



AseptiCap

Gamma Irradiatable Sterilization Grade Hydrophilic Polyethersulfone (PES) Membrane Devices for Liquid Streams in Biopharmaceuticals

Data Sheet

Biopharmaceutical processing requires sterilizing grade microfiltration at multiple stages to meet specific process requirements.

Processes managers are continuously looking for microfiltration solutions to upstream, downstream, intermediate processes and final biological preparations. Since bio manufacturing is a multi stage process and bio molecules by nature are extremely sensitive, they are looking for:

- Minimizing protein losses due to adsorption to improve overall product yields
- Minimizing filter extracts which add up due to multiple points of use in a process
- High throughputs to achieve process economy
- Choice of filter end connections for easy and reliable quick connections
- Absolute retentions for higher sterility assurance

mdi produces a wide range of Gamma compatible Sterilizing grade PES membrane devices to meet filtration requirements of biopharmaceutical processing. These filter devices are validated to meet compendia and regulatory requirements and are well characterized. They meet key process requirements such as high retention efficiency, very high protein recoveries, extremely low extractables, high throughputs, wide chemical compatibility and other important characteristics.

With the advantages of pre filtration layer built into the device for higher throughputs, linear scalability of filter area for smooth transitions from lab scale to pilot to process scale and widest range of end connections for quick and reliable connections to the existing fittings. **mdi AseptiCap** filters are a universal solution for process filtration.

Gamma Compatible PES Membrane Devices for Biopharmaceuticals

AseptiCap is a range of 0.1 and 0.2 micron capsule filters using **mdi** PES membrane in Gamma compatible Polypropylene housing. No adhesives or glue are used in the manufacturing process and all bonding is done by heat welding.

The products are deeply validated for use in Biopharmaceutical applications and specially recommended for single use systems. *AseptiCap* is manufactured in class 10,000 clean rooms and ISO 9001 : 2008 certified facilities. Packaging is done in double polybags for direct irradiation by gamma or for convenience of taking *AseptiCap* in clean areas for making disposable assemblies for subsequent sterilization.

Applications

Sterile Filtration of

- Cell culture media
- Cell culture media containing serum
- Media additives
- pH adjusters
- Final product concentrates

Bioburden Reduction/Particulate Removal

- Buffers
- Centrifuge supernatants
- Clarified cell lysates

Key Features

- Absolute retention
- 100% integrity tested
- Low protein binding
- Very low hold up volume in filters
- High flow rates
- Serial construction with prefilter for higher throughput with fouling streams
- Bioburden maintained below 1000 cfu/device
- Endotoxin level certified to be <0.25 EU/ml
- Widest range of end connections
- Products available for total scalability from a few ml to thousands of liters
- Total traceability through unique serial number for each filter
- Individual certificate of quality for each device
- Sterilizable by Gamma irradiation, EO gas or autoclaving

Validation Services

The regulatory requirements emphasize on the need to validate the efficacy of the 'Sterilizing Filter' with drug product under simulated worst-case conditions of use.

mdi provides validation services supported by customized validation protocols and world class test facilities to assist you in filter validations with your specific drug product.

mdi's quality management system emphasizes on quality by design rather by end product testing. Robust processes are developed for product manufacturing and are continuously monitored to ensure that the products meet their predetermined specifications and lot to lot reproducibility is ensured.

Certificate of Quality

Each capsule and cartridge filter is accompanied by individual certificate of quality to ensure traceable documentation at user's end.

It certifies the product compliance to various regulatory as well as user requirements.

Validated for Microbial Retention

Integrity test data have been correlated to actual microbial retention with *Brevundimonas diminuta* ATCC 19146 as per ASTM F838-05 to establish acceptable integrity test values.

Samples from each lot are subjected to microbial challenge test before final lot release.

100% Integrity Tested

Each *AseptiCap* is tested for integrity to comply with validated Acceptable Integrity Test Specifications.

Flow Rate

Each lot is tested for clean water flow rates to ensure that flow rates are within the specifications.

Adsorption

AseptiCap filters are validated for low protein binding to ensure minimal active ingredient losses when used for filtration of high value proteins.

Pressure, Temperature Endurance

AseptiCap filters are validated to endure high operating pressure and temperature conditions which may be encountered during use.

These filters are also validated for high burst pressure to ensure user safety in case of inadvertent pressure build-up.

Extractables

Extractables/leachables from sterilizing filters, used at various stages of a biopharmaceutical manufacturing process, will add on and may impact the impurity profile of the desired product.

AseptiCap filters are validated to exhibit low extractables under harsh extraction conditions.

Bioburden Testing

Device bioburden is tested as per ISO 117 37-1 and assured to be <1000 cfu/device.

Endotoxin Testing

Samples from each lot are subjected to LAL test before final lot release. The devices are tested as per USFDA CDER guidelines and exhibit <0.25 EU/ml endotoxin level.

Total Traceability

AseptiCap filters come with completely traceable lot numbers and unique identification number to facilitate easy and fast retrieval of manufacturing and quality control data associated with each filter.

These unique lot and identification numbers are embossed on each filter device and also printed on the labels of the box in which individual filter is packed.

Packaging Integrity

AseptiCap filters are fitted with vent caps and are packed in double polyethylene bags to ensure package integrity during transit as well as to prevent particulate contamination while transferring to clean room assembly or process areas.

Other Regulatory Compliance

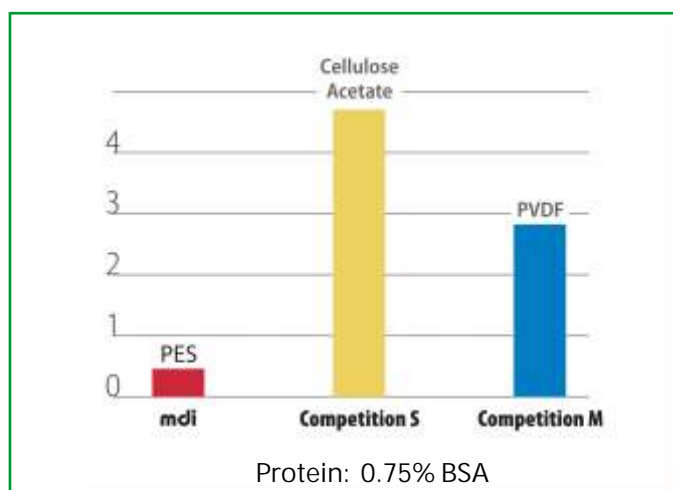
- Complies with USFDA 21 CFR 211.72 for fiber release
- Complies with USFDA 21 CFR 177.1520 for fractional dissolution
- Materials of construction tested for toxicity as per Biological Reactivity Tests, *in vivo*, USP <88> for class VI Plastics
- Complete filter devices tested for cytotoxicity as per Biological Reactivity Tests, *in vitro*, USP <87>

Low Protein Binding

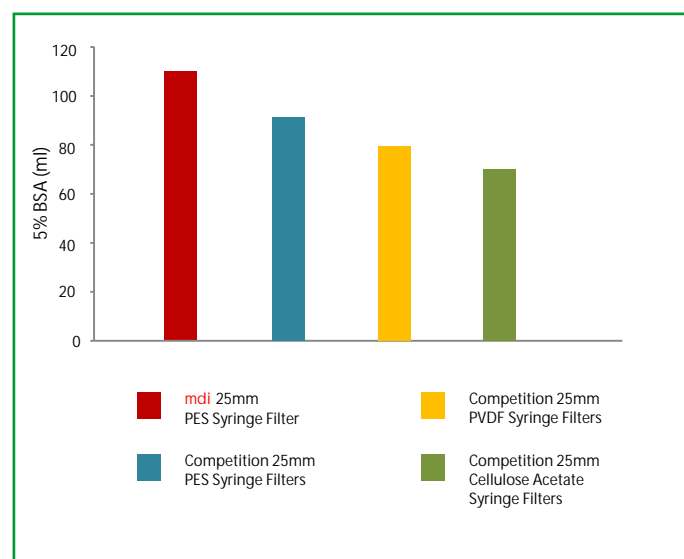
A comparative study on mdi PES membrane exhibits much lower protein adsorption than other competing membranes of Cellulose Acetate and PVDF.

The low protein binding results in increased overall product yield and higher throughputs with biological streams.

Protein Binding ($\mu\text{g}/\text{cm}^2$)



High Throughputs



mdi PES membrane exhibits higher throughput than either Cellulose Acetate or PVDF membranes.

The high throughput translates to lower filtration costs, less number of filter changes and overall economy of operations.

0.2 μm AseptiCap Filters	Protein Binding
25 mm Filter	1.45 μg
50 mm Filter	6.3 μg
AseptiCap DKS 1", 250 cm^2	80.5 μg
AseptiCap DKS 2", 500 cm^2	175 μg
AseptiCap LKS L10, 6000 cm^2	1925 μg

Extractables

It is useful to evaluate extractables that may be leached out of the filter and enter the process stream. mdi filters give low extractables well below the USP limits under harsh preconditioning and extraction conditions.

Low extractables mean less addition to impurity profile of the biological product from the filters.

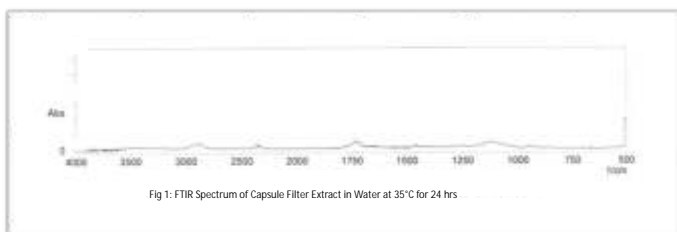
Preconditioning: Gamma Irradiated at 50kGy

Extraction Time: 24 hours

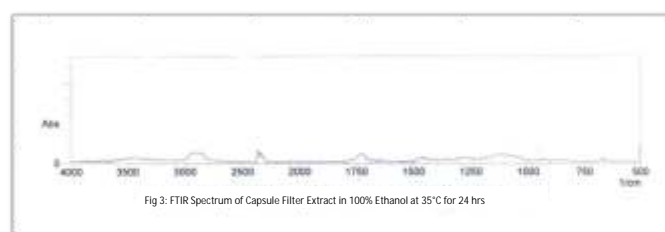
Model Solvent	Non Volatile Residue	
	AseptiCap 1" (230 cm ²)	AseptiCap L10 (5500 cm ²)
Water @ 35 °C	1.6 mg	38.26 mg
Water @ 80 °C	1.8 mg	43.04 mg

Model Solvent	Non Volatile Residue	
	AseptiCap 1" (230 cm ²)	AseptiCap L10 (5500 cm ²)
100% Ethanol @ 35 °C	13.4 mg	320.43 mg

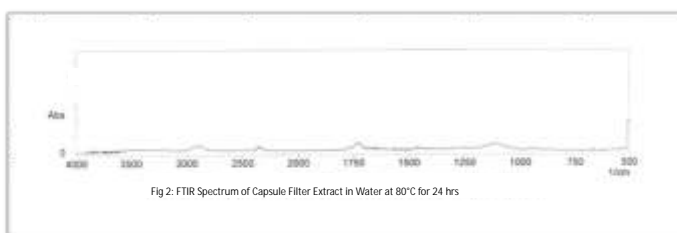
FTIR Analysis of Extractables From AseptiCap 1" Capsule Filter with Water @ 35 °C



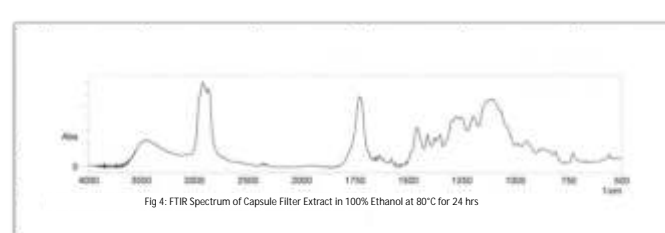
FTIR Analysis of Extractables From AseptiCap 1" Capsule Filter with 100% Ethanol @ 35 °C



FTIR Analysis of Extractables From AseptiCap 1" Capsule Filter with Water @ 80 °C



FTIR Analysis of Extractables From AseptiCap 1" Capsule Filter with 100% Ethanol @ 80 °C



The Spectrum of extracts from AseptiCap capsule filters with 100% ethanol under extreme extraction conditions show presence of various components used in the manufacture of mdi PES membrane capsule filters.

Widest Range of End Connections

Biopharmaceutical processes involve transfer of high value fluids through multiple process steps. Making high quality, reliable, flexible and functionally convenient connectivity with filters is of utmost value to the bio-processors.

mdi AseptiCap filters offer a wide range of reliable end connections for functional convenience and customized connectivity.

Validated for Performance

These end connections are manufactured with tight dimension tolerance and are validated for strength and connection integrity under extreme use conditions as well as for their ability to withstand prevalent sterilization methods including gamma irradiation, EO sterilization and autoclaving.



3/4" Sanitary Flange



1 1/2" Sanitary Flange



1/2" HB



Quick Connector



1/4" SHB

Some end connections available with AseptiCaps.

Customized Connectivity

mdi AseptiCap filters are available in a wide range of end connections and are also customized to offer different inlet-outlet combinations to meet the unique connectivity needs in biopharmaceutical process assemblies where, for example, stainless steel components with sanitary flange connections are sometimes required to be connected to single use disposable systems through quick-connectors or hose barb connections.



1 1/2" Sanitary Flange to 1/2" Barb Hose



1 1/2" Sanitary Flange to 3/4" Sanitary Flange



AseptiCap with HighSecurity 1/2" hose barb connection

Linear Upscaling from R&D to Production Process

Datasheet

Scientists are concerned about filter fluid interaction impacting the stability, purity, strength etc. of the drug product, and they take a keen interest in filter selection at the formulation development stage itself. Although preliminary compatibility data support initial filter selection, for stability studies detailed filter validations are required to provide enough documented evidence to justify specific filter use.

A critical requirement that needs to be addressed at this stage is of scalability from R&D to pilot scale to full scale production processes.

mdi offers a wide range of *AseptiCap* filters to provide linear scale up from lab scale to production process. While scaling up the process, the appropriate size filter can be selected by increasing the effective filtration area of filter proportionate to the process fluid volumes.

All Materials of construction of core, sleeve, end caps, support layers and housing as well as manufacturing process is identical for all filter devices starting from 4cm² to 19500cm² hence process scaling can be facilitated without triggering additional validation studies for given process conditions. **mdi** provides complete documentation for each of the *AseptiCap* filters thereby reducing the additional validation cost and time.



AseptiCap 25
5cm²



AseptiCap 50
18cm²



AseptiCap 1"
250cm²



AseptiCap 2"
500cm²



AseptiCap 5"
1000cm²



AseptiCap 8"
2000cm²

Filter Devices	EFA* (Nominal)	Hold up Volume
<i>AseptiCap</i> 25	5cm ²	< 50µl
<i>AseptiCap</i> 50	20cm ²	< 200µl
<i>AseptiCap</i> 1"	250cm ²	< 2ml
<i>AseptiCap</i> 2"	500cm ²	< 5ml
<i>AseptiCap</i> 5"	1000cm ²	< 5ml
<i>AseptiCap</i> 8"	2000cm ²	< 5ml
<i>AseptiCap</i> L10	6000cm ²	-



AseptiCap L10
6000cm²

0.1 μm AseptiCap DKS (with Prefilter)

Construction

Size	1"	2"	5"	8"	10"	
Membrane	0.1 μm Hydrophilic PES					
Prefilter Membrane	0.45 μm Hydrophilic PES					
Effective Filtration Area (Nominal)	250cm ²	500cm ²	1000cm ²	2000 cm ²	6000 cm ²	
Support Layers	Polyester					
Body and Core	Gamma Stable Polypropylene					
Dimension (End to End)	½" HBI I/O	99 mm	123 mm	175.5 mm	228 mm	337 mm
	1½" Sanitary Flange Inlet ½" Hose Barb Outlet	96 mm	118.5 mm	175.5 mm	228 mm	332 mm
	1½" Sanitary Flange I/O	100 mm	114 mm	168 mm	222 mm	327 mm
	Operational Radius (with Vent/ Drain)	30 mm	65 mm	65 mm	65 mm	106 mm
Vent and Drain	1/4" Hose Barb with double Silicone "O" rings					

Operational

Max. Operating Temperature	80 °C @ < 30 psi (2 Kg/cm ²)				
Max. Differential Pressure	60 psi (4 Kg/cm ²) @ 30 °C				
Bubble Point	≥ 34psi with 50% IPA/water solution				
Clean Water Flow Rate @ 10 psi with ½" Hose Barb Connection	0.8 lpm	1.6 lpm	3.6 lpm	5.6 lpm	10.8 lpm
Sterilization	By Irradiation	Gamma Irradiatable up to 50 kGy			
	By Gas	Sterilizable by Ethylene Oxide			
	By Autoclave	Autoclavable at 121°C for 30minute, 3 Cycles. Can not be steam sterilized			

Assurance

Toxicity	Passes Bioreactivity test, In Vivo, as per USP for Class VI plastics
Cytotoxicity	Passes Biological Reactivity Tests, invitro, USP <87> for cytotoxicity
Bacterial Retention	LRV> 7 for B. diminuta per cm ² of filter area as per ASTM F 838-05
Bacterial Endotoxin	Aqueous extracts exhibit < 0.25 EU/ml as established by Limulus Amebocyte Lysate (LAL) Test
Non Fiber Releasing	Passes test as per USP and comply with USFDA 21 CFR Part 211.72 for fiber release
pH Compatibility	Compatible with pH range of 1 - 10
Extractables with WFI	Passes test as per USP
Fractional Dissolution	Comply with USFDA 21 CFR Part 177.1520
Oxidizable Substances	Within limits as specified in USP
Quality Management System	ISO-9001:2008 Certified
CE Certification	Comply with the requirements of Medical Device Directive, 93/42/95 for Medical Device Class-1
USFDA	DMF Type V No. 15554

Ordering Information

Datasheet

0.1 µm AseptiCap PES Membrane Capsule filter

Type		Size		Pore Size		Inlet/Outlet		Radiation Sterilizable		Bell		Sterility		Pack Size	
	Code		Code		Code		Code	Yes	R	Yes	B	Non Sterile	Code	1	Code
DKS (0.45 µm Upstream)	DKSX	1"	51	0.1µm	36	¼" SHB	A		R	Yes	B	1	1	01	
		2"	52			½" Hose Barb	D			NoBell	X				
		5"	53			1½" Sanitary Flange	E								
LKS (0.45 µm Upstream)	LKSX	8"	57			¾" Sanitary Flange	S								
		10"	54			Quick Connector	J								
Example:															
DKSX		57		36		DD		R		X		1		01	

Note: Inlet/Outlet Connections available with different Sizes/Length as follows:

Inlet/Outlet	Size/Length					Bell at Outlet Available with (Size/Outlet)
	1"	2"	5"	8"	10"	
1/4" Stepped Hose Barb					X	1" / ¼" SHB
½" Hose Barb						
1-1/2" Sanitary Flange						
¾" Sanitary Flange	X					
Quick Connector					X	