

# VALIDATION GUIDE

## TETPOR PLUS

Pharmaceutical Grade

Cartridge & Capsule Filters



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# 1. Introduction

Sterilization grade filters that come into contact with pharmaceutical products, such as injectable or infusion liquids, must conform to strictly defined quality standards.

By using filter technology that conforms to the standards laid down by the various certifying bodies, the quality of the final product can be assured. Contamination can also be prevented from entering the final product by its comprehensive removal at each stage of the primary and secondary process.

When sterilizing grade filters are used in the manufacture of products, the interactions between product, filter and process must be fully investigated and validated.

Guidelines for validation can be sourced from publications issued by the FDA, EMEA, USP, EP, BP, PDA<sup>1</sup>, 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 instructions for the process.

## NOTE

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The Quality Assurance Department  
Parker Hannifin Manufacturing Ltd  
Durham Road, Birtley, Co. Durham, UK, DH3 2SF  
Tel: +44 (0)191 4105121  
Fax: +44 (0)191 410 5312  
E-mail: dhprocess@parker.com

Registered Holder Information	
Name:	.....
Company:	.....
Department:	.....
Address:	..... ..... .....
Registered No.	.....
Date Issued:	.....
Signed	.....

<sup>1</sup> 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 ISO9001                      Quality Management Systems
- BS EN ISO14001                  Environmental Management Standard
- PS 9100                              The application of ISO9001 GMP guide to pharmaceutical excipients
- BS EN ISO13485                  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 processes are categorised 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 and capsules.

## 2.5. Product and Lot Release Criteria

Prior to shipment all Parker domnick hunter cartridges and capsules 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.

In addition a sample is taken from each production lot and tested to demonstrate conformity to validated claims.

## 2.6. Product Traceability

The product code and type, lot number and unique capsule 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 / capsule is packed. The serial number provides complete traceability back to pleated materials used in the manufacture of each capsule and the manufacturing processes through the module routing sheet.



### 3. Product Description

All products within the TETPOR PLUS range have been designed for use in bioprocessing and pharmaceutical applications. All jointed surfaces are assembled by the use of heat sealing technology. No resins or binders are used in the manufacture of the filter and no surfactants are added to aid wetting.

#### 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	Polytetrafluoroethylene (PTFE)
■	Downstream support	Polytetrafluoroethylene (PTFE)
■	Inner core	PFA
■	Sleeve	PFA
■	Endcaps	PFA
■	Endcaps insert	316 Stainless Steel

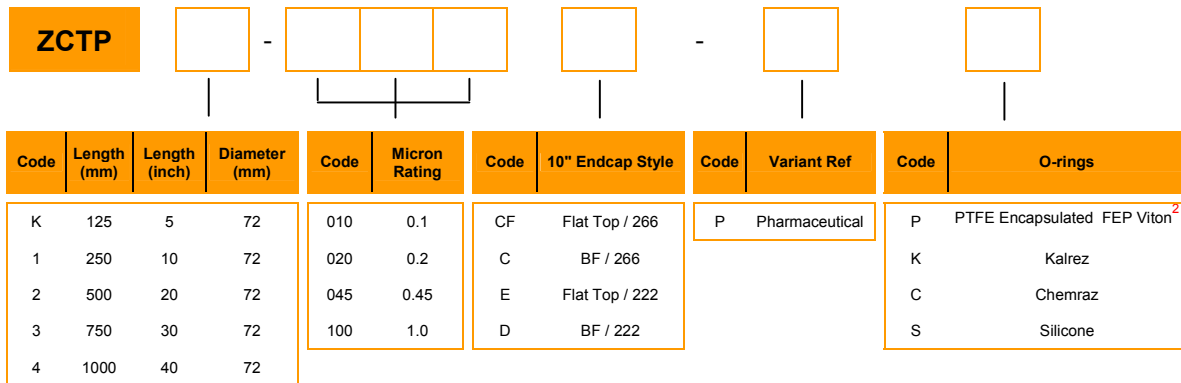
### 3.2. Product Coding

Product code structures indicate the cartridge / capsule sizes, micron ratings, endcap configurations and 'o'rings that are available within the product range.

#### Cartridges

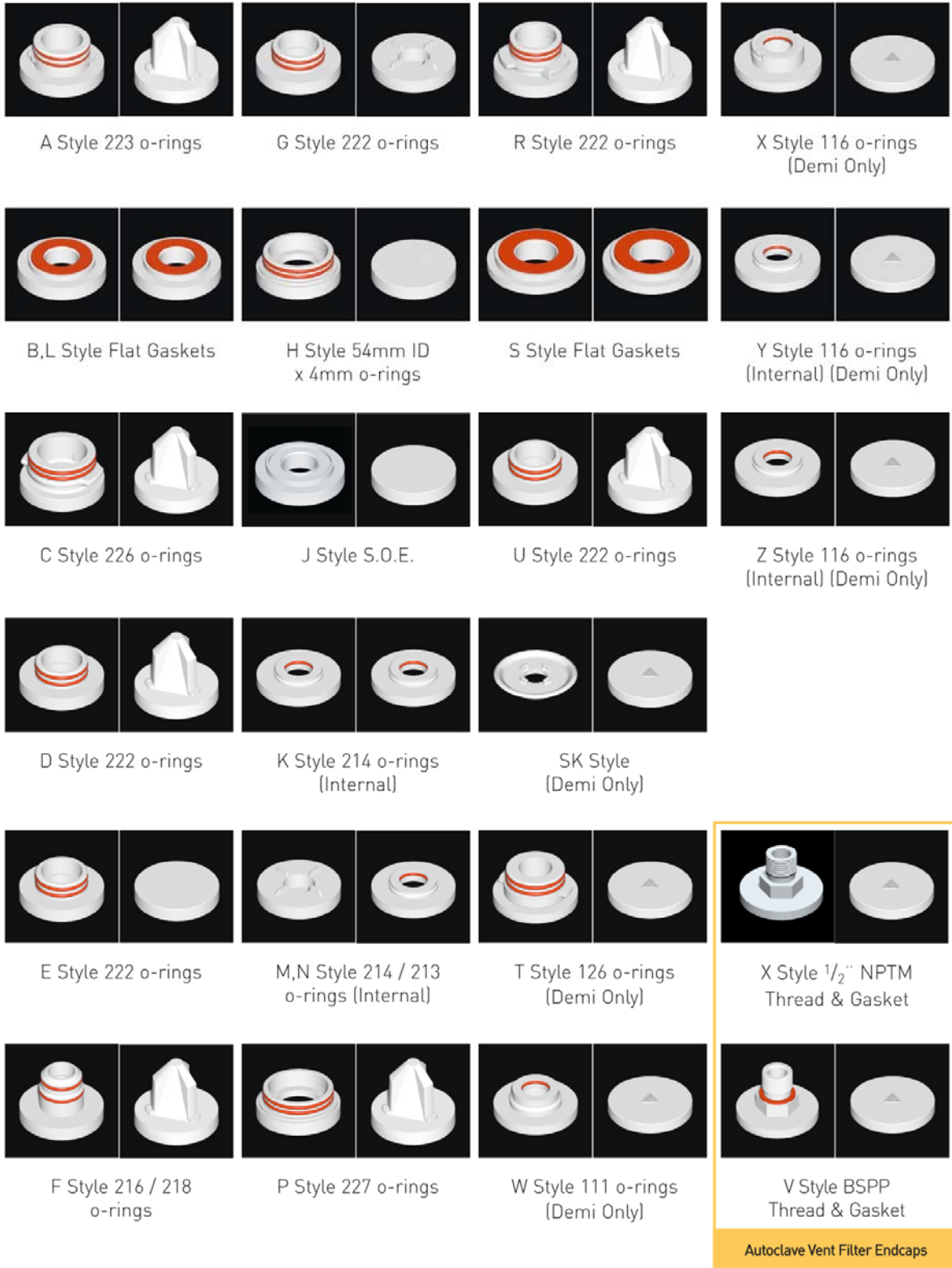
Example ZCTP2-020C-PP

500 mm (20") 0.2 micron TETPOR PLUS filter cartridge, pharmaceutical grade with 'C' style endcap and PTFE encapsulated FEP Viton o-rings.



<sup>2</sup> Viton™ is a registered trademark of DuPont Dow Corporation

### 3.3. Cartridge Endcap Configurations



## 4. Product Specifications

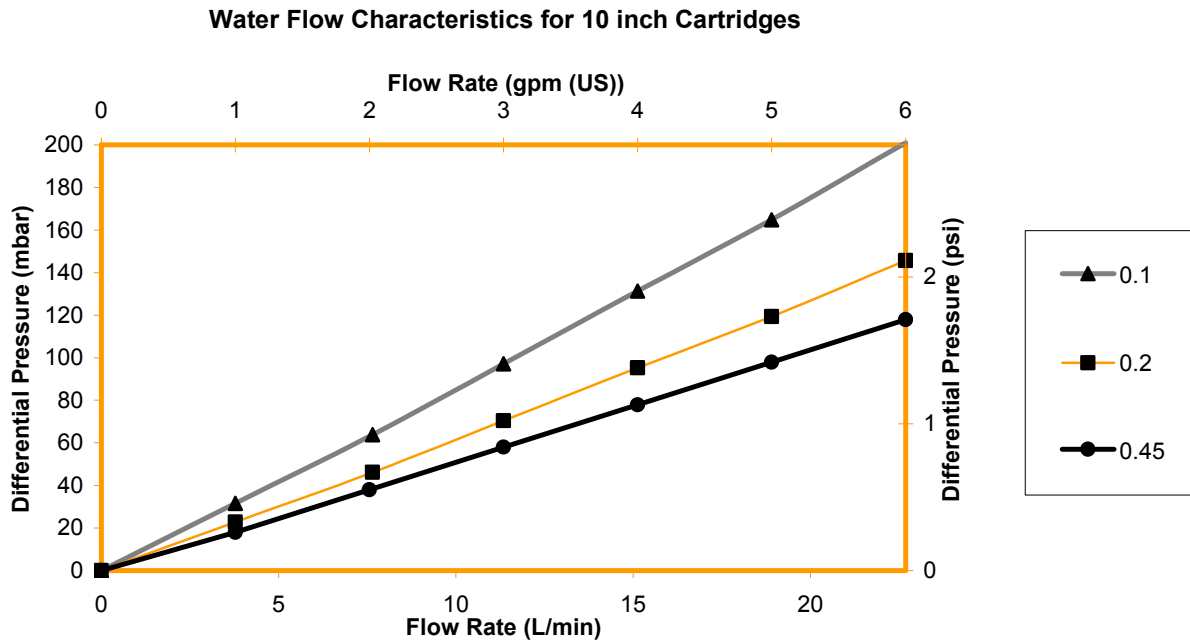
### 4.1. Cartridge Operating Differential Pressures and Temperatures

The recommended maximum differential operating pressures at various temperatures for products in the TETPOR PLUS range are shown below.

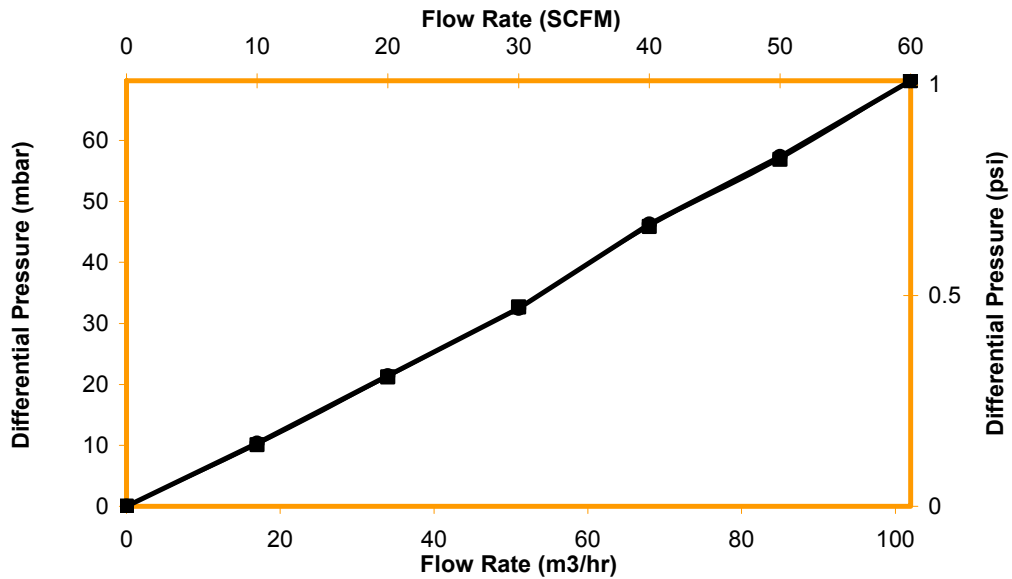
Temperature		Max forward dP	
°C	°F	bar	psi
20	68	5.5	80.0
75	167	3.8	55.0
125	257	2.0	30.0

### 4.2. Flow Rates

Flow rate performance characteristics were determined for filters from three separate lots of 10" cartridges.



**Air Flow Characteristics for 10 inch 0.2 micron Cartridges**



**4.3. Effective Filtration Area (EFA)**

Product Size	Surface Area (m <sup>2</sup> )	Surface Area (ft <sup>2</sup> )
3	1.89	20.34
2	1.26	13.56
1	0.63	6.78
K	0.32	3.44

**4.4. Autoclave Life**

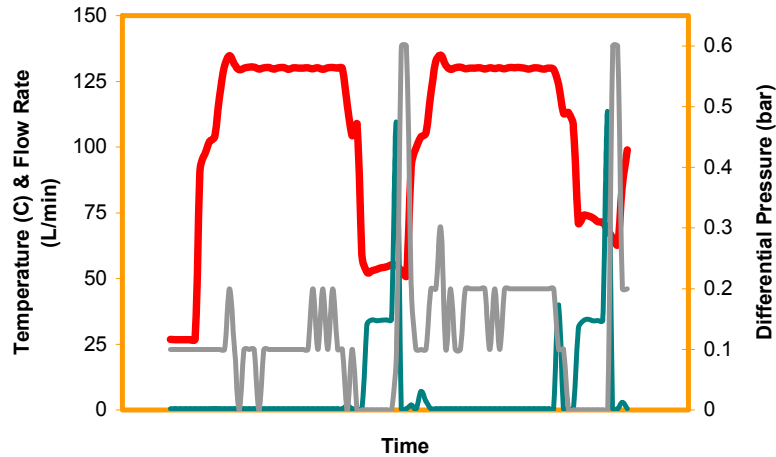
The autoclave life of TETPOR PLUS products was determined using a porous load cycle.

Product Format	SIP Temp		Number of Cycles	Cycle Time (minutes at temperature)
	°C	°F		
Cartridges	142	275	30	30

To maximize cartridge and capsule life, a slow exhaust cycle is recommended.

### 4.5. Cartridge Steam Life

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.



— Temperature    — Water flow    — Differential pressure

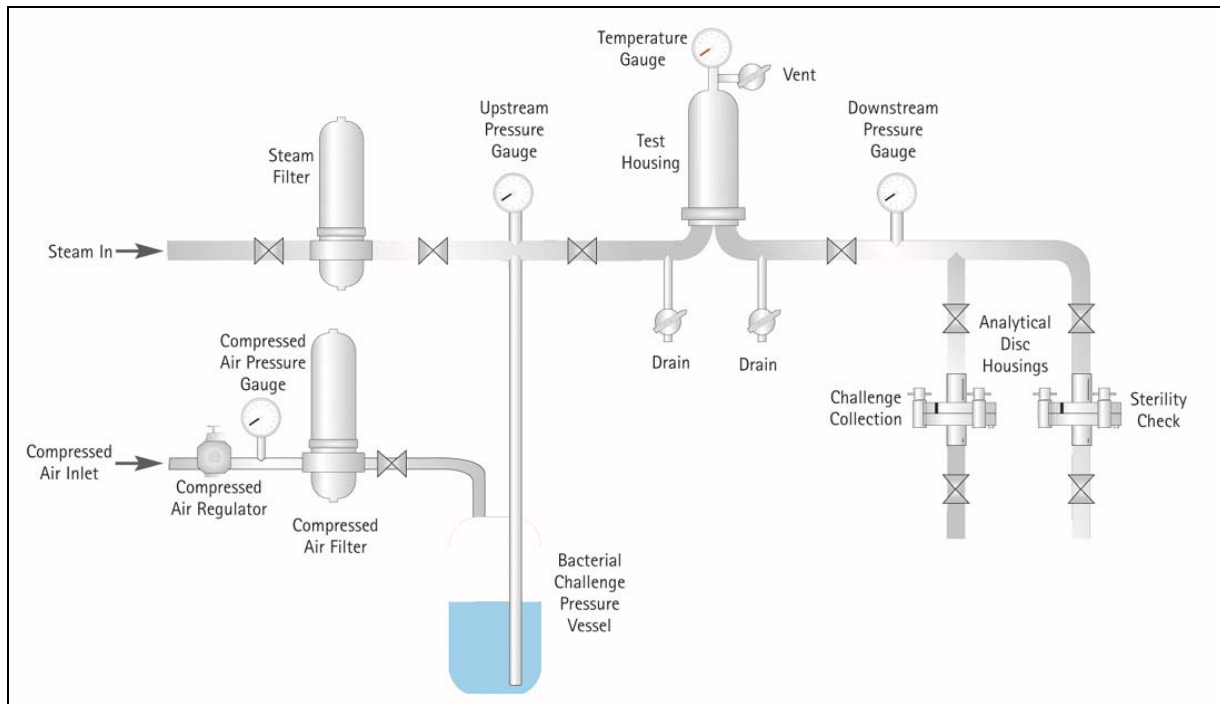
Product Format	SIP Temp		Number of Cycles	Cycle Time (minutes at temperature)
	°C	°F		
Cartridges	142	288	30	30

To maximize the life of the cartridge, the differential pressure across the cartridge should not exceed 0.3 bar (4.4 psi) at 142°C (288°C). For new applications it is recommended that the Parker domnick hunter guidance for the method of steam sterilization is followed.

## 4.6. Retention

The correlation between bacterial challenge and a non-destructive integrity test has been demonstrated using the procedure documented in ASTM F838-05 'Standard Test Method for Determining Bacterial Retention of Membrane Filters Utilized for Liquid Filtration'<sup>3</sup>.

### 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).

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

<sup>3</sup> Previous reference to the guidance document *Microbial Evaluation of Filters for Sterilising Liquids*, HIMA Document No. 3 Vol. 4, April 1982, referred to in USP<1211> *Sterilisation 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 TETPOR PLUS 0.2 micron cartridges is shown in the table below. This data shows that a 250mm (10") TETPOR PLUS 0.2 micron filter exhibiting a diffusional flow of <33.8 mL/min when completely wetted with 60:40<sub>v/v</sub> IPA:Water at a test pressure of 0.80 barg (11.6 psig) at 20°C (68°F) will produce a sterile filtrate.

Filter type: ZCPT1-020C TETPOR PLUS 0.2 µm 10" cartridge

Challenge organism: *Brevundimonas diminuta* (ATCC 19146)

Serial No.	Diffusional Flow (Air in Water) @ 0.80 barg (11.6 psig) mL/min	Total Challenge Level Cfu (x 10 <sup>11</sup> )	Organisms Passed cfu	LRV <sup>4</sup>
ME3035	1.2	23.22	0	11.51
ME4585	6.2	3.88	0	11.59
ME3033	6.6	3.62	0	11.56
ME4571	6.9	2.40	0	11.44
MF6503	7.6	2.44	0	11.38
MF6480	8.2	3.60	0	11.55
A5217/2	11.2	0.96	0	10.98
A5159/2	11.9	0.89	0	10.88
A5267/3	11.9	0.96	0	10.98
A5159/1	12.5	0.78	0	10.89
A5217/3	14.3	1.65	0	11.22
MH4293	17.0	0.87	0	10.94
A5267/1	18.2	1.36	0	11.00
ME4584	30.7	7.08	0	11.85
ME4566	33.8	3.82	0	11.58
ME4579	34.8	1.61	50	<7.00
ME3036	38.3	4.08	13	10.50
A5267/2	44.1	1.97	0	11.25
ME4552	57.6	1.55	12	10.11
ME4574	74.4	1.66	TNTC	<7.00
ME4553	100.8	4.00	TNTC	<7.00

#### Conclusion

A maximum diffusional flow of 16.5 mL/min for a water wetted 10" TETPOR PLUS filter cartridge provides complete assurance of a sterile effluent incorporating as it does a safety margin in relation to the correlation data above.

<sup>4</sup> Where organisms passed = 0, LRV is stated as *greater than*. TNTC = too numerous to count.

#### 4.8. Water Intrusion Correlation Data

The correlation between water intrusion and bacterial challenge for TETPOR PLUS 0.2 micron cartridges is shown in the table below. This data shows that a 250 mm (10") TETPOR PLUS 0.2 micron filter exhibiting a water intrusion value of  $\leq 16.5$  mL/10 min at a test pressure of 2.5 barg (36.3 psig) at 20°C (68°F) will produce a sterile filtrate.

Filter type: ZCTP1-020C

TETPOR PLUS 0.2µm 10" cartridge

Challenge organism:

*Brevundimonas diminuta* (ATCC 19146)

Serial No.	Water Intrusion @ 2.50 barg (36.3 psig) mL/10min	Challenge Level (x 10 <sup>11</sup> )	Organisms Passed	LRV <sup>5</sup>
ME4585	5.4	3.88	0	11.59
ME6480	5.7	3.60	0	11.55
A5159 / 2	6.0	0.89	0	10.88
MF6503	6.3	2.44	0	11.38
ME3035	7.4	3.22	0	11.51
ME3033	8.7	3.62	0	11.56
A5267 / 3	9.0	0.96	0	10.98
ME3034	9.2	4.30	0	11.63
ME4561	9.6	1.10	0	11.04
ME4580	9.9	4.68	0	11.67
A5217 / 3	10.8	1.65	0	11.22
A5217 / 2	11.7	0.96	0	10.98
A5159 / 1	12.3	0.78	0	10.89
ME4581	14.1	2.08	0	11.32
ME3037	14.4	2.68	0	11.43
ME4584	16.5	7.08	0	11.85
ME4566	18.6	3.82	0	11.58
A5267 / 1	20.1	1.36	0	11.13
ME4552	22.2	1.55	12	10.11
ME4574	30.0	1.66	Confluent	<7.00
ME4553	32.1	4.00	TNTC	<7.00

#### Conclusion

A maximum water intrusion value of 13.5 mL/10min (equivalent to a water flow value of 3857 µL/10mins) for a 10" TETPOR PLUS 0.2 micron filter cartridge provides complete assurance of a sterile effluent incorporating as it does a safety margin in relation to the correlation data above.

<sup>5</sup> Where Organisms passed = 0, LRV is stated as *greater than*.

#### 4.9. 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. These diffusional flow and bubble point limits are for 60:40<sub>v/v</sub> IPA:Water wet cartridges using air as the test gas.

Micron Rating	Minimum Bubble Point <sup>6</sup>		Diffusional Flow Test Pressure		Maximum Diffusional Flow (mL/min)	
	bar	psi	bar	psi	10"	K
0.1µm	1.45	21.0	1.17	17.0	35.0	16.3
0.2µm	1.00	14.5	0.8	11.6	16.5	7.7
0.45µm	0.48	7.0	0.35	5.00	50.0	23.3

Micron Rating		Water Intrusion Test Pressure		Maximum Water Intrusion (mL/10min)	
		bar	psi	10"	K
0.2µm		2.50	36.3	13.5	6.4

Micron Rating		Water Flow Test Pressure		Maximum Water Flow (µL/10min) <sup>7</sup>	
		bar	psi	10"	K
0.2µm		2.50	36.3	3857	1829

<sup>6</sup> 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.

<sup>7</sup> Values given for Water Flow (µL/10mins) and Water Intrusion (mL/10mins) are expressions of the same parameter, the first being the actual change in water volume during the test, the second being the pressurized gas volume change (expressed at atmospheric pressure) as a result of this water flow.

### 4.10. Chemical Compatibility

The following data is indicative of TETPOR PLUS cartridge & capsule 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 VENT AUTOCLAVE	PROCLEAR PP	PROCLEAR GF	PROPOR MR	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
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	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% <sub>v/v</sub>	NC	-	-	-	C	-	-	-	C	C	-	-	-	-	-	-	-	C	C	C
Ammonium Hydroxide 8N	NC	C	C	C	C	C	C	C	C	C	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	C	C	C	NC	NC	LC
Aqueous Ammonia 15.5N	NC	C	C	C	LC	C	LC	C	C	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
Benzalkonium 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	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	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	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% <sub>v/v</sub>	NC	-	-	-	NC	-	-	-	C	NC	C	C	C	C	-	-	-	C	C	LC
Diversey 212G 0.6% <sub>v/v</sub>	NC	-	-	-	C	-	-	-	C	C	-	-	-	-	-	-	-	C	C	C
Divosan Forte 0.5% <sub>v/v</sub>	LC	-	-	-	C	-	-	-	C	C	C	C	C	C	-	-	-	C	C	C
Divosan XT 1% <sub>v/v</sub>	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	LC
Ethanol 45%	LC	-	-	-	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	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
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
Hexane	LC	C	C	C	-	C	C	C	NC	-	-	-	-	-	-	-	-	NC	NC	NC

	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 SG	PROPOR HC	PROPOR BR	TETPOR AIR	TETPOR LIQUID	TETPOR PLUS	EPDM o-ring	VITON o-ring	SILICONE o-ring
Hydrochloric acid 1N	C	-	-	-	C	-	-	-	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	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	NC	C
Methyl-Iso-Butylketone	NC	C	C	C	C	C	C	C	C	C	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	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	-	-	-	-	-	-
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
Perchloroethylene	-	-	-	-	-	-	-	-	-	-	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	-	-	-	-	-	-
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	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
Propan-1-ol	NC	C	C	C	NC	C	C	C	C	NC	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	LC
Propan-2-ol, 60:40 H <sub>2</sub> O	C	C	C	C	NC	C	C	C	C	NC	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	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
Saline Lactose Broth	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
Sodium Hydroxide 7N 28%	NC	NC	NC	NC	NC	C	C	C	C	NC	NC	NC	NC	NC	C	C	C	C	C	LC
Sodium Hypochlorite (14% Free Cl <sub>2</sub> )	NC	C	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	HIGH FLOW TETPOR HT	HIGH FLOW TETPOR VENT AUTOCLAVE	PROCLEAR PP	PROCLEAR GF	PROPOR MR	PROPOR SG	PROPOR HC	PROPOR BR	TETPOR AIR	TETPOR LIQUID	TETPOR PLUS	EPDM o-ring	VITON o-ring	SILICONE o-ring
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	C	C
Sulphuric acid conc.	NC	NC	NC	NC	LC	LC	NC	LC	LC	LC	NC	NC	NC	NC	LC	LC	LC	-	-	-
Sulphurous acid	-	-	-	-	-	-	-	-	-	-	NC	NC	NC	NC	-	-	-	-	-	-
Toluene	-	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	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	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<sup>8</sup> 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.

<sup>8</sup> International Union of Pure and Applied Chemistry

## 5. Cartridge Cleanliness and Biocompatibility

### 5.1. Cartridge Cleanliness and Biocompatibility

TETPOR PLUS filters must meet stringent standards to be certified pharmaceutical (P) grade product by Parker domnick hunter.

- Conformance to the requirements for non-fibre releasing filters as laid down in the United States Food and Drug Administration Regulations 21CFR11.72 and 210.3(b), (6).
- Effluent quality following a purified water flush must also be met as determined by the following tests:
  - Test for oxidisable material per USP 23 Purified Water
  - Test for bacterial endotoxins using a gel clot LAL (Limulus Amoebocyte Lysate).
  - Test for particulates
  - Test for TOC (total organic carbon)
  - Test for conductivity
- All components conform to the Biological Safety Standards identified in USP<88> to Class VI-121°C levels.
- All filters must meet minimum defined integrity test values prior to despatch, defined from a correlation against an appropriate bacterial challenge.
- All filters are flushed with a high flux of purified water prior to despatch as a guarantee of product cleanliness.

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.

#### Quality of Purified Water used in the preparation of Pharmaceutical Grade Filters

The current USP and EP standards for Purified Water and Highly Purified Water specify a maximum conductivity of 1.1µS/cm at 20°C (68°F) and a maximum TOC content of 0.5 mg (500 ppb) of carbon per litre. The water used in the flushing stages of pharmaceutical grade filters exceeds these Pharmacopoeial requirements.

In addition, two other tests are carried out on samples taken from point of use and from a number of points in the supply pipework:

- A Membrane filtration Method Standard Plate Count Technique to establish the microbial content.
- A gel clot LAL test for detection of bacterial endotoxins at 0.125 EU/ml sensitivity.

## 5.2. Non-Volatile Extractables

All pharmaceutical grade filters are designed and manufactured to yield a minimum of extractables. Testing of TETPOR PLUS cartridges with various solvents is documented below.

Non-volatile extractables was performed using an autoclaved 250mm (10") TETPOR PLUS cartridge following a 24-hour static soak in the test solvents at the specified temperature. The solvent volume used was 1500mL.

Solvent Type	Cartridge Serial N°	Weight of Extract (mg)
Ultra Pure Water @ 21°C	P051003 / 1	1.3
Ultra Pure Water @ 82°C	P051003 / 2	0.3
Isopropanol @ 21°C	P051003 / 3	2.6

## 6. Certificate of Conformance

To certify that Parker domnick hunter's TETPOR PLUS filter products meet the highest pharmaceutical quality and performance requirements, a Certificate of Conformance is issued.

### Documentation Approval Section

Approved By:                     R. Strike                    

Title:                     Technical Manager                    

Signature:                     *R. Strike*                    

Date:                     July 2010                    



Parker Hannifin Manufacturing Ltd.  
Durham Road, Birtley, Co. Durham  
England, UK. DH3 2SF  
Tel: +44 (0)191 410 5121  
Fax: +44 (0)191 410 5312  
E-mail: [dhprocess@parker.com](mailto:dhprocess@parker.com)  
Website: [www.parker.com/processfiltration](http://www.parker.com/processfiltration)

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