Sterile Filter Transfer Sets

Validation Guide

SARTORIUS

Table of Contents

1. Introduction

The use of single use equipment in pharmaceutical and bio-pharmaceutical manufacturing processes is consistently increasing. For filtration applications filter capsules are integral part of many production processes since decades. These filter caspules are today available in a broad range of sizes and formats to facilitate small scale testing and clinical as well as commercial scale manufacturing. Typically the filter capsules are provided pre-sterilized (e.g. by autoclaving) and aseptically connected in a laminar flow system to the filtration system or the whole filtration system is assembled on-site and sterilized prior to use by the end user.

In the recent years single use flexible containers (bags) consistently replace conventional glass or stainless steel containers in bio-pharmaceutical manufacturing. These single use containers are pre-sterilized by gamma irradiation and ready to use. To allow for the integration of the filtration process and transport and storage of the filtered media, filter capsules are increasingly pre-connected to single use containers and pre-sterilized by gamma-irradiation as a complete assembly providing multiple benefits to the user. However, this requires that all materials of construction of the respective filter capsules are compatible with gamma irradiation to avoid subsequent polymer degradation and extractables release from the irradiated filter capsules. Therefore, special gamma irradiatable filter capsules have been designed by the industry.

However, a broad range of commercially available filter capsules which are widely used in bio-pharmaceutical manufacturing are not compatible with gamma irradiation due to the limited stability of their materials of construction. Therefore a concept is required to allow the integration of such non gamma irradiatable filter capsules into single use processing solutions. Such a concept allows the transfer of existing manufacturing processes employing such filter capsules towards single use technology or newly developed processes which have been validated with such filter capsules to utilize the benefits of single us technology right from the beginning.

For this reason Sartorius has developed the "Sterile Filter Transfer Sets (SFTS) – Concept". Within this concept non gamma irradiatable filter capsules are connected with tubing and aseptic or non-aseptic connectors on the inlet and/or outlet and pre-sterilized by autoclaving. The pre-sterilized sterile filter transfer sets can easily be connected under standard room conditions by the end user to pre-sterilized single use containers, avoiding the need for making the connection in a laminar flow system.

A comprehensive validation study has been carried out to provide information for the user required for validation of sterile filter transfer sets for bio-pharmaceutical manufacturing processes. This validation study focusses on a comparison of the validation data already established for the respective filter capules and the same filter capsule connected with tubing and connectors. The purpose of the study carried out is to demonstrate that the established validation data for a specific filter capsule product line are comparable with the data for the same filter capsule connected with tubing and connectors.

In a product life cycle project the Sterile Filter Transfer Set portfolio was extended with frequently requested components such as connectors and tubes, T-Style Maxicaps® as well as closed systems. Closed systems are Maxicaps® assemblies where a vent filter and sterile connector is attached to the vent valves of the filter capsules. Aditionally, in order to increase the robustness of the tube to hose barb connections, metal ear clamps were introduced for all connections, with the exception of the Maxicaps® valve connections.

The purpose of the new qualification study for the expanded portfolio was to test a representative set of assemblies with a combination of new and frequently used components to demonstrate, that the tube to hose barb connection using metal ear clamps meet the tightness and robustness requirements. Prior and within this study a comprehensive connection qualification of tube to hose barb connections using metal ear clamps were conducted, in order to be able to determine the maximum permissible operating pressures of the assemblies.

1.1 Study Design

Sterile Filter Transfer Sets will be provided for all non-gamma irradiatable Midicaps® from size 7 to size 0 and Maxicaps® from 10" to 30" connected with various tubings, various tubing length on inlet and|or outlet and different types of connectors.

Sartobran® P Midicaps® and Maxicaps®, representing one filter capsule product line which is non-gamma irradiatable have been selected to demonstrate the comparability of the validation data of the filter capsules product line and the same filter capsules connected with tubing and connectors.

For this purpose Sartobran® P Midicaps® of size 9 (most commonly used filter capsule size) and 30" Sartobran® P Maxicaps® (largest filter capsules size) from 3 different production lots have been connected with the longest possible tubing length of 300 mm on inlet and outlet. To simulate also the impact of different connector types they have been connected to the tubing on the inlet and outlet of the filter capsules. Those assemblies have been submitted in parallel to the un-connected filter capsules of the same lots to the identical validation tests and the test results are evaluated and compared.

Since the release of the expanded sterile Filter Transfer Sets, Filter Transfer Sets are provided with metal ear clamps for almost all tube to hose barb connections (Notification letter ECN 620177), instead of previously used cable ties, in order to increase the connection robustness and the maximum operating pressure of the assemblies.

A representive set of assemblies were selected to test a wide variety of combinations of connectors, tubings, filter types and filter capsule designs, including one assembly that covers the biggest possible product variant, in order to demonstrate the leak tightness of the assemblies.

A comprehensive connection qualification of tube to hose barb connections using metal ear clamps were conducted. Tube to hose barb connections with metal ear clamps were already proven in another similar product portfolio, where each single connection was tested for pressure resistance. Connections tested in the course of the similar product portfolio are similar in geometry and material. Additional tests were performed for new connections. Each available tube to hose barb connection was ultimately tested. The results which are presented in this validation guide are the summary of the performed tests. Detailed test reports can be viewed during an audit at the Sartorius site in Goettingen.

Test results of Filter Transfer Sets with cable ties such as particle, TOC, extractables and others test are unlikely to be influenced by the change to metal ear clamps, a component that is not in product contact.

1.2 Overview of Tested Elements

Assembly	Lot No.	Filter Part No.	Assembly Configuration	
1	50203479	5235307H9--OO	Inlet	None
			Filter	Sartobran® P Midicaps® Size 9
			Outlet	None
2	50203694	5235307H9--OO	Inlet	None
			Filter	Sartobran® P Midicaps® Size 9
			Outlet	None
3	50203899	5235307H9--OO	Inlet	None
			Filter	Sartobran® P Midicaps® Size 9
			Outlet	None
4	50204483	5235307H9--OO	Inlet	Connector: MPX ½"; Tubing: 300 mm Tuflux® SIL (½" × ¾"); Tube to hose barb connection: Cable ties
			Filter	Sartobran® P Midicaps® Size 9
			Outlet	Connector: MPX ½"; Tubing: 300 mm Tuflux® SIL (½" × ¾"); Tube to hose barb connection: Cable ties
5	50204861	5235307H9--OO	Inlet	Connector: OPTA® SFTS ½ "; Tubing: 300 mm Tuflux® SIL (½" × ¾"); Tube to hose barb connection: Cable ties
			Filter	Sartobran® P Midicaps® Size 9
			Outlet	Connector: OPTA® SFTS ½ "; Tubing: 300 mm Tuflux® SIL (½" × ¾"); Tube to hose barb connection: Cable ties
6	50205156	5235307H9--OO	Inlet	Connector: KleenpakTM HT ½"; Tubing: 300 mm Tuflux® SIL (½" × ¾"); Tube to hose barb connection: Cable ties
			Filter	Sartobran® P Midicaps® Size 9
			Outlet	Connector: Kleenpak™ HT ½"; Tubing: 300 mm Tuflux® SIL (½" × ¾"); Tube to hose barb connection: Cable ties
7	018118738	5237307H3--OO	Inlet	None
			Filter	Sartobran® P Maxicaps® 30"
			Outlet	None
8	028118737	5237307H3--OO	Inlet	None
			Filter	Sartobran® P Maxicaps® 30"
			Outlet	None

Assembly	Lot No.	Filter Part No.	Assembly Configuration	
9	038118737	5237307H3--OO	Inlet	None
			Filter	Sartobran® P Maxicaps® 30"
			Outlet	None
10	048118737	5237307H3--OO	Inlet	Connector: MPX ½"; Tubing: 300 mm Tuflux® SIL (½" × ¾"); Tube to hose barb connection: Cable ties
			Filter	Sartobran® P Maxicaps® 30"
			Outlet	Connector: MPX ½"; Tubing: 300 mm Tuflux® SIL (½" × ¾"); Tube to hose barb connection: Cable ties
11	058118737	5237307H3--OO	Inlet	Connector: OPTA® SFTS ½ "; Tubing: 300 mm Tuflux® SIL (½" × ¾"); Tube to hose barb connection: Cable ties
			Filter	Sartobran® P Maxicaps® 30"
			Outlet	Connector: OPTA® SFTS ½ "; Tubing: 300 mm Tuflux® SIL (½" × ¾"); Tube to hose barb connection: Cable ties
12	068118737	5237307H3--OO	Inlet	Connector: Kleenpak™ HT ½"; Tubing: 300 mm Tuflux® SIL (½" × ¾"); Tube to hose barb connection: Cable ties
			Filter	Sartobran® P Maxicaps® 30"
			Outlet	Connector: Kleenpak™ HT ½"; Tubing: 300 mm Tuflux® SIL (½" × ¾"); Tube to hose barb connection: Cable ties
FTS5002BN	909011813	5237307H2--OO	Inlet	Connector: Kleenpak™ Presto ½"; Tubing: 100 mm Sani-Tech® STHT®-R (½" × ⅞"); T-piece ½"; Tube to hose barb connection: Metal Ear Clamps
			Filter	Sartobran® P 20"
			Filter-Valve 1	Connector: OPTA® SFTS ¼ "; Tubing: 100 mm Tuflux® SIL ¼" × 7⁄16"; Tube to hose barb connection: Cable ties
			Filter-Valve 2	Midisart® 2000; Tubing: Tubing: 100 mm Tuflux® SIL ¼" × 7⁄16"; Tube to hose barb connection: Cable ties
			Outlet	Connector: Kleenpak™ HT ½"; Tubing: 100 mm Tuflux® SIL (½" × ⅞"); T-piece ½"; Tube to hose barb connection: Metal Ear Clamps
FTS5002BO	190003483	5237307H1--BB	Inlet	Connector: CPC® MPU ¾"; Tubing: 300 mm Sani-Tech® STHT®-R (¾" × ⅞"); Tube to hose barb connection: Metal Ear Clamps
			Filter	Sartobran® P 10"
			Outlet	Connector: OPTA® SFTS ¾"; Tubing: 300 mm Sani-Tech® STHT®-R (¾" × ⅞"); Tube to hose barb connection: Metal Ear Clamps

to be continued

Assembly	Lot No.	Filter Part No.	Assembly Configuration	
FTS5002BP	190003583	5237307H1--OO	Inlet	Connector: CPC® AseptiQuik G ½"; Tubing: 300 mm Pharma-80 (½" × ¾"); Tube to hose barb connection: Metal Ear Clamps
			Filter	Sartobran® P 10"
			Outlet	Connector: CPC® AseptiQuik G ½"; Tubing: 300 mm Pharma-80 (½" × ¾"); Tube to hose barb connection: Metal Ear Clamps
FTS5002BR	190003683	54A5358N9-OO	Inlet	Connector: 1.5" Sanitary Clamp ⅜" ; Tubing: 300 mm Tuflux® SIL (⅜" × ⅝"); Tube to hose barb connection: Metal Ear Clamps
			Filter	Virosart® Max Size 9
			Outlet	Connector: Kleenpak™ HT ⅜" ; Tubing: 300 mm Tuflux® SIL (⅜" × ⅝"); Tube to hose barb connection: Metal Ear Clamps

1.3 Overview Performed Tests

The following tests have been performed:

- Particle Content of the Filtrate (Capsules & Assemblies)
- Extractables Substances Testing According to USP (Capsules & Assemblies)
- TOC Flush Volumes (Capsules & Assemblies)
- Integrity Test of the assembled Filter Capsule of the Assemblies
- Mechanical Stability Testing of the tube to hose barb connections and Assemblies
- Endotoxin Testing of the Assemblies
- Sterilization Validation

1.4 Additional Information

The following additional information is provided

- Information on Biocompatibility of the Assemblies
- Information on Extractable Profile Testing of the Assemblies
- Information on transport validation of the assembly packaging

2. Performed Tests

2.1 Particle Content of the Filtrate

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

From the current USP, the following limits have been set as a maximum number of particles per mL of product (in this case, large volume injections for single dose infusion):
25 particles/mL > 10 µm
3 particles/mL > 25 µm

Standard Sartobran® P Midicaps®

Assembly: 1, 2, 3; Lot no.: 50203479, 50203694, 50203899

Particle Size [µm]	Particle Count per mL after 1 L Flush	Particle Count per mL after 5 L Flush	Particle Count per mL after 10 L Flush	Limits According to USP
≥ 10	0	0	0	25
≥ 25	0	0	0	3

Sartobran® P Midicaps® assembled with 300 mm tubing and MPX connectors on inlet and outlet

Assembly: 4; Lot no.: 50204483

Particle Size [µm]	Particle Count per mL after 1 L Flush	Particle Count per mL after 5 L Flush	Particle Count per mL after 10 L Flush	Limits According to USP
≥ 10	0	0	0	25
≥ 25	0	0	0	3

Sartobran® P Midicaps® assembled with 300 mm tubing and Opta® Connectors on inlet and outlet

Assembly: 5; Lot no.: 50204861

Particle Size [µm]	Particle Count per mL after 1 L Flush	Particle Count per mL after 5 L Flush	Particle Count per mL after 10 L Flush	Limits According to USP
≥ 10	0	0	0	25
≥ 25	0	0	0	3

Sartobran® P Midicaps® assembled with 300 mm tubing and KPC Connectors on inlet and outlet

Assembly: 6; Lot no.: 50205156

Particle Size [µm]	Particle Count per mL after 1 L Flush	Particle Count per mL after 5 L Flush	Particle Count per mL after 10 L Flush	Limits According to USP
≥ 10	0	0	0	25
≥ 25	0	0	0	3

Standard Sartobran® P Maxicaps®

Assembly: 7, 8, 9; Lot no.: 18118738, 028118737, 38118737

Particle Size [µm]	Particle Count per mL after 1 L Flush	Particle Count per mL after 5 L Flush	Particle Count per mL after 10 L Flush	Limits According to USP
≥ 10	0	0	0	25
≥ 25	0	0	0	3

Sartobran® P Maxicaps® assembled with 300 mm tubing and MPX Connectors on inlet and outlet

Assembly: 10; Lot no.: 048118737

Particle Size [µm]	Particle Count per mL after 1 L Flush	Particle Count per mL after 5 L Flush	Particle Count per mL after 10 L Flush	Limits According to USP
≥ 10	0	0	0	25
≥ 25	0	0	0	3

Sartobran® P Maxicaps® assembled with 300 mm tubing and Opta® Connectors on inlet and outlet

Assembly: 11; Lot no.: 058118737

Particle Size [µm]	Particle Count per mL after 1 L Flush	Particle Count per mL after 5 L Flush	Particle Count per mL after 10 L Flush	Limits According to USP
≥ 10	0	0	0	25
≥ 25	0	0	0	3

Sartobran® P Maxicaps® assembled with 300 mm tubing and KPC Connectors on inlet and outlet

Assembly: 12; Lot no.: 068118737

Particle Size [µm]	Particle Count per mL after 1 L Flush	Particle Count per mL after 5 L Flush	Particle Count per mL after 10 L Flush	Limits According to USP
≥ 10	0	0	0	25
≥ 25	0	0	0	3

Conclusion:
The tables show that for standard Sartobran® Midicaps® and Maxicaps® as well as for assembled Sartobran® P Maxicaps® and Midicaps® the requirements of the current USP for particle release are met in the very first liter of rinse volume. Accordingly standard and assembled Sartobran® P Maxicaps® and Midicaps® do not have to be rinsed prior to being able to produce a filtrate that conforms to the current USP for particle content. Thereby comparability between standard and assembled Sartobran® P Maxicaps® and Midicaps® for particle release has been demonstrated.

2.2 Extractable Substances Testing According to the Current USP

2.2.1 Determination of pH Values and Conductivity of the Filtrate

Test description
The filter capsules | assemblies were flushed with Water for Injection and samples were taken after 1, 5 and 10 L flush volumes. Conductivity and pH value of the samples were measured using appropriate calibrated pH meters and conductivity meters according to the USP regulations.

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 current USP is:

pH Value	Maximum Allowable Conductivity [µS/cm]
5.0	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

Standard Sartobran® P Midicaps®

A.) Results for pH

Blank: pH 5.8

Assembly	Lot No.	pH after 1 L Flush Volume	pH after 5 L Flush Volume	pH after 10 L Flush Volume
1	50203479	5.6	5.7	5.7
2	50203694	5.5	5.7	5.6
3	50203899	5.3	5.7	5.7

B.) Results for conductivity

Blank: 0.85 µS/cm

Assembly	Lot No.	Conductivity after 1 L Flush Volume [µS/cm]	Conductivity after 5 L Flush Volume [µS/cm]	Conductivity after 10 L Flush Volume [µS/cm]
1	50203479	0.97	0.98	0.94
2	50203694	0.93	0.98	0.98
3	50203899	0.92	0.97	0.89

Sartobran® P Midicaps® assembled with 300 mm tubing and 3 different connectors on inlet and outlet

A.) Results for pH

Blank: pH 5.9

Assembly	Lot No.	Connector Type	pH after 1 L Flush Volume	pH after 5 L Flush Volume	pH after 10 L Flush Volume
4	50204483	MPX	5.8	5.8	5.8
5	50204861	Opta®	5.6	5.7	5.8
6	50205156	KPC	5.7	5.8	5.8

B.) Results for conductivity

Blank: 0.95 µS/cm

Assembly	Lot No.	Connector Type	Conductivity after 1 L Flush Volume [µS/cm]	Conductivity after 5 L Flush Volume [µS/cm]	Conductivity after 10 L Flush Volume [µS/cm]
4	50204483	MPX	0.98	0.99	0.97
5	50204861	Opta®	1.01	0.91	0.92
6	50205156	KPC	0.97	0.92	0.93

Conclusion:
The tables show that for standard Sartobran® Midicaps® as well as for assembled Sartobran® P Midicaps® the requirements of the current USP for pH and conductivity are met in the very first liter of rinse volume. Accordingly standard and assembled Sartobran® P Midicaps® do not have to be rinsed prior to being able to produce a filtrate that conforms to the current USP for pH and conductivity. Thereby comparability between standard and assembled Midicaps® for pH and conductivity has been demonstrated.

Standard Sartobran® P Maxicaps®

A.) Results for pH

Blank: pH 5.8

Assembly	Lot No.	pH after 1 L Flush Volume	pH after 5 L Flush Volume	pH after 10 L Flush Volume
7	018118738	4.7	5.5	5.7
8	028118737	4.8	5.5	5.7
9	038118737	4.7	5.4	5.6

B.) Results for conductivity

Blank: 1.0 µS/cm

Assembly	Lot No.	Conductivity after 1 L Flush Volume [µS/cm]	Conductivity after 5 L Flush Volume [µS/cm]	Conductivity after 10 L Flush Volume [µS/cm]
7	018118738	9.80	1.67	1.00
8	028118737	8.30	1.51	1.09
9	038118737	10.91	1.99	1.14

Sartobran® P Maxicaps® connected with 300 mm tubing and 3 different connectors on inlet and outlet

A.) Results for pH

Blank: pH 5.8

Assembly	Lot No.	Connector Type	pH after 1 L Flush Volume	pH after 5 L Flush Volume	pH after 10 L Flush Volume
10	048118737	MPX	4.9	5.5	5.7
11	058118737	Opta®	5	5.5	5.7
12	068118737	KPC	4.9	5.5	5.8

B.) Results for conductivity

Blank: 1.0 µS/cm

Assembly	Lot No.	Connector Type	Conductivity after 1 L Flush Volume [µS/cm]	Conductivity after 5 L Flush Volume [µS/cm]	Conductivity after 10 L Flush Volume [µS/cm]
10	048118737	MPX	6.87	1.36	1.04
11	058118737	Opta®	4.70	1.61	1.26
12	068118737	KPC	6.27	1.10	0.97

Conclusion:
The tables show that for standard Sartobran® Maxicaps® as well as for assembled Sartobran® P Maxicaps® the requirements of the current USP for pH and conductivity are met after 5 L of rinse volume. Accordingly standard and assembled Sartobran® P Maxicaps® have to be rinsed with 5 L flush volume prior to being able to produce a filtrate that conforms to the current USP for pH and conductivity. Thereby comparability between standard and assembled Maxicaps® for pH and conductivity has been demonstrated.

2.2.2 Determination of Oxidizable Substances

Test description
The filter capsules | assemblies were flushed with Water for Injection, samples were taken after 1, 5 and 10 L flush volumes. As described in the current USP to the 100 mL samples 10 mL of 2 N sulfuric acid were added and heated to boiling. Then 0.2 mL of 0.1 N potassium permanganate were added and the solution was boiled for 5 minutes. If a precipitate forms, it is cooled to room temperature. If the precipitate remains its color after cooling to room temperature, the test sample and respectively the tested filter element meets the USP specifications for oxidizable substances.

Standard Sartobran® P Midicaps®

Assembly	Lot No.	After 1 L Flush Volume	After 5 L Flush Volume	After 10 L Flush Volume
1	50203479	passed	passed	passed
2	50203694	passed	passed	passed
3	50203899	passed	passed	passed

Sartobran® P Midicaps® assembled with 300 mm tubing and 3 different connectors on inlet and outlet

Assembly	Lot No.	Connector Type	After 1 L Flush Volume	After 5 L Flush Volume	After 10 L Flush Volume
4	50204483	MPX	passed	passed	passed
5	50204861	Opta®	passed	passed	passed
6	50205156	KPC	passed	passed	passed

Conclusion:
The tables show that for standard Sartobran® Midicaps® as well as for assembled Sartobran® P Midicaps® the requirements of the current USP for oxidizable substances are met in the very first liter of rinse volume. Accordingly standard and assembled Sartobran® P Midicaps® have not to be rinsed prior to being able to produce a filtrate that conforms to the current USP for oxidizable substances. Thereby comparability between standard and assembled Midicaps® for oxidizable substances has been demonstrated.

Standard Sartobran® P Maxicaps®

Assembly	Lot No.	After 1 L Flush Volume	After 5 L Flush Volume	After 10 L Flush Volume
7	018118738	not passed	passed	passed
8	028118737	not passed	passed	passed
9	038118737	not passed	passed	passed

Sartobran® P Maxicaps® with 300 mm tubing and 3 different connectors on inlet and outlet

Assembly	Lot No.	Connector Type	After 1 L Flush Volume	After 5 L Flush Volume	After 10 L Flush Volume
10	048118737	MPX	passed	passed	passed
11	058118737	Opta®	not passed	passed	passed
12	068118737	KPC	not passed	passed	passed

Conclusion:
The tables show that for standard Sartobran® Maxicaps® as well as for assembled Sartobran® P Maxicaps® the requirements of the current USP for oxidizable substances are met after 5 L of rinse volume. Accordingly standard and assembled Sartobran® P Maxicaps® have to be rinsed with 5 L flush volume prior to being able to produce a filtrate that conforms to the current USP for oxidizable substances. Thereby comparability between standard and assembled Maxicaps® for oxidizable substances has been demonstrated.

2.2.3 Determination of Residue on Evaporation

Test description
The filter capsules | assemblies were flushed with Water for Injection, samples were taken after 1, 5 and 10 L flush volumes. As described in the European Pharmacopoeia the samples where evaporated to dryness on a water-bath and dried in an oven at 100–105 °C. According to the European Pharmacopia for sterilised water for injections the test is passed if the concentration in the sample is < 3 mg/100 mL.

Standard Sartobran® P Midicaps®

Assembly	Lot No.	After 1 L Flush Volume	After 5 L Flush Volume	After 10 L Flush Volume
1	50203479	passed	passed	passed
2	50203694	passed	passed	passed
3	50203899	passed	passed	passed

Sartobran® P Midicaps® assembled with 300 mm tubing and 3 different connectors on inlet and outlet

Assembly	Lot No.	Connector Type	After 1 L Flush Volume	After 5 L Flush Volume	After 10 L Flush Volume
4	50204483	MPX	passed	passed	passed
5	50204861	Opta®	passed	passed	passed
6	50205156	KPC	passed	passed	passed

Standard Sartobran® P Maxicaps®

Assembly	Lot No.	After 1 L Flush Volume	After 5 L Flush Volume	After 10 L Flush Volume
7	018118738	passed	passed	passed
8	028118737	passed	passed	passed
9	038118737	passed	passed	passed

Sartobran® P Maxicaps® assembled with 300 mm tubing and 3 different connectors on inlet and outlet

Assembly	Lot No.	Connector Type	After 1 L Flush Volume	After 5 L Flush Volume	After 10 L Flush Volume
10	048118737	MPX	passed	passed	passed
11	058118737	Opta®	passed	passed	passed
12	068118737	KPC	passed	passed	passed

Conclusion:
The tables show that for standard Sartobran® Maxicaps® and Midicaps® as well as for assembled Sartobran® P Maxicaps® and Midicaps® the requirements of the current USP for NVR are met in the very first liter of rinse volume. Accordingly standard and assembled Sartobran® P Maxicaps® and Midicaps® have not to be rinsed prior to being able to produce a filtrate that conforms to the current USP for NVR content. Thereby comparability between standard and assembled Midicaps® NVR release has been demonstrated.

2.2.4 Determination of Chloride, Sulfate, Nitrate, Ammonium and Calcium

Standard Sartobran® P Maxicaps®

Test description for chloride determination
The filter capsules | assemblies were flushed with Water for Injection, samples were taken after 1, 5 and 10 L flush volumes. The test is passed if the chloride concentration in the sample is < 0.5 ppm.

Test description for sulfate determination
The filter capsules | assemblies were flushed with Water for Injection, samples were taken after 1, 5 and 10 L flush volumes. The test is passed if no sulfate could be detected in the sample.

Test description for nitrate determination
The filter capsules | assemblies were flushed with Water for Injection, samples were taken after 1, 5 and 10 L flush volumes. The test is passed if the nirate concentration in the sample is < 0.2 ppm.

Test description for ammonium determination
The filter capsules | assemblies were flushed with Water for Injection, samples were taken after 1, 5 and 10 L flush volumes. The test is passed if the ammonium concentration in the sample is < 0.2 ppm.

Test description for calcium determination
The filter capsules | assemblies were flushed with Water for Injection, samples were taken after 1, 5 and 10 L flush volumes. The test is passed if no calcium could be detected in the sample.

Standard Sartobran® P Midicaps®

Chloride

Assembly	Lot No.	After 1 L Flush Volume	After 5 L Flush Volume	After 10 L Flush Volume
1	50203479	passed	passed	passed
2	50203694	passed	passed	passed
3	50203899	passed	passed	passed

Sulfate

Assembly	Lot No.	After 1 L Flush Volume	After 5 L Flush Volume	After 10 L Flush Volume
1	50203479	passed	passed	passed
2	50203694	passed	passed	passed
3	50203899	passed	passed	passed

Nitrate

Assembly	Lot No.	After 1 L Flush Volume	After 5 L Flush Volume	After 10 L Flush Volume
1	50203479	passed	passed	passed
2	50203694	passed	passed	passed
3	50203899	passed	passed	passed

Ammonium

Assembly	Lot No.	After 1 L Flush Volume	After 5 L Flush Volume	After 10 L Flush Volume
1	50203479	passed	passed	passed
2	50203694	passed	passed	passed
3	50203899	passed	passed	passed

Calcium

Assembly	Lot No.	After 1 L Flush Volume	After 5 L Flush Volume	After 10 L Flush Volume
1	50203479	passed	passed	passed
2	50203694	passed	passed	passed
3	50203899	passed	passed	passed

Sartobran® P Maxicaps® assembled with 300 mm tubing and 3 different connectors on inlet and outlet

Chloride

Assembly	Lot No.	Connector Type	After 1 L Flush Volume	After 5 L Flush Volume	After 10 L Flush Volume
4	50204483	MPX	passed	passed	passed
5	50204861	Opta®	passed	passed	passed
6	50205156	KPC	passed	passed	passed

Sulfate

Assembly	Lot No.	Connector Type	After 1 L Flush Volume	After 5 L Flush Volume	After 10 L Flush Volume
4	50204483	MPX	passed	passed	passed
5	50204861	Opta®	passed	passed	passed
6	50205156	KPC	passed	passed	passed

Nitrate

Assembly	Lot No.	Connector Type	After 1 L Flush Volume	After 5 L Flush Volume	After 10 L Flush Volume
4	50204483	MPX	passed	passed	passed
5	50204861	Opta®	passed	passed	passed
6	50205156	KPC	passed	passed	passed

Ammonium

Assembly	Lot No.	Connector Type	After 1 L Flush Volume	After 5 L Flush Volume	After 10 L Flush Volume
4	50204483	MPX	passed	passed	passed
5	50204861	Opta®	passed	passed	passed
6	50205156	KPC	passed	passed	passed

Calcium

Assembly	Lot No.	Connector Type	After 1 L Flush Volume	After 5 L Flush Volume	After 10 L Flush Volume
4	50204483	MPX	passed	passed	passed
5	50204861	Opta®	passed	passed	passed
6	50205156	KPC	passed	passed	passed

Conclusion:
The tables show that for standard Sartobran® Maxicaps® and Midicaps® as well as for assembled Sartobran® P Maxicaps® and Midicaps® the requirements of the current USP for Chloride, Sulfate, Nitrate, Ammonium and Calcium are met in the very first liter of rinse volume. Accordingly standard and assembled Sartobran® P Maxicaps® and Midicaps® have not to be rinsed prior to being able to produce a filtrate that conforms to the current USP for Chloride, Sulfate, Nitrate, Ammonium and Calcium content. Thereby comparability between standard and assembled Midicaps® for Chloride, Sulfate, Nitrate, Ammonium and Calcium release has been demonstrated.

Standard Sartobran® P Maxicaps®

Chloride

Assembly	Lot No.	After 1 L Flush Volume	After 5 L Flush Volume	After 10 L Flush Volume
7	018118738	passed	passed	passed
8	028118737	passed	passed	passed
9	038118737	passed	passed	passed

Sulfate

Assembly	Lot No.	After 1 L Flush Volume	After 5 L Flush Volume	After 10 L Flush Volume
7	018118738	passed	passed	passed
8	028118737	passed	passed	passed
9	038118737	passed	passed	passed

Nitrate

Assembly	Lot No.	After 1 L Flush Volume	After 5 L Flush Volume	After 10 L Flush Volume
7	018118738	passed	passed	passed
8	028118737	passed	passed	passed
9	038118737	passed	passed	passed

Ammonium

Assembly	Lot No.	After 1 L Flush Volume	After 5 L Flush Volume	After 10 L Flush Volume
7	018118738	passed	passed	passed
8	028118737	passed	passed	passed
9	038118737	passed	passed	passed

Calcium

Assembly	Lot No.	After 1 L Flush Volume	After 5 L Flush Volume	After 10 L Flush Volume
7	018118738	passed	passed	passed
8	028118737	passed	passed	passed
9	038118737	passed	passed	passed

Sartobran® P Maxicaps® assembled with 300 mm tubing and 3 different connectors on inlet and outlet

Chloride

Assembly	Lot No.	Connector Type	After 1 L Flush Volume	After 5 L Flush Volume	After 10 L Flush Volume
10	048118737	MPX	passed	passed	passed
11	058118737	Opta®	passed	passed	passed
12	068118737	KPC	passed	passed	passed

Sulfate

Assembly	Lot No.	Connector Type	After 1 L Flush Volume	After 5 L Flush Volume	After 10 L Flush Volume
10	048118737	MPX	passed	passed	passed
11	058118737	Opta®	passed	passed	passed
12	068118737	KPC	passed	passed	passed

Nitrate

Assembly	Lot No.	Connector Type	After 1 L Flush Volume	After 5 L Flush Volume	After 10 L Flush Volume
10	048118737	MPX	passed	passed	passed
11	058118737	Opta®	passed	passed	passed
12	068118737	KPC	passed	passed	passed

Ammonium

Assembly	Lot No.	Connector Type	After 1 L Flush Volume	After 5 L Flush Volume	After 10 L Flush Volume
10	048118737	MPX	passed	passed	passed
11	058118737	Opta®	passed	passed	passed
12	068118737	KPC	passed	passed	passed

Calcium

Assembly	Lot No.	Connector Type	After 1 L Flush Volume	After 5 L Flush Volume	After 10 L Flush Volume
10	048118737	MPX	passed	passed	passed
11	058118737	Opta®	passed	passed	passed
12	068118737	KPC	passed	passed	passed

2.2.5 Total Organic Carbon (TOC)

Test Description
The test for TOC according to USP monograph is performed in dynamic extraction mode.

The samples are taken after 1, 5 and 10 liters flush volume. The test is passed if the sample has a value of ≤ 500 ppm of carbon.

A calibrated instrument is used and its suitability is periodically tested.

Standard Sartobran® P Midicaps®

Assembly	Lot No.	After 1 L Flush Volume	After 5 L Flush Volume	After 10 L Flush Volume
1	50203479	passed	passed	passed
2	50203694	passed	passed	passed
3	50203899	passed	passed	passed

Sartobran® P Midicaps® assembled with 300 mm tubing and 3 different connectors on inlet and outlet

Assembly	Lot No.	Connector Type	After 1 L Flush Volume	After 5 L Flush Volume	After 10 L Flush Volume
4	50204483	MPX	passed	passed	passed
5	50204861	Opta®	passed	passed	passed
6	50205156	KPC	passed	passed	passed

Conclusion:
The tables show that for standard Sartobran® Midicaps® as well as for assembled Sartobran® P Midicaps® the requirements of the current USP for TOC are met in the very first liter of rinse volume. Accordingly standard and assembled Sartobran® P Midicaps® have not to be rinsed prior to being able to produce a filtrate that conforms to the current USP for TOC. Thereby comparability between standard and assembled Midicaps® for TOC release has been demonstrated.

Standard Sartobran® P Maxicaps®

Assembly	Lot No.	After 1 L Flush Volume	After 5 L Flush Volume	After 10 L Flush Volume
7	018118738	not passed	not passed	passed
8	028118737	not passed	not passed	passed
9	038118737	not passed	not passed	passed

Sartobran® P Maxicaps® assembled with 300 mm tubing and 3 different connectors on inlet and outlet

Assembly	Lot No.	Connector Type	After 1 L Flush Volume	After 5 L Flush Volume	After 10 L Flush Volume
10	048118737	MPX	not passed	passed	passed
11	058118737	Opta®	not passed	not passed	passed
12	068118737	KPC	not passed	passed	passed

Conclusion:
The tables show that for standard Sartobran® Maxicaps® as well as for assembled Sartobran® P Maxicaps® the requirements of the current USP for TOC are met after 10 L of rinse volume. Accordingly standard and assembled Sartobran® P Maxicaps® have to be rinsed with 10 L flush volume prior to being able to produce a filtrate that conforms to the current USP for TOC. Thereby comparability between standard and assembled Maxicaps® for TOC has been demonstrated.

2.3 Integrity Test of the Filter Element

This test has been performed in order to demonstrate that the integrity of the assembled filter capsules is unaffected by the assembled components (connectors and tubing) after the sterilization process of the assembled Maxicaps® and Midicaps®.

For this purpose Sartobran® P Maxicaps® and Midicaps® as well as a Virosart® Max Midicaps have been assembled with tubing and connectors as specified under paragraph 1.2 and have been double wrapped into DuPont™ Tyvek® pouches and have subsequently been sterilized by autoclaving in a validated autoclaving procedure.

After sterilization the assembled Maxicaps® and Midicaps® have been taken out of the DuPont™ Tyvek® pouches. Connector and tubing have been removed from the filter elements. The filter elements have been wetted according to the directions for use of the respective filter elements and have been tested for integrity by a diffusion test as well as some by bubble point test.

Prior the filter integrity test all assemblies with metal ear clamps were autoclaved in DuPont™ Tyvek® pouches unpacked and used before for the water leak tight test.

Test result:

Sartobran® P Midicaps® assembled with 300 mm tubing and different connectors at inlet and outlet

Assembly	Lot No.	Connector Type	Test Pressure [bar | psi]	Max. allowed Diffusion Rate [mL/min]	Measured Diffusion Rate [mL/min]
4	50204483	MPX	2.5 | 36	5	3.9
5	50204861	Opta®	2.5 | 36	5	3.1
6	50205156	KPC	2.5 | 36	5	3.3

Sartobran® P Maxicaps® assembled with 300 mm tubing and 3 different connectors on inlet and outlet

Assembly	Lot No.	Connector Type	Test Pressure [bar | psi]	Max. allowed Diffusion Rate [mL/min]	Measured Diffusion Rate [mL/min]
10	048118737	MPX	2.5 | 36	45	21.1
11	058118737	Opta®	2.5 | 36	45	21.9
12	068118737	KPC	2.5 | 36	45	19.6

Assembly	Filter Capsule	Lot No.	Test Pressure [bar | psi]	Max. allowed Diffusion Rate [mL/min]	Measured Diffusion Rate [mL/min]	Minimum Bubble Point [bar | psig]	Measured Bubble Point [bar | psig]
FTS5002BN	5237307H2--OO	909011831	2.5 | 36	30	17.2	3.2 | 46.4	3.68 | 53.37
		909011831	2.5 | 36	30	16.4	3.2 | 46.4	3.63 | 52.65
		909011831	2.5 | 36	30	16.7	3.2 | 46.4	3.68 | 53.37
FTS5002BO*	5237307H1--BB	190003438	2.5 | 36	15	9.5	-	-
		190003438	2.5 | 36	15	10.2	-	-
		190003438	2.5|| 36	15	9.5	-	-
FTS5002BP	5237307H1--OO	190003583	2.5 | 36	15	9.6	3.2 | 46.4	3.83 | 55.55
		190003583	2.5 | 36	15	10.0	3.2 | 46.4	3.88 | 56.27
		190003583	2.5 | 36	15	10.2	3.2 | 46.4	3.78 | 54.82
FTS5002BR**	54A5358N9-OO	190003683	2 | 29	3	1.1	-	-
		190003683	2 | 29	3	1.0	-	-
		190003683	2 | 29	3	1.0	-	-

* Only diffusion test due to pressure limitation of the inlet connector
** Inlet tubing removed for filter IT test

Conclusion:
The test results clearly demonstrate that the integrity of the filter elements is unaffected by the assembled tubing and connectors after the sterilization process. Furthermore, it can be concluded that any leaks in the assembly, if any exist, are far below the maximum permissible diffusion rate of the filter elements.

2.4 Mechanical Stability of the Assemblies

2.4.1 Tube to Hose Barb Connections With Cable Ties

This test has been performed in order to determine the maximum operation pressure allowed during the filtration process of the Filter Transfer Sets.

For this purpose Filter Transfer Sets have been assembled as specified under paragraph 1.2 and have been double wrapped into DuPont™ Tyvek® pouches and have subsequently been sterilized by autoclaving in a validated autoclaving procedure.

After sterilization the assemblies have been taken out of the DuPont™ Tyvek® pouches. The outlet side of the respective assemblies has been closed by blind caps and the inlet of the assemblies has been pressurized for two hours at 2 bar|29 psi inlet pressure. The pressurized assemblies have been immersed in water and have been visually inspected for any leakages.

Test result:

Sartobran® P Midicaps® assembled with 300 mm tubing and different connectors at inlet and outlet

Assembly	Lot No.	Connector Type	Test Pressure [bar | psi]	Test Time [h]	Test Result
4	50204483	MPX	2.0 | 29	2	passed
5	50204861	Opta®	2.0 | 29	2	passed
6	50205156	KPC	2.0 | 29	2	passed

Sartobran® P Maxicaps® assembled with 300 mm tubing and different connectors at inlet and outlet

Assembly	Lot No.	Connector Type	Test Pressure [bar | psi]	Test Time [h]	Test Result
10	048118737	MPX	2.0 | 29	2	passed
11	058118737	Opta®	2.0 | 29	2	passed
12	068118737	KPC	2.0 | 29	2	passed

Conclusion:
The maximum allowed differential pressure during filtration with pre-assembled Maxicaps® and Midicaps® is set at 2 bar | 29 psi for 2 hours.

For integrity testing of the filter capsules the maximum allowed differential pressure is set according to the specifications given for Maxicaps® and Midicaps®.

2.4.2 Tube to Hose Barb Connections With Metal Ear Clamps

Pressure stability comparison of tube to hose barb conections, cable ties vs. metal ear clamps.

In order to increase the pressure stability of the tube to hose barb connections, metal ear clamps are used for almost all connections. The table below shows some examples of pressure stability increase for tube to hose barb connections using metal ear clamps instead of two cable ties. The samples used in this study were not autoclaved and not aged. Leakage tests with water were used as the measurement method.

Component	Tube [ID × OD]	Pressure Stability Increase [%]
Opta® SFT	Tuflux® SIL (½" × ¾")	50
MPX	Tuflux® SIL (½" × ¾")	20
MPX	Sani-Tech® STHT®-R (½" × ⅞")	38
Type O Filter Connector	Tuflux® SIL (½" × ¾")	50

The mechanical stability testing of the tube to hose barb connections with metal ear clamps was performed with water filled assemblies as this is the intended use of the product. Connection robustness towards compressed air was proven during the integrity test of the filter element by placing the Sartocheck® integrity test device on the inlet connector of the assemblies. The integrity test of the assembled filter capsules has been performed using the standard integrity test parameters and procedures of the integrated capsules.

Tube to hose barb connection test

Extensive tube to hose barb qualification tests have been performed in various studies. The following table shows an overview of tested tube to hose barb connections used within this product portfolio.

All connections are tested according to a standard Sartorius water leak test procedure at the maximum operation pressure plus 10 %. The test is passed if after the stabilisation time of 3 minutes and a test time of 5 minutes at maximum pressure plus 10 % no water drop is observed.

The maximum working pressure of the assembly is determined by lowest maximum working pressure from either connection, tube or component. The maximum operating pressures are printed on the product label and the Quality Assurance Certificate.

Test result:

¼" tube to hose barb connections

Component	Tube to Hose Barb Connection	Pharma-50 [¼" × 7/16"]	Tuflux® SIL [¼" × 7/16"]
Opta® SFT	Metal ear clamp	passed	passed
MPC	Metal ear clamp	passed	passed
AseptiQuik® S	Metal ear clamp	passed	passed
AseptiQuik® G	Metal ear clamp	passed	passed
Midisart® 2000	2 × cable tie	passed	passed
Maxicaps® valve	2 × cable tie	passed	passed

⅜" tube to hose barb connections

Component	Tube to Hose Barb Connection	Tuflux® SIL [⅜" × ⅝"]	Pharma-50 [⅜" × ⅝"]	Sani-Tech® STHT®-R [⅜" × ⅝"]
1.5" TC	Metal ear clamp	passed	passed	passed
Opta® SFT	Metal ear clamp	passed	passed	passed
MPC	Metal ear clamp	passed	passed	passed
STC II	Metal ear clamp	passed	passed	passed
KPC HT	Metal ear clamp	passed	passed	passed
AseptiQuik® G	Metal ear clamp	passed	passed	passed
Presto	Metal ear clamp	passed	passed	passed
Type O Filter Connector	Metal ear clamp	passed	passed	passed

½" tube to hose barb connections

Component	Tube to Hose Barb Connection	Tuflux® SIL [½" × ¾"]	Tuflux® SIL [½" × ⅞"]	Pharma-50 [½" × ¾"]	Pharma-80 [½" × ¾"]	Sani-Tech® STHT®-R [½" × ⅞"]
T-union (600 series)	Metal ear clamp	passed	passed	passed	passed	passed
1.5" TC	Metal ear clamp	passed	passed	passed	passed	passed
Opta® SFT	Metal ear clamp	passed	passed	passed	passed	passed
MPX	Metal ear clamp	passed	passed	passed	passed	passed
STC II	Metal ear clamp	passed	passed	passed	passed	passed
KPC HT	Metal ear clamp	passed	passed	passed	passed	passed
AseptiQuik® G	Metal ear clamp	passed	passed	passed	passed	passed
Presto	Metal ear clamp	passed	passed	passed	passed	passed
Type O Filter Connector	Metal ear clamp	passed	passed	passed	passed	passed

¾" tube to hose barb connections

Component	Tube to Hose Barb Connection	Tuflux® SIL (¾" × 1⅛")	Pharma-50 [¾" × ⅞"]	Sani-Tech® STHT®-R [¾" × ⅞"]
Opta® SFT	Metal ear clamp	passed	passed	passed
MPU	Metal ear clamp	passed	passed	passed
AseptiQuik® G	Metal ear clamp	passed	passed	passed
Type B Filter Connector	Metal ear clamp	passed	passed	passed

Water leak test of assemblies with metal ear clamps
The connection qualification tests within this study were performed with water inside the representative assemblies, as it is the intended use of the product.

The test was passed if during the test time of 3 minutes and test pressure of 2.2 bar respectively 3.3 bar (depending on the used components) no water drops were observed.

Test results:

Assembly	Lot No.	Test Pressure [bar | psi]	Test Result
FTS5002BN	909011813	2.2 | 32	passed
FTS5002BO	190003483	3.3 | 48	passed
FTS5002BP	190003583	3.3 | 48	passed
FTS5002BR	190003683	2.2 | 32	passed

Conclusion:
The test results demonstrate the robustness of the connections and the water tightness even at high pressure.

2.5 Endotoxin Testing

Assembled Sartobran® P Maxicaps® and Midicaps® as specified under paragraph 1.2 have been tested that the effluent released by these assemblies contains less than 0.25 EU/mL to meet the requirements of EP and USP monographs for "Sterile Water for Injection".

Test results:

Sartobran® P Midicaps® assembled with 300 mm tubing and different connectors at inlet and outlet

Assembly	Lot No.	Connector Type	LAL Test Result
4	50204483	MPX	passed
5	50204861	Opta®	passed
6	50205156	KPC	passed

Sartobran® P Maxicaps® assembled with 300 mm tubing and different connectors at inlet and outlet

Assembly	Lot No.	Connector Type	LAL Test Result
10	048118737	MPX	passed
11	058118737	Opta®	passed
12	068118737	KPC	passed

Conclusion:
The test results verify that assembled Sartobran® P Maxicaps® and Midicaps® comply with the limits of the current USP for endotoxin release.

3. Sterilization By Moist Heat

A sterilization validation study was performed in order to demonstrate the effectiveness of the steam sterilization method applied for assembled Maxicaps® and Midicaps®. This validation study follows the current standard DIN EN ISO 17665-1 (2006-11) for sterilization of health care product with moist heat.

Autoclaves
The autoclaves used for this study are located in the controlled clean room environment of the standard filter element manufacturing area at Sartorius and are also used for the routine sterilization of standard Maxicaps® and Midicaps® as well as for assembled Maxicaps® and Midicaps®. The equipment corresponds with the requirements of the standard DIN EN 285 for large steam sterilizers and is subject to the routine Sartorius maintenance and re-calibration program.

A daily control check of the autoclaves with a Bowie-Dick-Simulation-Test is performed.

The water to produce the steam for the autoclaves is monitored for chemical and microbiological parameters and the steam itself is checked for non-condensable gasses.

Challenging devices for the validation study
For the validation study specific load configurations are defined, following a worst-case-matrix approach to cover the complete product portfolio of assemblies.
The matrix considers the following criteria:

- Type of membrane
- Size of the capsule
- In- and outlet connector of the capsule
- Length of the tubing
- Connectors
- Primary packaging

Corresponding assembled Maxicaps® and Midicaps® are equipped with additional data loggers for temperature mapping and with bio-indicators (spore strips with ≥ 10^6 CFU of *Geobacillus Stearothemophilus*). These products are used as challenging devices in the validation study. The manufacture of these devices is done in the controlled clean room conditions of the standard manufacturing area for filter elements.

Autoclaving cycles
Due to the product properties (porous membranes, hollow body) the defined and applied "over kill" sterilization cycle consists of the following phases:

- Fractioned pre-vacuum for air removal
- Dwell time for sterilizing temperature
- Fractioned post-vacuum for drying

Parameter control
The following parameters are verified in each autoclaving cycle of the validation study:

- The temporal temperature gradient of every single challenge device is measured and documented.
- The temporal pressure gradient in the autoclave chamber is measured and documented.
- The steam penetration is checked by using a Hollow A-PCD (EN 867-5)
- The exposure time for the sterilizing temperature is determined.
- The spore stripes are evaluated.

The following parameters during routine sterilization of every lot of assembled Maxicaps® and Midicaps® are controlled, measured and documented:

- Temperature
- Pressure
- Dwell time
- Steam penetration

Result of the validation study
The evaluation of the physical and microbiological data demonstrates compliance with the requirements of the standard EN ISO 17665.

Consequently the defined autoclaving cycle is valid for sterilizing of assembled Maxicaps® and Midicaps®.

4. Additional Information

4.1 Biocompatibility

All components in fluid contact used for manufacturing of Filter Transfer Sets

- Filter elements
- Tubing
- Connectors

are biosafe and meet or exceed the requirements of the current USP Biological Reactivity tests <88> for plastics Class VI (Systemic Injection, Intracutaneous and Implantation tests).

Remaining product contact materials have passed USP <87> as a minimum requirement.

Corresponding certificates can be seen from the Validation Guides of the components provided by the individual suppliers of the components.

4.2 Extractable Profile Testing

Extractable profile testing has been carried out for all components in fluid contact for assembled Maxicaps® and Midicaps®.

Corresponding extractable profile information can be obtained from the suppliers of the individual components.

4.3 Packaging

- The seal seam of pouches have been validated based on EN ISO 11607.
- The proof of packaging concepts has been executed by performing transportation simulation tests based on ASTM D7386, enhanced by pre-conditioning at a tropical climate (ASTM D4332) and box compression test according to DIN 55441-1. After transport simulation tests, functional tests of products were performed and the integrity of the sterile barrier has been checked.

5. Summary

Since single use equipment is increasingly used in biopharmaceutical manufacturing processes, a concept was developed to integrate non gamma irradiatable filters into single use processing solutions. For this purpose non-gamma irradiatable filters are assembled with tubing and connectors, sterilized by autoclaving which allows integration into any single use processing solution.

It was the purpose of this study to demonstrate that Maxicaps® and Midicaps® assembled with defined tubing and connectors still comply with the specifications for:

- Particle Release
- pH and Conductivity
- Oxidizable Substances
- Non-volatile Residue
- Chloride, Sulfate, Nitrate, Ammonium and Calcium
- Total Organic Carbon
- Filter Integrity
- Endotoxin Release

compared to standard Maxicaps® and Midicaps®.

The results of the study verify that the parameters set in the corresponding Validation Guides of the respective product groups remain valid for assembled Maxicaps® and Midicaps®.

Furthermore it could be demonstrated, that the integrity of the filter elements is unaffected by the assembled components after sterilization.

It also could be demonstrated that the tube to hose barb connections with metal ear clamps fixations, for all component combinations used in the product portfolio of the Sterile Filter Transfer Sets, are robust and leak tight within their specifications.

Germany
Sartorius Stedim Biotech GmbH
August-Spindler-Strasse 11
37079 Goettingen
Phone +49 551 308 0

USA
Sartorius Stedim North America Inc.
565 Johnson Avenue
Bohemia NY 11716
Phone +1 800 368 7178

For further contacts, visit
www.sartorius.com

DIR No.: 2630981-000-00
Status 12 | 2020