{11}
IA1112174	4.0	$> 1.96 \times 10^{10}$
FR2832/0140	4.2	$> 2.30 \times 10^{11}$
FR2832/0088	4.2	2.22×10^{11}
FR2830/0133	4.2	$> 3.70 \times 10^{11}$
PILF304101	4.2	1.26×10^{6}
IA1112044	4.3	$> 1.96 \times 10^{10}$
FR2832/0119	4.3	$> 2.30 \times 10^{11}$
FR2830/0023	4.4	1.99×10^{11}
FR2832/0007	4.4	6.82×10^{7}
FR2831/0126	4.4	3.92×10^{10}
PILF304004	4.5	1.87×10^{8}
IA0717132	4.5	3.07×10^{8}
PILF304022	4.9	1.10×10^{9}
FR2831/0101	4.9	$> 2.37 \times 10^{11}$
IA1417011	5.1	$> 3.40 \times 10^{10}$
FR2832/0053	5.2	$> 2.50 \times 10^{11}$
IA1112064	5.3	$> 1.96 \times 10^{10}$
IA0717142	7.3	2.80×10^{6}
IA1417117	7.6	1.19×10^{8}
PILF304006	7.8	3.20×10^{6}
IA0717108	12.7	1.25×10^{8}
IA0717128	12.9	3.82×10^{7}
PILF304080	13.3	1.26×10^{6}
IA0717145	22.0	1.92×10^{8}

[1]*Forward Flow values determined at 1240 mbar (18 psi) air test pressure, wet with water at 20 °C ± 5 °C, maximum allowable limit of 13.0 mL/min.*

2.4 Conclusions

Based on the results of this study, the Forward Flow integrity test has been demonstrated to be a suitable non-destructive integrity test for Fluorodyne II grade DBL filter cartridges. The filters that were tested showed Forward Flow values ranging from 0.5 to 22.0 mL/min when tested water wet at 1240 mbar (18 psi) air test pressure.

Integrity test parameters for Fluorodyne II grade DBL filter cartridges, part number AB1DB(*)7* have been set, as shown in Table 6.

Table 6.

*Forward Flow integrity test parameters for Fluorodyne II grade DBL filter cartridges, part number AB1DB(*)7**

Test Parameters	
Test pressure	1240 mbar (18 psi)
Wetting liquid	Water
Temperature	20 °C ± 5 °C
Test gas	Air
Maximum allowable Forward Flow limit[1]	13.0 mL/min

[1] *During the test the temperature of the filter assembly should not vary by more than ±1 °C.*

Users of Fluorodyne II grade DBL filters can be assured that filters that pass the Forward Flow test will provide typical titer reductions in excess of 1 x 10^6 per cm^2 as demonstrated when challenged with aqueous solutions of *Serratia marcescens*.

3 Resistance to *In Situ* Steam and Autoclave Conditions

3.1 Introduction

The purpose of these tests was to determine the effects of repeated exposure to *in situ* steam cycles on filter integrity testing using standard AB-style Fluorodyne II grade DBL filter cartridges and from production.

3.2 Summary of Methods

Typical Fluorodyne II grade DBL filters from production were used for the tests (part number, AB1DB(*)7*).

Filters were installed in stainless steel filter housings and were steamed in place using saturated condensate-free steam. The steam pressure and flow were held constant during the sterilization. After each steam in place cycle, the filters were cooled by passing dry compressed air through the test assembly. The filter cartridges were Forward Flow integrity tested at appropriate intervals and steam tests performed at 125 °C, 140 °C and 142 °C.

3.3 Results

The Forward Flow integrity test results for Fluorodyne II grade DBL filters before (0 cycles) and after (n cycles) exposure to different one-hour *in situ* steam cycles for AB1DB(*)7*) at 125 °C, 140 °C and 142 °C are shown in Tables 7, 8 and 9.

All the filter cartridges retained integrity throughout the steam exposure tests.

Table 7.

*Effects of in situ steam exposure at 125 °C on filter integrity for Fluorodyne II grade DBL filter cartridges, part number AB1DB(*)7**

Pall Cartridge Serial Number	Forward Flow[1] (mL/min) Test Results after Following Number of 1-Hour Cycles at 125 °C			
	0 cycles	10 cycles	20 cycles	30 cycles
FR28300014	5.6	3.3	3.4	3.4
FR28300039	3.6	3.2	3.0	3.4
FR28300096	3.7	3.4	3.2	3.3
FR28300131	3.0	3.2	3.3	3.4
FR28310005	3.5	3.4	3.2	3.2
FR28310048	3.4	3.2	3.3	3.6
FR28310089	3.3	3.5	3.7	3.4
FR28310120	4.0	3.4	3.3	3.6
FR28320016	2.8	2.4	2.7	2.5
FR28320052	3.4	3.2	3.2	3.4
FR28320105	3.4	3.3	3.2	3.4
FR28320138	3.4	3.2	3.1	3.1

[1]*Forward Flow values determined at 1240 mbar (18 psi) air test pressure, wet with water at 20 °C ± 5 °C, maximum allowable limit of 13.0 mL/min.*

Table 8.

*Effects of in situ steam exposure at 140 °C on filter integrity for Fluorodyne II grade DBL filter cartridges, part number AB1DB(*)7**

Pall Cartridge Serial Number	Forward Flow[1] (mL/min) Test Results after Following Number of 1-Hour Cycles at 140 °C		
	0 cycles	5 cycles	10 cycles
FR28300021	3.3	3.0	2.7
FR28300066	3.2	2.9	2.5
FR28300107	3.8	2.9	2.8
FR28300138	5.5	2.9	2.6
FR28310021	3.1	2.8	2.9
FR28310060	3.2	2.8	2.8
FR28310093	3.3	3.2	2.8
FR28310114	3.3	2.9	2.5
FR28320024	3.5	2.9	2.7
FR28320059	3.2	3.0	2.7
FR28320099	2.9	3.3	2.6
FR28320130	3.2	2.8	2.6

[1]*Forward Flow values determined at 1240 mbar (18 psi) air test pressure, wet with water at 20 °C ± 5 °C, maximum allowable limit of 13.0 mL/min.*

Table 9.

*Effects of in situ steam exposure at 142 °C on filter integrity for Fluorodyne II grade DBL filter cartridges, part number AB1DB(*)7**

Pall Cartridge Serial Number	Forward Flow[1] (mL/min) Test Results after Following Number of 1-Hour Cycles at 142 °C	
	0 cycles	20 cycles
IA2096310	4.3	3.2
IA2096304	3.4	2.8
IA2096137	3.0	3.0
IA2096057	2.5	2.8
IA2096094	2.8	3.3

[1]*Forward Flow values determined at 1240 mbar (18 psi) air test pressure, wet with water at 20 °C ± 5 °C, maximum allowable limit of 13.0 mL/min.*

3.4 Conclusions

Fluorodyne II grade DBL filter cartridges (part number, AB1DB(*)7*) have been demonstrated to be capable of withstanding multiple *in situ* steam cycles. The data presented in this section of the guide support the following product claims (Table 10) for *in situ* steaming Fluorodyne II grade DBL filter cartridges.
The maximum recommended product claim for in situ steaming is 10 x 1-hour cycles at 140 °C, but also further data exist for 142 °C (Table 9).

Table 10.

Product claims for in situ Steaming of Fluorodyne II grade DBL filter cartridges (AB-style)

Fluorodyne II grade DBL Filter Styles	Steaming Conditions	Maximum Recommended Steam Life Claim[1]
High area AB-style filter cartridges	*In situ* steam cycles at 125 °C	30 x 1-hour cycles
	In situ steam cycles at 140 °C	10 x 1-hour cycles

[1] *The above claims are supported by data that incorporates a safety margin.*

4 Determination of Water Flow Characteristics

4.1 Introduction

The purpose of these tests was to determine the typical DP across Fluorodyne II grade DBL filter cartridges (part number, AB1DB(*)7*) at set water flow rate.

4.2 Summary of Methods

The tests were performed on standard production filter cartridge (part number, AB1DB(*)7*)

Pre-filtered DI water was pumped through the filters in the normal flow (out to in) direction. Pressure readings from transducers on the upstream and downstream sides of the test assembly were monitored to calculate the DP at set water flow rates.

Further flow measurements for AB style filter cartridges were taken with the test assembly with no filter cartridge or capsule installed, so that the piping/housing losses could be measured and then subtracted from the filter assembly results.

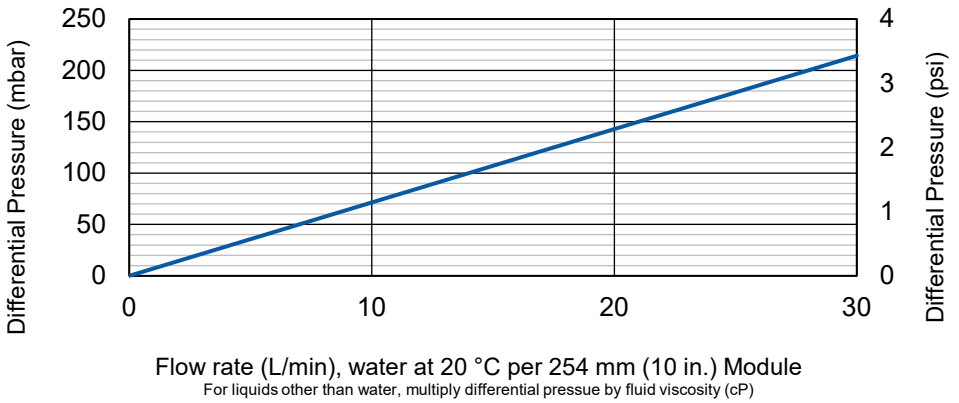
The results were corrected for a standard temperature of 20 °C.

4.3 Results

The water flow characteristics for typical Fluorodyne II grade DBL filter cartridges is presented in Figure 3. At 20 °C and DP of 100 mbar a water flow of 14 L/min were measured for a 254 mm (10 in.) module. To calculate the expected flow rate for fluids other than water, multiply the DP by the fluid viscosity (cP).

Figure 3.

*Water flow/differential pressure characteristics of the Fluorodyne II grade DBL, part number AB1DB(*)7**



4.4 Conclusions

DP measurements at a set water flow rate have been determined for typical Fluorodyne II grade DBL filter cartridges (part number, AB1DB(*)7*). The data presented can be used to size filtration systems employing Fluorodyne II grade DBL filter membrane.

5 Extractables Testing Using Water

5.1 Introduction

These series of tests aimed to quantify and to characterize the material that can be extracted from Fluorodyne II grade DBL filters (part number, AB1DB(*)7*) using water.

5.2 Summary of Methods

5.2.1 Preparation of Filter Samples

Before the extraction test, the filter samples were autoclaved to maximize the quantity of any present extractable material. The filter cartridges were wrapped in aluminum foil and autoclaved for one hour at 125 °C. Visible droplets of water remaining on the filter elements were allowed to evaporate at room temperature before the extraction was performed.

5.3 Extraction Procedure for Filter Cartridges

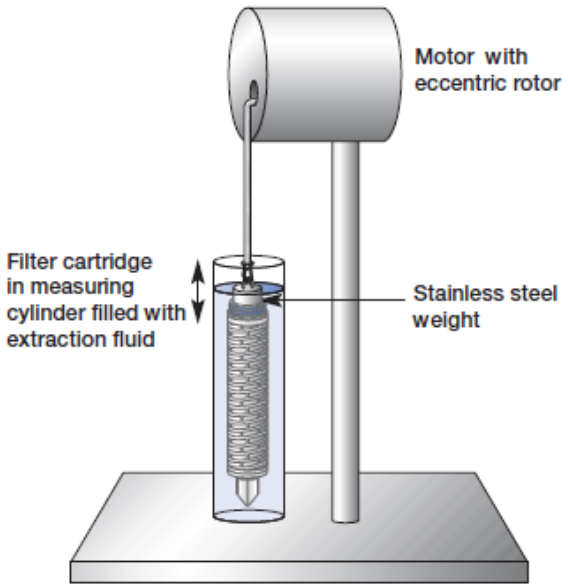
Dynamic extraction tests were performed in water at 23 °C ± 2 °C. The test filters were immersed in 1500 mL of water in a clean graduated cylinder, as shown in Figure 4. For 24 hours, the filter was gently moved up and down. This movement created flow through the filter membrane as a result of the pressure that was created each time the element was partially lifted out of the liquid.

Following the extraction period, a measured volume of the extraction liquid was evaporated to dryness and the non-volatile residue (NVR) were determined gravimetrically. A correction was made to the NVR value to account for the total extraction volume used.

The extractables were analyzed by Fourier Transform Infrared Spectroscopy (FTIR).

Figure 4.

Filter extraction apparatus for filter cartridges



5.4 Analysis of Extracted Material

After the extraction, a known volume of the extraction fluid was evaporated to dryness and the non-volatile extractable material was determined gravimetrically. A correction to the measured residue was made to take account of the material extracted in the full 1500 mL volume. A sample of the extracted material was analyzed by FTIR.

5.5 Results

Table 11 shows the typical level of aqueous extractables obtained from filters taken from four separate production batches (lot numbers ENG002, ENG003, ENG004 and IN3599) of Fluorodyne II grade DBL filters (part number, AB1DB(*)7*).

Table 11.

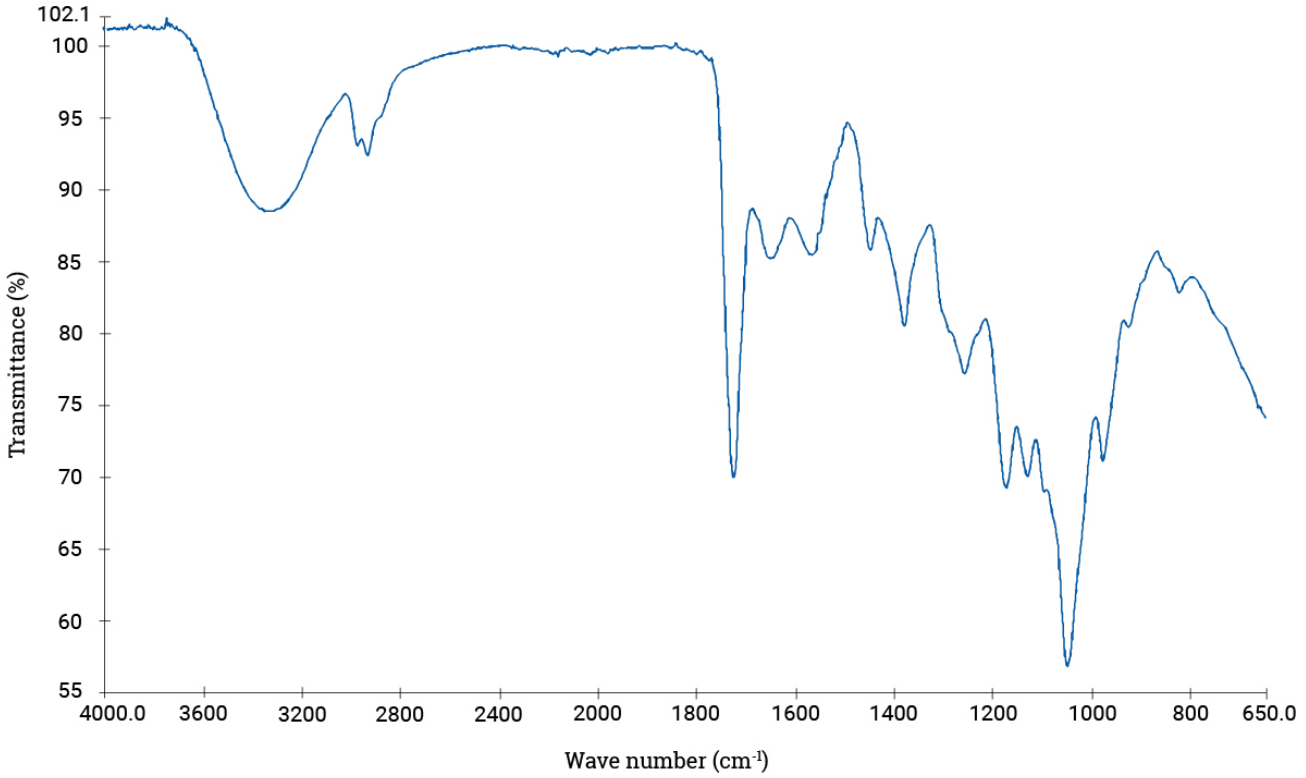
*Non-volatile aqueous extractables obtained using Fluorodyne II grade DBL filters, part number AB1DB(*)7**

Pall Filter Serial Number	Non-Volatile Residue (mg)
ENG00020004	2.1
ENG00020005	3.7
ENG00020006	2.9
ENG00020007	6.0
ENG00030001	2.2
ENG00030002	3.7
ENG00030003	5.4
ENG00030004	3.8
ENG00040003	4.3
ENG00040005	3.2
ENG00040006	2.5
ENG00040007	2.1
IN3599002	4.1
IN3599013	3.9
IN3599038	5.4
IN3599053	3.7

A typical infrared spectrum Figure 5 of an aqueous extract obtained from a Fluorodyne II grade DBL filter indicates the presence of extractables typical of polyvinylidene fluoride resins and the acrylate copolymer used to render the membrane hydrophilic.

Figure 5.

Infrared spectrum of the aqueous extractables from Fluorodyne II grade DBL filters



5.6 Conclusions

The typical amount of non-volatile residue extracted from Fluorodyne II DBL filters has been determined using water as the extraction fluid. For the 254 mm (10 in.) filter elements that were tested (part number, AB1DB(*)7*) the non-volatile residue measured was < 6 mg per 254 mm (10 in.) filter.

Actual service will impose different conditions, such as different exposure times, temperature, liquid purity etc. Evaluation under process conditions is recommended.

6 Biological Reactivity Tests on the Material of Construction

6.1 Introduction

This study aimed to evaluate the biological suitability of the materials of construction of Fluorodyne II grade DBL cartridges and capsules. The materials of construction of the filters are detailed in Table 12.

Table 12.

Materials of construction

Membranes	Double layered hydrophilic polyvinylidene fluoride (PVDF) membranes
Membrane support and drainage layer	Polypropylene
Core, cage and endcaps	Polypropylene
O-rings	Silicone elastomer for 'H4' option
Capsule housing for Kleenpak capsules	Polypropylene

6.2 Summary of Methods

The tests were performed in accordance with the Biological Reactivity Tests *in vivo* for Class VI-121 °C Plastics as described in the current United States Pharmacopoeia (USP) Chapter <88>.

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 cottonseed oil)

The USP states that extracts may be prepared at one of three standard conditions: 50 °C for 72 hours, 70 °C for 24 hours, or 121 °C for 1 hour. The most stringent condition not resulting in physical changes in the plastic is recommended. Therefore, the filter materials were extracted at 121 °C for one hour.

6.2.1 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. The sodium chloride injection and 1 in 20 solution of alcohol in sodium chloride injection were injected intravenously. The vegetable oil extract and polyethylene glycol 400 extract were injected intraperitoneally.

6.2.2 Intracutaneous 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.

6.2.3 Implantation Tests

Implantation tests were also performed, to subject the materials of construction to the most stringent conditions included in the USP. Each of the materials of the Fluorodyne II grade DBL cartridges and capsules was implanted separately.

6.3 Results

No biological response was observed in any of the tests performed. Therefore, the materials used in Fluorodyne II grade DBL cartridges and capsules passed all tests specified.

6.4 Conclusion

The materials used in Fluorodyne II grade DBL cartridges and capsules met the requirements of the USP Biological Reactivity Tests *(in vivo)* for Class VI-121 °C plastics. The tests included the systemic injection test, the intracutaneous test and the implantation test. Copies of the reports are available on request.

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