VALIDATION GUIDE

HIGH FLOW TETPOR HT

Sterilizing Grade
Cartridge Filters

Contents

1. Introduction

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

This validation guide provides proof of performance of HIGH FLOW TETPOR HT 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 HIGH FLOW TETPOR HT 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 TETPOR HT 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)*. The filter also conforms to ISO 8573-7 - Compressed Air Part 7. Test Methods 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 – PS9100 – 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. 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

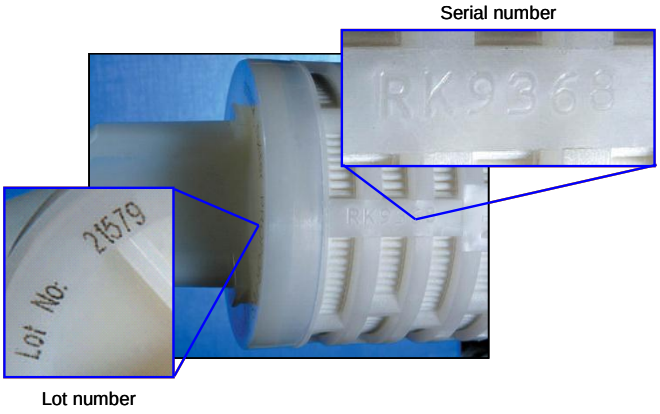
Parker domnick hunter works closely with suppliers to ensure materials supplied are of a consistently high quality and also to develop new materials as part of our ongoing product development activity. In addition to supplier certificates of conformity and analysis, incoming raw materials, including moulded parts, membranes and supports, and elastomeric seals, are subject to an appropriate level of incoming inspection. This includes bacterial challenge on each lot of membrane 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 testable products undergo a non-destructive integrity test (diffusional flow). This includes a high volume flush with water that meets or exceeds the current EP and USP standards for purified water. Products are dried using HEPA filtered air and sealed in a protective polyethylene bag within the controlled manufacturing environment prior to final pack and despatch.

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 TETPOR HT cartridges is 5 years.

3. Product Description

All products within the HIGH FLOW TETPOR HT range are fully validated to provide sterile air / gas under worst-case conditions in a wide range of applications through the food & beverage, dairy and pharmaceutical industries.

This performance has been qualified under worst-case condition (sterile gas system flooded with water) using the ASTM Standard Test Method F838-05 for sterilizing liquid filters. Their performance in gas streams has been qualified for full retention of both bacteria and bacteriophage 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)*.

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.

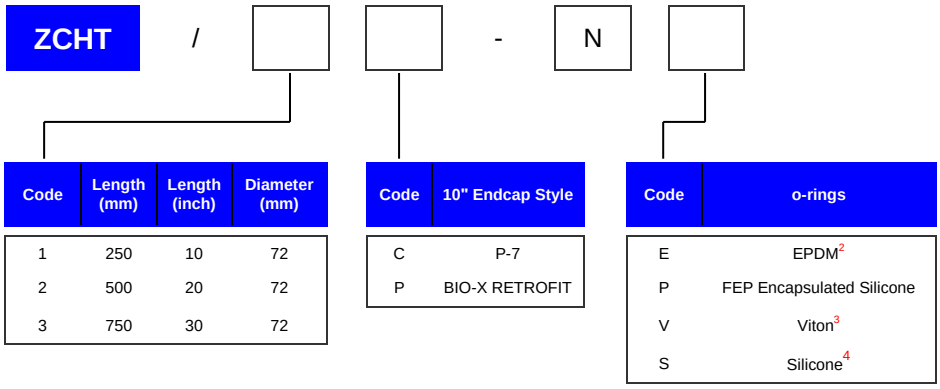
Filtration Membrane	Polytetrafluoroethylene (PTFE)
Upstream Support	Polyaramid
Downstream Support	Polyaramid
Inner Core	316L stainless steel
Outer Protection Cage	Heat stabilized polypropylene
Endcaps	Heat stabilized polypropylene
Endcap Insert	Stainless steel
Standard o-rings	Silicone

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: ZCHT/2C-NV 500 mm (20") HIGH FLOW TETPOR HT filter cartridge, pharmaceutical grade with 'C' style endcap and Viton o-rings.



Code	Length (mm)	Length (inch)	Diameter (mm)
1	250	10	72
2	500	20	72
3	750	30	72

Code	10" Endcap Style
C	P-7
P	BIO-X RETROFIT

Code	o-rings
E	EPDM[2]
P	FEP Encapsulated Silicone
V	Viton[3]
S	Silicone[4]

[2] **EPDM** – Ethylene Propylene Diene Monomer Rubber
[3] **Viton** is a registered trademark of DuPont Dow Corporation
[4] Silicone o-rings are fitted as standard without having to specify the S in the code.

4. Product Specifications

4.1. Cartridge Operating Differential Pressures and Temperatures

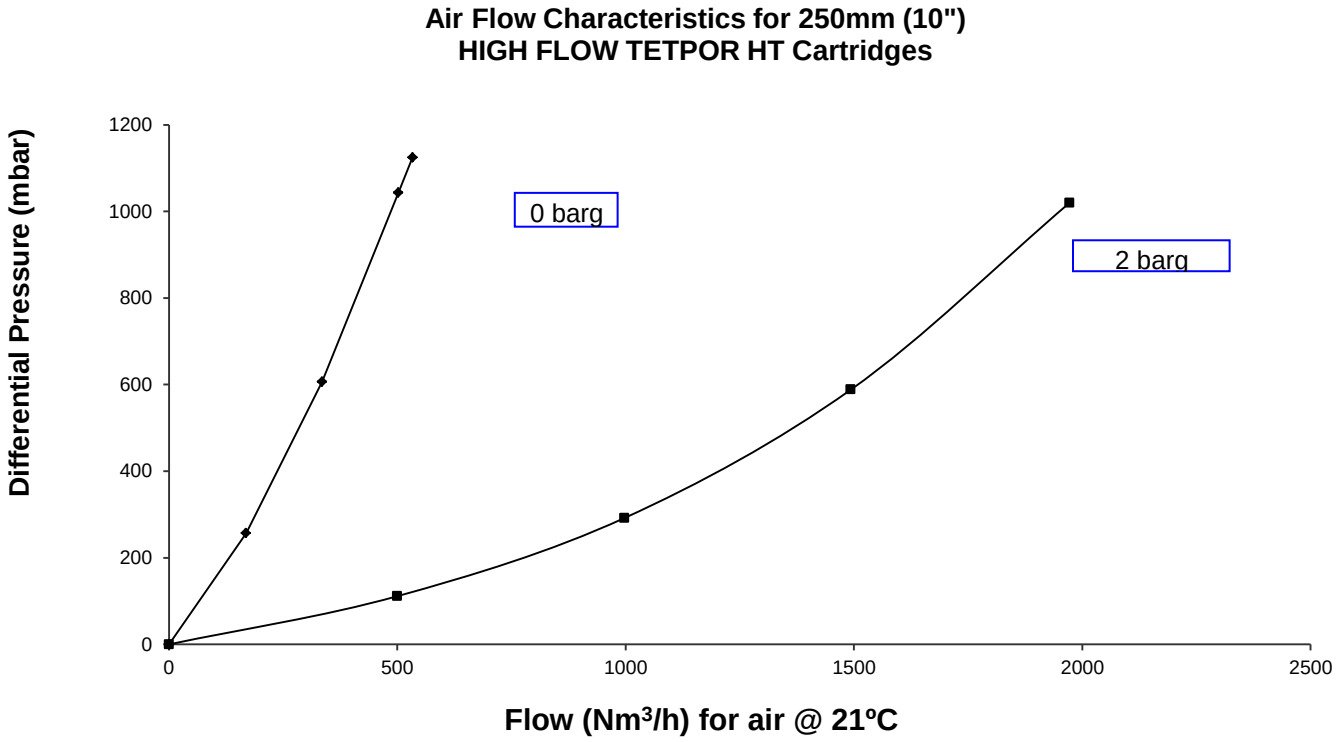
To obtain representative maximum differential pressures the filter cartridge membrane was first wet out in 60:40$_{v/v}$ IPA:Water then water was flowed through representative 10 inch cartridges at temperature to achieve the required differential pressure for 30 minutes.

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

Temperature		Differential Pressure Cartridges	
°C	°F	bar	psi
90	212	3.00	50.8

4.2. Flow Rates

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

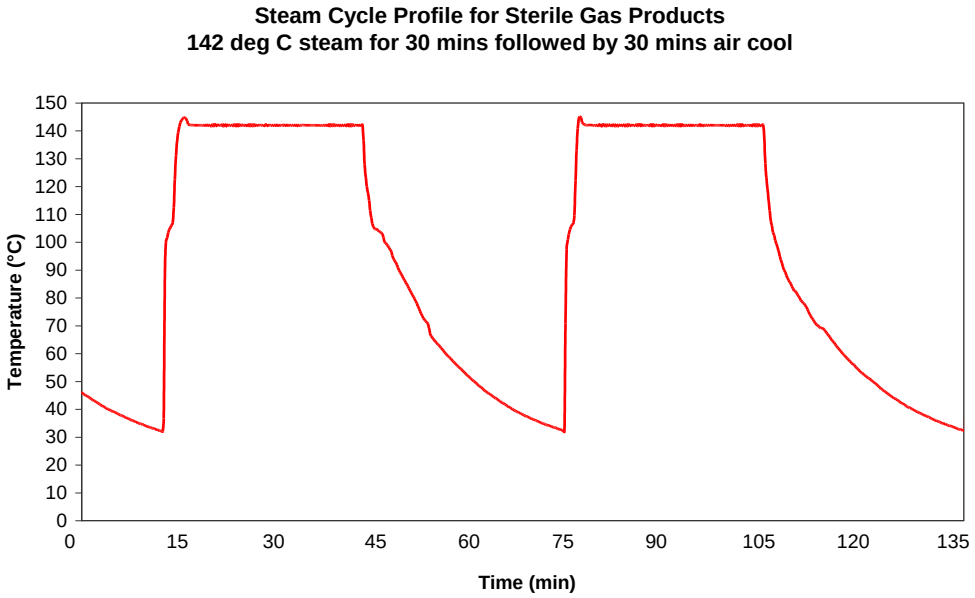


4.3. Effective Filtration Area (EFA)

Product Size	Surface Area (m^2)	Surface Area (ft^2)
10	0.85	9.1
20	1.7	18.2
30	2.55	27.3

4.4. Steam Sterilization (Autoclaving and Steam in Place)

The steam life of cartridges was determined using the 1 hour Steam in Place (SIP) cycle which replicates extreme conditions. This includes a combination of steaming for 30 minutes at temperature followed by rapid cooling with ambient temperature compressed air for 30 minutes.



Product Format	SIP / Autoclave Temp		Number of Cycles	Cycle Time (minutes at temperature)
	°C	°F		
Cartridge	142	288	120	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 sterilization be followed.

The resistance to steam sterilization was determined by evaluating three production batches of 10 inch cartridges. A representative sample is shown below.

Batch	Cartridge Size	Serial No	Integrity Test Values post SIP @ 142°C			
			0 cycles		132 cycles	
			Diff flow (mL/min)	B.pt (mbar)	Diff flow (mL/min)	B.pt (mbar)
1	10 Inch	EH9294	12.6	1620	13.5	1485
		EH9295	11.6	1600	9.7	1460
		EH9300	13.5	1552	10.6	1426
2	10 Inch	EJ0194	7.7	1637	11.6	1501
		EJ0196	7.7	1721	13.5	1574
		EJ0202	6.7	1681	11.6	1544
3	10 Inch	EJ2612	5.8	1616	13.5	1526
		EJ2618	8.7	1652	13.5	1522
		EJ2620	8.7	1657	14.5	1526

NOTE: Maximum allowable diffusional flow for a 10 inch HIGH FLOW TETPOR HT is 16.0 mL/min
Minimum bubble point for HIGH FLOW TETPOR HT is 1.0 bar.

Conclusion

The HIGH FLOW TETPOR HT range of filter cartridges can be steam sterilized up to 120 cycles at 142ºC (266ºF), which includes a 10% safety factor.

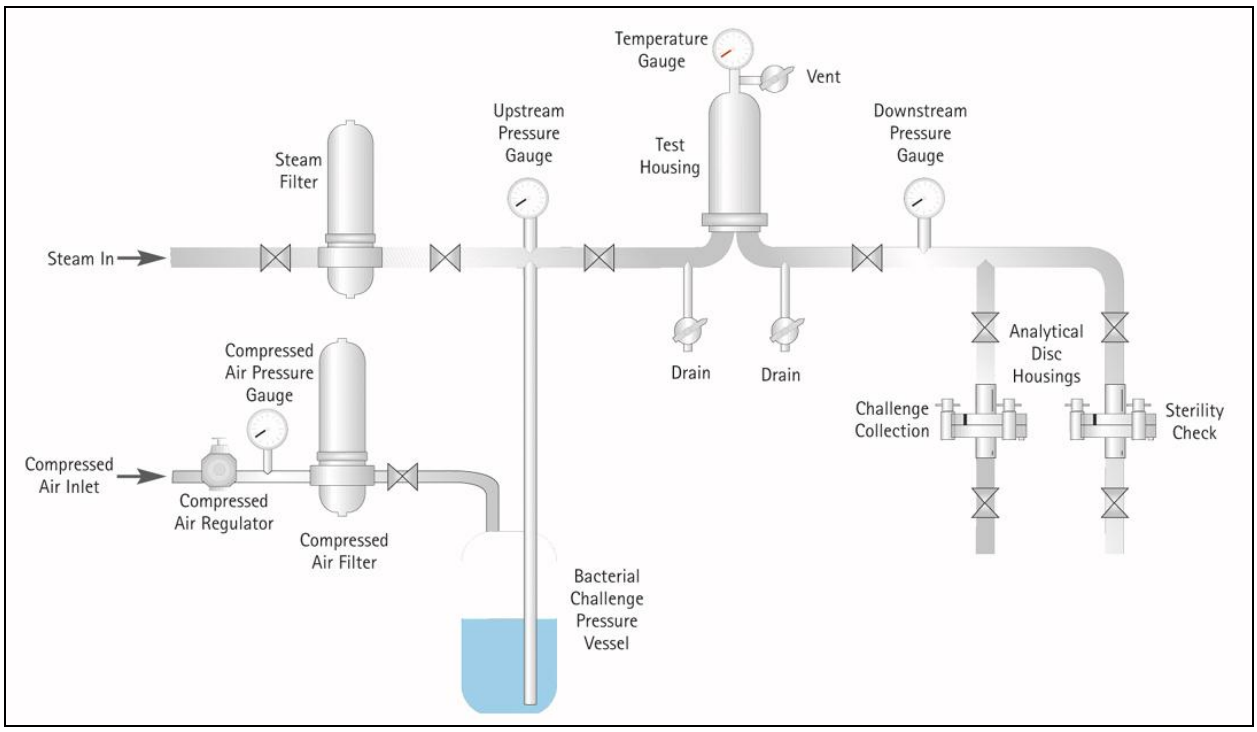
4.5. Retention

The retention of a sterilizing grade filter cartridge that may be used in the manufacture of a drug product needs to be correlated to both a liquid and gas phase challenge. Tests in the liquid phase are conducted because they are seen as worst-case i.e. if the compressed air system becomes flooded with water / condensate the filter will still maintain sterility of the process. This testing is a required when the process air comes into contact with the final drug product i.e. vent filters in sterile filling lines and compressed air used in BFS equipment. The industry recognized test procedure ASTM F838-05 'Standard Test Method for Determining Bacterial Retention of Membrane Filters Utilized for Liquid Filtration'[5] is used in this case.

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)*.

4.6. Liquid Bacterial Challenge

Liquid Bacterial Challenge Schematic



Under these test conditions, the test filter is challenged with a minimum of 10^7 viable *Brevundimonas diminuta* (ATCC 19146) per square centimetre of effective filtration area. Any organisms that pass through the test filter are collected and cultured on the surface of analytical discs. In this way colonies may be counted and bacterial species identified. The filter retention is quantified by expressing the filter's efficiency to remove the challenge organism from the challenge suspension as a Log Reduction Value (LRV).

$$LRV = Log_{10} \left({}^{\text{Number of organisms in the challenge}} / _{\text{Number of organisms in the filtrate}} \right)$$

[5] Previous reference to the guidance document *Microbial Evaluation of Filters for Sterilizing Liquids*, HIMA Document No. 3 Vol. 4, April 1982, referred to in USP<1211> *Sterilization by Filtration* has been superseded by the equivalent ASTM F838-05.

4.7. Diffusional Flow Correlation Data

The correlation between diffusional flow and bacterial challenge for representative Parker domnick hunter PTFE sterile gas cartridges is shown in the table below. This data shows that a 250mm (10") HIGH FLOW TETPOR HT filter exhibiting a diffusional flow of 17.7 mL/min when completely wet with 60:40$_{v/v}$ IPA:Water at a test pressure of 0.8 barg (11.6 psig) at 20ºC (68ºF) will produce a sterile filtrate.

Filter type: ZCHT/1C-N HIGH FLOW TETPOR HT 10" cartridge

Challenge organism: *Brevundimonas diminuta* (ATCC 19146)

Serial No.	Diffusional Flow Air in 60:40$_{v/v}$ IPA:Water @ 0.80 barg (11.6 psig) mL/min	Challenge Level (x 10^{11})	Organisms Passed	LRV[6]
N596898	17.7	2.3 x 10^{11}	0	11.3
N596897	16.7	4.0 x 10^{11}	0	11.6
EE6253	16.7	2.5 x 10^{11}	0	11.3
N596900	15.8	3.5 x 10^{11}	0	11.5
EE5524	15.8	3.0 x 10^{11}	0	11.4
EE6156	14.9	2.8 x 10^{11}	0	11.4
N596854	14.9	9.5 x 10^{10}	0	10.9
EF6181	13.9	2.4 x 10^{11}	0	11.3
EE1634	13.9	3.1 x 10^{11}	0	11.4
EF2309	13	6.7 x 10^{11}	0	11.8
EE1572	12.1	3.8 x 10^{11}	0	11.5
N557706	11.7	1.6 x 10^{11}	0	11.2
N567613	11.1	1.4 x 10^{11}	0	11.1
N567607	10.2	1.2 x 10^{11}	0	11
N608362	9.3	3.6 x 10^{11}	0	11.5
N558164	8.8	1.0 x 10^{11}	0	11
EE1580	8.3	4.4 x 10^{11}	0	11.6
N564406	6.8	1.2 x 10^{11}	0	11
N567597	6.5	2.0 x 10^{11}	0	11.3
N558182	5.8	1.2 x 10^{11}	0	11
N586194	4.9	2.2 x 10^{11}	0	11.3
N561311	4.6	1.2 x 10^{11}	0	11
N560087	3.9	1.8 x 10^{11}	0	11.2
N561333	2.9	1.4 x 10^{11}	0	11.1

Conclusion

A maximum diffusional flow of 16.0 ml/min for a 60:40$_{v/v}$ IPA:Water wetted 10” HIGH FLOW TETPOR HT filter cartridge provides complete assurance of a sterile effluent incorporating, as it does, a safety margin in relation to the correlation data above.

[6] Where Organisms passed = 0, LRV is stated as *greater than*.

4.8. Integrity Testing Data

The following integrity test limits have been determined from the 10 inch cartridge correlation data. Limits for other sizes have been calculated directly from effective filtration area ratios for each variant. Diffusional flow and bubble point values are given for cartridges wetted in 60:40$_{v/v}$ IPA : Water solution using air as the test gas.

Micron Rating	Minimum Bubble Point[7]		Diffusional Flow Test Pressure		Maximum Diffusional Flow (ml/min)
Liquid	bar	psi	bar	psi	10”
0.20	1.0	14.5	0.80	11.6	16.0

4.9. Retention to Aerosolized *Brevundimonas diminuta*

Tests have shown that HIGH FLOW TETPOR HT filters are 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.

PDA Technical Report 40 ‘Sterilizing Filtration of Gases’ states that, due to the mechanisms of retention, bacterial challenge testing in the liquid phase represents “worst-case” conditions for a filter. Therefore, aerosol bacterial challenge test data is included for information only.

[7] Parker domnick hunter does not recommend the use of bubble point as an integrity test method for cartridges, but values are given for use as an indicator of product integrity.

4.10. Retention of Aerosolized Bacteriophage

Independent tests have shown that HIGH FLOW TETPOR HT filters are fully retentive to aerosolized *MS-2 Coliphage* when challenged at between 4.39 x 10^7 and 4.69 x 10^7 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 serial no ME4567	Filter serial no ME4572
1	5.55	3.83 x 10^{11}	ND[8]	ND
2	5.09	3.51 x 10^{11}	ND	ND
3	5.32	3.67 x 10^{11}	ND	ND
4	5.23	3.61 x 10^{11}	ND	ND
5	5.34	3.69 x 10^{11}	ND	ND
6	5.43	3.75 x 10^{11}	ND	ND
7	5.41	3.74 x 10^{11}	ND	ND
8	5.13	3.54 x 10^{11}	ND	ND

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

5. Chemical Compatibility

The following data is indicative of HIGH FLOW TETPOR H.T. 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	HIGH FLOW TETPOR HT	HIGH FLOW TETPOR VENTAUTOCLAVE	PROCLEAR PP	PROCLEAR GF	PROPOR MR	PROPOR LR	PROPOR SG	PROPOR HC	PROPOR BR	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	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	NC	NC	NC	C	C	C	C	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	LC	LC	LC	LC	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	LC	LC	LC	C	C	C	NC	NC	LC
Aqueous Ammonia 15.5N	NC	C	C	C	LC	C	LC	C	C	LC	LC	LC	LC	LC	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	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	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	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	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	-	-	-	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	C	C	C	LC
Ethanol 45%	LC	-	-	-	C	-	-	-	C	C	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	NC	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	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	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	C	C	C

	ASYPOR	BIO-X II	HIGH FLOW BIO-X	HIGH FLOW BIO-X VENT AUTOCLAVE	HIGH FLOW PREPOR GFA	HIGH FLOW TETPOR	HIGH FLOW TETPOR HT	HIGH FLOW TETPOR VENTAUTOCLAVE	PROCLEAR PP	PROCLEAR GF	PROPOR MR	PROPOR LR	PROPOR SG	PROPOR HC	PROPOR BR	TETPOR AIR	TETPOR LIQUID	TETPOR PLUS	EPDM o-ring	VITON o-ring	SILICONE o-ring
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	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	C	C	C	NC	C
Methyl-Iso-Butylketone	NC	C	C	C	C	C	C	C	C	C	NC	NC	NC	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	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	NC	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	C	C	C
Perchloroethylene	-	-	-	-	-	-	-	-	-	-	NC	NC	NC	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	NC	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	LC	LC	LC	LC	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	C	C	C
Propan-1-ol	NC	C	C	C	NC	C	C	C	C	NC	C	C	C	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	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	C	C	C
Pyridine	NC	C	C	C	NC	C	C	C	C	NC	NC	NC	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	C	C	C
Saline Lactose Broth	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
Sodium Hydroxide 1N 4%	NC	NC	NC	NC	C	C	C	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	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	C	C	C
Sodium thiosulphate 0.1N	LC	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	HIGH FLOW TETPOR HT	HIGH FLOW TETPOR VENTAUTOCLAVE	PROCLEAR PP	PROCLEAR GF	PROPOR MR	PROPOR LR	PROPOR SG	PROPOR HC	PROPOR BR	TETPOR AIR	TETPOR LIQUID	TETPOR PLUS	EPDM o-ring	VITON o-ring	SILICONE o-ring
Sulphuric acid 1N	NC	C	C	C	LC	C	**C**	C	C	LC	C	C	C	C	C	-	-	-	C	C	C
Sulphuric acid conc.	NC	NC	NC	NC	LC	LC	**NC**	LC	LC	LC	NC	NC	NC	NC	NC	LC	LC	LC	-	-	-
Sulphurous acid	-	-	-	-	-	-	**-**	-	-	-	NC	NC	NC	NC	NC	-	-	-	-	-	-
Toluene	-	NC	NC	NC	-	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	NC	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	LC	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[9] 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.

[9] International Union of Pure and Applied Chemistry

6. Cartridge Cleanliness & Extractables

HIGH FLOW TETPOR HT filters must meet stringent standards to be certified pharmaceutical (P) grade product by Parker domnick hunter. One aspect of this is to confirm levels of potential contaminants that may be added to a process stream by the addition of the filter cartridge. Although this requirement is normally associated with sterile liquid filters a number of tests have been conducted to demonstrate the cleanliness of the product when in contact with some common fluids to prove acceptability in applications such as vent filtration on WFI holding tanks.

6.1. Cartridge Cleanliness

Bacterial Endotoxins: 10" Cartridges

Analysis of bacterial endotoxin content from purified water samples after flowing through three autoclaved 250mm (10") HIGH FLOW TETPOR HT cartridges is listed below. Testing was conducted in accordance with USP<85> methodology. The levels shown are the concentrations present in 1000mL samples of initial filtrate effluent.

Cartridge Serial Number	Bacterial Endotoxins USP <85>	Test Result
EJ2612	<0.00100 EU/mL	Pass
EH9298	0.00189 EU/mL	Pass
EJ0194	0.000976 EU/mL	Pass

Test results indicate that the bacterial endotoxin content of the first litre of filter effluent is below the maximum specified test limit of <0.025 EU/mL in each case.

Particle Shedding: 10" Cartridges

Analysis of particulate content from purified water samples after flowing through three autoclaved 250mm (10") HIGH FLOW TETPOR HT cartridges is listed below. Testing was conducted in accordance with USP<788> methodology. The levels shown are the concentrations present in 1000mL samples of initial filtrate effluent.

Cartridge Serial Number	Particles For Injection USP <788>
EJ2612	Pass
EH9298	Pass
EJ0194	Pass

Test results indicate that the particulate content of the first litre of filter effluent is below the maximum specified test limit of fewer than 25 particles of 10µm to 20µm in size per millilitre and fewer than 3 particles of 25µm to 100µm in size per millilitre in each case.

6.2. Extractables

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

Non-volatile Extractables: 10" Cartridges

Analysis of non-volatile extractables (by weight) recovered from purified water samples after flowing through three autoclaved 250mm (10") HIGH FLOW TETPOR HT cartridges is listed below. Testing was conducted in accordance with USP <661> methodology. The levels shown are the quantities present in 1000mL samples of initial filtrate effluent.

Cartridge Serial Number	Non-Volatile Extract USP <661>	Test Result
EJ2618	4mg	Pass
EH9294	4mg	Pass
EJ0204	0mg	Pass

Test results indicate that the non-volatile extractable content of the first litre of filter effluent is below the maximum specified test limit of <15mg in each case.

7. Tests for Biocompatibility

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

The materials used in the construction of HIGH FLOW TETPOR HT 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 TETPOR HT filter products meet the highest pharmaceutical quality and performance requirements, a Certificate of Conformance is issued.

Certificate of Conformance (2)

For Pharmaceutical Grade PRODUCT NAME Filters
Rated To RATING Micron(s)
This certifies that the Parker domnick hunter filter xxxxxxxxxx
Recorded Lot Number LOT NO

has been manufactured in a purpose-built facility within a controlled environment and subjected to a purified water flush.

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 Parker domnick hunter quality control and assurance standards.

Product Integrity
This product has successfully passed a non-destructive integrity test, which for sterilising grade cartridges is correlated to a bacterial challenge which gave a sterile effluent when challenged with a minimum of 10^7 organisms per sq cm.

The maximum diffusional flow value for this product is xx.x mL/min at a test pressure of xxxx mbar.

During validation, filter samples underwent the following tests and satisfactorily met the respective criteria specified:-

Effluent Quality
TOC
Met the requirements of USP Total Organic Carbon <643>

Bacterial Endotoxins
Cartridge aqueous extraction contains less than 0.125 EU/mL as determined using the Limulus Amebocyte Lysate (LAL) test, which meets the requirements of USP Water for Injection.

Water Conductivity
Met the requirements of USP Water Conductivity <645>

Particle Release
Met the requirements of USP Particulate Matter in Injections <788>

Thermal Stability
Integrity was maintained after STEAM_CYCLE steam cycles of DURATION minutes at TEMPERATURE°C

This product is registered with the Food & Drug Administration
Drug Master File No 7564

R. Thompson.

Parker | domnick hunter

Quality Manager

Date of Manufacture (dd/mm/yyyy) 1/1/2001
Use By Date (dd/mm/yyyy) 1/1/2001

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