Donaldson
FILTRATION SOLUTIONS

STERILE AIR JUNIOR PLEATED MEMBRANE FILTER ELEMENT
VALIDATION GUIDE

Process Filtration

Sterile Air Junior Pleated Membrane Filter Element Validation Guide

Contents

Thank You

Thank you for purchasing a quality-built Donaldson Filtration Solutions filter element. Donaldson takes pride in manufacturing state-of-the-art filtration for a variety of applications. Our commitment is to form lasting relationships with our customers by providing world-class products and service. If any questions or issues arise, do not hesitate to contact Donaldson.

Introduction

Donaldson Filtration Solutions has specifically designed Sterile Air filter elements for use in providing sterile air and gas for the processed food and beverage industry. Sterile Air filter elements utilize the inherently hydrophobic expanded polytetrafluoroethylene (ePTFE) membrane, which provides the highest levels of biosecurity throughout the process industry. When combined with quality all-polypropylene components and high integrity manufacturing techniques, the Sterile Air filter element is ideally suited to the most demanding process conditions.

Donaldson Sterile Air filter elements are constructed in ISO accredited clean rooms, under tightly controlled conditions, using advanced, highly-specialized machinery. Quality and consistency of product are managed by ISO 9001 accredited quality control and manufacturing procedures, which are in place throughout all stages of manufacture.

Donaldson Sterile Air ePTFE membrane elements are 100% integrity tested during manufacture by the forward flow diffusion method. Each module of every element is tested to ensure integrity is not compromised by any single module in a element.

Bacterial Challenge Test

This report describes the test results of the Sterile Air elements, under approved protocols, for the evaluation of bacterial retention characteristics of membrane filters used to sterilize liquids. This method uses Brevundimonas diminuta ATCC 19146 as the challenge organism.

The test filters were challenged with a suspension of Brevundimonas diminuta prepared at a concentration of approximately 1 x 10^7 Colony Forming Units (CFU) per cm^2 of Effective Filtration Area (EFA). The sterility of the complete apparatus was tested before the challenge. The challenge was conducted at a maximum differential pressure of 30 psig (206 kPa). The effluent was collected and assayed quantitatively on 0.45 micron assay membranes. Integrity testing was performed before and after the bacterial challenge procedure.

Justification

This test method was designed to determine the bacterial retention characteristics of membrane filter elements used to sterilize liquids. The selection of Brevundimonas diminuta as the challenge organism is based on its historical acceptance within the industry resulting from its very small size when grown under stress or starvation conditions.

The test procedure complies in intent and content with the ASTM F838-05 standard test method: ***Determining Bacterial Retention of Membrane Filters Utilized for Liquid Filtration*** and the Health Industry Manufacturers Association (HIMA) test method: ***Microbiological Evaluation of Filters for Sterilizing Liquids***. The test protocol, choice of organism, and parameters also meet the advisory information given by the Parenteral Drug Association (PDA) in ***PDA Technical Report No.26, Sterilizing Filtration of Liquids***.

When grown under carefully controlled conditions, many Brevundimonas diminuta will pass through 0.45 micron membranes. Due to the organism's size, Brevundimonas diminuta represents a most severe bacterial challenge to the filter. The organism's low pathogenicity also favors the use of Brevundimonas diminuta in laboratory studies. The challenge conditions include high pressure, high flow rates and a high bacterial concentration per cm^2 of EFA. The growth parameters, temperatures, and media were as detailed in the protocol as specified by ASTM and HIMA.

Log Reduction Value (LRV) Calculation:

$$\text{LRV / Filter} = \text{Log}_{10} \frac{\textit{Number of Organisms in Challenge}}{\textit{Number of Organisms in Filtrate}}$$

When filtrate is sterile, 1 is substituted in the denominated and the LRV is expressed as greater than (>) the calculated value.

Bacterial Retention Results

Sterile Air 0.2 micron (Brevundimonas diminuta ATCC 19146)

Filter ID	Flow Rate @30 psi (L/Sec)	Total Challenge (CFU)	Challenge/Sq. cm (CFU/cm^2)	Filtrate Count (CFUC)	Rinse Count (CFU)	Diffusion Rate (mL per Minute)*	LRV
F20 617525 001	10/18	7.7 x 10^{10}	1.1 x 10^7	<1	<1	1	>10.89
F20 617525 004	10/18	1.1 x 10^{11}	1.6 x 10^7	<1	<1	6	>11.05
F20 617525 005	12.5/30	1.1 x 10^{11}	1.6 x 10^7	<1	<1	22	>11.05

**At test pressure of 827 mbar – 60% IPA 40% water, wetted, prior to sterilization and bacterial challenge.*

Conclusion

Sterile Air 0.2 micron filter elements were effective in retaining the bacterial challenge as demonstrated by zero CFU present on the assay membranes.

Bacteriophage and Spore Retention

Hydrophobic membrane filters play a critical role in providing sterile air and gases in biotechnology and containment applications. The filters must be proficient in removing airborne viruses (bacteriophage) and spores from large volumes of moist air or gas streams over prolonged periods.

The aim of the following tests is to ensure Sterile Air filter elements are capable of retaining any bacteriophage and spores which might be present in moist air or gas streams.

The Sterile Air filter elements were challenged with high concentrations of MS-2 coliphage (26 nm diameter) and Bacillus atrophaeus spores (typically 1 micron × 0.7 micron), at a flow rate of 650 ± 50 L per minute, with a relative humidity greater than 90%, over a short period and an extended period of seven days. The test protocols, conditions and choice of organisms are in accordance with the advisory information given in the Parenteral Drug Association's ***PDA Technical Report 40, Sterilizing Filtration of Gases***.

Summary of Methods

Sterile Air 254 mm (10 in.) filter elements from a standard production batch were used for the tests listed below. Filter integrity was confirmed using the Diffusion Test method.

- Test 1: Elements challenged with aerosolized Bacillus atrophaeus spores for a period of ten (10) minutes, at 650 ± 50 L per minute, at a relative humidity greater than 90%.
- Test 2: Elements challenged with aerosolized MS-2 coliphage for a period of ten (10) minutes, at 650 ± 50 L per minute, at a relative humidity greater than 90%.
- Test 3: Elements challenged daily with aerosolized MS-2 coliphage for a period of ten (10) minutes, at 650 ± 50 L per minute, at a relative humidity greater than 90% over a period of seven (7) days.

Challenge Apparatus

A schematic diagram of the apparatus used in the filter tests is shown below. The challenge suspensions were placed in the collision sprays in the chamber. The suspensions were nebulized by applying compressed air. The relative humidity (>90%) of the air flowing through the system was checked before and after the challenge. A flow rate of 650 ± 50 L per minute was maintained during the challenge period.

A cyclone sampler was used to collect the organisms generated in the system. Sterile collecting fluid was fed into the cyclone sampler and particles in the air stream were deposited by centrifugal force onto the cyclone wall and were collected by the swirling liquid, which was then withdrawn by a syringe. At the end of the challenge period the fluid was measured and then assayed for the challenge organism using an appropriate technique.

The system was operated to determine the challenge concentration with the filter removed and the collision spray switched on. Background levels were determined with the filter in-situ and the collision spray switched off.

Log Reduction Value (LRV) Calculation:

$$\text{LRV / Filter} = \text{Log}_{10} \frac{\textit{Number of Organisms in Challenge}}{\textit{Number of Organisms in Filtrate}}$$

When filtrate is sterile, 1 is substituted in the denominated and the LRV is expressed as greater than (>) the calculated value.

Results

Table 1 - Ten Minute Challenge with Aerosolized Bacillus Atrophaeus Spores

Filter Batch No.	Diffusion Rate * (mL/Minute)	Total Challenge (CFU)	Filtrate Count (CFU)	Titer Reduction
146497017	8.1	6.28×10^{8}	<1	$>6.28 \times 10^{8}$
146497013	6.6	6.97×10^{8}	2	3.49×10^{8}
146497007	6.6	5.94×10^{8}	<1	$>5.94 \times 10^{8}$

** Test pressure 800 mbar: 60% IPA, 40% water wetted. Maximum allowable diffusion ≤10 mL per min.*

Table 2 - Ten Minute Challenge with Aerosolized MS-2 Coliphage

Filter Batch No.	Diffusion Rate * (mL/Minute)	Total Challenge (CFU)	Filtrate Count (CFU)	Titer Reduction
146497012	8.1	1.37×10^{13}	<15	$>9.13 \times 10^{11}$
146497016	7.3	1.39×10^{13}	138	1.01×10^{11}
146497018	7.3	1.40×10^{13}	436	$>3.21 \times 10^{10}$

** Test pressure 800 mbar: 60% IPA, 40% water wetted. Maximum allowable diffusion ≤10 mL per min.*

*Table 3 - Long-Term (7 Day) Aerosolized MS-2 Coliphage Challenge**

Day	Filter Batch Number	Total Challenge (CFU)	Filtrate Count (CFU)	Titre Reduction
1	146497014	4.820×10^{12}	196	2.459×10^{10}
	146497010	3.980×10^{12}	2168	1.836×10^{9}
	146497015	3.895×10^{12}	Data Not Used	–
2	146497014	1.040×10^{12}	27	3.852×10^{10}
	146497010	1.157×10^{12}	31	3.732×10^{10}
	146497015	1.146×10^{12}	986	1.162×10^{9}
3	146497014	1.299×10^{11}	16	8.116×10^{10}
	146497010	5.630×10^{11}	77	7.311×10^{9}
	146497015	1.132×10^{11}	71	8.636×10^{9}
4	146497014	3.951×10^{11}	352	1.122×10^{9}
	146497010	4.759×10^{11}	704	6.760×10^{8}
	146497015	4.462×10^{11}	1995	2.237×10^{8}
5	146497014	6.993×10^{11}	2065	3.386×10^{8}
	146497010	8.680×10^{11}	1285	6.755×10^{8}
	146497015	8.500×10^{11}	70	1.214×10^{10}
6	146497014	5.685×10^{11}	21	2.707×10^{10}
	146497010	7.861×10^{11}	558	1.409×10^{9}
	146497015	6.815×10^{11}	50	1.363×10^{10}
7	146497014	6.286×10^{11}	64	9.822×10^{9}
	146497010	5.574×10^{11}	<1.5	$>3.716 \times 10^{11}$
	146497015	6.346×10^{11}	641	9.900×10^{8}

** Filters were determined to be integral at the start of the test.*

Conclusion

The test data confirms that standard production filter elements retain very high challenge levels of aerosolized phage, as demonstrated using MS-2 coliphage and aerosols of non-vegetative spores, as demonstrated using spores of Bacillus atrophaeus.

Integrity Tests

For critical applications, filter validation requires testing with the bacteria Brevundimonas diminuta to confirm the retention characteristics of the filter. Since this is a destructive test, it cannot be performed on all filters. However, by correlating microbial challenge tests with non-destructive integrity tests, filter performance can be assured.

The bubble point, diffusion and pressure hold tests are industry accepted non-destructive methods for verifying the integrity of a membrane filter.

Test Parameters Summary

All Sterile Air 0.2 micron filter elements are 100% integrity tested during manufacture.

Test Procedure	Test Pressure (mbar)	Acceptable Flow Per 10 Inch Module
Bubble Point Test	960	–
Forward Flow Diffusion Test	800	10 mL/Minute
Pressure Hold Test	800	10 mL/Minute
Water Intrusion Test	2500	3714 µl/10 Minute (Microliter/Minutes)

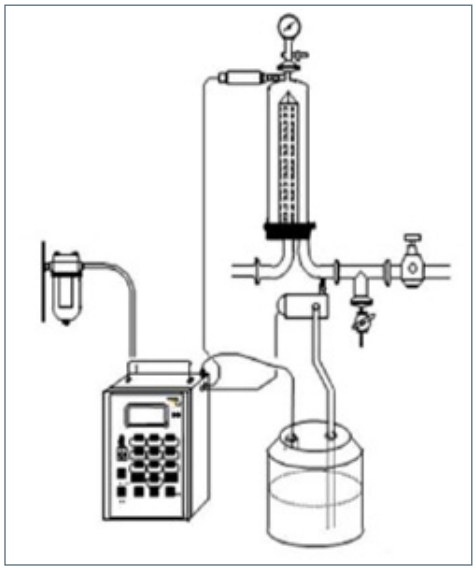
**All test data are valid for 60% IPA, 40% Water. The Water Intrusion Test should be carried out in pure water.*

Wetting

Before an integrity test, the hydrophobic ePTFE membrane must be completely wetted with a liquid having a surface tension of <28 dyne/cm. Therefore, to achieve thorough wetting, and to ensure an accurate diffusion rate, a solution of 60% Isopropyl alcohol (IPA) and 40% water is used.

Diffusion Test

The Sterile Air filter element is wetted with 60%, IPA 40% water and a test pressure of 800 mbar is applied to the upstream side of the filter assembly. After a stabilization stage, the gas flow through the wetted membrane can be measured manually on the downstream side or on the upstream side using automatic integrity test equipment, as illustrated below.



Materials of Construction

The Sterile Air filter element is manufactured using high-quality components. All components of the Sterile Air filter element are FDA listed for food contact use in the ***Code of Federal Regulations (CFR), Title 21*** as listed in the table below. Components meet ***EEC Directive EC10/2011*** for food contact.

Component	Materials of Manufacture	FDA Number
Membrane	PTFE	21CFR177.1550
Support Layers	Polypropylene	21CFR177.1520
Core	Polypropylene	21CFR177.1520
Sleeve	Polypropylene	21CFR177.1520
Adapters	Polypropylene	21CFR177.1520
End Caps	Polypropylene	21CFR177.1520
Seals	Silicone (Typically)	21CFR177.2600
Sealing Method	Thermal Bonding	–

Element Dimensions (Nominal)

Diameter:	56 mm (2.2 in.)
	70 mm (2.8 in.)
Lengths:	77.5 mm (2.5 in.)
	136 mm (5 in.)

Maximum Differential Pressure

Normal Flow Direction at:	20 C (68 F): 6.0 bar (87 lb/in^2)
	80 C (176 F): 4.0 bar (58 lb/in^2)
	100 C (212 F): 3.0 bar (43 lb/in^2)
	120 C (248 F): 2.0 bar (29 lb/in^2)
	125 C (257 F): 1.5 bar (22 lb/in^2)
Reverse Flow Direction at:	20 C (68 F): 2.1 bar (30 lb/in^2)
	80 C (176 F): 1.0 bar (15 lb/in^2)
	100 C (212 F): 0.5 bar (7 lb/in^2)

Elements are able to maintain integrity for an extended period of time at 60 C (140 F). Based on cyclic exposure to hot air and steam.

Chemical Compatibility

Compatibility is influenced by various factors such as temperature, concentration, and mixture. It is recommended that a compatibility test be performed with the solution medium before a full filtration run. The tests outlined in Chemical Compatibility Tables 1 and 2 were run using Sterile Air filter elements with O-rings under typical filtration application conditions of 20 C (68 F).

Chemical Compatibility Table 1

O-Ring Materials:	PTFE Encapsulated	Silicone	EPDM	Viton
Acids				
Acetic Acid (conc) 17.5 N	C	NC	C	LC
Acetic Acid, 8.75 N	C	C	NC	LC
Acetic Acid, 3.5 N	C	NC	LC	LC
Benzoic Acid	C	NC	C	LC
Citric Acid, 10%	C	LC	LC	LC
Chromic Acid	C	NC	NC	LC
Formic Acid (conc)	C	C	LC	NC
Hydrochloric Acid (conc)	C	NC	NC	NC
Hydrochloric Acid, 25%	C	C	C	C
Hydrochloric Acid, 5%	C	C	NC	NC
Hydrofluoric Acid, 25%	NC	NC	NC	NC
Nitric Acid, (conc), 15.8 N	C	NC	C	C
Nitric Acid, 2N	C	LC	C	LC
Perchloric Acid, 25%	C	LC	NC	NC
Phosphoric Acid, 85%	C	NC	NC	NC
Phosphoric Acid, 25%	C	C	C	C
Sulphuric Acid, 25%	C	LC	NC	NC
Sulphuric acid, 98%	C	LC	LC	LC
Trichloroacetic acid, 25%	C	LC	NC	LC
Bases				
Aqueous Ammonia, 15.5 N	C	LC	LC	C
Ammonium Hydroxide, 1 N	C	LC	LC	C
Ammonium Hydroxide, 3 N	C	LC	LC	C
Ammonium Hydroxide, 4 N	C	LC	LC	C
Calcium Hydroxide, 5%	C	LC	LC	LC
Potassium Hydroxide, 3 M	C	LC	LC	LC
Potassium Hydroxide, 32%	C	C	LC	C
Solium Carbonate, 0.5 N	C	LC	C	LC
Sodium Hydroxide, 2 N	C	LC	LC	LC

C - Compatible, LC - Limited Compatibility, NC - Not Compatible
NOTE: The information in the above table is offered as a guide only.

Chemical Compatibility Table 2

O-Ring Materials:	PTFE Encapsulated	Silicone	EPDM	Viton
Solvents				
Acetone	C	NC	C	NC
Benzene	C	NC	NC	LC
n-Butyl acetate	C	NC	C	NC
Cellosolve	C	NC	LC	C
Chloroform	C	NC	NC	LC
Cyclohexanone	C	NC	LC	NC
Diethyl ether	C	NC	NC	NC
Dimethyl formamide	C	LC	C	NC
Dimethyl sulfoxide	C	NC	C	NC
Dioxane	C	NC	C	NC
Ethanol, 98%	C	C	C	C
Ethyl acetate	C	LC	LC	NC
Formamide	C	NC	C	LC
Gasoline	C	NC	NC	C
n-Hexane	C	NC	NC	C
Iso-Butanol	C	C	C	C
Isopropanol	C	C	C	C
Methonol, 98%	C	C	C	C
Methylene chloride	C	NC	NC	LC
Methyl ethyl ketone	C	NC	C	NC
Tetrahydrofuran	C	NC	NC	NC
Toluene	C	NC	NC	LC
Trichlorethane	C	NC	NC	C
Trichlorethylene	C	NC	LC	C
Xylene	C	NC	NC	LC
Aqueous Solutions				
Ammonium persulfate, 25%	C	C	C	C
Ferric chloride, 25%	C	C	C	C
Formaldehyde, 30%	C	LC	C	C
Hydrogen peroxide, 5% - 35%	C	C	C	C
Sodium hypochlorite, 5%	C	C	C	C
Solvents				
Amuchina (bleach)	C	C	C	C
Ethylene diamine tetra-acetic acid	C	C	C	C
Quarternary ammonium compounds 2.5%	C	C	C	C
Sodium thiosulphate 0.1N	C	C	C	C
Sodium sulphite 0.1M	C	C	C	C
Sodium thiosulphate	C	C	C	C

C - Compatible, LC - Limited Compatibility, NC - Not Compatible
NOTE: The information in the above table is offered as a guide only.

Tests for Biological Safety - USP Class VI

Sterile Air 0.2 micron filter elements are manufactured using FDA approved materials as listed above. In addition, all material components used in this product range have been tested and meet the requirements of the USP guidelines for Class VI Plastics – 121 C.

The results from independent testing (Nelson Labs, Salt Lake City, Utah, USA) of filter materials are shown below. The test articles were extracted at 121 C for one (1) hour under dynamic conditions for systemic injection and intracutaneous injection tests.

Systemic Injection Test

Study Number	1211618-S01
Test Suite	USP Toxicity Class VI-121C
Specific Test	Systemic Injection
Species	Albino Swiss Mice

	Extract	No. of Test Subjects	Test Subjects Showing Signs of Toxicity After:				
			0 Hours	4 Hours	24 Hours	48 Hours	72 Hours
Controls	NaCl 0.9%	5	0	0	0	0	0
	Cottonseed Oil	5	0	0	0	0	0
	Ethanol 5%	5	0	0	0	0	0
	Peg 400	5	0	0	0	0	0
Tests	NaCl 0.9%	5	0	0	0	0	0
	Cottonseed Oil	5	0	0	0	0	0
	Ethanol 5%	5	0	0	0	0	0
	Peg 400	5	0	0	0	0	0

NOTE: No systemic toxicity observed at any of the observation points: non-toxic.

Intracutaneous Injection Test

Study Number	1211618-S01
Test Suite	USP Toxicity Class VI-121C
Specific Test	Intracutaneous Injection
Species	New Zealand White Rabbit

	Extract	No. of Test Subjects	Skin Irratation*		
			24 Hours	48 Hours	72 Hours
Controls	NaCl 0.9%	10	–	–	–
	Cottonseed Oil	10	–	–	–
	Ethanol 5%	10	–	–	–
	Peg 400	10	–	–	–
Tests	NaCl 0.9%	10	0	0	0
	Cottonseed Oil	10	0	0	0
	Ethanol 5%	10	0	0	0
	Peg 400	10	0	0	0

**Difference Between Test and Control: Overall Mean Score*
NOTE: No intracutaneous toxicity observed at any of the observation points: non-toxic.

Intramuscular Implantation Test

All test articles were prepared according to the USP guidelines.

Study Number	1211618-S01
Test Suite	USP Toxicity Class VI-121C
Specific Test	Intramuscular Implantation
Species	New Zealand White Rabbit

Extract	Number of Test Sites	Clinical Signs of Toxicity Over 7-Day Period
Filter Hardware	8	0
Filter Media	8	0
Control	8	0

NOTE: No intramuscular toxicity observed at any of the observation points: non-toxic.

Conclusion

The extracts of the test articles following intracutaneous injection in rabbits and systemic injection in mice, and the test articles following intramuscular implantation in rabbits, did not produce a biological response.

Based on the criteria of the protocol and the USP guidelines for Class VI Plastics -121 C, the test articles meet the requirements of the test.

In-line Steam Sterilization

Objective

Sterile Air filter elements have been demonstrated to retain integrity after repeated steam-in-place (SIP) cycles under the test conditions described below.

Procedure

Elements were sampled from a routine production batch; integrity tested by forward flow diffusion method, initially, and after every 12th cycle thereafter. Elements were steam sterilized by dynamic in-line steam at 125 C (257 F) and 135 C (275 F) for twenty (20) minutes, while maintaining differential pressure below 0.5 bar. Upstream and downstream condensate was drained throughout each cycle. The elements were air cooled for ten (10) minutes between steam cycles to simulate the highest levels of thermal shock likely to be encountered in use.

Results

Extract Element Batch Lot No.	No. of 20 Minute Cycles	Temperature C (F)	Tested	Failed
136927	150	125 (257)	5	0
137982	100	135 (275)	3	0
146497	100	135 (275)	5	0
107009	50*	135 (275)	1	0

**Reverse Flow*

Conclusion

All elements tested maintained integrity throughout differing test regimes.

Liquid Flow Rate Characteristics

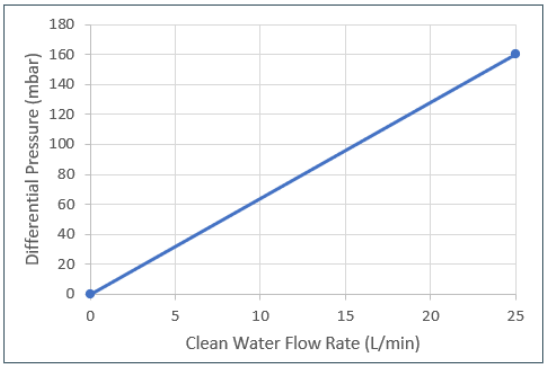
Clean Water

Sterile Air 0.2 micron filter element clean water flow rate, based on a 254 mm (10 in.) single element, with an effective filtration area of 0.73 m^2 (7.8 ft^2) in-situ, in a housing exhibiting the differential pressure characteristics indicated below.

Test Procedure

Clean water flow versus Δp: The test elements were immersed in a solution of 60%, IPA 40% water for approximately one (1) minute.

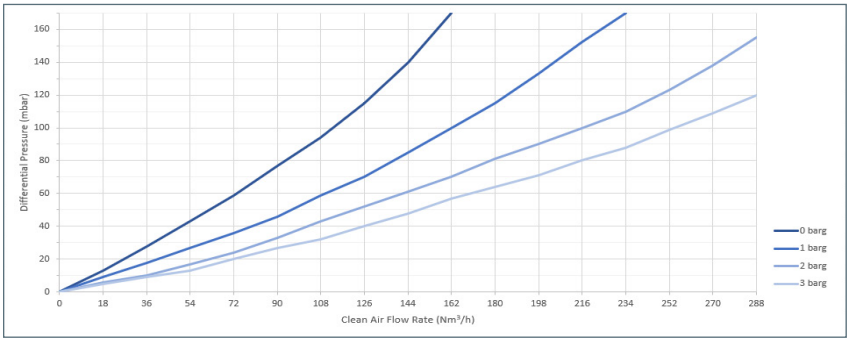
The water inlet valve was opened, and the water allowed to circulate, until the pressure differential across the clean-up filter stabilized. Test filters were installed, and the wetting solution flushed to waste. Water was then allowed to flow through the element for approximately ten (10) minutes before the differential pressure across the filter/housing, at a flow of 5, 10, 15, 20, and 25 L per minute, was recorded.



Air Flow Rate Characteristics

Clean Air Flow Rate

Sterile Air 0.2 micron filter element clean air flow rate, based on a 254 mm (10 in.) single element, with an effective filtration area of 0.73 m^2 (7.8 ft^2) in-situ, in a housing exhibiting the differential pressure characteristics indicated below.



Test Procedure

Standard production Sterile Air filter elements were installed in a stainless-steel air filter housing designed for use in compressed gas and vent applications. The differential pressure across the filter assembly was measured while clean compressed air was moving through the filter assembly, at a range of flow rates, under both **atmospheric vent** and **pressurized** operating conditions.

In **vent** conditions, the downstream side of the filter assembly was open to atmospheric pressure while air flow through the filter was controlled from the upstream side. Under **pressurized** conditions, predetermined air pressures were maintained upstream of the filter assembly while air flow rate through the filter was controlled by restricting flow on the downstream side.

Important Notice: Many factors beyond the control of Donaldson can affect the use and performance of Donaldson products in a particular application, including the conditions under which the product is used. Since these factors are uniquely within the user's knowledge and control, it is essential the user evaluate the products to determine whether the product is fit for the purpose and suitable for the user's application. All products, specifications, availability and data are subject to change without notice, and may vary by region or country.

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