3M Purification

Zeta Plus™ VR Series

Depth Filter Cartridges & Capsules

Zeta Plus VR Series For Enhanced Log Reduction of Viruses From Biological Fluids

Application

The removal and/or inactivation of contaminating viruses from biotherapeutics is a requisite for ensuring final product safety. Zeta Plus™ VR Series 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.

Virus Removal Applications for Zeta Plus™ VR Media:

- Processing of human plasma-derived proteins
- Recombinant proteins from cell culture and fermentation
- Monoclonal antibodies
- Serum and other raw materials derived from animal sources

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.

Features & Benefits

Combined ion exchange & physical entrapment virus removal mechanisms.
- Validatable viral log reduction.
- Provides added level of viral safety.

Economical "bolt-on" separation technology as adjunct or pre-filter to other viral clearance steps.
- Provides added level of validatable viral clearance.
- Can replace or augment chromatography columns or function as prefilter to final virus removal membrane filter.

Quality Control tested for media ion exchange capacity.
- Assurance of filter media consistency & performance.

Self-contained, single-use disposable capsules & cartridge modules
- Single-use, disposable design eliminates validation concerns associated with reusable clearance options (chromatography column sanitization & regeneration).

Range of cartridge sizes, sanitary design cartridge housings & disposable capsules.
- Facilitates scaleup from small volume feasibility trials & validation studies to production scale operations.

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

Zeta Plus™ VR Series filter media is a family of cellulosic depth filtration media designed to retain contaminants by both physical entrapment and ion exchange adsorption. It is composed of high-area process filter aids embedded in a cellulose fiber 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 electrokinetic 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 anion exchange 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 utilized world wide in the fractionation of human and animal plasma proteins.

Zeta Plus™ VR Series 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-inch diameter) make scale-up straight forward 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 BC capsules are available for laboratory scale and process development work and are ideal for scaled down viral validation studies.

Zeta Plus™ VR Series 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 milliliter lab volumes to production scale cGMP operations. Filter media is available in the following configurations:

Zeta Plus™ VR Series Filter Sheets: VR filter media is available in a range of filter sheet sizes to fit plate-and-frame filter presses.

Zeta Plus™ VR Series BC Disposable Filter Capsules: VR filter media is available in three different sizes of BC disposable capsules for bench scale and pilot scale filtration.

Zeta Plus™ VR Series Filter Cartridges and Sanitary Housings: VR filter media is available in 8-inch, 12-inch and 16-inch diameter, easy-to-use, disposable cartridges. A range of sanitary design Zeta Plus filter housings is available for VR Series cartridges.

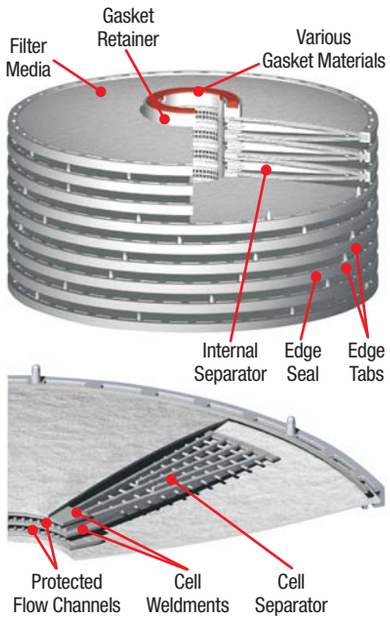
Table 1: Selection of Zeta Plus™ VR Series Filter Media

	Recommended For:					
Filter Media Choice	Plasma Proteins	Cell Culture Proteins	Nominal Retention Rating (µm)	20˚C Water Flow @ 5 psid (gpm/ft²)	Autoclavable or In-situ Steam Sterilizable	[Al3+] in 20°C water @ 5L/ft² (ppb)
VR 02	•	•	0.8	1.9	Yes	20
VR 03		•	0.8	1.2	Yes	40
VR 05		•	0.2	0.4	Yes	40
VR 06	•	•	0.2	0.6	Yes	20
VR 07	•	•	0.2	0.4	Yes	60

Recommended Operating Parameters

Nominal Retention Ratings	0.2 to 0.8 micron
Maximum Operating Pressure	**VR Cartridges:** 35 psi maximum cartridge pressure drop. **BC25 Capsules:** 40 psig max. inlet pressure, 35 psi max. media pressure drop. **BC1000/2000 Series Capsules:** 80 psig at 25° C, 40psig at 60° C, max. inlet pressure; 35 psi max. cartridge pressure drop.
Maximum Operating Temperature	**Zeta Plus™ VR 02, 03, 05, 06, & 07 Cartridges:** 82° C. **BC25 Capsules:** 40° C. **BC1000 / 2000 Capsules:** 60° C.
Recommended Pre-use Rinse	50 L/m² at 20 L/m²/min.
Sterilization Parameters	**All media grades can be autoclaved or *in-situ* steam sterilized** **Zeta Plus™ VR Series Cartridges:** In-situ steam sterilized or autoclaved, for 30 minutes at 121°C (1 cycle). **BC25:** Autoclave for 30 minutes at 121°C (1 cycle). **BC1000/2000:** Autoclave for 30 minutes at 121°C (up to 3 cycles).
Recommended Flow Rates	**BC25:** 3 - 30 ml/min. **BC1000/2000 & VR Cartridges:** 2.5 L/m²/min.

Cartridge Construction



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 model viruses 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 Series depth filters.

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

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.

Effective Filtration Area	
BC25 Capsule	25 cm²
BC1000 Capsule	650 cm²
BC2000 Capsule	1300 cm²
45109 (8-inch diameter cartridge, 8-cell)	0.26 m²
45167 (8-inch diameter cartridge, 7-cell, o-ring plug-in)	0.23 m²
Z8FA2NPX2 (8-inch diameter cartridge, 2-cell plug-in)	650 cm²
Z8FA4NPX2 (8-inch diameter cartridge, 4-cell plug-in)	1300 cm²
45264 (12-inch diameter cartridge, 7-cell bodyfeed)	0.67 m²
45245 (12-inch diameter cartridge, 16-cell)	1.5 m²
Z16P (16-inch, 14-cell, netted)	3.2 m²

Zeta Plus™ VR Series Ordering Guide

8" Diameter Cartridges

Catalog Number	Configuration	VR Series
45109 (8" 8-cell)	**11** - Nitrile **13** - Fluorocarbon **14** - EPR **22** - Silicone **23** - Expanded PTFE	**VR02 VR06** **VR03 VR07** **VR05**
45167 (8" 7-cell, O-ring plug-in)	**01** - Nitrile **02** - EPR **03** - Fluorocarbon **04** - Silicone	**VR02 VR06** **VR03 VR07** **VR05**

Catalog Number	Configuration	Pkg Code	VR Series
Z8FA2NP (8" 2-cell, plug-in) **Z8FA4NP** (8" 4-cell, plug-in)	**01** - Nitrile **02** - EPR **03** - Fluorocarbon **04** - Silicone	2	**VR02 VR06** **VR03 VR07** **VR05**

16" Diameter Cartridges

Catalog Number	Gasket Material	VR Series
Z16P (16" 14-cell)	**A** - Silicone **B** - Fluorocarbon **C** - EPR **D** - Nitrile	**VR02 VR06** **VR03 VR07** **VR05**

BC Capsules

Catalog Number	VR Series
BC0025L (Luer) **BC0025S** (Sanitary) **BC1000A** (Single pack) **BC1000B** (3 pack) **BC2000A** (Single pack) **BC2000B** (3 pack)	**VR02 VR06** **VR03 VR07** **VR05**

12" Diameter Cartridges

Catalog Number	Geometric Variation	Gasket Material	VR Series
45264 (12" 7-cell, Bodyfeed) **45245** (12" 16-cell)	**01** - Standard Polypropylene	**A** - Silicone **B** - Fluorocarbon **C** - EPR **D** - Nitrile	**VR02 VR06** **VR03 VR07** **VR05**

Important Notice

The information described in this literature is accurate to the best of our knowledge. A variety of factors, however, can affect the performance of the Product(s) in a particular application, some of which are uniquely within your knowledge and control. INFORMATION IS SUPPLIED UPON THE CONDITION THAT THE PERSONS RECEIVING THE SAME WILL MAKE THEIR OWN DETERMINATION AS TO ITS SUITABILITY FOR THEIR USE. IN NO EVENT WILL 3M PURIFICATION BE RESPONSIBLE FOR DAMAGES OF ANY NATURE WHATSOEVER RESULTING FROM THE USE OF OR RELIANCE UPON INFORMATION.

It is your responsibility to determine if additional testing or information is required and if this product is fit for a particular purpose and suitable in your specific application.

Limitation of Liability

3M Purification Pty Limited will not be liable, to the extent permitted by law, for any loss or damage from the use of the Product(s), whether direct, indirect, special, or consequential, regardless of the legal theory asserted, included warranty, contract, negligence or strict liability.

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