



**Comparability Study**  
for Filter Capsules of  
the Existing Design  
and MidiCaps



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## 1. Introduction

The use of disposable filter capsules in pharmaceutical and biopharmaceutical production has increased significantly in the last years. Meanwhile filter capsules are an integral part of many production processes. The extended use of filter capsules in bio-pharmaceutical manufacturing added new requirements onto these filter capsules. Therefore Sartorius AG has decided to introduce a new capsule design for its existing filter units into the market.

This new capsule design focuses on design improvements of the capsule housing, offering multiple advantages for users in biopharmaceutical production, while the filter elements inside the capsule housings remain completely unchanged compared to the existing capsule design. Of course, the polypropylene material of the capsule housing itself, remains unchanged compared to the existing capsule design.

The new capsule design will be implemented for all filter capsule product lines starting with 500 cm<sup>2</sup> (Size 7) up to 4.500 cm<sup>2</sup> (Size 0) filtration area of Sartorius AG, which includes the following product lines:

- Sartopore® 2 (544...)
- Sartopore® 2 Gamma Capsules (544.G...)
- Sartobran® P (523...)
- Sartolon® (510...)
- Sartofluor® (518...)
- Sartoclean® CA|GF (560...|562...)
- Sartopure® PP2|GF2 (557...|559-...)

To allow all current users of the existing Sartorius capsule design to benefit in an optimal way of the advantages combined with the implementation of the new design, we have conducted a comprehensive comparability study between the two capsule designs. The comparability study focuses on all application relevant chemical, physical and mechanical properties of both capsule designs and allows for fast track implementation of the new design into all processes currently using the existing design.

The comparability study was performed in the way that Sartopore® 2 0.2 µm rated capsules of the new design were used as model to compare all relevant data with Sartopore® 2 capsules 0.2 µm rated of the existing capsule design in order to demonstrate comparability.

As result out of this comprehensive comparability study it can be stated that the change from the existing capsule design to the new capsule design for each product line is classified as a **minor change** (Annual Report). The test results demonstrate full comparability between the filter capsules of the existing and the new capsule design.

Of course a comprehensive validation of each individual product line of the new capsule design will be performed by Sartorius AG and all validation data will be summarized in respective Validation Guides for each product line.

## 2. Performed Tests

The tests performed within this comparability study for the new capsule design were in detail:

- A.) Sterilizing Grade Filtration Capability
- B.) Particle Release Test
- C.) Extractable Substances according to the current USP
- D.) Extractables Profile Testing
- E.) Biocompatibility Testing
- F.) Flow Rate Performance
- G.) Total Throughput Performance
- H.) Mechanical and Thermal Stability
- I.) Endotoxin Testing

### 3. Test Descriptions

Sterilizing grade filtration capability was tested with autoclaved capsules according to HIMA and ASTM F 838-83 guidelines using *Brevundimonas diminuta* as challenging organism.

The tests for particle release and extractable substances are performed in dynamic extraction mode after defined flush volumes of 1, 2.5, 5 and 10 liters as this methodology represents best actual filtration conditions. The filters tested have been autoclaved prior to testing.

The extractables profile testing and the biocompatibility testing were done by two different qualified, independent laboratories, each one specialized in the respective disciplines.

The testing for flow rate, total throughput, thermal and mechanical stability was done with capsules according to Sartorius Standard Operating Procedures.

The Endotoxin testing was done according to the current USP standard stated under the section "Sterile Water for Injection".

## 4. Test Results

### 4.1 Sterilizing Grade Filtration Capability

The basic filter elements incorporated into the existing and the new capsule design are completely identical and have been validated for sterilizing grade filtration capability during the product validation of each sterilizing grade filter product line of the existing capsule design.

Besides the filter element itself, the welding of the filter element into the capsule housing and the structural integrity of the capsule housing itself can have an influence on the sterilizing grade filtration capability of sterilizing grade filter capsules. Therefore the sterilizing grade filtration capability of the new capsule design and the associated manufacturing technology has been validated using Sartopore® 2 sterilizing grade filter capsules of the new capsule design. Sartopore® 2 filter capsules of the new design from numerous lots were tested according to the Bacterial Challenge Test in accordance with the HIMA Document No. 3, Vol. 4 (April 1982) "Microbiological Evaluation of Filters for Sterilizing Liquids"|ASTM F 838-83 Guideline and DIN 58356, Part 1.

The following table summarizes the BC-Test results with *Brevundimonas diminuta* of numerous integral Sartopore® 2 sterilizing grade filter capsules of the new capsule design from 3 different production lots:

Lot.-No.	Bioburden [CFU/cm <sup>2</sup> ]	Bacterial Challenge Test after autoclaving
402243	$> 1 \times 10^7$	passed
402343	$> 1 \times 10^7$	passed
414243	$> 1 \times 10^7$	passed

#### Conclusion

Integral sterilizing grade filter capsules of the new capsule design provide sterile filtrates when challenged with  $> 1 \times 10^7$  *Brevundimonas diminuta*. The results demonstrate that the integrity and bacterial retentive properties of sterilizing grade filter capsules are not affected when changing from the existing to the new capsule design.

The basic filter elements for each product line and filter size of integrity testable filter capsules remain completely unchanged when changing from the existing to the new capsule design. Therefore the integrity test parameters for integrity testable filter capsules of the new capsule design remain completely unchanged compared to the integrity testing parameters of the existing capsule design for each product line and filter size. This is also valid for product specific integrity test data determined during product specific validation studies.

The integrity testing parameters for respective filters can be found in the corresponding directions for use

#### 4.2 Particle Release

In general the particle release from filters should be minimized. For parenteral solutions, the requirements are defined in the USP Monographs, which set maximum limits for particle content based on defined particle sizes. The particle release for filter capsules of the existing and the new capsule design was measured, using Sartopore® 2 capsules of the existing and the new design after autoclaving.

The following tables list the test results for the existing and the new capsule design.

#### Existing Capsule Design

Particle Size [µm]	Particle per ml after 1 l flush	Particle per ml after 2.5 l flush	Particle per ml after 5 l flush	Particle per ml after 10 l flush	Limits according to B.P.	Limits according to USP
< 2	72	199	122	128		
2-5	12	37	28	33	500	
5-10	3	8	6	8	80	
10-15	0	0	1	1		
15-20	0	0	0	0		25
20-25	0	0	0	0		
25-50	0	0	0	0		3
> 50	0	0	0	0	0	0

#### New Capsule Design

Particle Size [µm]	Particle per ml after 1 l flush	Particle per ml after 2.5 l flush	Particle per ml after 5 l flush	Particle per ml after 10 l flush	Limits according to B.P.	Limits according to USP
< 2	17	5	7	7		
2-5	8	3	3	2	500	
5-10	2	2	1	0	80	
10-15	0	1	0	0		
15-20	0	0	0	0		25
20-25	0	0	0	0		
25-50	0	0	0	0		3
> 50	0	0	0	0	0	0

#### Conclusion

The tables above show that for capsules of the existing as well as of the new design the requirements of the current USP and BP for particle release are met in the very first liter of rinse volume. Accordingly capsule filters of both designs do not have to be rinsed prior to being able to produce a filtrate that conforms with the current USP and BP for particle content. Thereby full comparability of the existing and the new capsule design with regard to particle release has been

#### 4.3 Extractable Substances according to the current USP

The determination of extractable substances serves to establish the minimum required rinse volume in order to use filter capsules of the existing and the new design to filter solutions where no addition of extractable substances are required. As a limit, the current USP requirements for "Sterile Water for Injection" are used. The samples of filtrates, of Sartopore® 2 capsules of the existing and the new design are taken for analysis of Oxidizable Substances, pH and Conductivity Changes, Chloride, Sulfate and Ammonia.

#### Determination of Oxidizable Substances in the Filtrate

##### Existing Capsule Design

Lot.-No.	Non-Volatile Residue after 1 l rinse volume	Non-Volatile Residue after 2.5 l rinse volume	Non-Volatile Residue after 5 l rinse volume	Non-Volatile Residue after 10 l rinse volume
935241	passed	passed	passed	passed
935341	passed	passed	passed	passed
935441	passed	passed	passed	passed

##### New Capsule Design

Lot.-No.	Non-Volatile Residue after 1 l rinse volume	Non-Volatile Residue after 2.5 l rinse volume	Non-Volatile Residue after 5 l rinse volume	Non-Volatile Residue after 10 l rinse volume
402243	passed	passed	passed	passed
402343	passed	passed	passed	passed
414243	passed	passed	passed	passed

#### Conclusion

Filter capsules of the existing and the new design produced filtrates after autoclaving that, when measured, were below the requirements set by the current USP Limits for Oxidizable Substances for "Sterile Water for Injection". Thereby full comparability between the existing and the new capsule design with regard to release of oxidizable substances has been demonstrated.

**Determination of pH Values and Conductivity of the Filtrate**

The following limits were used in conjunction with USP for "Purified Water" and the filters were tested in the pH range of 5 to 7. The relationship between the pH value and the maximum allowable conductivity for Water for Injection according to the USP is:

<b>pH Value</b>	<b>Maximum Allowable Conductivity [<math>\mu\text{S}/\text{cm}</math>]</b>
5	4.7
5.1	4.1
5.2	3.6
5.3	3.3
5.4	3.0
5.5	2.8
5.6	2.6
5.7	2.5
5.8-6.1	2.4
6.2	2.5
6.3	2.6
6.4	2.8
6.5	3.1
6.6	3.4
6.7	3.8
6.8	4.3

## Existing Capsule Design

### A. Results for pH Values

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Lot.-No.	Non-Volatile Residue after 1 l rinse volume	Non-Volatile Residue after 2.5 l rinse volume	Non-Volatile Residue after 5 l rinse volume	Non-Volatile Residue after 10 l rinse volume
935241	5.8	5.7	5.7	5.75
935341	5.8	5.8	5.8	5.8
935441	5.8	5.8	5.85	5.85

#### Note

Due to the interrelationship between the pH value determination and the measurement of the conductivity, results for both tests must be viewed together.

### B. Results for Conductivity

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Lot.-No.	Non-Volatile Residue after 1 l rinse volume	Non-Volatile Residue after 2.5 l rinse volume	Non-Volatile Residue after 5 l rinse volume	Non-Volatile Residue after 10 l rinse volume
935241	0.7	0.7	0.7	0.7
935341	0.65	0.7	0.7	0.7
935441	0.65	0.7	0.7	0.7

## New Capsule Design

### A. Results for pH Values

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Lot.-No.	Non-Volatile Residue after 1 l rinse volume	Non-Volatile Residue after 2.5 l rinse volume	Non-Volatile Residue after 5 l rinse volume	Non-Volatile Residue after 10 l rinse volume
402243	6.0	6.0	6.0	6.0
402343	5.9	6.0	6.0	6.0
414243	5.95	5.95	6.0	6.0

#### Note

Due to the interrelationship between the pH value determination and the measurement of the conductivity, results for both tests must be viewed together.

### B. Results for Conductivity

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Lot.-No.	Non-Volatile Residue after 1 l rinse volume	Non-Volatile Residue after 2.5 l rinse volume	Non-Volatile Residue after 5 l rinse volume	Non-Volatile Residue after 10 l rinse volume
402243	0.7	0.7	0.7	0.7
402343	0.75	0.7	0.7	0.7
414243	0.7	0.7	0.7	0.7

#### Conclusion

Both parameters, pH and pH dependent conductivity of the filtrate, when filtering with capsules of the new and the existing capsule design are well below the limit requirements of the current USP. Thereby full comparability between the existing and the new capsule design with regard to conductivity and pH-shift has been demonstrated.

## Determination of Chloride, Sulfate and Ammonia in the Filtrate

### Existing Capsule Design

#### Chloride

Lot.-No.	Non-Volatile Residue after 1 l rinse volume	Non-Volatile Residue after 2.5 l rinse volume	Non-Volatile Residue after 5 l rinse volume	Non-Volatile Residue after 10 l rinse volume
935241	passed	passed	passed	passed
935341	passed	passed	passed	passed
935441	passed	passed	passed	passed

#### Sulfate

Lot.-No.	Non-Volatile Residue after 1 l rinse volume	Non-Volatile Residue after 2.5 l rinse volume	Non-Volatile Residue after 5 l rinse volume	Non-Volatile Residue after 10 l rinse volume
935241	passed	passed	passed	passed
935341	passed	passed	passed	passed
935441	passed	passed	passed	passed

#### Ammonia

Lot.-No.	Non-Volatile Residue after 1 l rinse volume	Non-Volatile Residue after 2.5 l rinse volume	Non-Volatile Residue after 5 l rinse volume	Non-Volatile Residue after 10 l rinse volume
935241	passed	passed	passed	passed
935341	passed	passed	passed	passed
935441	passed	passed	passed	passed

## New Capsule Design

### Chloride

Lot.-No.	Non-Volatile Residue after 1 l rinse volume	Non-Volatile Residue after 2.5 l rinse volume	Non-Volatile Residue after 5 l rinse volume	Non-Volatile Residue after 10 l rinse volume
402243	passed	passed	passed	passed
402343	passed	passed	passed	passed
414243	passed	passed	passed	passed

### Sulfate

Lot.-No.	Non-Volatile Residue after 1 l rinse volume	Non-Volatile Residue after 2.5 l rinse volume	Non-Volatile Residue after 5 l rinse volume	Non-Volatile Residue after 10 l rinse volume
402243	passed	passed	passed	passed
402343	passed	passed	passed	passed
414243	passed	passed	passed	passed

### Ammonia

Lot.-No.	Non-Volatile Residue after 1 l rinse volume	Non-Volatile Residue after 2.5 l rinse volume	Non-Volatile Residue after 5 l rinse volume	Non-Volatile Residue after 10 l rinse volume
402243	passed	passed	passed	passed
402343	passed	passed	passed	passed
414243	passed	passed	passed	passed

### Conclusion

Filter capsules of the existing and the new capsule design produced filtrates were below the requirements set by the current USP Limits for Chloride, Sulfate and Ammonia for "Sterile Water for Injection". Thereby full comparability of the existing and the new capsule design has been demonstrated with regard to Chloride, Sulfate and Ammonia release.

#### 4.4 Extractables Profile Analysis

The current USP and European Ph. describe overall limits for contaminants in different solvents and liquids such as Water for Injection, etc. For the general evaluation and quantification of the contaminants, methods for the determination of the non-volatile residue (NVR), total organic content (TOC) as well as pH-conductivity determination are given among other testing methods.

For the explicit analysis of the individual extractables or leachables from polymeric devices or compounds and their chemical structure, no analytical method is described from a pharmaceutical point of view. This is due to the broad range of polymeric compounds and the various solvents used in the downstream processing, resulting a large variety of theoretically potential extractables from the polymers. Such extractables can be degradation products of the base polymer or its monomers, stabilizers, processing and protective additives, lubricants or surface modifying agents. As long as the polymer is compatible with the applied solvent, the extractables levels are well below the detection limits of the individual analytical methodologies.

To evaluate extractables and compare polymers or devices with respect to the individual extractables profile it is necessary to use a worst case scenario approach, where extractables are generated on purpose by using extreme extraction conditions. In the following, such an approach was used to compare the extractables profile of the capsule housings of the existing and the new capsule design.

As the identical base polymer is used in both designs, differences in the extractables profile could only be based on differences of tooling or device processing's. Even this is highly theoretic and has a very low probability, the following analysis was performed to verify the comparability of the extractable profile of the design formats under worst case extraction conditions.

#### Materials and Methods

For both housings of the existing and the new capsule design, identical procedures for extraction were used. The capsule housing materials of both designs were extracted in 1 l of WFI for 24 hours at 70 °C and in 1 l of Ethanol (HPLC grade) for 24 hours at 50 °C. Both extracts were analysed directly via RP-HPLC with UV detection with a peak identification using FT-IR and Head Space GC-MS. Furthermore 100 ml of the extracts were dried and the solid residue analysed by FT-IR. The sensitivity of the methodologies are in the range of ppm.

To provide a detailed analysis of the extractables under worst case conditions in the lower ppb range, 100 ml of the extracts were concentrated by the factor of 40 to 100 (depending on the solvent) via RP solid phase extraction. The eluates of the RP solid phase were analysed using the identical methods described above.

The scope of the combination of the methodologies is to provide a comprehensive extractables profile on the potential extractables such as high and low MW, volatile and non-volatile, stable and unstable compounds in the low ppb to the high ppm range under worst case conditions.

## Results

The following extractables could be identified under the selected worst case conditions.

Existing Capsule Design	New Capsule Design
4-Ethyl-benzylmethanol	4-Ethyl-benzylmethanol
Diethylhexylphthalat	Diethylhexylphthalat
2,4-bis(1,1-dimethylethyl)phenol	2,4-bis(1,1-dimethylethyl)phenol
Irgafos 168	Irgafos 168
Dibutylphthalat	Dibutylphthalat
Irganox 1010	Irganox 1010

## Conclusion

In general, all extractables could be determined only in the concentrated samples, thereby having only a concentration in the lower ppb range. The identified extractables are degradation products of the base polymer Polypropylene, UV-stabilizers, antioxidants and processing additives which are typical for polypropylene used in pharmaceutical applications and do not have toxicological relevance in the found concentrations.

As demonstrated with this investigation, the extractables profiles of the existing and the new capsule design is identical. This result could be expected, for the base polymers are identical and the different toolings in the capsule processing do not have an impact on the extractables of the capsule itself. The comparability of the existing and the new capsule design with regard to their extractables profiles is thereby given.

#### 4.5 **Biocompatibility**

These tests are to determine that all components used in the manufacture of filter capsules of the existing and the new design are biosafe and meet or exceed the requirements for the current USP Class VI-121 °C Plastic Tests.

Sartopore® 2 filter capsules of the new and the existing design were supplied to an independent testing facility for evaluation under the requirements of the current USP Class VI Plastics Tests, including the following test:

- Intracutaneous Test
- Systemic injection Test
- Implantation Test (7 days)

#### **Test Result**

Sartopore® 2 filter capsules of the new and the existing design passed the Biocompatibility Test according to the current USP. All materials used for construction of these filter elements meet or exceed the requirements of the USP Class VI-121 °C Plastics Tests. Thereby the comparability of the existing and the new capsule design with regard to Biocompatibility has been demonstrated.

Certificates are available on request.

#### 4.6 Flow Rate Performance

The tests for flow rate were performed in order to demonstrate that the flow rate performance of the filter capsules of the new design is at least as good as the flow rate performance of the filter capsules of the existing design. This will assure that the filtration time in a current applications will remain within defined worst case parameters when changing from the existing to the new capsule design. The tests were performed using Sartopore® 2 0.2 µm rated capsules of the existing and the new capsule design of each filter size and connector combination according to Sartorius Standard Operating Procedures.

**Existing Capsule Design with  
1½ inch Tri-Clamp inlet and  
outlet connector**

Flow Rate for filter element size 0  
(4.500 cm<sup>2</sup> filtration area)

Lot.-No.	Flow Rate at 0.1 bar dp [l/h]	Flow Rate at 0.5 bar dp [l/h]	Flow Rate at 1 bar dp [l/h]	Flow Rate at 2 bar dp [l/h]
004281	390	1.740	3.240	5.520

**New Capsule Design with  
1½ inch Tri-Clamp inlet and  
outlet connector**

Flow Rate for filter element size 0  
(4.500 cm<sup>2</sup> filtration area)

Lot.-No.	Flow Rate at 0.1 bar dp [l/h]	Flow Rate at 0.5 bar dp [l/h]	Flow Rate at 1 bar dp [l/h]	Flow Rate at 2 bar dp [l/h]
403043	440	2.100	3.840	7.020

**Existing Capsule Design with  
1½ inch Tri-Clamp inlet and hose  
barb outlet connector**

Flow Rate for filter element size 0  
(4.500 cm<sup>2</sup> filtration area)

Lot.-No.	Flow Rate at 0.1 bar dp [l/h]	Flow Rate at 0.5 bar dp [l/h]	Flow Rate at 1 bar dp [l/h]	Flow Rate at 2 bar dp [l/h]
311343	280	860	1.390	1.650

**New Capsule Design with  
1½ inch Tri-Clamp inlet and hose  
barb outlet connector**

Flow Rate for filter element size 0  
(4.500 cm<sup>2</sup> filtration area)

Lot.-No.	Flow Rate at 0.1 bar dp [l/h]	Flow Rate at 0.5 bar dp [l/h]	Flow Rate at 1 bar dp [l/h]	Flow Rate at 2 bar dp [l/h]
403243	290	940	1.470	2.210

**Existing Capsule Design with hose  
barb inlet and outlet connector**

Flow Rate for filter element size 0  
(4.500 cm<sup>2</sup> filtration area)

<b>Lot.-No.</b>	<b>Flow Rate at 0.1 bar dp [l/h]</b>	<b>Flow Rate at 0.5 bar dp [l/h]</b>	<b>Flow Rate at 1 bar dp [l/h]</b>	<b>Flow Rate at 2 bar dp [l/h]</b>
360603	230	670	1.050	1.580

**New Capsule Design with hose  
barb inlet and outlet connector**

Flow Rate for filter element size 0  
(4.500 cm<sup>2</sup> filtration area)

<b>Lot.-No.</b>	<b>Flow Rate at 0.1 bar dp [l/h]</b>	<b>Flow Rate at 0.5 bar dp [l/h]</b>	<b>Flow Rate at 1 bar dp [l/h]</b>	<b>Flow Rate at 2 bar dp [l/h]</b>
403143	240	740	1.110	1.630

**Existing Capsule Design with  
1½ inch Tri-Clamp inlet and  
outlet connector**

Flow Rate for filter element size 9  
(2.000 cm<sup>2</sup> filtration area)

Lot.-No.	Flow Rate at 0.1 bar dp [l/h]	Flow Rate at 0.5 bar dp [l/h]	Flow Rate at 1 bar dp [l/h]	Flow Rate at 2 bar dp [l/h]
343603	180	910	1.740	3.240

**New Capsule Design with  
1½ inch Tri-Clamp inlet and  
outlet connector**

Flow Rate for filter element size 9  
(2.000 cm<sup>2</sup> filtration area)

Lot.-No.	Flow Rate at 0.1 bar dp [l/h]	Flow Rate at 0.5 bar dp [l/h]	Flow Rate at 1 bar dp [l/h]	Flow Rate at 2 bar dp [l/h]
402243	190	1.020	1.950	3.480

**Existing Capsule Design with  
1½ inch Tri-Clamp inlet and hose  
barb outlet connector**

Flow Rate for filter element size 9  
(2.000 cm<sup>2</sup> filtration area)

Lot.-No.	Flow Rate at 0.1 bar dp [l/h]	Flow Rate at 0.5 bar dp [l/h]	Flow Rate at 1 bar dp [l/h]	Flow Rate at 2 bar dp [l/h]
311343	174	660	1.089	1.360

**New Capsule Design with  
1½ inch Tri-Clamp inlet and hose  
barb outlet connector**

Flow Rate for filter element size 9  
(2.000 cm<sup>2</sup> filtration area)

Lot.-No.	Flow Rate at 0.1 bar dp [l/h]	Flow Rate at 0.5 bar dp [l/h]	Flow Rate at 1 bar dp [l/h]	Flow Rate at 2 bar dp [l/h]
402243	180	708	1.150	1.830

**Existing Capsule Design with hose  
barb inlet and outlet connector**

Flow Rate for filter element size 9  
(2.000 cm<sup>2</sup> filtration area)

<b>Lot.-No.</b>	<b>Flow Rate at 0.1 bar dp [l/h]</b>	<b>Flow Rate at 0.5 bar dp [l/h]</b>	<b>Flow Rate at 1 bar dp [l/h]</b>	<b>Flow Rate at 2 bar dp [l/h]</b>
360603	140	510	850	1.350

**New Capsule Design with hose  
barb inlet and outlet connector**

Flow Rate for filter element size 9  
(2.000 cm<sup>2</sup> filtration area)

<b>Lot.-No.</b>	<b>Flow Rate at 0.1 bar dp [l/h]</b>	<b>Flow Rate at 0.5 bar dp [l/h]</b>	<b>Flow Rate at 1 bar dp [l/h]</b>	<b>Flow Rate at 2 bar dp [l/h]</b>
402343	144	560	900	1.380

**Existing Capsule Design with  
1½ inch Tri-Clamp inlet and  
outlet connector**

Flow Rate for filter element size 8  
(1.000 cm<sup>2</sup> filtration area)

Lot.-No.	Flow Rate at 0.1 bar dp [l/h]	Flow Rate at 0.5 bar dp [l/h]	Flow Rate at 1 bar dp [l/h]	Flow Rate at 2 bar dp [l/h]
402603	120	600	1.200	2.100

**New Capsule Design with  
1½ inch Tri-Clamp inlet and  
outlet connector**

Flow Rate for filter element size 8  
(1.000 cm<sup>2</sup> filtration area)

Lot.-No.	Flow Rate at 0.1 bar dp [l/h]	Flow Rate at 0.5 bar dp [l/h]	Flow Rate at 1 bar dp [l/h]	Flow Rate at 2 bar dp [l/h]
402843	132	630	1.200	2.220

**Existing Capsule Design with  
1½ inch Tri-Clamp inlet and hose  
barb outlet connector**

Flow Rate for filter element size 8  
(1.000 cm<sup>2</sup> filtration area)

Lot.-No.	Flow Rate at 0.1 bar dp [l/h]	Flow Rate at 0.5 bar dp [l/h]	Flow Rate at 1 bar dp [l/h]	Flow Rate at 2 bar dp [l/h]
205253	102	430	780	1.380

**New Capsule Design with 1½  
inch Tri-Clamp inlet and hose  
barb outlet connector**

Flow Rate for filter element size 8  
(1.000 cm<sup>2</sup> filtration area)

Lot.-No.	Flow Rate at 0.1 bar dp [l/h]	Flow Rate at 0.5 bar dp [l/h]	Flow Rate at 1 bar dp [l/h]	Flow Rate at 2 bar dp [l/h]
402243	120	520	900	1.500

**Existing Capsule Design with hose  
barb inlet and outlet connector**

Flow Rate for filter element size 8  
(1.000 cm<sup>2</sup> filtration area)

Lot.-No.	Flow Rate at 0.1 bar dp [l/h]	Flow Rate at 0.5 bar dp [l/h]	Flow Rate at 1 bar dp [l/h]	Flow Rate at 2 bar dp [l/h]
363203	108	420	720	1.140

**New Capsule Design with hose  
barb inlet and outlet connector**

Flow Rate for filter element size 8  
(1.000 cm<sup>2</sup> filtration area)

Lot.-No.	Flow Rate at 0.1 bar dp [l/h]	Flow Rate at 0.5 bar dp [l/h]	Flow Rate at 1 bar dp [l/h]	Flow Rate at 2 bar dp [l/h]
402943	108	432	740	1.200

**Existing Capsule Design with  
1½ inch Tri-Clamp inlet and  
outlet connector**

Flow Rate for filter element size 7  
(500 cm<sup>2</sup> filtration area)

Lot.-No.	Flow Rate at 0.1 bar dp [l/h]	Flow Rate at 0.5 bar dp [l/h]	Flow Rate at 1 bar dp [l/h]	Flow Rate at 2 bar dp [l/h]
402303	50	240	460	780

**New Capsule Design with  
1½ inch Tri-Clamp inlet and  
outlet connector**

Flow Rate for filter element size 7  
(500 cm<sup>2</sup> filtration area)

Lot.-No.	Flow Rate at 0.1 bar dp [l/h]	Flow Rate at 0.5 bar dp [l/h]	Flow Rate at 1 bar dp [l/h]	Flow Rate at 2 bar dp [l/h]
402443	60	300	630	1.080

**Existing Capsule Design with  
1½ inch Tri-Clamp inlet and hose  
barb outlet connector**

Flow Rate for filter element size 7  
(500 cm<sup>2</sup> filtration area)

Lot.-No.	Flow Rate at 0.1 bar dp [l/h]	Flow Rate at 0.5 bar dp [l/h]	Flow Rate at 1 bar dp [l/h]	Flow Rate at 2 bar dp [l/h]
256003	50	200	450	720

**New Capsule Design with  
1½ inch Tri-Clamp inlet and hose  
barb outlet connector**

Flow Rate for filter element size 7  
(500 cm<sup>2</sup> filtration area)

Lot.-No.	Flow Rate at 0.1 bar dp [l/h]	Flow Rate at 0.5 bar dp [l/h]	Flow Rate at 1 bar dp [l/h]	Flow Rate at 2 bar dp [l/h]
402643	70	300	540	960

**Existing Capsule Design with hose barb inlet and outlet connector**

Flow Rate for filter element size 7 (500 cm<sup>2</sup> filtration area)

Lot.-No.	Flow Rate at 0.1 bar dp [l/h]	Flow Rate at 0.5 bar dp [l/h]	Flow Rate at 1 bar dp [l/h]	Flow Rate at 2 bar dp [l/h]
415703	50	270	420	690

**New Capsule Design with hose barb inlet and outlet connector**

Flow Rate for filter element size 7 (500 cm<sup>2</sup> filtration area)

Lot.-No.	Flow Rate at 0.1 bar dp [l/h]	Flow Rate at 0.5 bar dp [l/h]	Flow Rate at 1 bar dp [l/h]	Flow Rate at 2 bar dp [l/h]
402343	70	300	540	960

**Conclusion**

Filter capsules of the new design show at least the same flow rate performance than filter capsules of the existing design. Especially for filter elements with higher effective filtration area (2.000 cm<sup>2</sup> and 4.500 cm<sup>2</sup>) at higher differential pressure the capsules of the new design show higher flow rates than capsules of the existing design due to the design optimization of the connectors of the capsules housing. As a result, the filtration time in a current application will be identical or lower when changing from the new to the existing design. Thereby full comparability between the existing and the new capsule design with regard to flow rate has been demonstrated.

4.7

**Total Throughput Performance**

The tests for total throughput performance were performed in order to demonstrate that the total throughput performance of the filter capsules of the new design is at least as good as the flow rate performance of the filter capsules of the existing design. This assures, that the filter sizing used for an application can remain unchanged when changing to the new capsules design from the existing design. The tests were performed using Sartopore® 2 0.2 µm rated capsules of the existing and the new capsule design according to Sartorius Standard Operating Procedures.

**Existing Capsule Design Total Throughput for filter element size 0 (4.500 cm<sup>2</sup> filtration area)**

Lot.-No.	Total Throughput at 95% blockage [kg]
	41.5

**New Capsule Design Total Throughput for filter element size 0 (4.500 cm<sup>2</sup> filtration area)**

Lot.-No.	Total Throughput at 95% blockage [kg]
	42.0

**Existing Capsule Design Total Throughput for filter element size 9 (2.000 cm<sup>2</sup> filtration area)**

Lot.-No.	Total Throughput at 95% blockage [kg]
935541	26.2

**New Capsule Design Total Throughput for filter element size 9 (2.000 cm<sup>2</sup> filtration area)**

Lot.-No.	Total Throughput at 95% blockage [kg]
402243	26.6

**Existing Capsule Design Total Throughput for filter element size 8 (1.000 cm<sup>2</sup> filtration area)**

Lot.-No.	Total Throughput at 95% blockage [kg]
935641	15.3

**New Capsule Design Total Throughput for filter element size 8 (1.000 cm<sup>2</sup> filtration area)**

Lot.-No.	Total Throughput at 95% blockage [kg]
402843	15.7

**Existing Capsule Design Total  
Throughput for filter element  
size 7 (500 cm<sup>2</sup> filtration area)**

<b>Lot.-No.</b>	<b>Total Throughput at 95 % blockage [kg]</b>
935941	6.4

**New Capsule Design Total  
Throughput for filter element  
size 7 (500 cm<sup>2</sup> filtration area)**

<b>Lot.-No.</b>	<b>Total Throughput at 95 % blockage [kg]</b>
402443	6.9

**Conclusion**

The filter elements incorporated into the existing filter capsule design and into the new filter capsule design are completely identical. The total throughput performance of these filter elements is unaffected by the different capsules designs. For all current applications using the existing capsule design the filter sizing can remain completely unchanged when changing to the new capsule design. Thereby full comparability between the existing and the new capsule design with regard to total throughput performance has been demonstrated.

#### 4.8 Mechanical and Thermal Stability

##### Determination of max. allowable differential pressure

Sartopore® 2 0.2 µm rated filter capsules of 3 different production lots of the existing and the new capsule design were sterilized by autoclaving and subsequently pressurized with an inlet pressure of 6 bar|87 psi with pressurized air for 24 hours with outlet closed.

After 24 hours capsules leakage was determined using the automatic integrity test device Sartocheck 4 to check for leakages at 6 bar. Any significant pressure decrease during this test would lead to a non passed statement.

##### Existing Capsule Design

Lot.-No.	Test Pressure [bar psi]	Integrity Test
935241	6 87	passed
935341	6 87	passed
935441	6 87	passed

##### New Capsule Design

Lot.-No.	Test Pressure [bar psi]	Integrity Test
402243	6 87	passed
402343	6 87	passed
414243	6 87	passed

##### Conclusion

Filter capsules of the existing and the new capsule design retain their structural filter integrity after autoclaving when pressurized with 6 bar|87 psi for 24 hours. In order to guarantee a high degree of safety during use the max. allowed differential pressure for the new capsule design was set at 5 bar|72.5 psi in comparison to 4 bar|58 psi for the old capsule design.

**Burst Pressure determination**

In order to determine the burst pressure of filter capsules of the existing and the new design, Sartopore® 2 capsules 0.2 µm rated, from 3 different production lots were sterilized by autoclaving and subsequently pressurized with air until a crack of the capsule housing occurred.

**Existing Capsule Design**

Lot.-No.	Determined burst pressure after 1 autoclaving cycle [bar psi]
935241	> 10 145
935341	> 10 145
935441	> 10 145

**New Capsule Design**

Lot.-No.	Determined burst pressure after 1 autoclaving cycle [bar psi]
402243	> 10 145
402343	> 10 145
414243	> 10 145

**Conclusion**

The test results verify that filter capsules of the existing and the new capsule design do withstand comparable physical stress. Thereby full comparability between the existing and the new capsule design with regard to mechanical stability has been demonstrated.

**Burst Pressure determination after thermal stress**

In order to verify that filter capsules of the new capsule design can withstand multiple autoclaving cycles, Sartopore® 2 0.2 µm rated from 3 different production lots were sterilized 25 times by autoclaving and subsequently pressurized with air until a crack of the capsule housing occurred.

**New Capsule Design**

Lot.-No.	Determined burst pressure after 25 autoclaving cycles [bar psi]
402243	> 10 145
402343	> 10 145
414243	> 10 145

**Conclusion**

The test results verify that filter capsules of the new capsule design are unaffected by multiple autoclaving cycles at 134 °C for 20 minutes. Thereby full comparability between the existing and the new capsule design has been demonstrated.

**4.9****Endotoxin Testing**

Sartopore® 2 capsules of 3 different lots of the existing and the new capsule design have been tested that the effluent produced by these capsules contains less than 0.18 EU/ml.

**Existing Capsule Design**

<b>Lot-No.</b>	<b>LAL Test Result</b>
935241	passed
935341	passed
935441	passed

**New Capsule Design**

<b>Lot-No.</b>	<b>LAL Test Result</b>
402243	passed
402343	passed
414243	passed

**Conclusion**

The test results verify that capsules of the existing and the new capsule design comply with the limits of the current USP for endotoxin release. Therefore comparability for the new and the existing capsule design is given with regard to endotoxin release. Thereby full comparability between the existing and the new capsules design with regard to content of endotoxins has been demonstrated.

## 5. Summary

The new capsule design incorporates the identical filter elements compared to the existing capsule design for each product line of capsules manufactured by Sartorius AG. Furthermore the base polymer for manufacturing capsules housings of the existing and the new capsule design remains completely unchanged.

The implementation of the new capsule design into processes using the existing capsule design will allow for significant improvements on process safety and ease of operation. This comparability study between the existing and the new capsule design was performed to demonstrate full comparability between both designs, to allow a fast implementation of the new capsule design in all process currently using the existing design.

Thereby Sartopore® 2 capsules 0.2 µm rated of the existing and the new design were used to compare all application relevant specifications of the new and the existing capsule design in order to demonstrate full comparability between both designs. This study serves as a model for implementation of the new capsule design for all capsule product lines of Sartorius AG.

The results of the tests reported in this document give documented evidence that there is full comparability between filter capsules of the existing and the new capsule design. As a result of this study the change from the existing to the new capsule design for Sartorius filter capsules has been classified as minor change.







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