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3M Separation and Purification Sciences Division

3M™ Zeta Plus™ Filters with SP Series Media

Regulatory Support File

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I. Regulatory Support Information

3M Separation and Purification Sciences Division is a leader in advanced filtration and purification solutions, offering a wide range of products and services for various stages of pharmaceutical and biologics manufacturing.

3M, a U.S. based multinational high technology company, has operations in more than 65 countries. Facilities that participate in the manufacturing of 3M™ Zeta Plus™ Filters with SP Series Media as shown below, have quality systems registered to quality system standards as noted below.

Stafford Springs, CT, USA	Wroclaw, Poland	Columbia, MO, USA	Blacktown, Australia
Registered to: ISO 9001	Registered to: ISO 9001	Registered to: ISO 9001	Registered to: ISO 9001

This Regulatory Support File provides information pertinent to the 3M™ Zeta Plus™ Filters with SP Series Media. Contained herein are detailed test methods, product specifications, product performance information and regulatory documentation related to pharmaceutical and biologics manufacturing processes. 3M supplied documentation can be used to support risk assessments and regulatory submissions, prepare standard operating procedures, and streamline testing requirements, all of which save time and cost for the manufacturer. The manufacturer of a pharmaceutical or biologic product is ultimately responsible for registration through regulatory authorities in each country or region where their product will be produced or used.

The U.S. Federal Food, Drug, and Cosmetics Act designated the United States Pharmacopeia (USP) and the National Formulary (NF) as official compendia for drugs marketed in the United States. USP-NF is a combination of two public compendia of pharmacopeia standards. The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) brings together the regulatory authorities and pharmaceutical industry to discuss various aspects of drug registration and to achieve greater international harmonization. These standards form the primary basis for technical information provided in this product support document. 3M routinely completes a thorough review of the USP and ICH standards and this regulatory support file to ensure that the claims and data package are current.

Complementary product information, use and operating instructions and guidelines, and technical data can be found in the 3M™ Zeta Plus™ Filters with SP Series Media literature and product quality certifications. Further information can be obtained by contacting your local 3M representative.

The intended use(s), restrictions on use, and production selection and use for 3M™ Zeta Plus™ Filters with SP Series Media are stated below.

Intended Use(s): 3M™ Zeta Plus™ Filters with SP Series Media are single-use filter products intended for use in biopharmaceutical processing applications of aqueous and chemical based pharmaceuticals (drugs) and vaccines in accordance with the product instructions and specifications, and cGMP requirements, where applicable.

Since there are many factors that can affect a product's use, the customer and user remain responsible for determining whether the 3M product is suitable and appropriate for the user's specific application, including user conducting an appropriate risk assessment and evaluating the 3M product in user's application.

Restrictions on Use: 3M advises against the use of these 3M products in any application other than the stated intended use(s), since other applications have not been evaluated by 3M and may result in an unsafe or unintended condition. Do not use in any manner whereby the 3M product, or any leachable from the 3M product, may become part of or remains in a medical device that is regulated by any agency, and/or globally exemplary agencies, including but not limited to: a) FDA, b) European Medical Device Regulation (MDR), c) Japan Pharmaceuticals and Medical Devices Agency (PMDA) or in applications involving permanent implantation into the body; Life-sustaining medical applications; Applications requiring food contact compliance.

Product Selection and Use: Many factors beyond 3M's control and uniquely within user's knowledge and control can affect the use and performance of a 3M product in a particular application. As a result, end-user is solely responsible for evaluating the product and determining whether it is appropriate and suitable for end-user's application, including completing a risk assessment that considers the product leachable characteristics and its impact on drug safety, conducting a workplace hazard assessment and reviewing all applicable regulations and standards. Failure to properly evaluate, select, and use a 3M product and appropriate safety products, or to meet all applicable safety regulations, may result in injury, sickness, death, and/or harm to property.

II. Drug Master File Reference

3M™ Zeta Plus™ SP Series filters are listed in a Drug Master File (DMF) registered with the United States Food and Drug Administration (FDA).

The information contained in the DMF may be utilized by regulatory reviewers to support a New Drug Application (NDA), Investigational New Drug Application (INDA), Abbreviated New Drug Application (ANDA), another DMF, an Export Application, or supplements to any of these.

Permission by 3M for review of a DMF is granted only to appropriate United States Food and Drug Administration (FDA) or similar regulatory agency personnel as the document contains 3M proprietary information. Following the FDA Code of Federal Regulations (CFR) Title 21 Section 314.420, before FDA may review the DMF in support of an application, 3M Purification Inc. must provide a letter of authorization permitting FDA to reference the DMF. The applicant is required to include a copy of the letter of authorization in their application. Contact 3M Separation and Purification Sciences Division to initiate a review of the DMF. 3M will update this Regulatory Support File as a routine aspect of product maintenance.

III. Product Descriptions

3M™ Zeta Plus™ Filters with SP Series Media are a family of advanced depth filters designed for clarification of various bioprocess, biological and pharmaceutical fluids. 3M™ Zeta Plus™ SP Series Filter Media has the widest nominal pore size range relative to 3M™ Zeta Plus™ LA and ZB Series Filter Media offerings, including grades with larger nominal pore sizes. 3M™ Zeta Plus™ SP Series Filter Media has a lower charge level than 3M™ Zeta Plus™ ZB Series Filter Media, which may reduce the likelihood of removing (binding) product along with contaminants.

3M™ Zeta Plus™ 01SP Grade Filter Media contains a mixture of cellulose and a crosslinking polymer binder resin while the remaining grades of 3M™ Zeta Plus™ SP Series Filter Media contains a mixture of inorganic filter aids, cellulose, and a crosslinking polymer binder resin. The polymer resin has a mixed amine structure including a quaternary amine, which imparts the anion exchange functionality of the media.

The 3M™ Zeta Plus™ SP Series Filter Media exhibits a combination of mechanical and electrokinetic mechanisms for particulate removal as a result of its physical and chemical attributes. The 3M™ Zeta Plus™ SP Series Filter Media is a porous depth filter media that is a tortuous network of charge-enhanced flow channels capable of reducing negatively charged DNA, endotoxins, and other host cell proteins to a level which mechanical screening alone cannot achieve. Whole cells and cell debris can be removed by mechanical entrapment within the 3M™ Zeta Plus™ SP Series Filter Media depth filter matrix. Note that the charge capacity of the 3M™ Zeta Plus™ SP Series Filter Media is a general attribute but not a controlled qualification or release specification. Therefore, formal process validation of charged contaminant removal must be fully assessed as part of the customer's rigorous risk management process.

3M™ Zeta Plus™ EXT Series Filter Cartridges and Capsules with SP Series Media are dual layer versions that consist of two distinct layers, or "zones," of filter media with the upstream zone more open than the downstream zone. The media used for each layer is a standard grade. The structure of the 3M™ Zeta Plus™ EXT Series Filters with SP Series Media enhances the contaminant holding capacity of the filter media. The dual layer structure allows larger particles to be trapped in the upstream zone of the more open filter media and smaller particles to be trapped in the downstream zone, reducing premature plugging and helping extend service life of the media. The structure of dual layer media can provide enhanced contaminant holding capacity when the challenge process stream has a wide particle distribution, compared to that of a single layer, single zone product.

A wide range of product configurations are available including converted media sheets, lenticular cartridges and single-use capsules.

3M has global manufacturing and supply chain capabilities. The products described below may be produced at multiple global locations. 3M assigns a unique ID number to each product specific to its country of origin and will ensure lot traceability to each manufacturing facility.

Product configurations listed below may not be commercially available or may not be available to all customers. Please contact your 3M account representative for questions on available product configurations in your country.

There may be additional product configurations not listed here that are still covered by this Regulatory Support File or the associated RSF Supplement. Please contact your 3M Account Representative with questions regarding product configurations not listed below that may be covered by this document.

3M™ Zeta Plus™ 8-Inch Filter Cartridges

Table 1a. 3M™ Zeta Plus™ 8-Inch Filter Cartridge Product Descriptions: Single Layer Media

Manufacturing Facility	Product Description Examples: 451092260SP, Z8FA4NPA230SP, Z08P2A05SP, Z08CA30SP						
United States	**Diameter Designation**				**Gasket Material**		**Grade**
	45109 - 8 cell				13 – Fluorocarbon (FPM) 22 – Silicone (VMQ) 23 – Fluoropolymer (PTFE)		05SP 10SP 30SP 50SP 60SP 90SP
	45167 - 7 cell Plug-in				03 – Fluorocarbon (FPM) 04 – Silicone (VMQ) 09 –PTFE-Encapsulated Fluorocarbon		
	Diameter Designation	**Number of Cells**	**Configuration**	**Material**	**O-Ring Material**	**Package**	**Grade**
	Z8FA -Plug-in	2 - 2 cell 4 - 4 cell	N - None	P - Polypropylene	A – Silicone (VMQ) B – Fluorocarbon (FPM) K – PTFE-Encapsulated Fluorocarbon	2 - Standard	05SP 10SP 30SP 50SP 60SP 90SP
Poland	**Diameter Designation**		**Cartridge Construction**		**Gasket Material**		**Grade**
	Z08		P - Plug-in 7 cells P2 - Plug-in 2 cells P4 - Plug-in 4 cells		A – Silicone (VMQ)		05SP 10SP 30SP
			D - Standard 8 cells		A - Silicone (VMQ) B – Fluorocarbon (FPM)		50SP 60SP 90SP
Australia	**Diameter Designation**	**Number of Cells**		**Gasket Material**		**Grade**	
	Z08	M – 9 cell		A – Silicone (VMQ)		30SP 60SP	

Table 1b. 3M™ Zeta Plus™ 8-Inch Filter Cartridge Product Descriptions: Dual Layer (EXT) Media						
Manufacturing Facility	**Product Description Examples: Z08E05PA60SP05A, Z08E07AA60SP02A**					
	Diameter Designation	**Media Configuration**	**Number of Cells**	**Cartridge Construction**	**Gasket Material[1]**	**Grade**
United States	Z08	E	05 – 5 cell 06 – 6 cell 07 – 7 cell	A - Stainless Steel Bands B - Hastelloy® Bands P – Polypropylene Plug-in	A – Silicone (VMQ)	05SP01A (5 & 6 cell) 10SP01A (5 & 6 cell) 10SP02A (5 & 6 cell) 30SP02A (5 & 6 cell) 30SP03A (5 & 6 cell) 60SP01A (5 & 6 cell) 60SP02A (5 & 6 cell) 60SP03A (5 & 6 cell) 60SP05A (5 & 7 cell) 90SP05A (5 & 7 cell) 90SP08A (5 & 7 cell)
Poland	**Diameter Designation**	**Media Configuration**	**Number of Cells**	**Cartridge Construction**	**Gasket Material[1]**	**Grade**
	Z08	E	06 – 6 cell	A - Stainless Steel Bands	A – Silicone (VMQ)	05SP01A (6 cell) 30SP02A (7 cell) 60SP02A (7 cell)
	Z08	E	07 – 7 cell	A - Stainless Steel Bands B - Hastelloy® Bands	A – Silicone (VMQ)	

1 Dual layer (EXT) media configurations are designed for biopharmaceutical applications, where gasket material is Silicone (VMQ)

3M™ Zeta Plus™ 12-Inch Filter Cartridges

Table 2a. 3M™ Zeta Plus™ 12-Inch Filter Cartridge Product Descriptions: Single Layer Media

Manufacturing Facility	Product Description Examples: 4523702A90SP, Z12DA90SP					
United States	Diameter Designation		Material	Gasket Material	Grade	
	45244 - 9 cell DOE 45237 - 12 cell DOE 45245 - 16 cell DOE		01 - Polypropylene (PP) 02 – Mineral-filled PP 03 – PP, Hastelloy® Bands	A – Silicone (VMQ) B – Fluorocarbon (FPM) E – Fluoropolymer (PTFE)	05SP 10SP 30SP 50SP 60SP 90SP	
Poland	Diameter Designation	Cartridge Construction	Optional Lifting Handle	Gasket Material	Grade	Optional Material
	Z12	C – 9 cells /small B – 12 cells D – 16 cells[1] M – 15 cells, Netting S – 7 cells	H[2] – with Handle	A – Silicone (VMQ) B – Fluorocarbon (FPM)	05SP 10SP 30SP 50SP 60SP 90SP	H[3] – Hastelloy Bands
Australia	Diameter Designation		Cartridge Construction	Gasket Material	Grade	
	Z12		C – 9 cells /small D – 16 cells	A – Silicone (VMQ)	10SP 30SP 50SP 60SP 90SP	

1 15 cells for 05SP media

2 Omit "H" from product description if lifting handle is not required.

3 "H" for Hastelloy® bands. Omit "H" for Stainless Steel Bands.

Table 2b. 3M™ Zeta Plus™ 12-Inch Filter Cartridge Product Descriptions: Dual Layer (EXT) Media

Manufacturing Facility	Product Description Example: Z12E11AA60SP05A					
Poland	Diameter Designation	Cartridge Construction	Number of Cells	Cartridge Construction	Gasket Material[1]	Grade
	Z12	E	11 – 11 cell	A - Stainless Steel Bands B - Hastelloy® Bands	A – Silicone (VMQ)	05SP01A 30SP02A 60SP05A 90SP05A

1 Dual layer (EXT) media configurations are designed for biopharmaceutical applications, where gasket material is Silicone (VMQ).

3M™ Zeta Plus™ 16-Inch Filter Cartridges

Table 3a. 3M™ Zeta Plus™ 16-Inch Filter Cartridge Product Descriptions: Single Layer Media

Manufacturing Facility	Product Description Examples: Z16PA90SP, Z16DA90SP				
United States	Diameter Designation	Configuration	Gasket Material	Grade	Lifting Handle
	Z16	P – 14 cell H – High Area[1] R – 14 cell (Hastelloy® Bands) T – High Area (Hastelloy® Bands)	A – Silicone (VMQ) B – Fluorocarbon (FPM) E – Fluoropolymer (PTFE)	05SP 10SP 30SP 50SP 60SP 90SP	H – with Handle[2]

	Diameter Designation	Cartridge Construction	Gasket Material	Grade	Lifting Handle
Poland	Z16	M – 14 cell, Netting P – 14 cell, Netting D – 15 cell S – 9 cell H – High Area[3], Netting, Stainless Steel Bands T – High Area[3], Netting, Hastelloy® Bands R – 14 cell, Netting, Hastelloy® Bands	A – Silicone (VMQ) B – Fluorocarbon (FPM) E – Fluoropolymer (PTFE)	05SP 10SP 30SP 50SP 60SP 90SP	H – with Handle[2]
Australia	**Diameter Designation**	**Cartridge Construction**	**Gasket Material**	**Grade**	
	Z16	M – 14 cell, Netting D – 15 cell	A – Silicone (VMQ)	10SP 30SP 50SP 60SP 90SP	

1 High Area Cell Count – 16 cells for grades 30SP & 50SP; 17 cells for grades 60SP & 90SP; not available for 05SP. Bodyfeed cartridge available, please order 45802 (16", 9 cell).

2 Omit "H" from product description if film lifting handle is not required.

3 16 cells for grades 30SP and 50SP, 17 cells for grades 60SP and 90SP.

Table 3b. 3M™ Zeta Plus™ 16-Inch Filter Cartridge Product Descriptions: Dual Layer (EXT) Media						
Manufacturing Facility	**Product Description Example: Z16E08AA60SP05A, Z16E08AA90SP05A**					
	Diameter Designation	**Media Configuration**	**Number of Cells**	**Cartridge Construction**	**Gasket Material[1]**	**Grade**
United States	Z16	E	01 - 1 cell 02 - 2 cell 08 - 8 cell 12 - 12 cell	A - Stainless Steel Bands	A – Silicone (VMQ)	05SP01A 10SP01A 10SP02A 30SP02A 30SP03A 60SP01A 60SP02A 60SP03A 60SP05A 90SP05A 90SP08A
	Diameter Designation	**Cartridge Construction**	**Number of Cells**	**Cartridge Construction**	**Gasket Material[1]**	**Grade**
Poland	Z16	E	01 - 1 cell 02 - 2 cell 08 - 8 cell 12 - 12 cell	A - Stainless Steel Bands B - Hastelloy® Bands	A – Silicone (VMQ)	05SP01A 10SP01A 10SP02A 30SP02A 30SP03A 60SP01A 60SP02A 60SP03A 60SP05A 90SP05A 90SP08A

1 Dual layer (EXT) media configurations are designed for biopharmaceutical applications, where gasket material is Silicone (VMQ).

3M™ Zeta Plus™ BC Series Filter Capsules (Laboratory Capsules)

Table 4a. 3M™ Zeta Plus™ BC Series Filter Capsule (Laboratory Capsule) Product Descriptions: Single Layer Media			
Manufacturing Facility	**Product Description Example: BC0025L90SP**		
	Diameter Designation	**Configuration**	**Grade**
United States and Poland	BC0025	L - Luer S - Sanitary	05SP 10SP 30SP 50SP 60SP 90SP

Table 4b. 3M™ Zeta Plus™ BC Series Filter Capsule (Laboratory Capsule) Product Descriptions: Dual Layer (EXT) Media			
Manufacturing Facility	**Product Description Example: BC0025L90SP08A**		
	Diameter Designation	**Configuration**	**Grade**
United States and Poland	BC0025	L - Luer S - Sanitary	05SP01A 10SP01A 10SP02A 30SP01A 30SP02A 30SP03A 60SP01A 60SP02A 60SP03A 60SP05A 90SP05A 90SP08A

3M™ Zeta Plus™ Encapsulated System Scale-Up Filter Capsules

Table 5a. 3M™ Zeta Plus™ Encapsulated System Scale-Up Filter Capsule Product Descriptions: Single Layer Media				
Manufacturing Facility	**Product Description Example: E0340FSA90SP**			
	Diameter Designation	**EFA (cm^2)**	**Capsule Material**	**Grade**
United States and Poland	E	0170 0340 1020	FSA - Polysulfone	05SP 10SP 30SP 50SP 60SP 90SP

Table 5b. 3M™ Zeta Plus™ Encapsulated System Scale-Up Filter Capsule Product Descriptions: Dual Layer (EXT) Media				
Manufacturing Facility	**Product Description Example: E0340FSA90SP08A**			
	Diameter Designation	**EFA (cm^2)**	**Capsule Material**	**Grade**
United States and Poland	E	0170 0340 1020	FSA - Polysulfone	05SP01A 10SP01A 10SP02A 30SP02A 30SP03A 60SP01A 60SP02A 60SP03A 60SP05A 90SP05A 90SP08A

3M™ Zeta Plus™ Encapsulated System Filter Capsules (Production Capsules)

Table 6a. 3M™ Zeta Plus™ Encapsulated System Filter Capsule (Production Capsule) Product Descriptions: Single Layer Media					
Manufacturing Facility	**Product Description Example: E16E01A90SP**				
	Diameter Designation	**Configuration**	**Number of Cells**	**Gasket Material**	**Grade**
United States and Poland	E16	E - Standard R - Alkaline Resistant[1]	01 - 1 cell 07 – 7 cell[2] 11 - 11 cell	A – Silicone (VMQ)	05SP 10SP 30SP 50SP 60SP 90SP

1 Alkaline resistance is based on testing with 1M NaOH and 5% NaClO (Bleach).
2 Only available with 05SP, 50SP and 90SP in standard configuration

Table 6b. 3M™ Zeta Plus™ Encapsulated System Filter Capsule (Production Capsule) Product Descriptions: Dual Layer (EXT) Media					
Manufacturing Facility	**Product Description Example: E16E07A05SP01A**				
	Diameter Designation	**Configuration**	**Number of Cells**	**Gasket Material**	**Grade**
United States and Poland	E16	E - Standard R - Alkaline Resistant[1]	01 - 1 cell 07 - 7 cell	A – Silicone (VMQ)	05SP01A 10SP01A 10SP02A 30SP02A 30SP03A 60SP01A 60SP02A 60SP03A 60SP05A 90SP05A 90SP08A

1 Alkaline resistance is based on testing with 1M NaOH and 5% NaClO (Bleach).

3M™ Manifolds

Table 7. 3M™ Manifold Product Descriptions	
Manufacturing Facility	**Product Description Example: 6128901**
United States and Poland	**Product Description**
	6128901 – Standard Set 6129001 – Alkaline Resistant Set[1]

1 Alkaline resistance is based on testing with 1M NaOH and 5% NaClO (Bleach).

IV. Product Design

All components used in the manufacture of 3M™ Zeta Plus™ Filters with SP Series Media are traceable. Intermediate products are packaged and labeled throughout the manufacturing process to provide complete traceability from the raw materials to media batch to finished product.

All grades of the 3M™ Zeta Plus™ SP Series Filter Media are composed of the same materials of construction at varying ratios. Therefore, the test results reported herein are generally applicable to all grades and product configurations.

Multiple manufacturing facilities in various global locations produce 3M™ Zeta Plus™ Filters with SP Series Media. Raw materials are purchased consistent with global specifications.

A. Media

3M™ Zeta Plus™ SP Series Filter Media contains a mixture of inorganic filter aid, cellulose, and a crosslinking polymer binder resin. The polymer binding resin used in 3M™ Zeta Plus™ SP Series Filter Media is a polyamide epichlorohydrin (PAE) polymer that contains a mixture of secondary, tertiary, and quaternary amines. The media is produced by a wetlaid process.

Media or filter sheets may be die cut to various shapes and dimensions per customer specifications. Converted filter sheets are generally used in commercially available filter presses. Each distinct pattern is assigned a unique stock number.

3M™ Zeta Plus™ EXT Series Filters with SP Series Media are dual layer versions that consist of two distinct layers, or "zones," of filter media with the upstream zone more open than the downstream zone. Smaller numbers indicate more open grades; for example, 30SP is more open than 90SP. The media used for each layer is a standard grade.

B. Cartridges

The lenticular cells of cartridges are comprised of single or dual (EXT) opposing layers of the filter media and an inner cell separator with a polymeric molded edge seal. The lenticular cells are sealed to one another by ring seals that are aligned to the inner fluid effluent core and rest on the media under predetermined compression by three 316 stainless steel or Hastelloy® binder bands or, in the case of certain 8-inch cartridges that are designated as Plug-in, by a plug-in post and a connector. Netting is added to selected model numbers to maintain flow path between lenticles. Each cartridge has two gaskets, one at the top and one at the bottom. Depending on the cartridge configuration, three standard gasket materials may be offered: silicone (VMQ), fluorocarbon (FPM) or fluoropolymer (PTFE).

Filter cartridges are available in 8-inch, 12-inch and 16-inch nominal diameters, with surface areas ranging from 0.26 m^2 to 3.9 m^2 per cartridge. The cartridge lenticles have an outside-to-in flow path. The flow passes through the filter media and is directed to a central exit flow path along the separators.

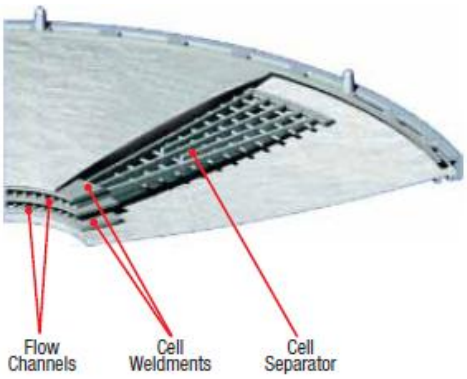


Figure 1a. 3M™ Zeta Plus™ Filter Cartridge lenticle configuration with single media layer

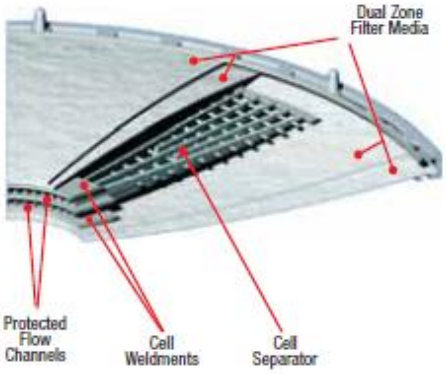


Figure 1b. 3M™ Zeta Plus™ EXT Series Filter Cartridge lenticle configuration with dual media layers

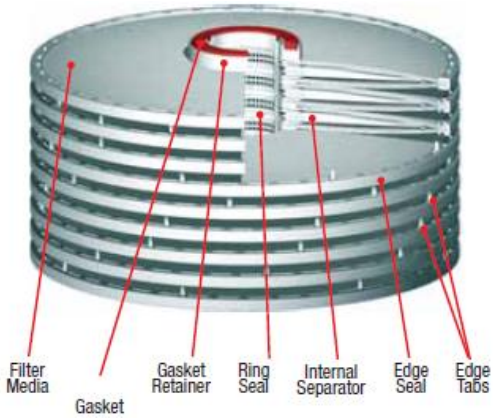


Figure 1c. 3M™ Zeta Plus™ Filter Cartridge and components

Figure 1d. 3M™ Zeta Plus™ Filter Cartridges shown with housings

Figure 1e. 3M™ Zeta Plus™ 8-Inch Plug-In Filter Cartridge

Figure 1f. 3M™ Zeta Plus™ Plug-In Filter Cartridge housing

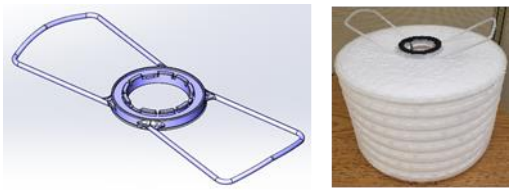


Figure 1g. Optional Molded Lifting Handle on Gasket Retainer for 3M™ Zeta Plus™ 12-Inch Filter Cartridges

Figure 1h. Optional Film Lifting Handle for 3M™ Zeta Plus™ 16-Inch Filter Cartridges

C. Capsules

There are three capsule categories for the 3M™ Zeta Plus™ Encapsulated System Filter Capsules: Laboratory (BC Series), Scale-up and Production Capsules.

The Laboratory capsule (BC0025, 3M™ Zeta Plus™ BC Series Filter Capsule) is constructed by compressing the single or dual layer (EXT) filter media between the inlet and outlet capsule components, then overmolding this entire unit with a glass fiber filled polypropylene. The Laboratory capsule is available with either luer lock or ½-inch mini sanitary matched inlet and outlet connections. The Laboratory capsule has a nominal surface area of 25 cm².

Scale-up capsules (3M™ Zeta Plus™ Encapsulated System Scale-Up Filter Capsules) are constructed from a lenticular media cell design with an 8-inch diameter. The lenticle comprises single or dual (EXT) opposing layers of the filter media and an inner separator with a polymeric molded edge seal. This lenticle is first compressed and then held together by injection molding at the outer and inner diameter by a thermoplastic resin, which simultaneously seals all edges and forms the inner fluid outlet manifold. A polypropylene spacer is placed between the lenticles in 3-cell design capsule. The lenticles have an outside-to-in flow path. The flow passes through the filter media and is directed to a central exit flow path along the separators. Scale-up capsules have three configurations with nominal surface areas of 170 cm², 340 cm² and 1020 cm² per capsule. For the 170 cm² lenticle, one of the opposing filter media layers is replaced with an injection molded polypropylene disk, thereby, reducing the accessible surface area by a factor of two. The 1020 cm² capsules contain three stacked and sealed lenticles. The lenticles, or lenticle stack, are sealed to the outlet side of the capsule with a polypropylene support ring and fluorocarbon o-ring. The top and bottom pieces of the capsule are sealed together by a thermal bond. The Scale-up capsules have mini sanitary connections on the inlet and outlet.

Production capsules (3M™ Zeta Plus™ Encapsulated System Filter Capsules) are also constructed from a lenticular media cell design with a 16-inch diameter. Each lenticle has two opposing layers of the filter media and an inner separator with a polymeric molded edge seal. The lenticle is first compressed and then held together by injection molding at the outer and inner diameter by a thermoplastic resin, which simultaneously seals all edges and forms the inner fluid outlet manifold. A polypropylene spacer is placed between the lenticles in 7-cell and 11-cell capsules. The lenticles have an outside-to-in flow path. The flow passes through the filter media and is directed to a central exit flow path along the separator. The production capsules have three single-use capsule configurations. The 0.23 m² capsule has one lenticle of single or dual layer (EXT) media. The 1.6 m² capsule has seven (7) lenticles of dual layer (EXT) media. The 2.5 m² capsule has eleven (11) lenticles of single layer media.

The outermost lenticles of the lenticle stack have respective male and female connectors thermally attached to provide connection to adjacent capsules or manifolds. The connectors use silicone o-rings. The top and bottom capsule shells are sealed together by a thermal bond. The multicell production capsule has a self-guiding locking mechanism for a robust capsule-to-capsule connection. The standard production capsule material is translucent polycarbonate. An opaque, alkaline-resistant, polyphenylene/oxide polystyrene capsule material option is available, enabling exposure to strong bases. The multicell production capsules have two handles for convenient loading and unloading.

A set of 3M™ Manifolds is required for connecting the production capsules to external components of the purification train. The 3M™ Manifolds have 1.5" sanitary connections on the inlet and outlet. Manifold and capsule materials should always be the same; materials of construction should not be mixed. For example, polycarbonate capsules should only be used with polycarbonate manifolds.

The 3M™ Zeta Plus™ Encapsulated System Filter Capsules (Production capsules) may be used in a multi-stage filtration or purification train with a single 3M™ Encapsulated System Holder. Production capsules of the same or different media configurations can be installed in a single 3M™ Encapsulated System Holder. Additionally, one of the stages may include 3M™ Emphaze™ AEX Hybrid Purifier. An extra pair of manifolds is required between each stage of the multi-stage train within the 3M™ Encapsulated System Holder.

Figure 2. 3M™ Zeta Plus™ BC Series Filter Capsules (Laboratory Capsules)

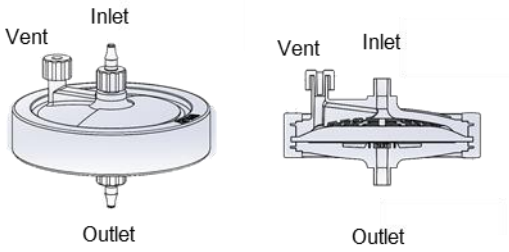


Figure 2a. 3M™ Zeta Plus™ BC Series Filter Capsule (BC0025 Laboratory Capsule) – Luer Style

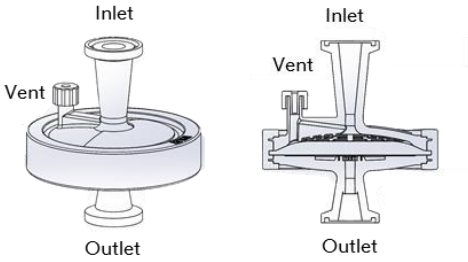


Figure 2b. 3M™ Zeta Plus™ BC Series Filter Capsule (BC0025 Laboratory Capsule) – Sanitary Style

Figure 3. 3M™ Zeta Plus™ Encapsulated System Scale-Up Filter Capsules

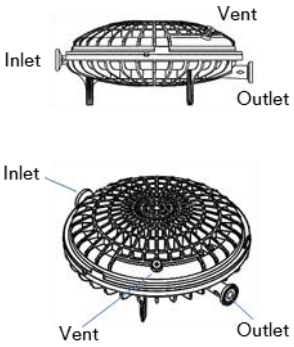


Figure 3a. 3M™ Zeta Plus™ Encapsulated System 170 cm² & 340 cm² Scale-Up Filter Capsules

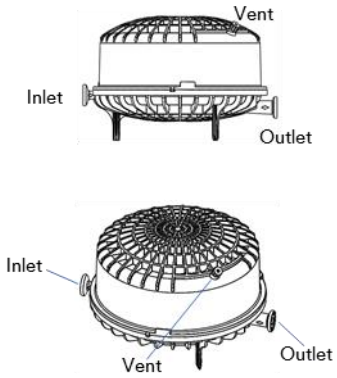


Figure 3b. 3M™ Zeta Plus™ Encapsulated System 1020 cm² Scale-Up Filter Capsule

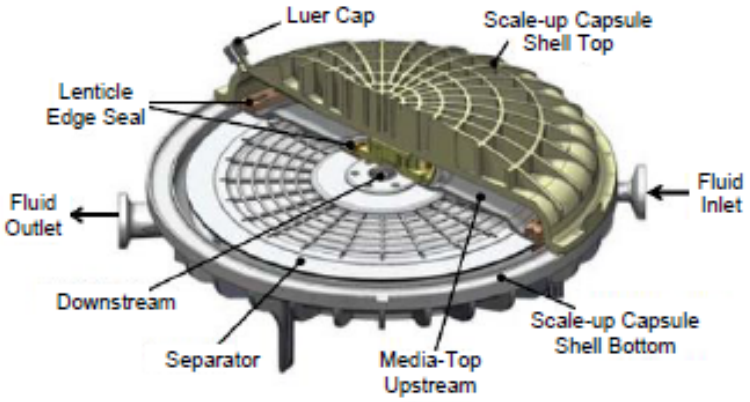


Figure 3c. 3M™ Zeta Plus™ Encapsulated System Scale-up Filter Capsule cross-section

Figure 4. 3M™ Zeta Plus™ Encapsulated System Filter Capsules (Production Capsules)

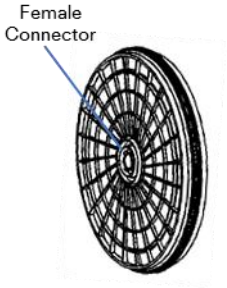


Figure 4a. 3M™ Zeta Plus™ Encapsulated System 0.23 m² Filter Capsule

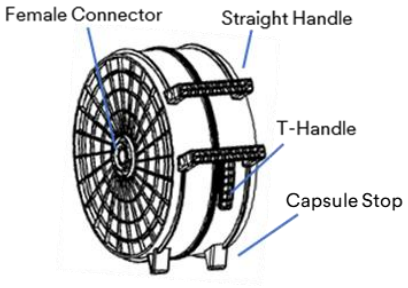


Figure 4b. 3M™ Zeta Plus™ Encapsulated System 1.6 m² & 2.5 m² Filter Capsules

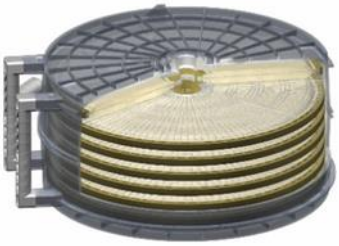


Figure 4c. 3M™ Zeta Plus™ Encapsulated System Filter Capsule (Production Capsule) cross-section

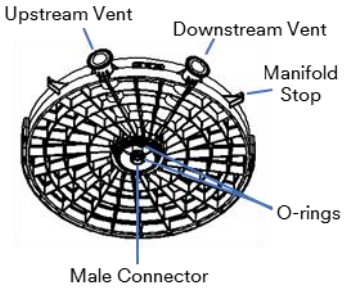


Figure 4d. 3M™ Manifolds – Top manifold

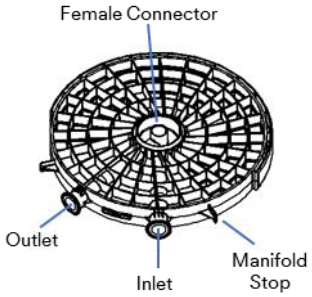


Figure 4e. 3M™ Manifolds – Bottom manifold

Figure 4f. 3M™ Zeta Plus™ Encapsulated System Filter Capsules (Production capsules) installed in 3M™ Encapsulated System Holders

D. Materials of Construction

Table 8. Materials of Construction – 3M™ Zeta Plus™ Filter Cartridges	
Part Type	**Materials**
Filter Media	Natural Silica, Cellulose, Polymer Resin
Separators	Polypropylene or Mineral-filled Polypropylene
Netting[1]	Polypropylene
Edge Seal	Polypropylene or Mineral-filled Polypropylene (single layer media) or Thermoplastic Elastomer (dual layer media)
Ring Seal	Polypropylene
Gasket Retainers	Polypropylene or Mineral-filled Polypropylene
Optional Molded Lifting Handle on Gasket Retainer	Polypropylene or Mineral-filled Polypropylene
Gaskets	Silicone, Fluorocarbon or PTFE
Optional Film Lifting Handle	Polypropylene
Binder Bands	316 Stainless Steel or Hastelloy®
8-inch Cartridge Plug-in Unitizing Post	Polypropylene

1 Specific 12-inch and 16-inch cartridges

Table 9. Materials of Construction – 3M™ Zeta Plus™ BC Series Filter Capsule (Laboratory Capsule)	
Part Type	**Materials**
	BC0025
Nominal Surface Area	25 cm^2
Filter Media	Natural Silica, Cellulose, Polymer Resin
Shells	Polypropylene
Ring Seal (dual layer media)	Polypropylene
Edge Seal Overmold	Glass Fiber Filled Polypropylene
Luer cap & luer-barb connector	Polypropylene

Table 10. Materials of Construction – 3M™ Zeta Plus™ Encapsulated System Scale Up Filter Capsules			
Part Type	**Materials**		
	E0170 Capsule	**E0340 Capsule**	**E1020 Capsule**
Nominal Surface Area	170 cm^2	340 cm^2	1020 cm^2
Filter Media	Natural Silica, Cellulose, Polymer Resin		
Separators	Polypropylene		
Spacers	N/A		Polypropylene
Flow Inhibitor Disc	Polypropylene	N/A	
Edge Seal	Thermoplastic Elastomer		
Inner Seal	Thermoplastic Elastomer		
Endcap	Thermoplastic Elastomer		
Shells	Polysulfone		
Back-up O-ring	Polypropylene		
O-ring	Fluorocarbon (FKM)		
Luer Cap	Polypropylene		

Table 11. Materials of Construction – 3M™ Zeta Plus™ Encapsulated System Filter Capsules (Production Capsules)			
Part Type	**Materials**		
	E16E01, E16R01 Capsules	**E16E07, E16R07 Capsules**	**E16E11, E16R11 Capsules**
Nominal Surface Area	0.23 m^2	1.6 m^2	2.5 m^2
Filter Media	Natural Silica, Cellulose, Polymer Resin		
Separators, Spacers	Polypropylene		
Edge Seal	Thermoplastic Elastomer		
Ring Seal	Thermoplastic Elastomer		
Connectors (Male & Female)	Polypropylene		
Shells	Either Polycarbonate or Polyphenylene Oxide/Polystyrene		
O-ring Retainer	Either Polycarbonate or Polyphenylene Oxide/Polystyrene		
O-rings	Silicone		
Handles	N/A	Nylon	
Manifold	Polycarbonate or Polyphenylene Oxide/Polystyrene		

E. 3M™ Zeta Plus™ Encapsulated System Filter Capsule and 3M™ Manifold Design Characteristics

Weights and Volumes shown in Tables 12-15 below were experimentally determined from samples of various representative grades and families of 3M™ Zeta Plus™ Filter Media. **Please note that these values are presented for guidance only and are not specifications**; actual amounts depend upon individual capsule variability, exact blow-down conditions, media type in capsule, the number of capsules in the system, the process fluid, and loading level of the capsule.

1) Dry Weight – Weight of capsule prior to use.
2) Wet, Post Blow-down Weight - Liquid retained in the system, as measured by the differential between the capsule dry weight and the capsule weight after blow-down. This predominantly reflects the liquid left in the filter media. Actual amount depends upon exact blow-down conditions, media type in capsule, the number of capsules in the system, the process fluid, and loading level of the capsule.
3) Capsule Fill Volume - Amount of liquid necessary to fill the capsule from inlet to outlet, including media, calculated using the filled capsule weight and flush fluid density.
4) Post Blow-down Hold-Up Volume - Estimated volume of residual preconditioning flush liquid after air/gas blow-down using water as the flush fluid and calculated by post-blow-down weight and flush fluid density. Actual amount depends upon exact blow-down conditions, media type in capsule, the number of capsules in the system, the process fluid, and loading level of the capsule.

Table 12. Capsule Design Characteristics – 3M™ Zeta Plus™ BC Series Filter Capsules (Laboratory Capsules)		
Product Name	**BC25, Luer**	**BC25, Sanitary**
Nominal Surface Area	25 cm²	25 cm²
Inlet/Outlet	Luer	½" - ¾" Sanitary Style
Nominal Dimensions		
Single Layer (height by diameter)	6.5 cm x 7.6 cm (2.6 inches x 3 inches)	7.9 cm x 7.6 cm (3.1 inches x 3 inches)
Dual Layer (height by diameter)	6.9 cm x 7.6 cm (2.7 inches x 3 inches)	8.3 cm x 7.6 cm (3.3 inches x 3 inches)
Weight		
Dry – Single Layer	≈ 60 g	≈ 64 g
Dry – Dual Layer	≈ 69 g	≈ 75 g
Wet, post blow-down[1] – Single Layer	≈ 70 g	≈ 75 g
Wet, post blow-down[1] – Dual Layer	≈ 86 g	≈ 93 g
Volume		
Capsule Fill Volume[2] – Single Layer	≈ 17 mL	
Capsule Fill Volume[2] – Dual Layer	≈ 25 mL	
Post blow-down Hold-Up Volume[3] – Single Layer	≈ 11 mL	
Post blow-down Hold-Up Volume[3] – Dual Layer	≈ 17 mL	

1 Post blow-down wet weight is defined as the experimentally measured weight of the capsule after air/gas blow-down using water as the flush fluid. Actual amount depends upon exact blow-down conditions, media type in capsule, the number of capsules in the system, the process fluid, and loading level of the capsule.

2 Capsule Fill Volume is defined as the volume of liquid required to fill the capsule (experimentally measured).

3 Post blow-down hold-up volume is defined as the estimated volume of the residual flush liquid after air/gas blow-down using water as the flush fluid and calculated by post-blow-down weight and flush fluid density. Actual amount depends upon exact blow-down conditions, media type in capsule, the number of capsules in the system, the process fluid, and loading level of the capsule.

Table 13. Capsule Design Characteristics – 3M™ Zeta Plus™ Encapsulated System Scale Up Filter Capsules			
Product Name	**E170**	**E340**	**E1020**
Nominal Surface Area	170 cm²	340 cm²	1020 cm²
Inlet/Outlet	½" Sanitary Style		
Nominal Dimensions			
Height by Diameter	10.3 cm x 21.6 cm (4.1 inches x 8.5 inches)		15.2 cm x 21.6 cm (6.0 inches x 8.5 inches)
Weight			
Dry – Single Layer	1.0 kg (2.2 lb)	1.0 kg (2.2 lb)	1.4 kg (3.0 lb)
Dry – Dual Layer	1.0 kg (2.2 lb)	1.0 kg (2.3 lb)	1.6 kg (3.5 lb)
Wet, post blow-down[1] – Single Layer	1.1 kg (2.4 lb)	1.1 kg (2.5 lb)	1.8 kg (4.0 lb)
Wet, post blow-down[1] – Dual Layer	1.2 kg (2.6 lb)	1.3 kg (2.9 lb)	2.4 kg (5.2 lb)
Volume			
Capsule Fill Volume[2] – Single Layer	≈ 0.67 L (≈ 1.5 gal)	≈ 0.69 L (≈ 1.5 gal)	≈ 1.7 L (≈ 3.7 gal)
Capsule Fill Volume[2] – Dual Layer	≈ 0.63 L (≈ 1.4 gal)	≈ 0.65 L (≈ 1.4 gal)	≈ 1.6 L (≈ 3.5 gal)
Post blow-down Hold-Up Volume[3] – Single Layer	≈ 0.12 L (≈ 0.26 gal)	≈ 0.16 L (≈ 0.35 gal)	≈ 0.46 L (≈ 1.0 gal)
Post blow-down Hold-Up Volume[3] – Dual Layer	≈ 0.15 L (≈ 0.34 gal)	≈ 0.26 L (≈ 0.58 gal)	≈ 0.80 L (≈ 1.8 gal)

1 Post blow-down wet weight is defined as the experimentally measured weight of the capsule after air/gas blow-down using water as the flush fluid. Actual amount depends upon exact blow-down conditions, media type in capsule, the number of capsules in the system, the process fluid, and loading level of the capsule.

2 Capsule Fill Volume is defined as the volume of liquid required to fill the capsule (experimentally measured).

3 Post blow-down hold-up volume is defined as the estimated volume of the residual flush liquid after air/gas blow-down using water as the flush fluid, and calculated by post-blow-down weight and flush fluid density. Actual amount depends upon exact blow-down conditions, media type in capsule, the number of capsules in the system, the process fluid, and loading level of the capsule.

Table 14. Capsule Design Characteristics – 3M™ Zeta Plus™ Encapsulated System 0.23 m² Filter Capsules (Production Capsules, Single Cell)				
	Single Layer Media		**Dual Layer (EXT) Media**	
Product Name	**Standard Production Capsule E16E01**	**Alkaline Resistant[1] Production Capsule E16R01**	**Standard Production Capsule E16E01**	**Alkaline Resistant[1] Production Capsule E16R01**
Nominal Surface Area	0.23 m²			
Nominal Dimensions				
Height by Diameter	5.7 cm x 45.2 cm (2.2 inches x 17.8 inches)			
Weight				
Dry	3.0 kg (6.6 lbs)	3.1 kg (6.8 lbs)	3.3 kg (7.3 lbs)	3.4 kg (7.5 lbs)
Wet (post Blow-Down)[2]	3.8 kg (8.3 lbs)	3.9 kg (8.5 lbs)	4.6 kg (10 lbs)	4.8 kg (11 lbs)
Volume				
Capsule Fill Volume[3]	≈ 3.8 L (≈ 1.0 gal)		≈ 3.4 L (≈ 0.89 gal)	
Capsule Post Blow-Down Hold-up Volume[4]	≈ 0.7 L (≈ 0.20 gal)		≈ 1.3 L (≈ 0.35 gal)	

1 Alkaline resistance is based on testing with 1M NaOH and 5% NaClO (Bleach).
2 Post blow-down wet weight is defined as the experimentally measured weight of the capsule after air/gas blow-down using water as the flush fluid. Actual amount depends upon exact blow-down conditions, media type in capsule, the number of capsules in the system, the process fluid, and loading level of the capsule.
3 Capsule Fill Volume is defined as the volume of liquid required to fill the capsule (experimentally measured).
4 Post blow-down hold-up volume is defined as the estimated volume of the residual flush liquid after air/gas blow-down using water as the flush fluid, and calculated by post-blow-down weight and flush fluid density. Actual amount depends upon exact blow-down conditions, media type in capsule, the number of capsules in the system, the process fluid, and loading level of the capsule.

Table 15. Capsule Design Characteristics – 3M™ Zeta Plus™ Encapsulated System 2.5 m² & 1.6 m² Filter Capsules (Production Capsules, Multi-Cell)				
	Single Layer Media		**Dual Layer (EXT) Media**	
Product Name	**Standard Production Capsule E16E11**	**Alkaline Resistant[1] Production Capsule E16R11**	**Standard Production Capsule E16E07**	**Alkaline Resistant[1] Production Capsule E16R07**
Nominal Surface Area	2.5 m²		1.6 m²	
Nominal Dimensions				
Height by Diameter	20.3 cm x 45.2 cm (8.0 inches x 17.8 inches)			
Weight				
Dry	10.2 kg (23 lbs)	10.4 kg (23 lbs)	10.5 kg (23 lbs)	10.7 kg (24 lbs)
Wet (post Blow-Down)[2]	17.6 kg (39 lbs)	18 kg (40 lbs)	19.3 kg (43 lbs)	19.7 kg (43 lbs)
Volume				
Capsule Fill Volume[3]	≈ 18.1 L (≈ 4.8 gal)		≈ 18.8 L (≈ 5.0 gal)	
Capsule Post Blow-Down Hold-up Volume[4]	≈ 7.5 L (≈ 2.0 gal)		≈ 9.0 L (≈ 2.4 gal)	

1 Alkaline resistance is based on testing with 1M NaOH and 5% NaClO (Bleach).
2 Post blow-down wet weight is defined as the experimentally measured weight of the capsule after air/gas blow-down using water as the flush fluid. Actual amount depends upon exact blow-down conditions, media type in capsule, the number of capsules in the system, the process fluid, and loading level of the capsule.
3 Capsule Fill Volume is defined as the volume of liquid required to fill the capsule (experimentally measured).
4 Post blow-down hold-up volume is defined as the estimated volume of the residual flush liquid after air/gas blow-down using water as the flush fluid, and calculated by post-blow-down weight and flush fluid density. Actual amount depends upon exact blow-down conditions, media type in capsule, the number of capsules in the system, the process fluid, and loading level of the capsule.

Weights and Volumes shown in Table 16 below for standard and alkaline resistant manifolds were experimentally determined. **Please note that these values are presented for guidance only and are not specifications**.

Table 16. 3M™ Manifold Design Characteristics		
Component	**Standard Manifold, Top or Bottom**	**Alkaline Resistant[1] Manifold, Top or Bottom**
Nominal Dimensions, Height by Diameter	5.2 cm x 45.2 cm (2.0 inches x 17.8 inches)	
Connector	1½" Sanitary Style	
Dry Weight	4.4 kg per set (10 lbs per set)	4.7 kg per set (10 lbs per set)
Hold-up Volume[2]	<250 mL per set	

1 Alkaline resistance is based on testing with 1M NaOH and 5% NaClO (Bleach).

2 Post blow-down hold-up volume is defined as the estimated volume of the residual flush liquid after air/gas blow-down using water as the flush fluid, and calculated by post-blow-down weight and flush fluid density.

F. Wetted Surface Areas

The wetted surface areas of components in 3M™ Zeta Plus™ Filter Cartridges, 3M™ Zeta Plus™ BC Series Filter Capsules, 3M™ Zeta Plus™ Encapsulated System Scale-Up Filter Capsules, and 3M™ Zeta Plus™ Encapsulated System Filter Capsules are listed in Tables 17-20, respectively. For O-rings, it is estimated that 50% of the surface area is wetted. Nominal media surface areas for capsules and cartridges are listed in Table 23.

Wetted surface area calculations are based on 3D models where all geometries are represented by a finely spaced discrete set of points; curves are approximated by linear interpolation between these points. A numerical quadrature algorithm is used to estimate the surface area and volume. The listed wetted surface areas represent the nominal values with tolerances allowed in component dimensions.

Table 17. Wetted Surface Areas of 3M™ Zeta Plus™ Filter Cartridge Components			
Components	**Wetted Surface Area [cm²]**		
	8-inch Cartridge	**12-inch Cartridge**	**16-inch Cartridge**
Separator (per lenticle)	415	1373	4361
Netting[1] (per lenticle)	-	5970	12900
Edge Seal (per lenticle)	174	312	426
Ring Seal (per lenticle)	23	12	22
Gasket Retainer (each)	46	57	57
Molded Lifting Handle[2] on Gasket Retainer	-	181	-
Gasket (each)	28	37	37
Film Handle[3]	-	-	1245
Binder Bands	19	28	28
8" Plug-in Unitizing Post	397	--	--

1 Specific 12-inch and 16-inch cartridges

2 Specific 12-inch cartridges

3 Specific 16-inch cartridges

Table 18. Wetted Surface Areas of 3M™ Zeta Plus™ BC Series Filter Capsule (Laboratory Capsule) Components	
Components	**Wetted Surface Area [cm²]**
	BC0025
Shell (Inlet – Luer)	41
Shell (Inlet – Sanitary)	48
Shell (Outlet - Luer)	54
Shell (Outlet – Sanitary)	58
Ring Seal (dual layer media)	36
Edge Seal	Non-wetted Surface

Table 19. Wetted Surface Areas of 3M™ Zeta Plus™ Encapsulated System Scale Up Filter Capsule Components			
Components	**Wetted Surface Area [cm²]**		
	E0170 Capsule	**E0340 Capsule**	**E1020 Capsule**
Separator (per lenticle)	324		
Spacer	-	-	3.7
Flow Inhibitor Disc	439	-	-
Edge Seal (per lenticle)	250	208	
Inner Seal (per lenticle)	47		
End Cap	14.7		
Shell Top	388		679
Shell Bottom	420		
Back-up O-ring	2.5		
O-ring	1.4		

Table 20. Wetted Surface Areas of 3M™ Zeta Plus™ Encapsulated System Filter Capsule (Production Capsule) Components			
Components	**Wetted Surface Area [cm²]**		
	E16E01, E16R01 Capsules	**E16E07, E16R07 Capsules**	**E16E11, E16R11 Capsules**
Number of Cells	1 cell	7 cells	11 cells
Separator Assembly	2,178		
Spacer	825		
Edge Seal (per lenticle)	592	516	592
Inner Seal (per lenticle)	68	79	68
Connectors (Male and Female)	377		
Capsule Shells (2)	3,554	5,477	
O-ring large retainer	28		
O-ring large	14		
O-ring small	4		
Manifold (Total Top and Bottom)	1,047		

V. Product Specifications and Operation Parameters

A. Product Release Specifications

The product specifications verified during filter manufacturing and prior to the release of media lots include but are not limited to the following.

1) Pressure Drop at constant air flow – Determined by testing a 5-inch diameter disc of media sheet when challenged at a specific air flow rate.

2) Wet Tensile Strength - Determined by soaking a media coupon in water for two minutes then measuring the peak force (in kilograms) to break the sample. The result is normalized for the cross-sectional width and length.

3) Calcium Extraction - Determined after completing a pre-conditioning flush with deionized (DI) water, then soaking media in DI water at a ratio of 1 gram of media to 10 mL of water for 24 hours at ambient temperature and analyzing the water for soluble calcium. The result is normalized as mg of calcium per gram of media.

4) Iron Extraction - Determined after completing a pre-conditioning flush with DI water, then soaking media in DI water at a ratio of 1 gram of media to 10 mL of water for 24 hours at ambient temperature and analyzing the water for soluble iron. The result is normalized as mg of iron per gram of media.

5) Color Extraction - Determined by flushing a media sample with 100 mL of 0.4% w/v 180° F sodium citrate solution through a 45 mm disc sample of the media. The pooled effluent is analyzed for percent transmittance at 420 nm.

6) Total Nitrogen (TN) - Determined by autoclaving media in deionized (DI) water at a ratio of 1 gram of media to 12 mL of water for 1 hour at 121 °C. The extract is analyzed for Total Nitrogen content.

7) Endotoxin Extraction - *Limulus* Amebocyte Lysate (LAL) bacterial endotoxin reactivity - Determined by filtering sterile water through a 45 mm disc of media at a flow rate of 18-20 mL/min then collecting a 2 mL effluent sample after 49 mL. The effluent sample is tested for endotoxins using a Kinetic Turbidimetric LAL Assay.

The above specification limits for each grade of 3M™ Zeta Plus™ SP Series Filter Media are presented in Table 21. The dual layer (EXT) media specifications represent the specifications of the tighter media layer. The tighter media layer has the smaller nominal pore size of the two layers; the larger the grade number, the tighter or smaller the nominal media pore size. In the Dual Layer (EXT) Media section of Table 21, the dual layer configuration is shown in parentheses beneath the media grade; the upstream layer is shown first, followed by the downstream layer. Each layer is released according to the single layer media specification, and then assembled into dual layer products.

Table 21. Product Release Properties for 3M™ Zeta Plus™ SP Series Filter Media

Product Release Properties	Single Layer Media Specifications[1]							
	01SP	**05SP**	**10SP**	**30SP**	**50SP**	**60SP**	**90SP**	**Units**
Pressure Drop at Air Flow	≤ 2.8	2.7 – 5.0	8.5 – 13.0	16.0 – 26.0	50.0 – 68.0	81.0 – 107.0	148.0 - 202.0	Inch H_2O
Wet Tensile Strength	≥ 1.5	≥ 3.0	≥ 3.0	≥ 4.0	≥ 5.0	≥ 5.5	≥ 6.5	Kg/in
Ca Extraction	≤ 0.040 (PL ≤ 0.080)	≤ 0.040	≤ 0.040	≤ 0.040	≤ 0.040	≤ 0.040	≤ 0.040	mg/g
Fe Extraction	≤ 0.010	≤ 0.010	≤ 0.010	≤ 0.010	≤ 0.010	≤ 0.010	≤ 0.010	mg/g
Color Extraction	≤ 8.0	≤ 8.0	≤ 8.0	≤ 8.0	≤ 8.0	≤ 8.0	≤ 8.0	Color Units
Total Nitrogen	≤ 60	≤ 60	≤ 60	≤ 60	≤ 60	≤ 60	≤ 60	ppm
Endotoxin Extraction	< 0.25	< 0.25	< 0.25	< 0.25	< 0.25	< 0.25	< 0.25	EU/mL

Product Release Properties	Dual Layer (EXT) Media[1] (Specification of Tighter Media Layer)						
	05SP01 (01SP/05SP)	**10SP01** (01SP/10SP)	**10SP02** (05SP/10SP)	**30SP02, 30SP03** (05SP/30SP, 10SP/30SP)	**60SP02, 60SP03, 60SP05** (05SP/60SP, 10SP/60SP, 30SP/60SP)	**90SP05, 90SP08** (30SP/90SP, 60SP/90SP)	**Units**
Pressure Drop at Air Flow	2.7 – 5.0	8.5 – 13.0	8.5 – 13.0	16.0 – 26.0	81.0 – 107.0	148.0 - 202.0	Inch H_2O
Wet Tensile Strength	≥ 3.0	≥ 3.0	≥ 3.0	≥ 4.0	≥ 5.5	≥ 6.5	Kg/in
Ca Extraction	≤ 0.040	≤ 0.040	≤ 0.040	≤ 0.040	≤ 0.040	≤ 0.040	mg/g
Fe Extraction	≤ 0.010	≤ 0.010	≤ 0.010	≤ 0.010	≤ 0.010	≤ 0.010	mg/g
Color Extraction	≤ 8.0	≤ 8.0	≤ 8.0	≤ 8.0	≤ 8.0	≤ 8.0	Color Units
Total Nitrogen	≤ 60	≤ 60	≤ 60	≤ 60	≤ 60	≤ 60	ppm
Endotoxin Extraction	< 0.25	< 0.25	< 0.25	< 0.25	< 0.25	< 0.25	EU/mL

1 Manufacturing facilities have the same specification except as noted in parentheses. (US: USA; PL: Poland)

B. Installation and Operation Instructions

The installation and operation of the 3M™ Zeta Plus™ Filters with SP Series Media should follow the appropriate use instruction for each filter configuration. Always operate within the specified pressure and temperature limits.

Note: Installation and Operation Instructions are available upon request from your local representative.

Prior to filtration operation, end-user should verify that the housing for filter cartridges is integral and filter cartridges or capsules have been properly installed and sealed. Therefore, a pre-use Installation Qualification test (IQ) should be performed per recommended test procedure contained in 3M's Installation and Operating Procedures manuals (70-0201-8802-8 for cartridges, 70-0202-6945-5 for capsules).

C. Minimum Required Preconditioning Flush

3M™ Zeta Plus™ Filters with SP Series Media are comprised primarily of natural products and are considered fiber-releasing filters. Trace amounts of polymer resin, cellulosic fibers and natural extractables such as endotoxin, beta

glucan, and inorganic ions, are released by these filters during use. Therefore, customers must flush the filters before exposure to their product. 3M™ Zeta Plus™ Filters with SP Series Media can be flushed with water or buffer at temperature and pressure not to exceed the maximum product specification. The required minimum preconditioning flush volume for all products is 54 L/m². Pressure drop across the filter should not exceed 2.4 bar [35 psid]. The maximum recommended preconditioning flush flux for the required preconditioning flush is 1200 L/m²/hour (LMH) for cartridges. The maximum recommended preconditioning flush flux for the required preconditioning flush is 210 LMH for capsules.

If the filter is autoclaved or steam sterilized *in-situ* prior to use, the product must be flushed after sterilization using the required preconditioning flush.

Detailed preconditioning flush protocols are provided in 3M Installation and Operating Instructions (see Section V.B.). Based on the required minimum preconditioning flush of 54 L/m² and the nominal surface area for each filter, flush volumes for each filter configuration are provided in Table 23.

The data package of effluent quality presented in this Regulatory Support File is developed based on the maximum recommended flux of the required preconditioning flush for cartridges.

Table 22. Minimum Required Preconditioning Flush Volume and Maximum Recommended Flux

Minimum Required Preconditioning Flush Volume	All Products	54 L/m²
Maximum Recommended Flux of Required Preconditioning Flush	Cartridges	1200 LMH
	Capsules	210 LMH

Table 23. Minimum Required Preconditioning Flush Volume & Nominal Surface Area		
3M™ Zeta Plus™ Filter Cartridge Configuration	**Nominal Surface Area**	**Minimum Required Preconditioning Flush Volume [L]**
45109 (8-inch diameter cartridge, 8-cell)	0.26 m^2	14
45167 (8-inch diameter cartridge, 7-cell O-ring plug-in)	0.23 m^2	12
Z8FA2NPx2 (8-inch diameter, 2-cell plug-in)	0.065 m^2	3.5
Z8FA4NPx2 (8-inch diameter, 4-cell plug-in)	0.13 m^2	7.0
Z08E05 (8-inch diameter cartridge, 5-cell plug-in)	0.16 m^2	8.6
Z08E07 (8-inch diameter cartridge, 7-cell)	0.23 m^2	12
45244 (12-inch diameter cartridge, 9-cell)	0.85 m^2	46
45237 (12-inch diameter cartridge, 12-cell)	1.1 m^2	59
45230 (12-inch diameter cartridge, 15-cell)	1.4 m^2	76
45245 (12-inch diameter cartridge, 16-cell)	1.5 m^2	81
Z12E11 (12-inch diameter cartridge, 11-cell)	1.0 m^2	54
Z16D (16-inch diameter cartridge, 15-cell)	3.5 m^2	189
Z16P (16-inch diameter cartridge, 14-cell)	3.2 m^2	173
Z16H (16-inch diameter cartridge, 16-cell) 30SP & 50SP only	3.7 m^2	200
Z16H (16-inch diameter cartridge, 17-cell) 60SP & 90SP only	3.9 m^2	211
Z16E01 (16-inch diameter cartridge, 1-cell)	0.23 m^2	12
Z16E02 (16-inch diameter cartridge, 2-cell)	0.46 m^2	25
Z16E08 (16-inch diameter cartridge, 8-cell)	1.8 m^2	97
Z16E12 (16-inch diameter cartridge, 12-cell)	2.7 m^2	146
3M™ Zeta Plus™ BC Series and Encapsulated Series Filter Capsule Configuration	**Nominal Surface Area**	**Minimum Required Preconditioning Flush Volume [L]**
BC0025 Laboratory Capsule	25 cm^2	0.14
E0170 (Scale-Up capsule)	0.017 m^2	0.9
E0340 (Scale-Up capsule)	0.034 m^2	1.8
E1020 (Scale-Up capsule)	0.102 m^2	5.5
E16E01 & E16R01 (Production capsule)	0.23 m^2	12
E16E07 & E16R07 (Production capsule)	1.6 m^2	86
E16E11 & E16R11 (Production capsule)	2.5 m^2	135

D. Operating Conditions

Table 24. Operating Conditions		
Maximum Operating Pressure	Laboratory Capsule	2.8 bar (40 psig) maximum inlet pressure
	Scale-Up Capsule	3.1 bar (45 psig)
	Production Capsule	3.4 bar @40 °C (50 psig @104 °F)
Maximum Differential Pressure Forward	All Products	2.4 bar (35 psig)
Maximum Operating Temperature	Cartridge	82 °C (180 °F)
	Capsules	40 °C (104 °F)
Minimum Required Preconditioning Flush Volume	All Products	See Section V. C.
Maximum Recommended Flux of Required Preconditioning Flush	Cartridges	
	Capsules	
Pre-Use Sterilization	Cartridges	See Section V. E.
	Capsules	

E. Pre-Use Sterilization

3M™ Zeta Plus™ Filters with SP Series Media are not bioburden controlled. They can be autoclaved or *in-situ* steam sterilized per recommended conditions listed in Table 25. The 3M™ Zeta Plus™ Filter Cartridges can be steam

sterilized per 3M procedure 70-0201-8840-8. Studies were conducted to ensure sterility after autoclave or *in situ* steam sterilization. If the filter is autoclaved or steam sterilized *in-situ* prior to use, it must be flushed after sterilization using the required preconditioning flush.

Table 25. Pre-Use Sterilization Conditions	
Product Class	**Autoclave / Steam-in-Place Parameters[1]**
Cartridges	*in situ* steam sterilization, 30 minutes @ 126 °C (259 °F) maximum (3 cycles Max)
Laboratory Capsules	Autoclave only, 30 minutes @ 121 °C (250 °F) maximum (1 cycle)
Scale-Up Capsules	Autoclave only, Pre-vac cycle, 30 minutes @ 126 °C (259 °F) maximum (1 cycle)
Production Capsules	Autoclave only, Pre-vac cycle, 30 minutes @ 126 °C (259 °F) maximum (1 cycle)

1 Do not exceed maximum pressure and temperature ratings during sterilization.

F. Post-Use Sanitization

3M™ Zeta Plus™ Filters with SP Series Media may be sanitized by the procedure in Table 26 prior to disposal, if necessary, to comply with local regulations or customer requirements.

Note that the Standard Production Capsules (E16E01, E16E07, E16E11) have a polycarbonate shell and CANNOT be exposed to NaOH or NaClO (Bleach).

Table 26. Post-Use Sanitization Conditions[1]		
Product Class	**Caustic Sanitization**	**Autoclave / Steam-in-Place Parameters**
Cartridges	Can be treated with 1M NaOH or 5% NaClO post-use.	Same as Pre-Use Sterilization Conditions (See Table 25)
Laboratory Capsules	Capsule soak for 1 hour with 1M NaOH or 5% NaClO (bleach)[2] post-use.	
Scale-Up Capsules		
Production Capsules	Alkaline-Resistant[3] Production Capsules can be treated with 1M NaOH or 5% NaClO (bleach)[2] post-use. **Not applicable to polycarbonate Standard Production Capsules.**	

1. Do not exceed maximum pressure and temperature ratings during sanitization.
2. Do not use NaClO (bleach) for pre-use sanitization.
3. Alkaline resistance is based on testing with 1M NaOH and 5% NaClO (Bleach).

VI. Performance Verification

A. Media Pressure Drop vs. Water Flow Rate

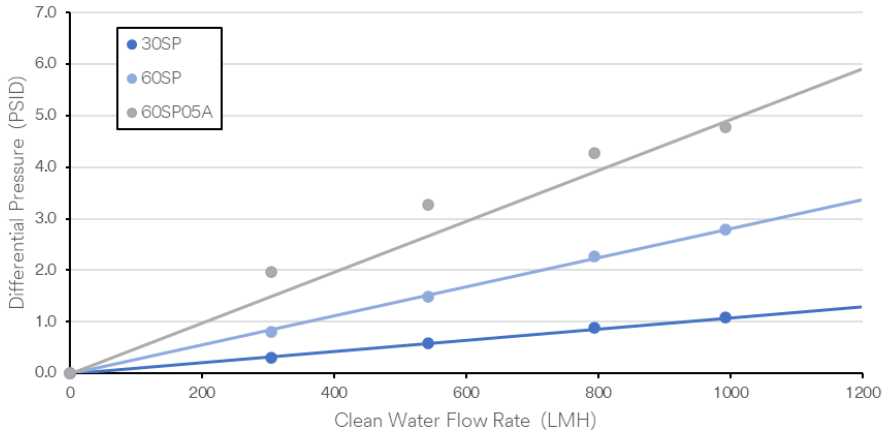
The 90-mm discs of 3M™ Zeta Plus™ 30SP, 60SP and 60SP05A Grade Filter Media produced at different global plants were tested for pressure drop as a function of water flow rate in liters/m²/hour (LMH) with 18 Megohm water (25°C), as shown in Table 27 and Figure 5.

3M™ Zeta Plus™ SP Series Filter Media has variations within each manufacturing lot and from lot-to-lot. The chart is based on test data for representative manufacturing lots from each global facility and should be considered typical values.

The water flow rate differentiation by grade of 3M™ Zeta Plus™ SP Series Filter Media indicated here is for guidance only. Factors that influence actual customer flow rates include fluid viscosity, density, flow restriction due to fluid path, and normal fouling of media by contaminant load.

Table 27. Pressure Drop vs. Water Flow Rate of 3M™ Zeta Plus™ 30SP, 60SP and 60SP05A Grade Filter Media at 25°C									
	Single Layer Media						Dual Layer (EXT) Media		
	30SP			60SP			60SP05A		
	Number of Manufacturing Lots: 5			Number of Manufacturing Lots: 6			Number of Manufacturing Lots: 6		
Flow Rate	Differential Pressure (PSID)								
LMH	Average	Max	Min	Average	Max	Min	Average	Max	Min
0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
304	0.3	0.2	0.5	0.8	0.7	0.9	2.0	1.2	2.6
542	0.6	0.5	0.8	1.5	1.3	1.7	3.3	2.1	4.4
794	0.9	0.6	1.3	2.3	2.1	2.6	4.3	2.8	5.5
992	1.1	0.7	1.6	2.8	2.5	3.2	4.8	3.3	5.7
1204	1.3	0.7	1.9	3.4	3.1	3.8	5.4	3.8	6.9

Figure 5. Average Pressure Drop vs. Clean Water Flow Rate of 3M™ Zeta Plus™ 30SP, 60SP and 60SP05A Media at 25°C



VII. Effluent Quality

Various regulatory organizations require that equipment used in pharmaceutical manufacturing that is in direct contact with the drug product should not add to or change the drug in any way other than what is intended by the manufacturer.

Distribution of Responsibility

3M Separation and Purification Sciences Division has adopted the following supplier collaborative model (D. Jenke, Pharma Ed Conference on Extractables & Leachables, keynote address Oct 2011) relative to Extractable and Leachable evaluation.

In this Regulatory Support File, 3M provides effluent quality data relating to the required preconditioning flush based on the requirements listed in Table 28. The data provided is on a limited number of lots with product close to its date of manufacture. Except where noted, data should be considered as representative of typical product performance, but not a product specification. 3M has also performed Extractable/Leachable studies consistent with guidance from the USP chapter <665> (draft) and the BioPhorum Operating Group (BPOG) extractable protocol. The extractable/leachable data package is available as an addendum to this RSF upon request.

Table 28. Reference Industry Standards	
USP Standards	**Applicable Methods**
<643>	Total Organic Carbon
<645>	Conductivity
<791>	pH
<232>, <233>, ICH* Q3D	Elemental Impurities
<788>	Particulate Matter in Injections
<85>	Bacterial Endotoxin
<88>	Biological Reactivity

* ICH – International Conference for Harmonisation, Guideline for Elemental Impurities, Q3D

A. USP <643> Total Organic Carbon (TOC) and Total Nitrogen (TN)

The 90-mm discs of 3M™ Zeta Plus™ 30SP, 60SP and 60SP05A Grade Filter Media produced at different global plants were challenged with 18 Megohm water (25°C) at a constant flux of 1200 LMH to a total volume of two times the minimum required preconditioning flush volume of 54 L/m². Effluent samples were collected at 10%, 20%, 30%, 40%, and so on at 10% increments to 200% of the preconditioning flush volume. The effluent samples were then analyzed for TOC and TN. The TOC data at selected preconditioning flush volume percentages is shown in Table 29 and Figure 6. The TN data at selected preconditioning flush volume percentages is shown in Table 30 and Figure 7.

Table 29. Effluent TOC [ppm] vs. Preconditioning Flush Volume % - 3M™ Zeta Plus™ 30SP, 60SP and 60SP05A Media - No Treatment

	Single Layer Media						Dual Layer (EXT) Media		
	30SP			60SP			60SP05A		
Flush Vol %	Number of Manufacturing Lots: 6			Number of Manufacturing Lots: 9			Number of Manufacturing Lots: 6		
[%]	Average	Max	Min	Average	Max	Min	Average	Max	Min
10%	152.2	201.6	115.5	236.7	443.3	83.0	352.0	548.7	190.2
20%	25.0	37.6	13.7	28.3	41.3	10.2	67.9	93.8	29.3
30%	13.7	22.5	8.5	15.1	21.9	5.6	27.6	34.4	19.1
40%	10.0	15.3	6.5	10.7	15.8	4.3	17.2	18.0	16.9
50%	8.3	11.8	5.4	8.4	12.6	4.0	12.5	15.9	10.2
60%	7.1	10.0	4.6	6.8	9.8	3.7	10.3	13.9	7.8
100%	**4.5**	**7.0**	**3.2**	**3.3**	**4.6**	**2.4**	**5.9**	**7.0**	**4.7**
150%	3.9	6.3	1.9	2.8	5.1	1.4	4.7	6.2	3.8
200%	2.4	3.3	1.6	1.8	2.9	0.9	2.9	3.2	2.5

Figure 6. Average TOC vs. Flush Volume % of 3M™ Zeta Plus™ Media 30SP, 60SP and 60SP05 - No Treatment

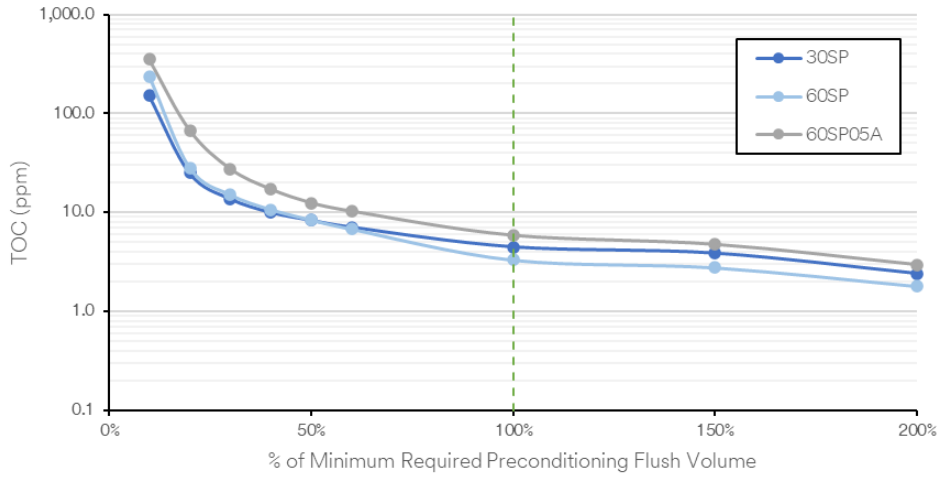
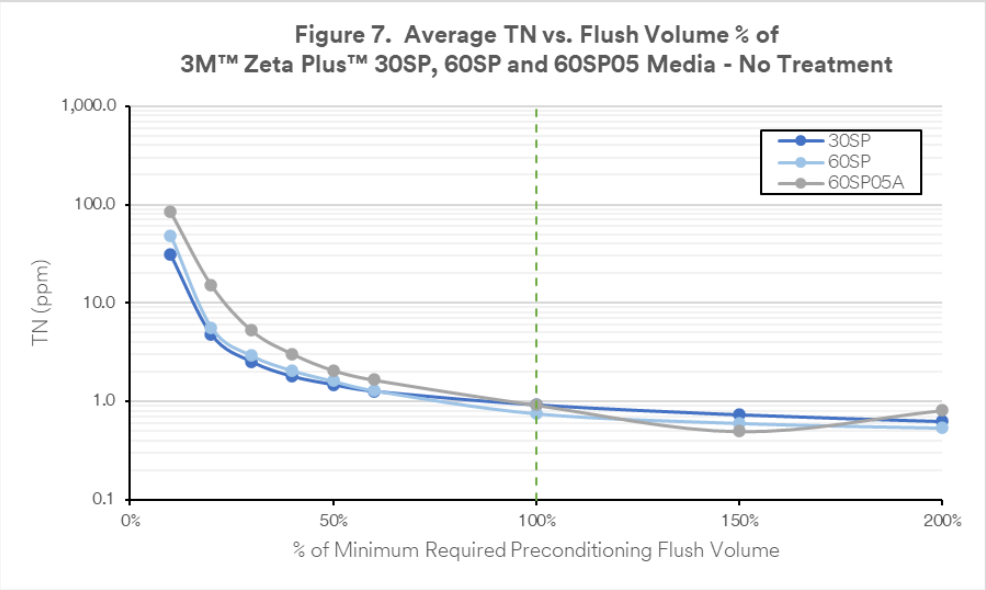


Table 30. Effluent TN [ppm] vs. Preconditioning Flush Volume % of 3M™ Zeta Plus™ 30SP, 60SP and 60SP05A Grade Filter Media – No Treatment

	Single Layer Media						Dual Layer (EXT) Media		
	30SP			60SP			60SP05A		
Flush Vol %	Number of Manufacturing Lots: 7			Number of Manufacturing Lots: 9			Number of Manufacturing Lots: 5		
[%]	Average	Max	Min	Average	Max	Min	Average	Max	Min
10%	30.9	39.7	23.8	48.6	73.7	19.7	84.6	109.8	42.7
20%	4.8	7.4	3.0	5.7	9.1	2.1	15.3	20.8	6.2
30%	2.5	4.1	1.9	2.9	4.5	1.0	5.3	6.7	3.8
40%	1.8	2.9	1.2	2.1	2.9	0.7	3.1	3.6	2.5
50%	1.5	2.3	0.9	1.6	2.1	0.7	2.1	3.2	1.6
60%	1.3	2.0	0.7	1.3	1.8	0.5	1.7	2.8	1.2
100%	**0.9**	**1.5**	**0.4**	**0.8**	**1.0**	**0.4**	**0.9**	**1.2**	**0.7**
150%	0.7	1.0	0.3	0.6	0.8	0.3	0.5	0.6	0.4
200%	0.6	0.8	0.3	0.5	0.7	0.3	0.8	3.1	0.3



Additional 90-mm discs of 3M™ Zeta Plus™ 60SP Grade Filter Media were autoclaved using a pre-vac cycle at 126°C for 60 minutes prior to the preconditioning flush. The same preconditioning flush sampling and test procedures which were used for the non-autoclaved samples were followed for the autoclaved samples. The TOC data for autoclaved samples is shown in Table 31 and Figure 8. The TN data for autoclaved samples is shown in Table 32 and Figure 9.

Table 31. Effluent TOC [ppm] vs. Preconditioning Flush Volume % of 3M™ Zeta Plus™ 60SP Grade Filter Media – Post Autoclave

	Single Layer Media		
	60SP		
Flush Volume	Number of Manufacturing Lots: 4		
[%]	Average	Max	Min
10%	341.4	504.5	252.9
20%	43.3	48.5	36.9
30%	19.5	25.4	14.8
40%	13.9	20.0	9.4
50%	10.9	15.7	7.5
60%	9.3	13.1	6.6
100%	**4.8**	**5.6**	**3.7**
150%	4.1	5.8	2.4
200%	2.6	3.1	1.9

Figure 8. Average TOC vs. Flush Volume % of 3M™ Zeta Plus™ 60SP Media- Post Autoclave

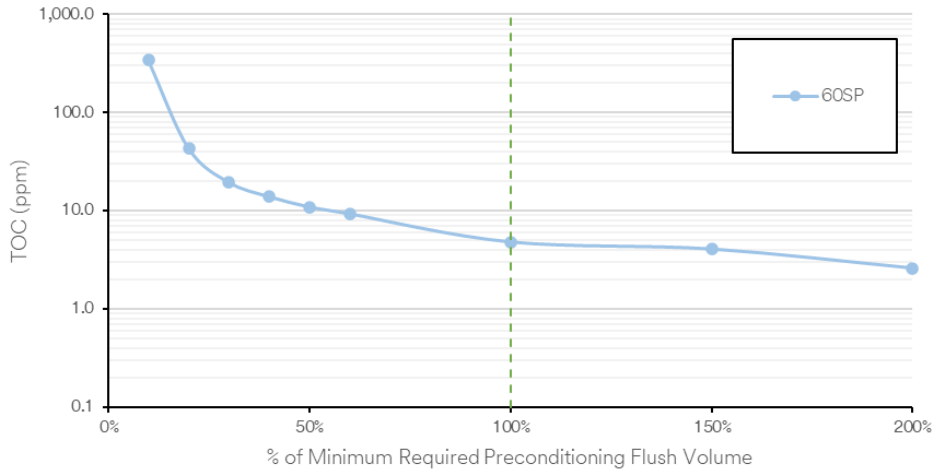
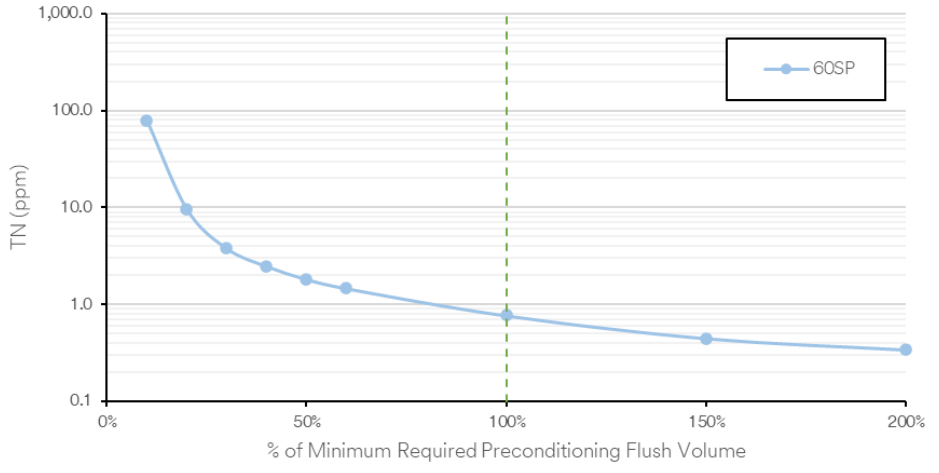


Table 32. Effluent TN [ppm] vs. Preconditioning Flush Volume % of 3M™ Zeta Plus™ 60SP Grade Filter Media – Post Autoclave

	Single Layer Media		
	60SP		
Flush Volume	Number of Manufacturing Lots: 4		
[%]	Average	Max	Min
10%	78.6	106.8	66.4
20%	9.6	10.5	8.1
30%	3.8	4.9	2.9
40%	2.5	3.6	1.7
50%	1.8	2.7	1.2
60%	1.5	2.1	1.1
100%	**0.8**	**1.1**	**0.5**
150%	0.4	0.7	0.3
200%	0.3	0.5	0.2

Figure 9. Average TN vs. Flush Volume % of 3M™ Zeta Plus™ 60SP Media - Post Autoclave



B. USP <645> Conductivity

The 90-mm discs of 3M™ Zeta Plus™ 30SP, 60SP and 60SP05A Grade Filter Media produced at different global plants were challenged with 18 Megohm water (25°C) at a constant flux of 1200 LMH to a total volume of two times the minimum required preconditioning flush volume of 54 L/m². Effluent samples were collected at 10%, 20%, 30%, 40%, and so on at 10% increments to 200% of the minimum required preconditioning flush volume. The effluent samples were then measured for conductivity. The conductivity at selected preconditioning flush volume percentages are shown in Table 33 and Figure 10.

Additional 90-mm discs of 3M™ Zeta Plus™ 30SP, 60SP and 60SP05A Grade Filter Media were autoclaved using a pre-vac cycle at 121°C for 60 minutes prior to the preconditioning flush. The same preconditioning flush sampling and test procedures which were used for the non-autoclaved samples were followed for the autoclaved samples. The conductivity at selected preconditioning flush volume percentages are shown in Table 34 and Figure 11.

Table 33. Effluent Conductivity [µS/cm] vs. Preconditioning Flush Volume % of 3M™ Zeta Plus™ 30SP, 60SP and 60SP05A Grade Filter Media – No Treatment

	Single Layer Media						Dual Layer (EXT) Media		
	30SP			60SP			60SP05A		
Flush Vol %	Number of Manufacturing Lots: 7			Number of Manufacturing Lots: 9			Number of Manufacturing Lots: 6		
[%]	Average	Max	Min	Average	Max	Min	Average	Max	Min
10%	158.2	183.9	134.4	247.2	363.7	139.8	374.0	515.1	242.2
20%	36.9	60.8	25.2	49.7	79.8	33.5	90.1	135.8	53.5
30%	25.0	43.1	15.7	32.2	45.2	23.0	46.2	63.6	36.0
40%	18.2	30.6	11.3	25.6	39.1	19.5	33.9	41.6	28.9
50%	15.7	26.2	10.1	20.9	28.4	16.4	27.8	31.6	22.9
60%	13.9	24.3	9.4	17.8	24.6	14.0	24.6	29.1	19.7
100%	**9.8**	**17.3**	**6.7**	**10.8**	**16.9**	**7.5**	**15.8**	**25.6**	**11.0**
150%	8.1	12.7	6.1	8.8	17.0	5.4	12.3	21.0	8.2
200%	6.8	10.0	4.4	7.3	14.1	4.5	9.5	14.9	6.3

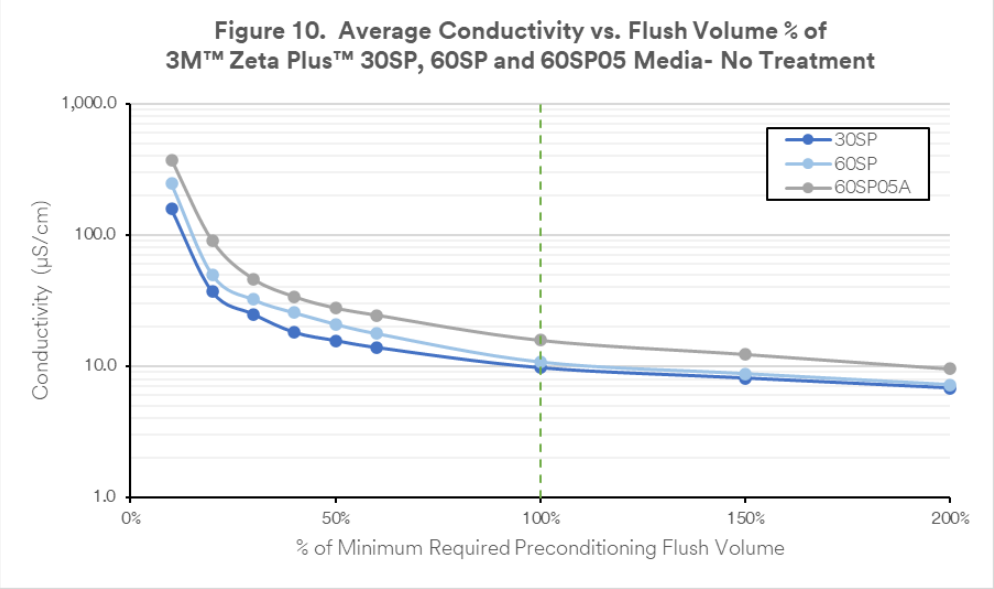
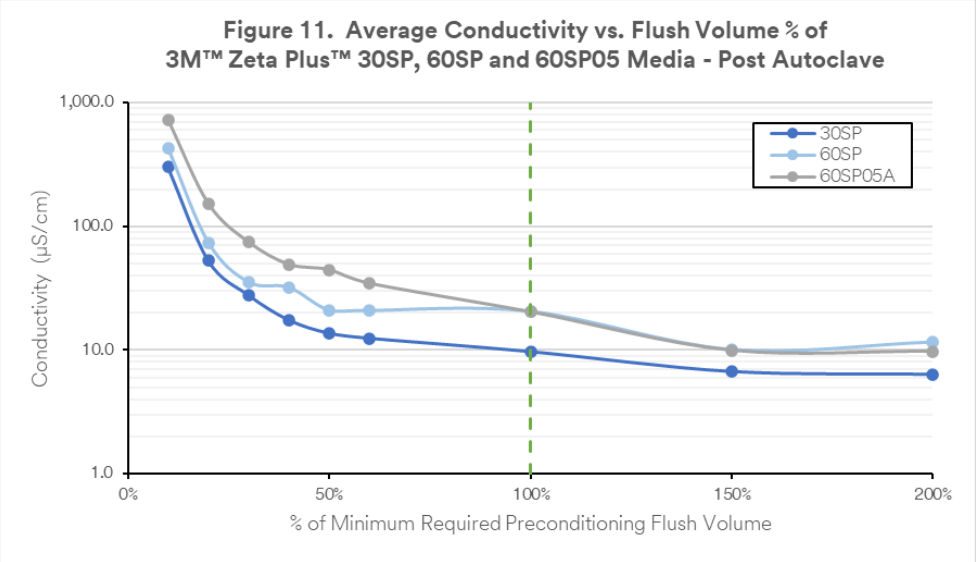


Table 34. Effluent Conductivity [µS/cm] vs. Preconditioning Flush Volume % of 3M™ Zeta Plus™ 30SP, 60SP and 60SP05A Grade Filter Media – Post-Autoclave									
	Single Layer Media						Dual Layer (EXT) Media		
	30SP			60SP			60SP05A		
Flush Vol %	Number of Manufacturing Lots: 6			Number of Manufacturing Lots: 6			Number of Manufacturing Lots: 6		
[%]	Average	Max	Min	Average	Max	Min	Average	Max	Min
10%	300.7	378.2	264.4	430.3	588.8	310.2	726.5	962.0	510.2
20%	52.7	88.9	34.7	73.9	116.3	43.5	152.9	246.9	76.5
30%	27.6	55.7	17.0	35.2	54.5	20.3	74.6	107.1	49.5
40%	17.4	31.0	11.4	31.9	69.3	14.7	49.2	61.6	41.9
50%	13.6	22.1	8.9	20.9	31.4	13.2	44.6	74.8	30.6
60%	12.4	23.6	7.8	20.8	32.6	11.7	34.6	41.4	23.1
100%	**9.7**	**23.2**	**4.9**	**20.5**	**50.5**	**8.1**	**20.4**	**36.9**	**9.3**
150%	6.7	11.8	3.7	10.0	20.6	6.0	10.0	18.6	6.4
200%	6.3	13.5	3.4	11.5	27.7	5.4	9.8	19.3	5.6



C. USP <791> pH

The 90-mm discs of 3M™ Zeta Plus™ 30SP, 60SP and 60SP05A Grade Filter Media produced at different global plants were challenged with 18 Megohm water (25°C) at a constant flux of 1200 LMH to a total volume of two times the minimum required preconditioning flush volume of 54 L/m². Effluent samples were collected at 10%, 20%, 30%, 40%, and so on at 10% increments to 200% of the minimum required preconditioning flush volume. The effluent samples were then measured for pH.

The effluent pH at selected preconditioning flush volume percentages, along with pH of DI water controls, are shown in Table 35 and Figure 12. Note that the DI water used as the flush solution is not buffered. Its low resistance to pH change due to small amount of acid or base is reflected in the extract pH difference shown here.

Additional 90-mm discs of 3M™ Zeta Plus™ 30SP, 60SP and 60SP05A Grade Filter Media were autoclaved using a pre-vac cycle at 121°C for 60 minutes prior to the preconditioning flush. The same preconditioning flush sampling and test procedures which were used for the non-autoclaved samples were followed for the autoclaved samples. The effluent pH for autoclaved samples at selected preconditioning flush volume percentages, along with pH of DI water controls, are shown in Table 36 and Figure 13.

Table 35. Effluent pH vs. Preconditioning Flush Volume % of 3M™ Zeta Plus™ 30SP, 60SP and 60SP05A Grade Filter Media – No Treatment									
	Single Layer Media						Dual Layer (EXT) Media		
	30SP			60SP			60SP05A		
Flush Vol %	Number of Manufacturing Lots: 6			Number of Manufacturing Lots: 9			Number of Manufacturing Lots: 6		
[%]	Average	Max	Min	Average	Max	Min	Average	Max	Min
DI Water Control	5.3	5.6	5.0	5.4	5.6	5.0	5.3	5.6	5.0
10%	5.6	5.9	5.2	5.6	5.9	5.4	5.6	5.7	5.5
20%	5.3	5.7	4.7	5.1	5.6	4.8	5.4	5.6	5.3
30%	5.1	5.6	4.6	4.9	5.1	4.6	5.2	5.5	5.0
40%	5.1	5.7	4.6	4.8	5.0	4.6	5.1	5.4	4.7
50%	5.1	5.5	4.6	4.8	4.9	4.5	5.0	5.4	4.7
60%	5.2	5.7	4.7	4.9	5.0	4.6	5.0	5.3	4.7
100%	**5.4**	**5.6**	**5.1**	**5.0**	**5.2**	**4.7**	**5.1**	**5.3**	**4.8**
150%	5.3	5.4	5.2	5.1	5.2	4.9	5.2	5.4	4.9
200%	5.4	5.6	5.3	5.2	5.3	5.0	5.3	5.5	5.1

Figure 12. Average pH vs. Flush Volume % of 3M™ Zeta Plus™ 30SP, 60SP and 60SP05A Media - No Treatment

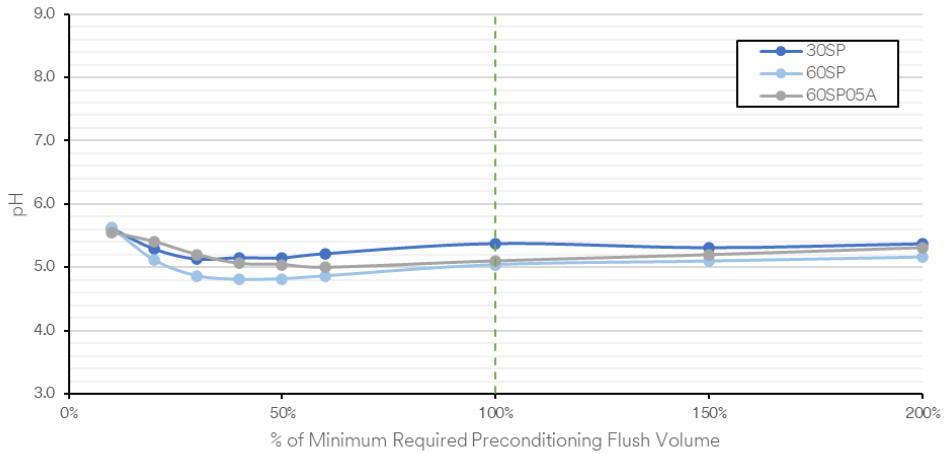
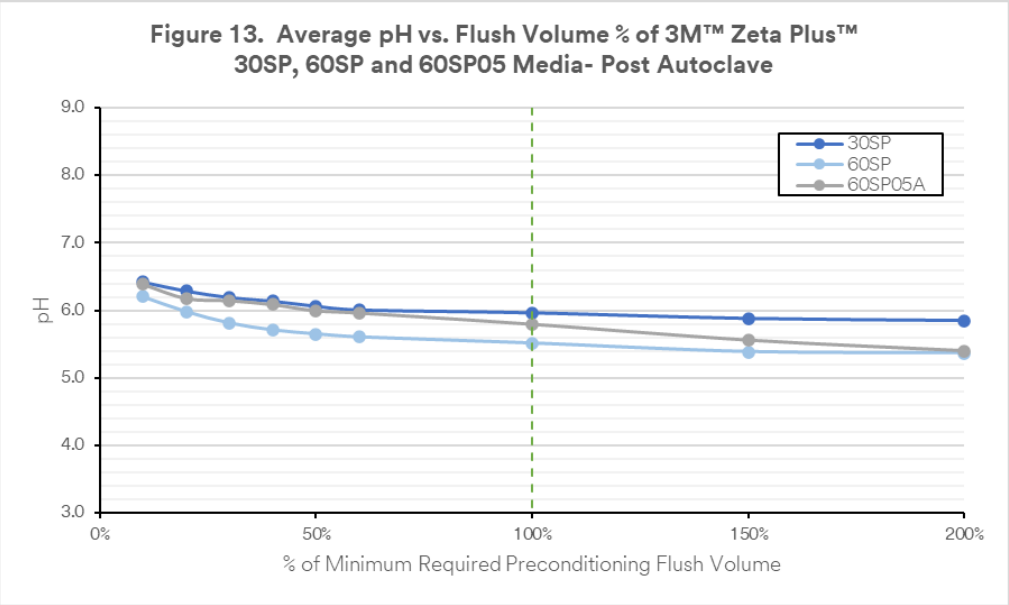


Table 36. Effluent pH vs. Preconditioning Flush Volume % of 3M™ Zeta Plus™ 30SP, 60SP and 60SP05A Grade Filter Media – Post-Autoclave									
	Single Layer Media						Dual Layer (EXT) Media		
	30SP			60SP			60SP05A		
Flush Vol %	Number of Manufacturing Lots: 6			Number of Manufacturing Lots: 6			Number of Manufacturing Lots: 6		
[%]	Average	Max	Min	Average	Max	Min	Average	Max	Min
DI Water Control	5.4	5.5	5.4	5.3	5.4	5.2	5.3	5.5	5.2
10%	6.6	6.7	6.3	6.4	6.5	5.8	6.6	7.2	6.4
20%	6.5	6.7	6.2	6.1	6.3	5.8	6.3	6.7	6.1
30%	6.4	6.6	6.1	5.9	6.1	5.7	6.3	6.5	6.2
40%	6.3	6.5	6.0	5.9	6.1	5.6	6.3	6.4	6.2
50%	6.2	6.4	6.0	5.8	5.9	5.5	6.2	6.3	6.0
60%	6.2	6.4	6.0	5.8	5.8	5.6	6.2	6.4	6.0
100%	**6.1**	**6.3**	**5.9**	**5.7**	**5.7**	**5.5**	**6.0**	**6.2**	**5.7**
150%	6.1	6.2	5.8	5.5	5.5	5.4	5.7	5.8	5.6
200%	6.0	6.2	5.7	5.5	5.5	5.4	5.5	5.5	5.4



D. USP <232>/<233> and ICH Q3D Elemental Impurities

The 90-mm discs of 3M™ Zeta Plus™ 30SP, 60SP and 60SP05A Grade Filter Media produced at different global plants were challenged with 18 Megohm DI water (25°C) at a constant flux of 1200 LMH to a total volume of two times the minimum required preconditioning flush volume of 54 L/m². Effluent samples were collected at 10%, 20%, 30%, 40%, and so on at 10% increments to 200% of the preconditioning flush volume. The 10%, 100% and 200% effluent samples were then analyzed for extractable elements.

Additional 90-mm discs of 3M™ Zeta Plus™ 30SP, 60SP and 60SP05A Grade Filter Media were autoclaved using a pre-vac cycle at 121°C for 60 minutes prior to the preconditioning flush. The same preconditioning flush sampling and test procedures which were used for the non-autoclaved samples were followed for the autoclaved samples.

Elemental profiles for effluent from both autoclaved and non-autoclaved samples are shown in Tables 37 and 38. The designation "<LOQ" indicates that the measured value is below the Limit of Quantification (LOQ). 3M™ Zeta Plus™ SP Series Filter Media contains natural silica; naturally occurring differences are anticipated, and the values below should be taken as representative.

Table 37. Flush Effluent Elemental Impurities for 3M™ Zeta Plus™ 30SP, 60SP and 60SP05A Grade Filter Media (ppb) – No Treatment												
ICH Class	**Element**	**LOD [ppb]**	**30SP**			**60SP**			**60SP05A**			
			Max. of 6 Lots			**Max. of 6 Lots**			**Max. of 6 Lots**			
At % of Flush Volume			10%	**100%**	200%	10%	**100%**	200%	10%	**100%**	200%	
1	**As**	2	3	*	*	5	**1**	*	9	*	*	
	Cd	0.3	*	*	*	1.0	*	*	1.2	*	*	
	Hg	2	*	*	*	*	*	*	*	*	*	
	Pb	0.5	5.6	*	*	0.8	*	*	1.4	**0.6**	*	
2A	**Co**	0.2	0.5	*	*	1.0	*	*	1.4	*	*	
	Ni	0.5	13.0	*	0.9	27.0	**0.6**	*	42.0	**0.8**	*	
	V	0.5	6.4	**1.5**	1.1	162.5	**6.0**	5.4	150.0	**5.7**	5.6	
2B	**Ag**	0.3	*	*	*	*	*	*	*	*	*	
	Au	0.5	*	*	*	*	*	*	*	*	*	
	Ir	0.6	*	*	*	*	*	*	*	*	*	
	Os	0.2	*	*	*	*	*	*	*	*	*	
	Pd	0.6	*	*	*	*	*	*	*	*	*	
	Pt	0.8	*	*	*	*	*	*	*	*	*	
	Rh	0.2	*	*	*	*	*	*	*	*	*	
	Ru	0.5	*	*	*	*	*	*	*	*	*	
	Se	70	*	*	*	*	*	*	*	*	*	
	Tl	1	*	*	*	2	*	*	*	*	*	
3	**Ba**	0.1	56.2	**2.5**	1.2	51.0	**2.7**	2.8	93.0	**3.3**	1.8	
	Cr	0.3	4.3	*	*	5.5	*	*	10.0	**0.5**	0.3	
	Cu	0.5	5.3	*	*	28.0	**1.1**	0.7	32.0	**2.0**	0.6	
	Li	0.3	4.6	**0.3**	*	27.0	**1.0**	0.1	31.0	**0.6**	0.3	
	Mo	0.5	7.1	*	*	31.0	**0.8**	0.8	38.0	**1.4**	1.2	
	Sb	0.2	*	*	*	1.0	*	*	1.2	*	*	
	Sn	0.2	*	*	*	*	*	*	*	*	*	
Other Elements	**Al**	0.5	940.0	**20.7**	10.1	1400.0	**91.7**	19.2	2500.0	**130.9**	29.7	
	B	5	18	**6**	*	60	**1**	*	49	*	*	
	Ca	30	3000	**75**	55	5600	**57**	48	9200	**92**	45	
	Fe	50	1000	*	*	1212	*	*	1800	**70**	*	
	K	50	1397	**112**	400	5442	**1700**	1500	6300	**800**	224	
	Mg	0.2	580.0	**11.0**	10.0	1600.0	**12.9**	5.4	2600.0	**17.8**	7.3	
	Mn	0.3	140.7	**3.2**	1.4	140.0	**1.6**	0.8	300.0	**5.9**	1.8	
	Na	0.6	16144.4	**863.8**	598.5	36000.0	**665.7**	292.0	44000.0	**1701.4**	836.9	
	Si	10	535	**25**	28	808	**52**	33	1036	**81**	48	
	Sr	0.1	13.0	**0.5**	0.2	45.0	**0.6**	0.3	58.0	**0.5**	0.3	
	W	0.2	0.9	*	*	1.7	*	*	2.4	*	*	
	Zn	0.6	27.0	**3.2**	4.3	43.0	**3.4**	3.3	64.0	**3.1**	2.9	
	Zr	2	2	*	*	*	*	*	*	*	*	

*** = Below LOD**

Table 38. Flush Effluent Elemental Impurities for 3M™ Zeta Plus™ 30SP, 60SP and 60SP05A Grade Filter Media (ppb) – Post-Autoclave												
ICH Class	**Element**	**LOD [ppb]**	**30SP**			**60SP**			**60SP05A**			
			Max. of 7 Lots			**Max. of 9 Lots**			**Max. of 6 Lots**			
At % of Flush Volume			10%	**100%**	200%	10%	**100%**	200%	10%	**100%**	200%	
1	**As**	2	6	*	*	5	*	*	11	*	*	
	Cd	0.3	*	*	*	2.5	*	*	2.9	*	*	
	Hg	2	*	*	*	*	*	*	*	*	*	
	Pb	0.5	0.9	*	*	*	*	*	1.5	*	*	
2A	**Co**	0.2	0.6	*	*	2.0	*	*	2.7	*	*	
	Ni	0.5	15.0	**0.7**	*	33.0	**1.0**	*	35.0	**1.1**	0.5	
	V	0.5	3.2	*	*	297.6	**46.4**	24.2	400.0	**47.6**	41.0	
2B	**Ag**	0.3	*	*	*	*	*	*	*	*	*	
	Au	0.5	*	*	*	*	*	*	*	*	*	
	Ir	0.6	*	*	*	*	*	*	*	*	*	
	Os	0.2	*	*	*	*	*	*	*	*	*	
	Pd	0.6	*	*	*	*	*	*	*	*	*	
	Pt	0.8	*	*	*	*	*	*	*	*	*	
	Rh	0.2	*	*	*	*	*	*	*	*	*	
	Ru	0.5	*	*	*	*	*	*	*	*	*	
	Se	70	*	*	*	*	*	*	*	*	*	
	Tl	1	*	*	*	*	*	*	*	*	*	
3	**Ba**	0.1	54.0	**4.2**	1.5	71.0	**24.0**	12.1	90.0	**19.5**	10.4	
	Cr	0.3	18.0	**0.3**	3.2	15.0	**0.4**	*	27.0	**0.6**	*	
	Cu	0.5	4.6	**1.4**	*	35.0	**5.9**	2.0	53.0	**8.3**	3.9	
	Li	0.3	35.3	**0.9**	0.5	150.0	**1.7**	0.8	180.0	**2.1**	0.5	
	Mo	0.5	5.7	*	*	58.0	**5.8**	4.0	67.9	**9.0**	4.8	
	Sb	0.2	0.3	*	*	1.7	**0.2**	*	2.0	**0.2**	*	
	Sn	0.2	0.3	*	*	*	*	*	0.3	*	*	
Other Elements	**Al**	0.5	220.0	**15.0**	5.9	890.0	**42.1**	18.4	980.0	**50.0**	20.8	
	B	5	29	*	*	90	**5**	*	87	**5**	10	
	Ca	30	2100	**130**	61	7541	**228**	101	7400	**290**	110	
	Fe	50	620	*	*	1400	**88**	*	2500	**100**	56	
	K	50	14000	**800**	4100	10679	**9000**	1400	32000	**1800**	700	
	Mg	0.2	1178.7	**35.4**	25.2	6520.6	**183.5**	47.2	6031.6	**155.5**	48.7	
	Mn	0.3	450.0	**11.0**	4.1	470.0	**11.0**	4.8	750.0	**17.0**	4.0	
	Na	0.6	44956.8	**1099.0**	780.5	72066.7	**1638.2**	783.3	100000.0	**3493.3**	940.2	
	Si	10	2425	**58**	40	2554	**85**	50	2620	**140**	40	
	Sr	0.1	9.9	**0.7**	0.5	33.2	**4.0**	1.6	35.4	**3.1**	1.4	
	W	0.2	26.0	**2.0**	1.6	51.0	**3.7**	1.7	76.0	**6.2**	2.3	
	Zn	0.6	6.0	**0.7**	0.7	20.0	**3.1**	5.2	23.6	**2.1**	1.0	
	Zr	2	*	*	*	*	*	*	*	*	*	

*** = Below LOD**

E. USP <788> Particulate Matter in Injections

90-mm discs of 3M™ Zeta Plus™ 30SP, 60SP and 60SP05A Grade Filter Media produced at different global plants were challenged with 18 Megohm water (25°C) at a constant flux of 1200 LMH to a total volume of two times the minimum required preconditioning flush volume of 54 L/m². Effluent samples were collected at 33%, 66%, 100% and 200% of the preconditioning flush volume. After the 200% extract sample was collected, the remaining extract was left to soak in the housing. After one hour, the static soak extract was then pushed through the filter and collected. For dual layer products, media discs were stacked in the housing with the tighter grade media downstream of the more open grade.

Additional 90-mm discs of 3M™ Zeta Plus™ 30SP, 60SP and 60SP05A Grade Filter Media were autoclaved using a pre-vac cycle at 121°C for 60 minutes prior to the preconditioning flush. The same preconditioning flush sampling and test procedures which were used for the non-autoclaved samples were followed for the autoclaved samples.

Samples were analyzed following USP <788> Method 1 (Light Obscuration Particle Count Test) for particulate release. Three to four aliquots of 5 mL each were measured from each sample, with particles counted and measured at the size ranges specified in the USP chapter: particles greater than 10 µm but less than 25 µm; and particles > 25 µm. The solution meets the USP <788> requirement if it contains less than 25 particles/mL >10 µm and less than 3 particles/mL >25 µm.

The results of this analysis including results of control water samples are shown in Tables 39-42.

Table 39. Particulate Matter of 3M™ Zeta Plus™ 30SP and 60SP Grade Filter Media

	Single Layer Media											
	30SP						60SP					
	Number of Manufacturing Lots: 5						Number of Manufacturing Lots: 5					
Particulate Size	18 Megohm Water (25°C)	Flush Volume				Static Soak	18 Megohm Water (25°C)	Flush Volume				Static Soak
		33%	66%	100%	200%			33%	66%	100%	200%	
>10 µm	2.1	418.5	14.0	**13.0**	4.4	44.3	2.1	21.5	29.0	**17.8**	3.6	24.8
>25 µm	0.0	24.7	0.7	**0.6**	0.3	1.4	0.0	1.6	2.9	**2.2**	0.4	2.4

Table 40. Particulate Matter of 3M™ Zeta Plus™ 60SP05A Grade Filter Media

	Dual Layer (EXT) Media					
	60SP05A					
	Number of Manufacturing Lots: 4					
Particulate Size	18 Megohm Water (25°C)	Flush Volume				Static Soak
		33%	66%	100%	200%	
>10 µm	2.1	43.9	55.3	**51.0**	11.6	221.6
>25 µm	0.0	0.8	3.0	**6.9**	1.4	44.3

Table 41. Particulate Matter of 3M™ Zeta Plus™ 30SP and 60SP Grade Filter Media– Post-Autoclave

	Single Layer Media											
	30SP						60SP					
	Number of Manufacturing Lots: 3						Number of Manufacturing Lots: 3					
Particulate Size	18 Megohm Water (25°C)	Flush Volume				Static Soak	18 Megohm Water (25°C)	Flush Volume				Static Soak
		33%	66%	100%	200%			33%	66%	100%	200%	
>10 µm	2.1	53.6	23.2	**57.2**	63.4	566.6	2.1	10.2	39.1	**64.1**	14.4	48.1
>25 µm	0.0	5.6	1.2	**2.1**	2.7	26.0	0.0	2.2	3.8	**9.6**	1.5	9.2

Table 42. Particulate Matter of 3M™ Zeta Plus™ 60SP05A Grade Filter Media – Post Autoclave						
	Dual Layer (EXT) Media					
	60SP05A					
	Number of Manufacturing Lots: 2					
Particulate Size	18 Megohm Water (25°C)	Flush Volume				Static Soak
		33%	66%	**100%**	200%	
>10 µm	0.3	10.3	40.3	**90.3**	19.5	61.8
>25 µm	0.1	3.1	5.1	**14.2**	2.1	13.1

F. USP <85> Bacterial Endotoxin

As part of the product release tests for every media lot at each global plant, a 45-mm disc of 3M™ Zeta Plus™ SP Series Filter Media produced is challenged with Sterile Water For Injection (SWFI) at a constant flux of 1200 LMH to a total volume equivalent to the minimum required preconditioning flush volume of 54 L/m^2. A 2 mL effluent sample collected at the end of flush is analyzed per USP <85> for extractable endotoxin concentration by a *Limulus Amebocyte Lysate* (LAL) reactivity method. The extractable endotoxin release specification for all grades of 3M™ Zeta Plus™ SP Series Filter Media is < 0.25 EU/mL. The specification is based on a flush of single layer media, even for dual layer media products. Therefore, the 3M™ Zeta Plus™ SP Series Filter Media flush effluent as prepared per above conditions meets the bacterial endotoxin limits for WFI of <0.25 EU/mL.

Note the release specification is based on a dynamic flush protocol that does not necessarily reflect the total endotoxin amount in the media. Therefore, the extractable endotoxin amount may be impacted if using a different challenge fluid under different test conditions (*i.e.*, pH, conductivity, protein, *etc.*).

Cellulose is a raw material used in 3M™ Zeta Plus™ Filter Media. Cellulose may contain β-Glucan, which is a non-endotoxin LAL-reactive material. The presence of β-Glucan in any 3M™ Zeta Plus™ Filter Media flush effluent may cause an interference or enhancement of endotoxin measurement. Thus, a β-Glucan blocking buffer or LAL reagent may be used to minimize interference in the product release test. USP <85> "Bacterial Endotoxins Tests" supports these strategies during extractable endotoxin measurement in the presence of β-Glucan.

VIII. Shelf Life

Shelf Life of 3M™ Zeta Plus™ Filter Sheets, Filter Cartridges, BC Series Filter Capsules, Encapsulated System Filter Capsules, and Encapsulated System Scale-Up Filter Capsules with SP Series Media:

3 years at a recommended storage temperature of 5ºC - 30ºC, stored in original package

Shelf Life of 3M™ Manifolds:

3 years at a recommended storage temperature of 5ºC - 30ºC, stored in original package

All 3M™ Zeta Plus™ Filters with SP Series Media and 3M™ Manifolds should be stored in a controlled environment with an average temperature between 5 and 30°C with short term excursions to 50°C, and relative humidity less than 90%. All 3M™ Zeta Plus™ Filters with SP Series Media and 3M™ Manifolds should be inspected before use to determine if any unanticipated damage has occurred during shipping and storage. This includes an inspection of the O-rings to confirm that they have no nicks or cuts, are not cracked or do not exhibit a loss of elasticity that would prevent a normal sealing operation.

IX. Regulatory Compliance

The following Regulatory Compliance items apply to 3M™ Zeta Plus™ Filters with SP Series Media and 3M™ Manifolds.

A. USP <88> Class VI - 70°C$_{minimum}$ Biological Reactivity Tests, *In Vivo*

Representative media grade samples and wetted components or wetted component materials were tested and met the requirements of USP <88> Class VI, Biological Reactivity Tests, *In Vivo* at either 121˚C or 70˚C extraction temperature.

B. BSE/TSE (animal derived materials)

3M understands the continued public interest and the increased regulatory scrutiny concerning the transmission of bovine spongiform encephalopathy (BSE) and other transmissible spongiform encephalopathies (TSE).

In order to address these issues, the following statement is offered: In order to assess the BSE/TSE risk associated with the above products, we have contacted our suppliers of raw materials and performed an evaluation of our production processes to determine if any of the materials used are of animal origin. The result of our survey and inquiries of our raw material suppliers has revealed that the resins used in the molded parts and over-molds may contain tallow derivatives and certain elastomer gaskets could contain a stearic acid that is used as an activator in the vulcanization process. We can state, however, that our suppliers have indicated that these parts which use tallow derivatives and stearic acid are processed at conditions conforming to the requirements of the European Medicines Agency note for guidance EMEA/410/01 rev.3.

X. Quality Assurance

Pharmaceutical and Biological products manufacturers routinely visit 3M manufacturing sites to audit production quality management systems and documentation. The ISO certifications for 3M Separation and Purification Sciences Division global plants are available on request.

Certificates are provided in support of the release of the 3M™ Zeta Plus™ Filters with SP Series Media.

The 3M™ Zeta Plus™ Filters with SP Series Media are defined as non-hazardous articles under REACH and do not require a Safety Data Sheet under Article 31 of Regulation (EC) No. 1907/2006.

The 3M™ Zeta Plus™ Filters with SP Series Media are not regulated under the OSHA Hazard Communication Standard (CFR Title 29 1910.1200). A Safety Data Sheet (SDS) is not required for these products.

Article Information Sheets for 3M™ Zeta Plus™ Filters with SP Series Media are available in the US as courtesy.

Intended Use(s): 3M™ Zeta Plus™ Filters with SP Series Media are single-use filter products intended for use in biopharmaceutical processing applications of aqueous and chemical based pharmaceuticals (drugs) and vaccines in accordance with the product instructions and specifications, and cGMP requirements, where applicable.

Since there are many factors that can affect a product's use, the customer and user remain responsible for determining whether the 3M product is suitable and appropriate for the user's specific application, including user conducting an appropriate risk assessment and evaluating the 3M product in user's application.

Restrictions on Use: 3M advises against the use of these 3M products in any application other than the stated intended use(s), since other applications have not been evaluated by 3M and may result in an unsafe or unintended condition. Do not use in any manner whereby the 3M product, or any leachable from the 3M product, may become part of or remains in a medical device that is regulated by any agency, and/or globally exemplary agencies, including but not limited to: a) FDA, b) European Medical Device Regulation (MDR), c) Japan Pharmaceuticals and Medical Devices Agency (PMDA) or in applications involving permanent implantation into the body; Life-sustaining medical applications; Applications requiring food contact compliance.

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