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Zeta Plus™ VR Series

Viral Reduction Depth Filter Cartridges

Application

The removal and inactivation of contaminating viruses from biotherapeutics is a requisite for ensuring final product safety. Zeta Plus VR cartridge depth filters remove significant levels of viruses from biological fluids. They provide validatable viral titer reduction, high flow rates, scalability, economy, disposability and ease-of-use in the biological manufacturing environment. The Zeta Plus VR Series includes specific filter media recommendations for virus removal from blood plasma proteins and bioprocess derived cell culture fluids.

Zeta Plus depth filtration offers an attractive and economical alternative to other available technologies for reduction of viral burden. Zeta Plus VR Series depth filters can be used as a bolt-on processing step to existing in-process viral clearance methodologies, providing an added measure of end-product safety.

Regulators (FDA) recommend validation clearance via a combination of removal (filtration, chromatography) and inactivation (temperature, pH, solvent) steps where multiple methods of virus clearance are required to assure product safety.

Features & Benefits

Combined adsorption & physical entrapment virus removal mechanisms

- Validatable viral log reduction
- Provides added level of viral safety

Quality Control tested for media adsorption capacity

- Assurance of filter media consistency & performance
- Single-use, disposable design eliminates validation concerns associated with reusable clearance options (chromatography column sanitisation & regeneration)

Self-contained, single-use disposable capsules & cartridge modules

- Eliminates concern over virus carryover from one purification cycle to the next

Range of cartridge sizes, sanitary design cartridge housings & disposable capsules

- Facilitates scaleup from small volume feasibility trials & validation studies to production scale operations
- Enable high flow processes

Optimised cartridge designs for biologicals filtration

- Robust *in-situ* steam-sterilisable cartridges
- Drug Master Files simplify FDA submissions

Complete technical, regulatory & validation support

- Regulatory Support Files detail filter media regulatory compliance & safety data
- Provides added level of validatable viral clearance

Economical “bolt-on” separation technology as adjunct or prefilter to other viral clearance steps

- Can replace or augment chromatography columns or function as prefilter to final virus removal membrane filter



Picture 1: Zeta Plus VR Series Family For Enhanced Log Reduction of Viruses From Biological Fluids

Applications

Processing of human plasma-derived proteins

Recombinant proteins from cell culture and fermentation

Monoclonal antibodies

Serum and other raw materials derived from animal sources

3M

Table 1: Selection of Zeta Plus VR Series Filter Media

Filter Media Choice	VR 01	VR 02	VR 03	VR 04	VR 05	VR 06	VR 07
Recommended for Plasma Proteins	◆	◆		◆		◆	◆
Recommended for Cell Culture Proteins		◆	◆		◆	◆	◆
Nominal Retention Rating (µm)	0.8	0.8	0.8	0.45	0.2	0.2	0.2
20 °C Water Flow @ 345 mbar (Litre per min/m²)	50	77	50	37	16	24	16
Auto-clavable or <i>In-situ</i> Steam Sterilisable	No	Yes	Yes	No	Yes	Yes	Yes
[Al³⁺] in 20°C water @ 54 l/m²	40	20	40	20	40	20	60

Table 2: Viral Clearance In An Immunoglobulin Production Process

Cumulative Virus Titer Reduction (Log ₁₀)					
Process Step	BVD	EMC	HIV	PPV	PRV
Solvent detergent	> 4.3	—	> 5.3	—	> 7.3
Supernatant III	1.4	4.3	6.1	4.7	3.8
Zeta Plus VR 03 Depth Filtration	4.8	4.5	4.7	3.7	5.4
Total Cumulative Reduction	> 10.5	8.8	> 16.1	8.4	> 16.6

Source : D. Revie, *Novel Validation Approaches to Obtain Maximum Viral Clearance from an Immunoglobulin Production Process*, IBC 2nd International Symposium on Viral Clearance, Philadelphia, PA, June, 1998.

Table 3: Quality Control of Zeta Plus VR Series Filters

Filter media (µm)	VR 01 (0.8)	VR 02 (0.8)	VR 03 (0.8)	VR 04 (0.45)	VR 05 (0.2)	VR 06 (0.2)	VR 07 (0.2)
Test for Filter Media Charge Capacity *	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Optimised & Tested for Low Al Extractables *	No	Yes	No	Yes	No	Yes	Yes
Filter Materials Optimised for Low LAL-RM *	No	Yes	No	No	No	Yes	No
Non-pyrogenic per USP Endotoxin Test	Yes	Yes	Yes	Yes	Yes	Yes	Yes
100% 21 CFR Listed Materials	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Supplied with Certificate of Quality	Yes	Yes	Yes	Yes	Yes	Yes	Yes
USP Class VI Biological Tests	Pass	Pass	Pass	Pass	Pass	Pass	Pass

* Indicates filter media manufacturing lot is sampled and tested as lot release test criteria.

Zeta Plus VR Filter Selection

A range of cartridge sizes is available for varying batch size, so scale-up is easy and predictable from lab-scale, to pilot plant, to full production scale. Three different cartridge sizes (8, 12 and 16" diameter) make scale-up straightforward and predictable. Zeta Plus cartridges are used in a flow-through mode, enabling the process stream to be passed through the filter cartridge while viruses are retained within the depth filter matrix. Small, low area disposable Zeta Plus BC capsules are available for laboratory scale and process development work and are ideal for scaled down viral validation studies.

Zeta Plus Filter Mechanisms of Virus Removal

Zeta Plus filter media is a family of cellulosic depth filtration media designed to retain contaminants by both physical entrapment and adsorption. It is composed of high-area process filter aids embedded in a cellulose fibre depth matrix. During the manufacturing process, a cationic charge modifier is chemically bound to the matrix components, forming a permanent, interconnected, rigid depth filter with positively-charged electro-kinetic capture sites. The resulting porous depth filter structure is a tortuous network of adsorptive flow channels capable of retaining contaminating viruses through a combination of adsorption and mechanical entrapment. Cumulative viral titer reduction may also be attainable through a staged two-step Zeta Plus system.

Zeta Plus depth filtration is a key component in biopharmaceutical production schemes for clarifying cell culture fluids (cell separation) and is utilised worldwide in the fractionation of human and animal plasma proteins.

Selection Guide - Zeta Plus VR Filter Media

A range of Zeta Plus VR depth filter media is available for viral reduction from plasma proteins and bioprocess-derived (cell culture) proteins. Specific recommendations for each application are provided in Table 1. Zeta Plus VR filter media is available in a range of porosities. Each Zeta Plus VR filter media is tested and optimised for biologicals and bioprocess filtration (pharmaceutical-grade).

All cartridge and capsule components have been USP Class VI tested for biological safety.

Viral Reduction Validation

Many factors influence the choice of process steps to be studied when performing viral clearance evaluation and validation. Viral clearance validation studies are performed with a select panel of model viruses. Different virus panels are chosen to validate blood and plasma products, and separately, cell-culture derived products.

Virus removal efficiency may be dependent on fluid and processing conditions and is best determined during qualification and validation studies using suitable virus model systems in a controlled laboratory study. Contact 3M Purification Scientific Applications Support Services (SASS) for further technical advice concerning validation of viral reduction with Zeta Plus VR depth filters.

Data is available which confirms the ability of Zeta Plus VR depth filter media to function as an effective and validatable viral log reduction filter. Table 2 illustrates results for a reported viral clearance study utilising Zeta Plus VR depth filters.

Quality Control of Zeta Plus VR Series Filters

3M Purification applies rigorous Quality Control testing and standards both during in-process manufacturing and during final lot release. This testing ensures consistent filter media performance in critical virus removal applications. A Certificate of Quality is provided with each Zeta Plus VR Series filter cartridge and disposable Zeta Plus BC capsule.

Each grade of Zeta Plus VR Series filter media is Quality Control tested on a lot release basis for the presence and magnitude of positive charge. Summarised in Table 3 are key quality control test parameters and lot release test criteria applied to Zeta Plus VR Series filters.

Zeta Plus VR Disposable Capsules, Filter Cartridges and Filter Sheets - Configured to Suit Your Every Need

Zeta Plus VR Series filter products are highly scaleable and can be used for applications ranging from millilitre lab volumes to production scale operations. Filter media is available in sheets, capsules and cartridges.

Zeta Plus VR Filter Sheets

Zeta Plus VR filter media is available in a range of filter sheet sizes to fit plate-and-frame filter presses (contact 3M Purification for specific sheet sizes and part numbers).

Zeta Plus BC Disposable VR Filter Capsules

Zeta Plus VR filter media is available in three different sizes of Zeta Plus BC disposable capsules for bench scale and pilot scale filtration (filter areas of 25 cm², 650 cm² and 1300 cm²).

Zeta Plus VR Filter Cartridges and Sanitary Housings

Zeta Plus VR filter media is available in 8", 12" and 16" diameter easy-to-use cartridges providing surface areas from 650 cm² to 3.2 m² per cartridge. A range of sanitary design Zeta Plus filter housings is available for Zeta Plus VR Series cartridges.

Zeta PlusVR Series filter media is available in a wide range of cartridge sizes including 8", 12", and 16" diameter filter cartridges for varying flow rates and batch volumes. 3M Purification's sanitary design filter housings are designed for pharmaceutical and biological manufacturing environments. For more information on Sanitary filter housings, contact 3M Purification.

Operating Parameters

	Maximum Operating Pressure	Maximum Operating Temperature	Recommended Flush	Sterilisation Parameters	Maximum Flow Rate (FLUX) (in l/min per m ²)
Standard and Special pre-coat Zeta Plus Cartridges	2.4 bar	82 °C VR 01 & 04: 60 °C	54 l/m ² at 20 lpm/m ²	autoclave or <i>in-situ</i> steam sterilisation for 30 minutes at 121 °C (1 cycle) except VR 01 & 04 (see Table 1)	1.2 to 12
Zeta Plus BC25 Capsules	Inlet pressure: 2.75 bar Media pressure: 2.4 bar	40 °C	54 l/m ² at 20 lpm/m ²	Autoclave for 30 minutes at 121 °C (1 cycle)	1.2 to 12
Zeta Plus BC1000 and BC2000 Series Capsules	Inlet pressure: 5.5 bar at 25 °C 2.75 bar at 60 °C Media pressure: 2.4 bar	60 °C	54 l/m ² at 20 lpm/m ²	Autoclave for 30 minutes at 121 °C (up to 3 cycles)	1.2 to 12
Nominal Ratings: 0.2 to 0.8 micron.					

Zeta Plus BC25 Capsule	25 cm ²	Z8FA2NPX2 (8" diameter cartridge, 2-cell plug-in)	650 cm ²
Zeta Plus BC1000 Capsule	650 cm ²	Z8FA4NPX2 (8" diameter cartridge, 4-cell plug-in)	1300 cm ²
Zeta Plus BC2000 Capsule	1300 cm ²	45264 (12" diameter cartridge, 7-cell bodyfeed)	0.67 m ²
45109 (8" diameter cartridge, 8-cell)	2600 cm ²	45245 (12" diameter cartridge, 16-cell)	1.5 m ²
45167 (8" diameter cartridge, 7-cell, O-ring, plug-in)	2300 cm ²	Z16P (16", 14-cell, netted)	3.20 m ²

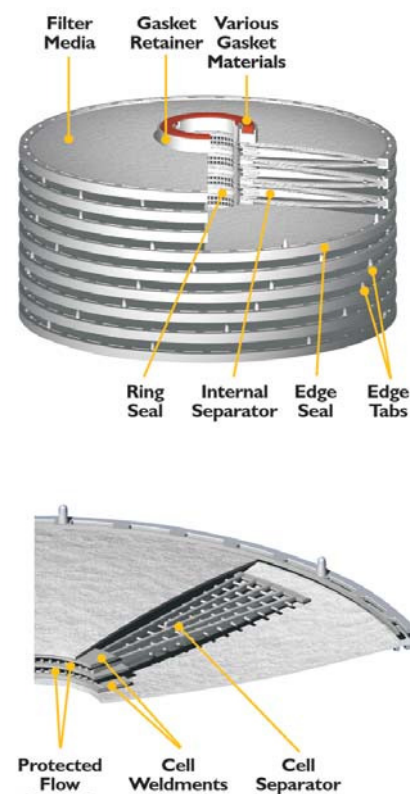
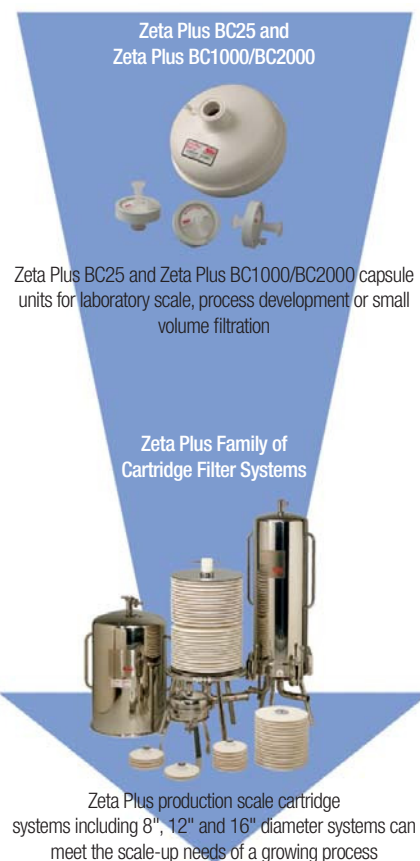


Figure 1: Zeta Plus Cartridge Construction



Zeta Plus VR Series Ordering Guide

8" Diameter Cartridges

CATALOGUE NUMBER	GASKET	VR SERIES
45109 (8", 8-Cell)	11 - Nitrile 13 - Fluorocarbon 14 - EPR 22 - Silicone	VR 01 VR 05 VR 02 VR 06 VR 03 VR 07 VR 04
45167 (8", 7-Cell, O-ring Plug-in)	01 - Nitrile 02 - EPR 03 - Fluorocarbon 04 - Silicone	VR 01 VR 05 VR 02 VR 06 VR 03 VR 07 VR 04
		PKG. CODE
Z8FA2NP (8", 2-Cell, Plug-in)	A - Silicone B - Fluorocarbon C - EPR D - Nitrile	VR 01 VR 05 VR 02 VR 06 VR 03 VR 07 VR 04
Z8FA4NP (8", 4-Cell Plug-in)		

16" Diameter Cartridges

CATALOGUE NUMBER	GASKET	VR SERIES
Z16P (16", 14-Cell)	A - Silicone B - Fluorocarbon C - EPR D - Nitrile	VR 01 VR 05 VR 02 VR 06 VR 03 VR 07 VR 04

Zeta Plus BC Capsules

CATALOGUE NUMBER	VR SERIES
BC0025L (Luer) BC0025S (Sanitary) BC1000A (Single Filter) BC1000B (3 Filter Pack) BC2000A (Single Filter) BC2000B (3 Filter Pack)	VR 01 VR 05 VR 02 VR 06 VR 03 VR 07 VR 04

12" Diameter Cartridges

CATALOGUE NUMBER	GEOMETRIC VARIATION	GASKET	VR SERIES
45264 (12", 7-Cell Bodyfeed)	01 - Standard Polypropylene	A - Silicone B - Fluorocarbon C - EPR D - Nitrile	VR 01 VR 05 VR 02 VR 06 VR 03 VR 07 VR 04
45245 (12", 16-Cell)			

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Limited Warranty

3M Purification warrants this product to be free from defects in material and workmanship during normal use for a period of one (1) year from the date of shipment from the factory. If the Product(s) is (are) defective within this warranty period, your exclusive remedy and 3M Purification's sole obligations shall be, at 3M Purification's option, to replace or repair the Product(s) or refund the original purchase price of the Product(s). This warranty does not apply to failures that result from abuse, misuse, alteration or damage not caused by 3M Purification or failure to properly follow installation and use instructions.

Limitation of Liability: 3M Purification will not be liable for any loss or damage arising from the use of the Product(s), whether direct, indirect, special, incidental, or consequential, regardless of the legal theory asserted, including warranty, contract, negligence or strict liability. Some states do not allow the exclusion or limitation of incidental or consequential damages, so the above limitation may not apply to you.

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45109 11 VR 01	Z16P A VR 01	BC0025L VR 01	Z8FA2NP C 2 VR 01	45264 01 C VR 01
45109 11 VR 02	Z16P A VR 02	BC0025L VR 02	Z8FA2NP C 2 VR 02	45264 01 C VR 02
45109 11 VR 03	Z16P A VR 03	BC0025L VR 03	Z8FA2NP C 2 VR 03	45264 01 C VR 03
45109 11 VR 04	Z16P A VR 04	BC0025L VR 04	Z8FA2NP C 2 VR 04	45264 01 C VR 04
45109 11 VR 05	Z16P A VR 05	BC0025L VR 05	Z8FA2NP C 2 VR 05	45264 01 C VR 05
45109 11 VR 06	Z16P A VR 06	BC0025L VR 06	Z8FA2NP C 2 VR 06	45264 01 C VR 06
45109 11 VR 07	Z16P A VR 07	BC0025L VR 07	Z8FA2NP C 2 VR 07	45264 01 C VR 07
45109 13 VR 01	Z16P B VR 01	BC0025S VR 01	Z8FA2NP D 2 VR 01	45264 01 D VR 01
45109 13 VR 02	Z16P B VR 02	BC0025S VR 02	Z8FA2NP D 2 VR 02	45264 01 D VR 02
45109 13 VR 03	Z16P B VR 03	BC0025S VR 03	Z8FA2NP D 2 VR 03	45264 01 D VR 03
45109 13 VR 04	Z16P B VR 04	BC0025S VR 04	Z8FA2NP D 2 VR 04	45264 01 D VR 04
45109 13 VR 05	Z16P B VR 05	BC0025S VR 05	Z8FA2NP D 2 VR 05	45264 01 D VR 05
45109 13 VR 06	Z16P B VR 06	BC0025S VR 06	Z8FA2NP D 2 VR 06	45264 01 D VR 06
45109 13 VR 07	Z16P B VR 07	BC0025S VR 07	Z8FA2NP D 2 VR 07	45264 01 D VR 07
45109 14 VR 01	Z16P C VR 01	BC1000A VR 01	Z8FA4NP A 2 VR 01	45245 01 A VR 01
45109 14 VR 02	Z16P C VR 02	BC1000A VR 02	Z8FA4NP A 2 VR 02	45245 01 A VR 02
45109 14 VR 03	Z16P C VR 03	BC1000A VR 03	Z8FA4NP A 2 VR 03	45245 01 A VR 03
45109 14 VR 04	Z16P C VR 04	BC1000A VR 04	Z8FA4NP A 2 VR 04	45245 01 A VR 04
45109 14 VR 05	Z16P C VR 05	BC1000A VR 05	Z8FA4NP A 2 VR 05	45245 01 A VR 05
45109 14 VR 06	Z16P C VR 06	BC1000A VR 06	Z8FA4NP A 2 VR 06	45245 01 A VR 06
45109 14 VR 07	Z16P C VR 07	BC1000A VR 07	Z8FA4NP A 2 VR 07	45245 01 A VR 07
45109 22 VR 01	Z16P D VR 01	BC1000B VR 01	Z8FA4NP B 2 VR 01	45245 01 B VR 01
45109 22 VR 02	Z16P D VR 02	BC1000B VR 02	Z8FA4NP B 2 VR 02	45245 01 B VR 02
45109 22 VR 03	Z16P D VR 03	BC1000B VR 03	Z8FA4NP B 2 VR 03	45245 01 B VR 03
45109 22 VR 04	Z16P D VR 04	BC1000B VR 04	Z8FA4NP B 2 VR 04	45245 01 B VR 04
45109 22 VR 05	Z16P D VR 05	BC1000B VR 05	Z8FA4NP B 2 VR 05	45245 01 B VR 05
45109 22 VR 06	Z16P D VR 06	BC1000B VR 06	Z8FA4NP B 2 VR 06	45245 01 B VR 06
45109 22 VR 07	Z16P D VR 07	BC1000B VR 07	Z8FA4NP B 2 VR 07	45245 01 B VR 07
Z8FA2NP A 2 VR 01	45264 01 A VR 01	BC2000A VR 01	Z8FA4NP C 2 VR 01	45245 01 C VR 01
Z8FA2NP A 2 VR 02	45264 01 A VR 02	BC2000A VR 02	Z8FA4NP C 2 VR 02	45245 01 C VR 02
Z8FA2NP A 2 VR 03	45264 01 A VR 03	BC2000A VR 03	Z8FA4NP C 2 VR 03	45245 01 C VR 03
Z8FA2NP A 2 VR 04	45264 01 A VR 04	BC2000A VR 04	Z8FA4NP C 2 VR 04	45245 01 C VR 04
Z8FA2NP A 2 VR 05	45264 01 A VR 05	BC2000A VR 05	Z8FA4NP C 2 VR 05	45245 01 C VR 05
Z8FA2NP A 2 VR 06	45264 01 A VR 06	BC2000A VR 06	Z8FA4NP C 2 VR 06	45245 01 C VR 06
Z8FA2NP A 2 VR 07	45264 01 A VR 07	BC2000A VR 07	Z8FA4NP C 2 VR 07	45245 01 C VR 07
Z8FA2NP B 2 VR 01	45264 01 B VR 01	BC2000B VR 01	Z8FA4NP D 2 VR 01	45245 01 D VR 01
Z8FA2NP B 2 VR 02	45264 01 B VR 02	BC2000B VR 02	Z8FA4NP D 2 VR 02	45245 01 D VR 02
Z8FA2NP B 2 VR 03	45264 01 B VR 03	BC2000B VR 03	Z8FA4NP D 2 VR 03	45245 01 D VR 03
Z8FA2NP B 2 VR 04	45264 01 B VR 04	BC2000B VR 04	Z8FA4NP D 2 VR 04	45245 01 D VR 04
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Z8FA2NP B 2 VR 06	45264 01 B VR 06	BC2000B VR 06	Z8FA4NP D 2 VR 06	45245 01 D VR 06
Z8FA2NP B 2 VR 07	45264 01 B VR 07	BC2000B VR 07	Z8FA4NP D 2 VR 07	45245 01 D VR 07