VALIDATION GUIDE

HIGH FLOW BIO-X

Sterilizing Grade

Cartridge Filters

Contents

1. Introduction

Sterilizing grade filters used to sterilize gases that come into contact with products must conform to strictly defined quality standards.

This validation guide provides proof of performance of the High flow Bio-X filter cartridges with respect to bacterial retention and physical performance characteristics such as flow rates and resistance to steam sterilization. The performance tests conducted for the High Flow Bio-X products have been designed to guarantee that sterile gas will continue to be provided even under the most arduous operating conditions.

Guidelines for validation can be sourced from publications issued by the FDA, EMEA, USP, EP, BP, PDA[1], etc. This validation document has been produced with these guidelines in mind to enable the end user to incorporate this information within their own validation documentation or standard operating procedures for the process.

The performance of HIGH FLOW BIO-X filter cartridges has been tested in accordance with - and exceeds - the specific guidelines of PDA Technical Report 40 'Sterilizing Filtration of Gases' *(Supplement Volume 58 No.S-1 Jan / Feb 2005),* sections 7.2 to 7.3. These filters also conform to current ISO 8573-7 Compressed Air Part 7: Test method for viable microbiological contaminant content.

NOTE

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[1] FDA, EMEA, USP, EP, BP, PDA – Food and Drug Administration, European Medicines Evaluation Agency, United States, European and British Pharmacopoeia, Parenteral Drug Association.

2. Quality Assurance

Quality is built into all Parker domnick hunter filtration products through a rigorous product design process, careful selection of suppliers and materials, and manufacture within a highly controlled environment using validated production technologies in adherence to cGMP.

2.1. Quality and Environmental Management Systems

Parker domnick hunter is certified by Lloyds Register Quality Assurance to current versions of the following quality standards:

- BS EN ISO 9001 Quality Management Systems
- BS EN ISO 14001 Environmental Management Standard
- PS 9100 The application of ISO9001 GMP guide to pharmaceutical excipients
- BS EN ISO 13485 Medical Devices

Copies of the original certificates are available upon request.

2.2. PS 9100 within Parker domnick hunter

The pharmaceutical Quality Group of the Institute of Quality Assurance has developed and produced an application standard – PS 9100 – which defines the application of ISO 9001 to pharmaceutical excipients; Parker domnick hunter filter products used within pharmaceutical and sterilizing processes are categorized as excipients.

PS 9100 introduces three levels of GMP, written in the ICH Q7A style. One of the key practical elements in this document is to assign an appropriate level of GMP for excipients using a risk assessment approach based on end-user safety. The Parker domnick hunter quality system defines, at an appropriate (intermediate) risk level, standards of GMP for the manufacture of filtration products under an appropriate system for managing quality.

Compliance to PS 9100 is independently assessed at regular intervals by Lloyds Register Quality Assurance.

2.3. Manufacturing Facilities

Parker domnick hunter continues to invest substantially in installation of the latest clean room and manufacturing technology. All manufacturing systems are validated using statistical methodologies (process, product and software) and constantly monitored using statistical process control charts. All personnel within the manufacturing operations are fully trained in cGMP and against competency frameworks to ensure their suitability to operate within specific manufacturing areas.

2.4. Material Conformity

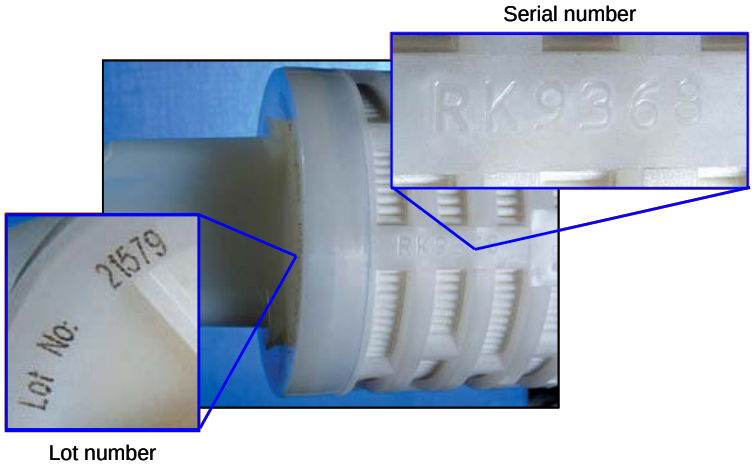
Parker domnick hunter works closely with suppliers to ensure materials supplied are of a consistently high quality and also to develop new materials as part of our ongoing product development activity. In addition to supplier certificates of conformity and analysis, incoming raw materials, including moulded parts, media and supports, and elastomeric seals, are subject to an appropriate level of incoming inspection. This includes aerosol bacterial challenge on each lot of media used in the manufacture of sterilizing grade filter cartridges.

2.5. Product and Lot Release Criteria

Prior to shipment all Parker domnick hunter cartridges undergo final product quality control. 100% of HIGH FLOW BIO-X cartridges undergo a non-destructive aerosol integrity test which is correlated to an aerosol bacterial challenge.

2.6. Product Traceability

The product code and type, lot number and unique serial number are printed on all products. Additionally, the lot number is identified on the protective bag label and the box label within which the cartridge is packed. The serial number provides complete traceability back to pleated materials used in the manufacture of each product and the manufacturing processes through the module routing sheet.



2.7. Product Shelf Life

The shelf life for HIGH FLOW BIO-X cartridges is 5 years.

3. Product Description

All products within the HIGH FLOW BIO-X sterilizing grade filter range are fully validated to provide sterile air / gas under worst case conditions in a wide range of applications throughout the food & beverage, dairy and pharmaceutical industries

Their performance has been qualified for full retention of both bacteria and bacteriophage in the gas phase when tested in accordance with the recommendations in PDA Technical Report 40 'Sterilizing Filtration of Gases' *(Supplement Volume 58 No. S-1 Jan / Feb 2005),* sections 7.2 to 7.3.

3.1. Materials of construction

All materials meet the FDA requirements as defined in Title 21 Code of Federal Regulations and the BioSafety Tests as defined in the current USP including the Class VI Plastics Testing.

Filtration Media	Polytetrafluoroethylene (PTFE) Impregnated Borosilicate Microfibre
Upstream Support	Polypropylene
Downstream Support	Polypropylene
Inner Core	316L Stainless Steel
Outer Protection Cage	Polypropylene
Endcaps	Polypropylene
Endcap Insert	316 Stainless Steel
Standard o-rings	Silicone

3.2. Product Coding

Product code structures indicate the cartridge sizes, endcap configurations and o-rings that are available within the product range.

Cartridges

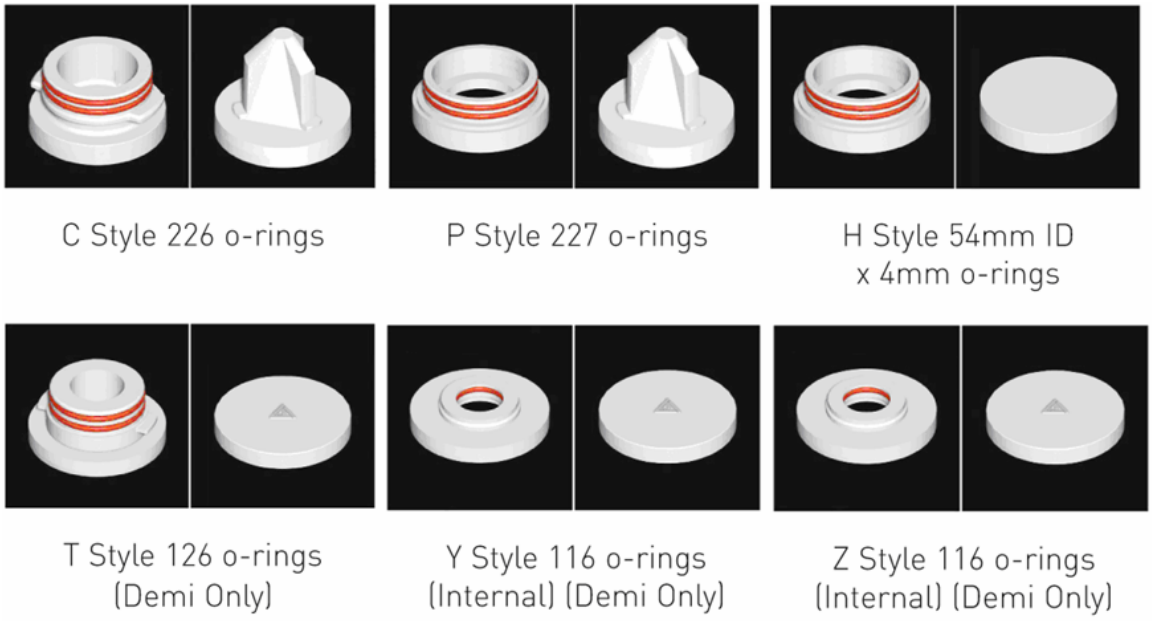
Example ZCHB-1C 250 mm (10”) HIGH FLOW BIO-X filter cartridge, with ‘C’ style endcap and Silicone o-rings.

ZCHB - [ ][ ]

Code	Length (mm)	Length (inch)	Diameter (mm)
B	65	2.5	56
A	125	5	56
K	125	5	72
1	250	10	72
2	500	20	72
3	750	30	72

Code	10” Endcap Style
C	P-7
P	Bio-X Retrofit
H	Donaldson UF Retrofit
Code	**10” Endcap Style**
H	Donaldson **UF** Retrofit
T	TRUESEAL
Y	DEMI MCY
Z	DEMI A&B Std

3.3. Cartridge Endcap Configurations



4. Product Specifications

4.1. Cartridge Operating Differential Pressures and Temperatures

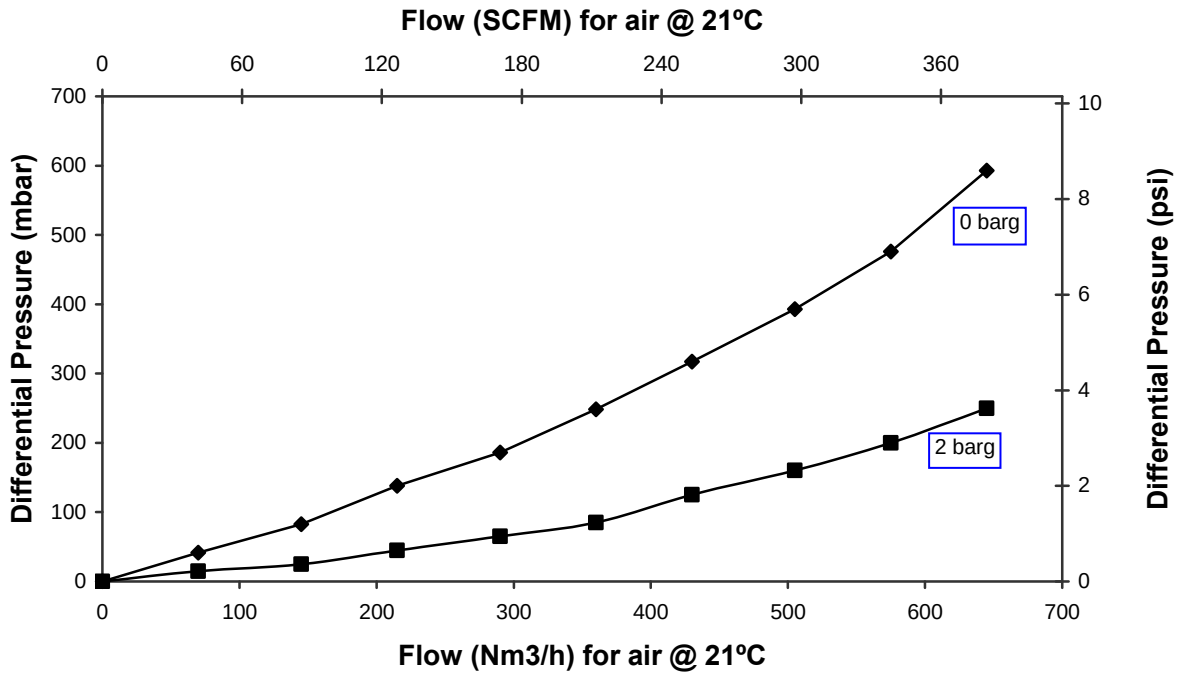
The recommended continuous maximum differential operating pressure and temperature is shown below.

Temperature		Differential Pressure	
°C	°F	bar	psi
70	158	3.50	50.8

4.2. Flow Rates

Cartridge flow rates were determined for filters from three separate lots.

Air Flow Characteristics for 250mm (10") High Flow Bio-X Cartridges

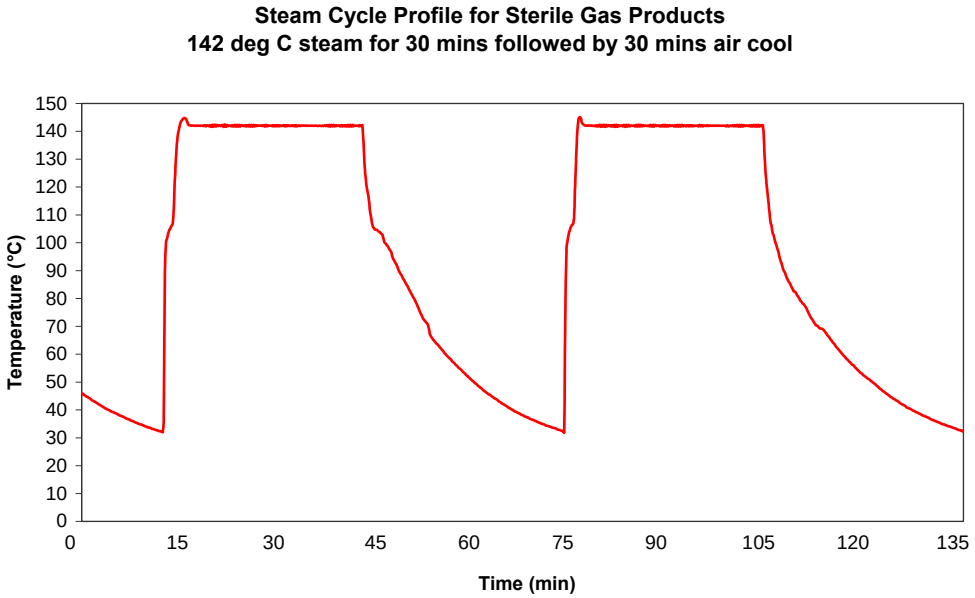


4.3. Effective Filtration Area (EFA)

Product Size	Surface Area (m^2)	Surface Area (ft^2)
10”	0.38	4.09

4.4. Steam Sterilization (Autoclaving and Steam in Place)

The steam life of cartridges was determined using the Steam in Place (SIP) cycle shown below which replicates extreme conditions. This includes a combination of steaming for 30 minutes at temperature followed by ambient water flow during the cooling phase of each cycle. The resistance to steam sterilisation was determined by evaluating three production batches of 10 inch cartridges.



Product Format	SIP Temp		Number of Cycles	Cycle Time (minutes at temperature)
	°C	°F		
Cartridges	142	288	150	30

It should be noted that the number of times the temperature is cycled from ambient to the sterilization temperature rather than the time at temperature determines the lifetime of the cartridge in steam.

To maximize the life of the cartridge, the differential pressure across the cartridge should not exceed 0.30 bar (4.4 psi) at 142°C (288°F). For new applications it is recommended that the Parker domnick hunter guidance for the method of steam sterilisation be followed.

4.5. Retention

To guarantee filter performance a filter must be capable of being non-destructively integrity tested. This is recognized by the FDA in the "Guideline on Sterile Drug Products produced by Aseptic Processing" (June 1987), which states:

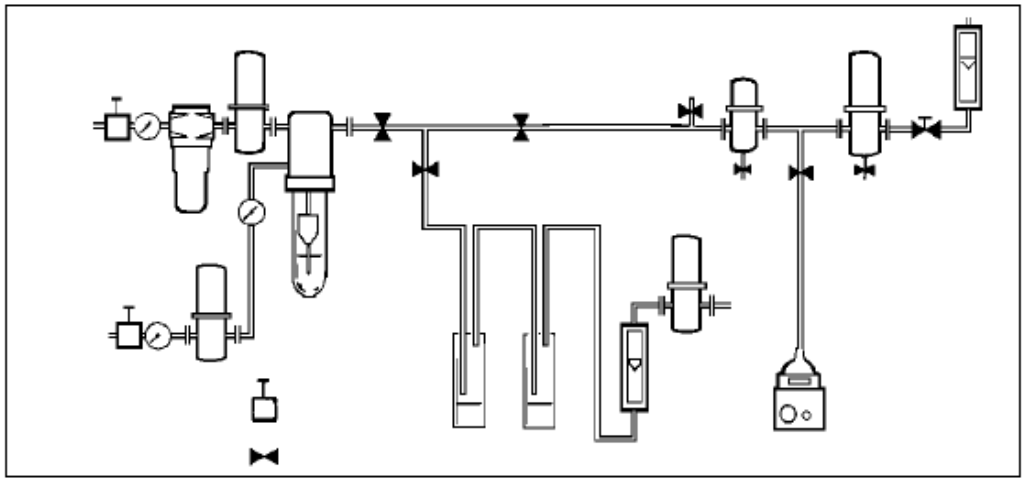
"After a filtration process is properly validated for a given product process and filter, it is important to assure that identical filter replacements…used in production runs will perform in the same manner. One way of achieving this is to correlate filter performance data with filter integrity testing 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 the filtration."

To achieve this objective the correlation between bacterial challenge retention and a non-destructive integrity test must be proven. To ensure the filter is capable of sterilizing in the gas phase it is subjected to aerosol bacterial and bacteriophage challenges. These tests are conducted in line with the guidelines published in PDA Technical Report 40 'Sterilizing Filtration of Gases' *(Supplement Volume 58 No.S-1 Jan / Feb 2005),* sections 7.2-7.3.

The filter must be challenged with a minimum of 10^7 viable Brevundimonas diminuta (ATCC 19146) per cm^2 of effective filtration area. The methodology is also referenced in "Integrity Testing Air Sterilisation Filters, A Comparison of Aerosol Challenge with Airborne Microbiological Challenge Methods, Pharmaceutical Technology Europe, April 1995"[2]

Non-destructive testing of filter integrity is carried out using a Parker domnick hunter VALAIRDATA integrity test instrument with a minimum sensitivity of 0.00005%.

Aerosol Bacterial Challenge Schematic



1. Nebuliser
2. Test filter housing
3. Impinger samplers
4. Slit sampler
5. Flowmeters
6. Inlet air sterilising filters
7. Pressure meters
8. Steam inlet
9. Exhaust gas sterilising filter
10. Sampling ports
11. Drainage ports
12. Flow control valve
13. Prefilter

[2] S. Johnston, A.M. Bennett, S.R.Parks, Dr. J.E. Benbough – Biosafety Investigation Unit, Centre for Applied Micro-biology and Research, Porton Down, UK

4.6. Retention to Aerosolized *Brevundimonas diminuta*

Tests have shown that the Parker domnick hunter High Flow Bio-X series is fully retentive to aerosolized *Brevundimonas diminuta* (ATCC 19146) bacteria when challenged with a total of $2x10^{11}$ cfu over a 1-hr test at the rated flow of the cartridge.

No penetration was detected, which is equivalent to a log reduction value (LRV) of >8 per cm^2 of effective filtration area.

4.7. Retention of Aerosolized Bacteriophage

Independent tests have shown that High Flow Bio-X filters are fully retentive to aerosolized *MS-2 Coliphage* when challenged at between $4.39x10^7$ and $4.69x10^7$ pfu per cm^2 daily over a period of 8 days.

No penetration was detected over this time which is equivalent to a log reduction value (LRV) of > 11.5 for the 8 day period.

Day	Volume MS-2 nebulized (ml)	Total MS-2 challenge (pfu)	MS-2 (pfu) in effluent	
			Filter 1	Filter 2
1	7.0	2.38×10^{11}	ND[3]	ND
2	7.1	2.41×10^{11}	ND	ND
3	7.0	2.38×10^{11}	ND	ND
4	6.1	2.07×10^{11}	ND	ND
5	5.8	1.97×10^{11}	ND	ND
6	7.1	2.41×10^{11}	ND	ND
7	8.3	2.82×10^{11}	ND	ND
8	7.0	2.38×10^{11}	ND	ND

[3] None detected (i.e. less than 1 pfu, or less than background level)

4.8. VAL*AIR*DATA Aerosol Correlation

The table below lists HIGH FLOW BIO-X cartridges that were aerosol integrity tested before and after bacterial challenge. The bacterial challenge was conducted using ASTM F838-83 so providing the necessary correlation between a bacterial challenge and a non-destructive diffusional flow test.

These results indicate that a 250 mm (10") HIGH FLOW BIO-X filter exhibiting and integrity test reading of 0.00068% using a VAL*AIR*DATA integrity test instrument is fully retentive to an aerosol challenge of *Brevundimonas diminuta*.

Parker domnick hunter has applied a margin of safety and gives a PASS level based on the sensitivity of the instrument. The sensitivity of a VAL*AIR*DATA integrity test instrument is 0.00005%.

Filter type: ZCHB-1C HIGH FLOW BIO-X 10" cartridge

Challenge organism: *Brevundimonas diminuta*

Serial No.	Total Challenge Level (x 10^{10})	Silt Samples		LRV[4]	Aerosol Penetration VAL*AIR*DATA (%)
		Initial	Final		
143309	3.53	0	0	10.55	< 0.00005
132777	3.64	0	0	10.56	< 0.00005
143253	7.33	0	0	10.87	< 0.00005
143061	2.51	0	0	10.40	< 0.00005
143037	1.76	0	0	10.24	< 0.00005
143243	0.80	0	0	9.90	< 0.00005
143286	0.0963	0	0	8.98	0.00011
143337	0.00168	0	0	7.23	0.00014
132784	0.00222	0	0	7.35	0.00024
143182	5.34	0	0	10.72	0.00068
143268	0.109	21	5	7.62	> 0.01
142985	0.0494	41	65	6.67	> 0.01

Conclusion

Any filter when tested for integrity that gives a PASS reading using the VALAIRDATA, i.e. 0.00005% or less, is validated as fully retentive to aerosol bacterial challenge.

[4] Where organisms passed = 0, LRV is stated as *greater than*.

5. Chemical Compatibility

The following data is indicative of HIGH FLOW BIO-X cartridge compatibility with a range of chemicals at ambient temperature and 72 hour exposure. However it is recommended that specific process conditions are reviewed with your local Parker domnick hunter representative.

	ASYPOR	BIO-X II	HIGH FLOW BIO-X	HIGH FLOW BIO-X VENT AUTOCLAVE	HIGH FLOW PREPOR GFA	HIGH FLOW TETPOR II	HIGH FLOW TETPOR H.T.	HIGH FLOW TETPOR VENT AUTOCLAVE	PEPLYN PLUS & PEPLYN PLUS DC	PREPOR GF	PREPOR PES	PROPOR PES / FS	TETPOR AIR	TETPOR LIQUID	TETPOR PLUS	EPDM 'O'Ring	VITON 'O'Ring	SILICONE 'O'Ring
Acetic acid 3.5N	LC	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
Acetic acid 8.75N	LC	C	C	-	C	C	C	C	C	C	-	-	C	C	C	LC	LC	NC
Acetic acid conc.17.5N	NC	C	C	-	C	C	C	C	C	C	-	-	C	C	C	LC	NC	NC
Acetone	NC	C	C	-	C	C	C	C	C	C	NC	NC	C	C	C	NC	NC	NC
Acetonitrile	NC	C	C	-	LC	C	C	C	C	LC	-	-	C	C	C	NC	NC	NC
Acidbrite 4 (Diversey) 3.0%$_{v/v}$	NC	-	-	-	C	-	-	-	C	C	-	-	-	-	-	C	C	C
Ammonium Hydroxide 8N	NC	C	C	C	C	C	C	C	C	C	C	LC	C	C	C	C	C	C
Ammonium Oxalate 0.07N	-	C	C	C	C	C	C	C	C	C	-	-	C	C	C	C	C	C
Amyl Acetate	NC	C	C	C	LC	C	C	C	C	LC	LC	LC	C	C	C	NC	NC	LC
Aqueous Ammonia 15.5N	NC	C	C	C	LC	C	LC	C	C	LC	C	LC	C	C	C	C	C	C
Benzyl Alcohol	NC	C	C	C	NC	C	C	C	NC	NC	-	-	C	C	C	C	C	C
Benzyalkonium Chloride 0.1%	LC	C	C	C	C	C	C	C	C	C	-	-	C	C	C	C	C	C
Boric acid,saturated	C	C	C	C	C	C	C	C	C	C	-	-	C	C	C	C	C	C
Butan-1-ol	NC	C	C	C	C	LC	LC	LC	C	C	C	C	NC	NC	NC	C	C	C
Butan-2-ol	NC	C	C	C	C	C	C	C	C	C	C	C	C	C	C	LC	C	C
Carbon Tetrachloride	NC	C	C	C	NC	C	C	C	NC	NC	-	-	NC	NC	NC	NC	C	NC
Chloroform	NC	C	C	C	NC	C	C	C	NC	NC	NC	NC	NC	NC	NC	NC	LC	NC
Cyclohexane	NC	C	C	C	NC	-	-	-	NC	NC	-	-	LC	LC	LC	NC	NC	NC
1,4 – Dioxane	NC	C	C	C	LC	C	C	C	C	LC	-	-	C	C	C	NC	NC	NC
Diverflow (Diversey) 3%v/v	NC	-	-	-	NC	-	-	-	C	NC	C	C	-	-	-	C	C	LC
Diversey 212G 0.6%v/v	NC	-	-	-	C	-	-	-	C	C	-	-	-	-	-	C	C	C
Divosan Forte 0.5%v/v	LC	-	-	-	C	-	-	-	C	C	C	C	-	-	-	C	C	C
Divosan XT 1%v/v	C	-	-	-	C	-	-	-	C	C	-	-	-	-	-	C	C	C
Ethanol	NC	C	C	C	C	C	-	C	C	C	C	C	C	C	C	C	C	LC
Ethanol 45%	LC	-	-	-	C	-	-	-	C	C	C	C	C	C	C	C	C	C
Ethyl Acetate	NC	LC	LC	LC	LC	LC	LC	LC	LC	LC	NC	NC	LC	LC	LC	C	NC	LC
Formaldehyde 0.3%	LC	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
Formaldehyde 37%	NC	C	C	C	C	C	C	C	C	C	-	-	C	C	C	C	C	C
Formic acid conc.	NC	C	C	C	NC	C	C	C	C	NC	-	-	C	C	C	C	NC	NC
Glycerol	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
Hexane	LC	C	C	C	-	C	C	C	NC	-	-	-	-	-	-	NC	NC	NC
Hydrochloric acid 1N	C	-	-	-	C	-	-	-	C	C	C	C	C	C	C	C	C	C
Hydrochloric acid conc.	NC	-	-	-	NC	-	-	-	C	NC	-	-	C	C	C	NC	NC	NC
Hydrochloric acid conc.13%	-	C	C	C	-	C	C	C	-	-	-	-	-	-	-	NC	NC	NC
Hydrogen Peroxide	-	C	C	C	-	-	-	-	C	-	-	-	-	-	-	C	C	C
Hydrogen Peroxide 10% Volume	C	-	-	-	C	-	-	-	C	C	C	C	C	C	C	C	C	C
Hydrogen Peroxide 100% Volume	LC	-	-	-	C	C	C	C	C	C	-	-	C	C	C	C	C	C
Methanol	NC	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	NC	C
Methyl-Iso-Butylketone	NC	C	C	C	C	C	C	C	C	C	NC	NC	C	C	C	NC	NC	LC
Methylene Chloride @ 40°C	-	-	-	-	LC	-	-	-	LC	LC	-	-	-	-	-	-	-	-
Nitric acid 2N 14.4%	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	LC	C	C
Nitric acid 15.8N	NC	C	C	C	NC	C	NC	C	C	NC	-	-	C	C	C	NC	NC	NC
Ozone	-	-	-	-	-	-	-	-	-	-	NC	NC	-	-	-	-	-	-
Paraffin yellow	LC	LC	LC	LC	LC	C	C	C	C	LC	-	-	C	C	C	NC	C	NC
Pentane	LC	C	C	C	LC	-	-	-	LC	LC	-	-	LC	LC	LC	NC	C	NC
Peracetic acid 0.5% (10 wk test)	C	-	-	-	-	C	C	C	-	-	-	-	-	-	-	C	C	C
Peracetic acid 4%	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C

	ASYPOR	BIO-X II	HIGH FLOW BIO-X	HIGH FLOW BIO-X VENT AUTOCLAVE	HIGH FLOW PREPOR GFA	HIGH FLOW TETPOR II	HIGH FLOW TETPOR H.T.	HIGH FLOW TETPOR VENT AUTOCLAVE	PEPLYN PLUS & PEPLYN PLUS DC	PREPOR GF	PREPOR PES	PROPOR PES / FS	TETPOR AIR	TETPOR LIQUID	TETPOR PLUS	EPDM 'O'Ring	VITON 'O'Ring	SILICONE 'O'Ring
Perchloroethylene	-	-	-	-	-	-	-	-	-	-	NC	NC	-	-	-	-	-	-
Petroleum spirits	NC	-	-	-	NC	C	C	C	NC	NC	-	-	LC	LC	LC	NC	C	NC
Phenol (aq) 0.5N	-	C	C	C	-	NC	-	NC	-	-	-	-	-	-	-	-	-	-
Phenol 5%	NC	-	-	-	C	-	-	-	C	C	-	-	C	C	C	C	C	C
Phenol 0.25%	C	-	-	-	C	-	-	-	C	C	-	-	C	C	C	C	C	C
Polyethylene Glycol 600	NC	LC	LC	LC	NC	C	C	C	LC	NC	NC	NC	-	-	-	-	-	-
Polyglycol 2000-E	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	C	C	C
Potassium Dichromate 0.1N	LC	C	C	C	C	C	C	C	C	C	-	-	C	C	C	C	C	C
Potassium Iodine 0.6N	C	C	C	C	C	C	C	C	C	C	-	-	C	C	C	C	C	C
Potassium Hydroxide 10N	NC	C	C	C	NC	C	C	C	C	NC	C	LC	C	C	C	C	C	C
Potassium Permanganate 0.1N	NC	C	C	C	NC	C	LC	C	C	NC	C	C	C	C	C	C	C	C
Propan-1-ol	NC	C	C	C	NC	C	C	C	C	NC	C	C	C	C	C	C	C	LC
Propan-2-ol	C	C	C	C	NC	C	C	C	C	NC	C	C	C	C	C	C	C	LC
Propan-2-ol, 60:40 H_2O	C	C	C	C	NC	C	C	C	C	NC	C	C	C	C	C	C	C	C
Pyridine	NC	C	C	C	NC	C	C	C	C	NC	NC	NC	C	C	C	C	NC	C
Sodium Chloride 0.5N	LC	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
Saline Lactose Broth	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
Sodium Hydroxide 2N 8%	NC	NC	NC	NC	C	C	C	C	C	C	C	C	C	C	C	C	C	C
Sodium Hydroxide 7N 28%	NC	NC	NC	NC	NC	C	C	C	C	NC	NC	NC	C	C	C	C	C	LC
Sodium Hypochlorite (14% Free Cl_2)	NC	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
Sodium thiosulphate 0.1N	LC	C	C	C	C	C	C	C	C	C	-	-	C	C	C	C	C	C
Sulphuric acid 1N	NC	C	C	C	LC	C	C	C	C	LC	C	C	-	-	-	C	C	C
Sulphuric acid conc.	NC	NC	NC	NC	LC	LC	NC	LC	LC	LC	NC	NC	LC	LC	LC	-	-	-
Sulphurous acid	-	-	-	-	-	-	-	-	-	-	NC	NC	-	-	-	-	-	-
Toluene	-	NC	NC	NC	-	NC	NC	NC	NC	-	NC	NC	-	-	-	NC	LC	NC
1,1,1 Trichloroethane	LC	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1,1,2 Trichloroethane	-	C	C	C	LC	C	LC	C	LC	LC	NC	NC	LC	LC	LC	NC	LC	LC
Trichloroacetic Acid 80%	LC	-	-	-	LC	-	-	-	C	LC	-	-	C	C	C	NC	LC	NC
Trichloroacetic Acid 5N	-	C	C	C	-	C	C	C	-	-	-	-	-	-	-	---		
Toluene	NC	-	-	-	NC	-	-	-	-	NC	-	-	-	-	-	NC	LC	NC
Xylene	NC	LC	LC	LC	NC	LC	LC	LC	NC	NC	LC	LC	NC	NC	NC	C	LC	NC

Chemical Compatibility User Instructions and Notes

- The chemicals are arranged in alphabetical order using their most common or trade names. If the chemical in question does not appear to be listed, it may be found elsewhere in the table under a pseudonym, in particular its IUPAC[5] name.

- **Please note:**
  - Any product that has limited compatibility (LC) at ambient temperatures should not be used at a higher temperature.
  - The list of compatibilities does not take into account any synergistic effects of more than one chemical present in the solution to be filtered.

[5] International Union of Pure and Applied Chemistry

6. Cartridge Cleanliness

The following tests are designed to determine if contaminants can be released or extracted from the filter and, where identified, a quantitative assessment is made.

6.1. Extractables

All pharmaceutical grade filters are designed and manufactured to yield a minimum of extractables. Testing of a purified water filtrate with HIGH FLOW BIO-X is documented below.

Test Method (1)

Non-volatile extractables from purified water samples after flowing through an autoclaved 250mm (10") HIGH FLOW BIO-X cartridge are listed below. The levels shown are the quantities present in 100ml samples of filtrate, which were taken at stages throughout a 10-litre flush.

Cartridge Serial No. W309149

Flush Quantity (litres)	Non-volatile Extract (mg per 100 ml)	Oxidisables (per USP 23 Test Method)
1	0.7	PASS
2	0.4	PASS
4	<0.1	PASS
6	0.5	PASS
8	0.5	PASS
10	<0.1	PASS

Test Method (2)

Non-volatile extractables from an autoclaved 250mm (10") HIGH FLOW BIO-X cartridge following a 4-hour dynamic immersion in a variety of commonly used solvents. Solvent volume used 1500ml.

Solvent	Weight of extract (mg)
Water @ 20^{0}C	20.1
Water @ 80^{0}C	14.1
ISO Propyl Alcohol (IPA)	39.2
Ethanol	34.5

7. Tests for Biocompatibility

An independent research establishment has assessed the biological safety associated with the use of HIGH FLOW BIO-X filters designed for processing pharmaceutical products.

The materials used in the construction of HIGH FLOW BIO-X products meet the requirements of the current USP <88> Biological Reactivity tests at Plastics Class VI – 121^{o}C.

8. Certificate of Conformance

To certify that Parker domnick hunter's HIGH FLOW BIO-X filter products meet the highest pharmaceutical quality and performance requirements, a Certificate of Conformance is issued.

Certificate of Conformance (9)

For Sterile Gas	HIGH FLOW BIO-X **Filters**
Rated To	0.01 Micron(s)
*This certifies that the **domnick hunter** filter*	ZCHB-1C
Recorded Lot Number	1234567

has been manufactured in a purpose-built facility within a controlled environment.

Materials of Construction
All components of the cartridge are manufactured from materials suitable for contact with food and conform to the biological safety requirements laid down in the current USP Class VI - 121°C Plastics. They also conform with the requirements for non fibre releasing filters as laid down in the United States FDA Title 21 CFR 211.72 and 210.3(b), (6).

The filters also meet the **domnick hunter** quality control and assurance standards.

Product Integrity
This product has successfully passed a non-destructive aerosol integrity test that is correlated to an aerosol bacterial challenge of Brevundimonas diminuta. This proves the filters ability to sterilise gas. The product also exceeds the filter efficiency requirements of the latest HTM 10 and EN285 (supercedes BS3970) guidelines and standards.

Thermal Stability (Sterilisable Grades)
Integrity was maintained after 150 steam cycles of 30 minutes at 142°C

R. Thompson.

Quality Manager

Parker domnick hunter

Date of Manufacture 13/8/2009
Use (Install) by Date 13/8/2014

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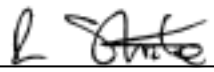
Signature: 

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