sartorius stedim biotech

Validation Guide
Sartolab® P20



Table of Contents

1.	**Introduction**	**4**
2.	**Quality and Its Assurance**	**5**
2.1	Quality Assurance from Sartorius Stedim Biotech	5
2.2	Prevention of Contamination	5
2.3	Complete Traceability	5
2.4	DIN EN ISO Certificates	5
2.5	Test Methods for the Quality Assurance of Sartorius Stedim Sartolab® P20 and Sartolab® P20 Plus Filters	5
3.	**Technical Specifications**	**6**
3.1	Product Description	6
3.2	Order Number Overview	6
3.3	Specifications	7
3.4	Packaging and Storage Conditions	9
3.5	Lot Release Criteria	9
4.	**Integrity Test Limits**	**10**
4.1	Correlation of Bubble Point Values with the HIMA|ASTM Bacteria Challenge Tests	10
4.2	Results	11
5.	**Sterilization Validation**	**15**
5.1	Presterilization Bioburden	15
5.2	Ethylene Oxide Gas Sterilization	16
6.	**Physical Tests**	**17**
6.1	Burst Pressure	17
6.2	Pressure Hold Test	18
6.3	Flow Rate Performance Test	19
6.4	Air Flow Rate Performance Test of the Vent Filter	20
6.5	PTFE Leakage Test	21
7.	**Chemical Compatibility – Sartolab® P20 and Sartolab® P20 Plus Filters**	**22**
8.	**Analytical Tests**	**24**
8.1	Endotoxin Test	24
8.2	Biocompatibility Test	25
8.3	Extractables Analysis	26
8.4	Visual Inspections	27

1. Introduction

Sartolab® P20 is manufactured by Sartorius Stedim Biotech in accordance with the applicable Current Good Manufacturing Practice Standards and facility whose Quality Management System is certified for compliance with the DIN EN ISO 9001 Quality System Standard and DIN EN ISO 13485.

The desired quality of the final product can only be obtained when the entire production process is adequately safeguarded against contamination.

When sterilizing grade filters are used, the aseptic process must be validated, taking all aspects of the product and the production process into consideration. Sartolab® P20 and Sartolab® P20 Plus pressure filter units reliably fulfill the product-specific requirements which have to be imposed on a sterilizing grade filter for liquid filtration.

We have compiled this validation guide so users of Sartolab® P20 and Sartolab® P20 Plus pressure filters can plan, implement and document their own validation procedures.

2. Quality and Its Assurance

2.1 Quality Assurance from Sartorius Stedim Biotech

Consistent high quality of Sartolab® P20 and Sartolab® P20 Plus filters is assured by careful selection of the raw materials, well planned and validated production technologies and an exceptionally efficient Quality Assurance Department, all of which results in high batch-to-batch reproducibility. The test procedures used are based both on external standard methods, such as the USP, EP and ASTM, and on in-house methods, which are the result of Sartorius Stedim's experience over the past 60 years.

For quality assurance, all materials are selected carefully in accordance with current regulations, such as the FDA CFR's, in-house guidelines and the specifications of our Research and Development Department, including the terms of delivery and acceptance of our supply chain management. Documentation begins with the inspection of the incoming raw materials including in-process materials, molded parts and sealing materials, etc., for manufacture.

Sartolab® P20 and Sartolab® P20 Plus are completely manufactured under clean-room conditions. Compliance with applicable requirements (clean-room conditions, gowning and employee hygiene, etc.) which is monitored by documented in-process controls, ensures optimal quality control in standard operating procedures for production. Finished Sartolab® P20 and Sartolab® P20 Plus filters undergo final product quality control. This involves 100 % non-destructive testing of each individual product. Other individual tests are carried out on a representative number of samples. A lot is not released until all in-process and final quality control data are available and meet the required specifications.

2.2 Prevention of Contamination

Sartolab® P20 and Sartolab® P20 Plus filters are individually sealed in PE bags with a DuPont™ Tyvek® window under clean-room conditions. Afterwards the filters are sterilized by EO gas to reliably prevent microbial growth.

2.3 Complete Traceability

The product name, order number, lot number, consecutive number, pore size and expiration date are printed on the housing of each filter.

Furthermore, the quantity inside the package and the barcodes for the order number and the lot number are printed on the label of the box. The traceable lot number allows convenient retrieval of all data complied on the materials used, production steps and QC tests.

2.4 DIN EN ISO Certificates

The complete Quality System Certificates are continuously updated and can be downloaded from our website: www.sartorius-stedim.com/qm-certificates

2.5 Test Methods for the Quality Assurance of Sartorius Stedim Sartolab® P20 and Sartolab® P20 Plus Filters

Lot-related Tests

Non-destructive Tests 100 % Individual Testing

- Integrity Leakage Test

Destructive Tests on Randomly Sampled Sartolab® P20 and Sartolab® P20 Plus

- Bacteria Challenge Test
- Bubble Point Test
- Sterility
- Burst Pressure
- Pressure Hold Test
- Flow Rate Performance
- Endotoxin Test
- Visual Inspections

Testing Conducted for the Validation of Sartolab® P20 and Sartolab® P20 Plus

- Bacteria Challenge Test
- Bubble Point Test
- Correlation of Bubble Point Values with the HIMA|ASTM Bacteria Challenge Tests
- Validation of Ethylene Oxide Gas Sterilization
- Burst Pressure
- Pressure Hold Test
- Flow Rate Performance
- Endotoxin Test
- USP Biological Tests
- Visual Inspections
- Bioburden Test
- Sterility
- Extractables
- Air Flow Rate Performance
- Pressure Hold Test of Vent Filter

3. Technical Specifications

3.1 Product Description

Sartolab® P20 is a ready-to-use pressure filtration unit for sterile filtration of media and aqueous solutions in batches ranging from 100 ml to 5 liters. For media that contain sera and difficult-to-filter solutions, a Sartolab® P20 Plus unit with an incorporated pre-filter is also available.

The single–use products consist of a hydrophilic surfactant-free cellulose acetate (SFCA) or polyethersulfone (PES) membrane filter sealed in polycarbonate housing. They do not contain endotoxins and they are non-toxic. Sartolab® P20 Plus contains an additional 100 % binder-free glass fiber pre-filter on top of the cellulose acetate membrane. Vent ports on the inlet side of the housing are protected against liquid passage by a hydrophobic PTFE membrane. The units are available with either a hose nipple or a luer lock inlet, and each type has a filling bell on the outlet side. A typical application is sterile filtration of protein solutions, tissue culture additives, buffer and water.

Lot-related certificates are available on request.

3.2 Order Number Overview

Table 3.1 - Order Number Overview

Order No.	Product Name	Membrane Filter	Venting Filter PTFE	Pore Size [µm]	Connectors Female Luer Lock	Stepped Hose Nipple
18052-D	Sartolab® P20	SFCA	+	0.2	–	Inlet and Outlet
18053-D	Sartolab® P20	SFCA	+	0.2	Inlet	Outlet
18056-D	Sartolab® P20 Plus	SFCA + GF	+	0.2	–	Inlet and Outlet
18058-D	Sartolab® P20 Plus	SFCA + GF	+	0.2	Inlet	Outlet
18068-D	Sartolab® P20 Plus	PES + GF	+	0.2	Inlet	Outlet
18075-D	Sartolab® P20	PES	–	0.2	Inlet	Outlet

SFCA – Surfactant-free Cellulose Acetate
PES – Polyethersulfone
PTFE – Polytetrafluoroethylene
GF – Glass Fiber

3.3 Specifications

Table 3.2 – Specifications for Sartolab® P20 and Sartolab® P20 Plus Units with SFCA Membrane

Properties	Description Sartolab® P20 18052 18053	Sartolab® P20 Plus 18056 18058
Filter material	SFCA, type 12587, 0.2 µm pore size and PTFE	SFCA, type 12587 0.2 µm pore size plus GF, 100 % free of binding agents and PTFE
Housing material	Polycarbonate	Polycarbonate
Color code	Transparent	Transparent
Filter diameter	64 mm	64 mm
Connector inlet Connector outlet	Female luer lock or stepped hose nipple with 6-12 mm outer diameter (Table 3.1) Hose nipple	Female luer lock or stepped hose nipple with 6–12 mm outer diameter (Table 3.1) Hose nipple
Filling bell	Available	Available
Filtration area	20 cm^2	20 cm^2
Hold-up volume before bubble point	1 ml	Approx 1.5 ml
Housing burst pressure	> 5 bar|72.5 psi	> 5 bar|72.5 psi
Bubble point	≥ 3.2 bar|46.4 psi	≥ 3.2 bar|46.4 psi
Max. recommended inlet pressure	3 bar|43.5 psi	3 bar|43.5 psi
Flow rate for water	≥ 250 ml/min at Δp = 1 bar|14.5 psi	≥ 250 ml/min at Δp = 1 bar|14.5 psi
Filtration range	100 ml–max. 5 l	100 ml–max. 10 l
pH-range	4–8	4–8
Non-specific protein adsorption	No loss of protein detectable (filtration of γ globulin, method acc. to Bradford)	< 80 µg/cm^2 (filtration of γ globulin, method acc. to Bradford)
Sterilization	EO sterilization	EO sterilization
Biosafety	Class VI Plastics Test	Class VI Plastics Test
Operating instructions	Directions for use included in each box	Directions for use included in each box

Table 3.3 – Specifications for Sartolab® P20 and Sartolab® P20 Plus Units with PES Membrane

Properties	Description Sartolab® P20 Plus 18068	Sartolab® P20 18075
Filter material	PES, type 15407 MI, 0.2 µm pore size plus GF, 100 % free of binding agents and PTFE	PES, type 15407 MI, 0.2 µm pore size
Housing material	Polycarbonate	Polycarbonate
Color code	Transparent	Transparent
Filter diameter	64 mm	64 mm
Connector inlet: Connector outlet:	Female luer lock or stepped hose nipple with 6–12 mm outer diameter (Table 3.1) Hose nipple	Female luer lock or stepped hose nipple with 6–12 mm outer diameter (Table 3.1) Hose nipple
Filling bell	Available	Available
Filtration area	20 cm^2	20 cm^2
Hold-up volume before bubble point	Approx 1.5 ml	1 ml
Housing burst pressure	> 5 bar|72.5 psi	> 5 bar|72.5 psi
Bubble point	≥ 3.2 bar|46.4 psi	≥ 3.2 bar|46.4 psi
Max. recommended inlet pressure	3 bar|43.5 psi	3 bar|43.5 psi
Flow rate for water	400 ml/min at Δp = 1 bar|14.5 psi	400 ml/min at Δp = 1 bar|14.5 psi
Filtration range	100 ml–max. 5 l	100 ml–max. 10 l
pH range	1–8	1–8
Non-specific protein adsorption	< 80 µg/cm^2 (filtration of γ globulin, method acc. to Bradford)	No loss of protein detectable (filtration of γ globulin, method acc. to Bradford)
Sterilization	EO sterilization	EO sterilization
Biosafety	Class VI Plastics Test	Class VI Plastics Test
Operating instructions	Directions for use included in each box	Directions for use included in each box

3.4 Packaging and Storage Conditions

Label on the Outer Box

- Product name
- Product description
- Order number
- Pore size
- Sterilization method
- Expiration date
- Product lot number
- Quantity per package and the barcodes for order number and lot number
- Expiration date: three years (36 months) from date of manufacture

Storage Conditions

- Store in a closed, dry area, in the original package
- Temperature: 5 °C–40 °C, frost-free (for max. 7 d at -10 °C – +50 °C))
- Humidity: 10 %–75 %
- No direct exposure to sunlight
- No direct contact with moisture
- Prevent any mechanical influence or damage
- Products with damaged packaging must be discarded

Warning

- Do not use product if package is damaged.
- Do not resterilize or re-use the unit.
- Do not use this product to filter fluids at temperature above 50 °C.

3.5 Lot Release Criteria

Table 3.4 - Lot Release Criteria

Sterility	Sterilization process has been approved and certified
Endotoxin test	< 0.06 EU/ml, meets current USP bacterial endotoxins test for devices
Integrity leakage test	100 % tested during manufacture
Bacteria challenge test (Sterile Filtration Capability)	Retention of 10^7 bacteria/ml cm^2 of Brevundimonas diminuta
Bubble point test	≥ 3.2 bar | 46.4 psi
Water flow rate performance at 1.0 bar|14.5 psi	18052, 18053, 18056, 18058 with SFCA membrane: > 250 ml/min 18068, 18075 with PES membrane: > 400 ml/min
Pressure hold test [bar]	18052, 18053, 18056, 18058 with SFCA membrane: no air passage at 2 bar|29 psi 18068, 18075 with PES membrane: no air passages at 2 bar|29 psi
Burst pressure testing of the housing	≥ 5 bar|72.50 psi
Visual inspection	No particles > 0.5 mm^2, 1 particle < 0.5 mm^2
PTFE leakage test	No leakage at > 2 bar|29 psi

4. Integrity Test Limits

4.1 Correlation of Bubble Point Values with the HIMA|ASTM Bacteria Challenge Tests

Background for the Determination of Integrity Test Values
Establishing a correlation between bacterial retention of a sterilizing grade filter, such as a Sartolab® P20 filter, and a non-destructive integrity test is decisive for the reliability of a sterile filtration procedure. According to the Health Industry Manufacturers Association (HIMA) Guidelines for "Microbiological Evaluation of Filters for Sterilizing Liquids" Doc. No. 3, Vol. 4, 1982, the ASTM F 838-83 Guideline and the FDA "Guideline on Sterile Drug Products Produced by Aseptic Processing", June 1987, a sterilizing grade filter should produce a sterile effluent when challenged with a minimum concentration of 10^7 Brevundimonas diminuta organisms/cm^2 of filter area.

Since the bacteria challenge test is a destructive method, it must be correlated with a non-destructive a test series.

The FDA "Guidelines on Sterile Drug Products Produced by Aseptic Processing", June 1987, states: "After a filtration process is properly validated for a given product, process and filter, it is important to assure that identical filter replacements (membrane or cartridge) used in production runs will perform in the same manner. One way of achieving this is to correlate filter performance data with filter integrity testing data. Normally, integrity testing of the filter is performed after the filter unit is assembled prior to use. More importantly, however, such testing should be conducted after the filter is used in order to detect any filter leaks or perforations that may have occurred during filtration."

Method
Sartolab® P20 and Sartolab® P20 Plus filters from different production lots were tested according to a bacteria challenge test in accordance with the HIMA Document No. 3, Vol. 4 (April 1982) "Microbiological Evaluation of Filters for Sterilizing Liquids", the ASTM F 838-83 Guideline and DIN 58356, Part 1. A bacterial suspension is filtered through each Sartolab® P20 and Sartolab® P20 Plus filters a bacterial suspension is filtered at a constant pressure of 4 bar|58.0 psi. The suspension consists of Saline Lactose broth medium according to ASTM and Brevundimonas diminuta ATCC 19146.

For the validation studies of the Sartolab® P20 and Sartolab® P20 Plus filters, a minimum concentration of 1×10^7 B. diminuta per cm^2 filtration area was used for each tested unit. Pressure gauges and valves were installed for controlling and monitoring the prevailing pressure during the bacteria challenge test. Each filtrate that passes through the Sartolab® P20 and Sartolab® P20 Plus filters was collected separately and incubated for 7 days at 28–32 °C. The number of bacteria retained was quantified in parallel by filtering half of the filtrates through a microbiological gridded membrane filter, which was placed on agar and incubated under the same conditions.

Integrity Test
After the bacteria challenge test the Sartolab® P20 and Sartolab® P20 Plus filters units were integrity tested by the bubble point test method in order to correlate the results of the destructive bacteria challenge test with this non-destructive integrity test.

The bubble point test is performed by two methods:
- Utilizing a Sartocheck® automated integrity test unit
- Manually, visual detection

For the determination of the bubble point, air pressure is slowly increased on the upstream side of the Sartolab® P20 and Sartolab® P20 Plus filter housing. The pressure at which a constant air flow passes through the membrane filter is detected by measuring the pressure drop on the upstream side of the Sartolab® P20 and Sartolab® P20 Plus filters. For the visual test, a tube is attached to the Sartolab® outlet. This tube is immersed in a water-filled vessel. When the first continuous stream of bubbles appears, the bubble point is detected.

DuPont™ and Tyvek® are trademarks or registered trademarks of E.I. du Pont de Nemours and Company.

4.2 Results

Since most of the filters tested during the validation studies had high bubble point values and produced a sterile filtrate, the following data is a sampling of all filters examined during validation testing, and show that the results are within the bubble point|sterile filtrate limits.

Table 4.1 – Bubble Point for Sartolab® with SFCA Membrane

Lot Number		Bubble Point, Sartocheck® [bar]	Bubble Point, Visual [bar]	Result Bacteria Challenge Test
Test lot	500123	2.812	3.00	Non-sterile
Test lot	500123	2.813	3.00	Non-sterile
Test lot	0500093R5Z3	2.815	3.05	Sterile
Test lot	0500093R5Z3	2.859	3.05	Sterile
Test lot	0500093R8Z3	2.872	3.10	Sterile
18052	40897	3.219	3.30	Sterile
18052	40897	3.223	3.35	Sterile
18052	40897	3.246	3.40	Sterile
18052	40897	3.313	3.50	Sterile
18052	40897	3.352	3.50	Sterile
18053	41059	3.467	3.60	Sterile
18053	90012113	3.530	3.70	Sterile
18053	90012113	3.558	3.73	Sterile
18053	90012113	3.575	3.74	Sterile
Test lot	0500093R1	3.667	3.85	Sterile
Test lot	0500093R1	3.707	3.85	Sterile
Test lot	0500093R1	3.713	3.95	Sterile
Test lot	0500093R1	3.713	4.00	Sterile
18053	90012113	3.782	3.99	Sterile
18053	90012113	3.783	3.98	Sterile

Diagram 4.1 – Sartolab® P20 and P20 Plus with SFCA Membrane Bubble Point|BCT Correlation – Sartocheck®

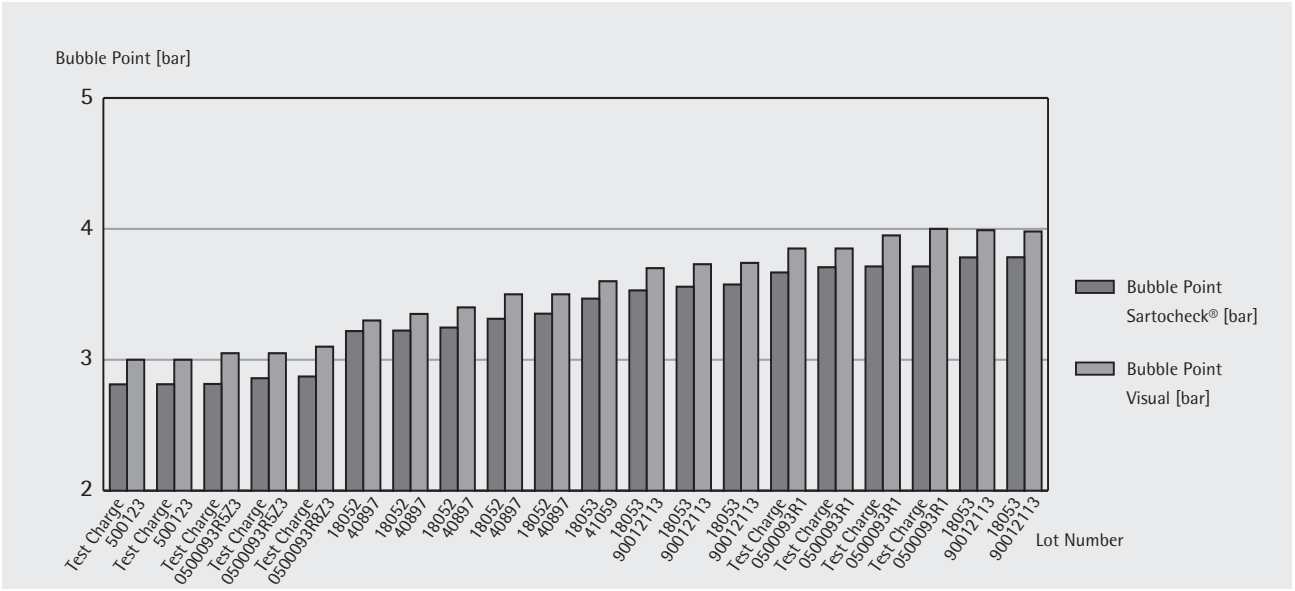
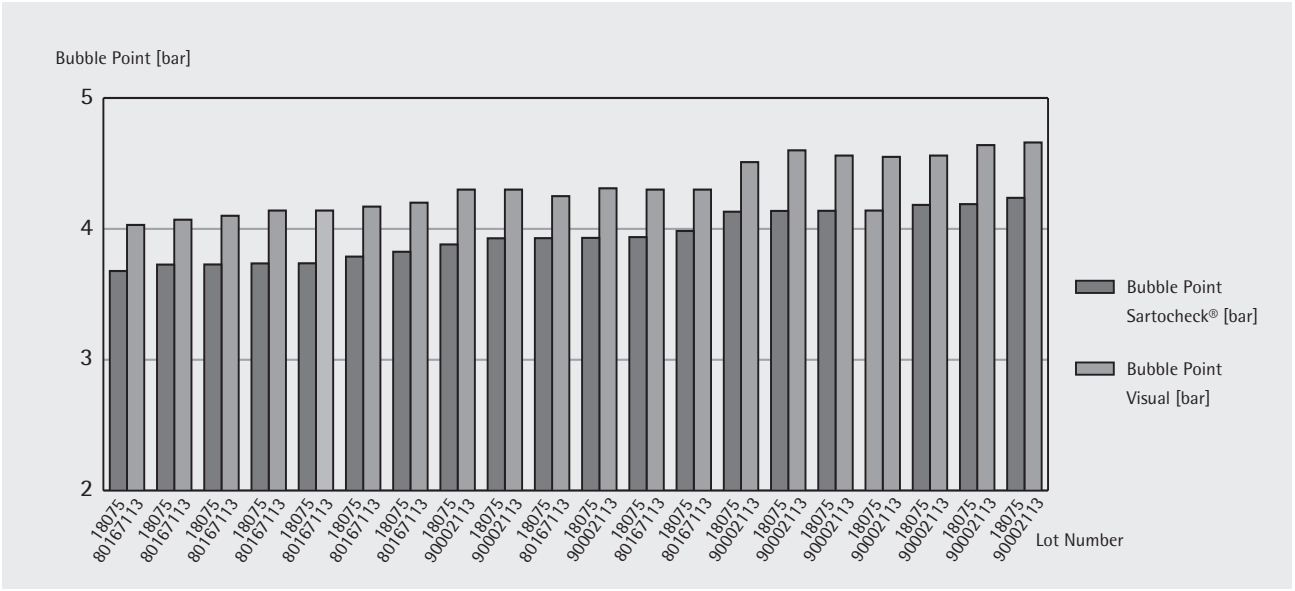


Table 4.2 – Bubble Point for Sartolab® with PES Membrane

Lot Number		Bubble Point, Sartocheck® [bar]	Bubble Point, Visual [bar]	Results Bacterial Challenge Test
18075	80167113	3.678	4.03	Sterile
18075	80167113	3.727	4.07	Sterile
18075	80167113	3.728	4.10	Sterile
18075	80167113	3.736	4.14	Sterile
18075	80167113	3.737	4.14	Sterile
18075	80167113	3.788	4.17	Sterile
18075	80167113	3.825	4.20	Sterile
18075	90002113	3.881	4.30	Sterile
18075	90002113	3.928	4.30	Sterile
18075	80167113	3.929	4.25	Sterile
18075	90002113	3.931	4.31	Sterile
18075	80167113	3.937	4.30	Sterile
18075	80167113	3.984	4.30	Sterile
18075	90002113	4.131	4.51	Sterile
18075	90002113	4.137	4.60	Sterile
18075	90002113	4.138	4.56	Sterile
18075	90002113	4.140	4.55	Sterile
18075	90002113	4.183	4.56	Sterile
18075	90002113	4.189	4.64	Sterile
18075	90002113	4.237	4.66	Sterile

Chart 4.2 – Sartolab® P with PES Membrane Bubble Point|BCT Correlation – Visual Determination



Conclusion
The data determined by the Sartocheck® automated device show that Sartolab® P20 and Sartolab® P20 Plus filters with bubble point values ≥ 3.2 bar|46.4 psi always produced a sterile filtrate with 100 % retention of the test organism, Brevundimonas diminuta.

Note
The bubble point test results are influenced by the nature of the wetting medium. The bubble point values listed in this validation guide are for Sartolab® P20 and Sartolab® P20 Plus filters wetted with water at 20 °C. It should be noted that a modification of the test conditions, such as temperature, wetting liquid or type of gas, may require different integrity test limits than those mentioned above.

5. Sterilization Validation

Background
A series of tests is needed to confirm that a sterilization procedure has been carried out successfully. Sterility testing of a system is used to prove that the entire contents of the interior packaging are sterile. The performance test ensures that the sterilization procedure does not damage any part of the product or lead to system malfunctions. Sartolab® P20 and Sartolab® P20 Plus are sterilized with EO gas in compliance with DIN EN 550 and ISO 11135

5.1 Presterilization Bioburden

Background
The bioburden of a system is determined before sterilization to ensure that it is not too high in order for the sterilization process to be reliable.

Method
The bioburden was determined for all interior and exterior Sartolab® P20 filter surfaces by filling, shaking and rinsing the units in succession. The rinsing solution collected was filtered through a 0.45 µm gridded membrane filter made of cellulose nitrate (cellulose ester). The filter was transferred to nutrient agar (order no. 14144) and incubated for 7 days at 30–35 °C. The resulting colonies were counted and averaged from the individual totals.

Table 5.1 – Bioburden Results

Type	Lot No.	No. of Units Tested	Average Bioburden Exterior Surfaces of Sartolab® P20 and Interior Surfaces of Packaging [cfu]	Average Bioburden Interior Surfaces of Sartolab® P20 [cfu]	Average Bioburden Total [cfu]
18052	070707	10	6.9	2.6	9.5
18053	80147113	10	11.0	2.2	13.2
18056	070239	10	2.6	3.0	5.6
18058	080113	10	1.4	1.1	2.5
18056	060271	10	14.1	4.7	18.8
18075	060913	10	2.1	1.5	3.6

Conclusion
The bioburden of the Sartolab® P20 filters is low enough to ensure that any standard sterilization procedure using ethylene oxide gas will reduce the bioburden to zero.

5.2 Ethylene Oxide Gas Sterilization

Sterilization Method
The process of sterilization with ethylene oxide gas is validated according to DIN EN 550 and ISO 11135; all documents and data of this validation may be consulted within the scope of an audit. The compliance with the specified parameters of the sterilization process is certified for each sterilization lot.

Sterilization validation has been performed with our most difficult-to-sterilize products, Sterisart®, type 16467 ACD, and the medical device Minisart®, type 16534 – K. The Sterilization Assurance Level (SAL) is demonstrated by half-cycle validation.

Quantitative Assay of Residual Ethylene Oxide Gas
Head Space Method according to DIN EN ISO 10993–7.

Maximum allowance level may not exceed 4 mg/product.

Table 5.2 – Sterilization Conditions

Stage	Parameter	Conditions
Before sterilization	Time	≥ 24 hours
	Temperature	≥ 15 °C
Pre-conditioning	Time	7–48 hours
	Temperature	40–50 °C
	Humidity	≥ 50 % RH
Sterilization	Initial vacuum	85–95 mbar absolute (1.2–1.4 psi)
	Ethylene oxide gas concentration	820 mg/l
	Time	4 hours
	Humidity	≥ 50 % RH
	Degassing time	≥ 60 minutes
	Desorption steps	3 to 5 times
Aeration	Time	20–48 hours
	Temperature	37–47 °C

After a full-cycle and aeration time we found: 1.69 mg ethylene oxide/product.

Sterility Test with Bioindicators

Method
The Sterisart® and Minisart® filters were prepared with Bacillus subtilis endospore strips with a concentration of 10^6 spores per strip. Some units were sterilized with ethylene oxide using minimum half-cycle exposure (concentration 820 mg/l). The remaining units were gassed with ethylene oxide for 4 hours (concentration 820 mg/l). ETO gas sterilization was repeated three times. After sterilization, the spore strips were removed under aseptic conditions and poured into liquid Soybean Casein Digest broth medium and incubated for 7 days at 28–32 °C. Sterility was demonstrated by the absence of microbial growth.

Results
After the ethylene oxide gas sterilization, all bioindicators (Bacillus subtilis spore strips) were sterile. The SAL of 10^{-6} has been demonstrated.

Number and Distribution of Bioindicators

Table 5.3 – Number and Distribution of Bioindicators

Cycle	No.	Number of Bioindicators Used	Result
Half-cycle	11040411	120	Sterile
Half-cycle	25040411	130	Sterile
Half-cycle	29040411	260	Sterile
Full-cycle	11050411	20	Sterile
Half-cycle (minimum load)	19050412	34	Sterile

Table 5.4 - Results of Bioindicator Tests

Type	Lot	Gassing Time	Result of the Bioindicator Test
16534	040019	4 hours	All bioindicators sterile

Conclusion
The results demonstrate that even half-cycle exposure with ethylene oxide sterilizes all bioindicators tested. The standard procedure of sterilizing the Sartolab® P20 and Sartolab® P20 Plus filters for 4 hours with a concentration of 820 mg/l ethylene oxide gas always produces sterile products.

6. Physical Tests

6.1 Burst Pressure

Background
Sartolab® P20 and Sartolab® P20 Plus filters are capable of withstanding high pressure within a system. Their high burst pressure assures that the system maintains its integrity and does not leak during usage and prevents a sample from bypassing the membrane.

Method
Positive pressure was applied from the top of the Sartolab® P20 and Sartolab® P20 Plus filters and gradually increased (about 1 bar|14.5 psi per second). The outlet connector of the Sartolab® P20 and Sartolab® P20 Plus filters was closed. The pressure was increased to the burst pressure of the Sartolab® P20 and Sartolab® P20 Plus filters or to a maximum of 9 bar|130.5 psi. The burst pressure values listed in the table below are substantially higher than the normal maximum operating pressure used.

Results

Table 6.1 – Burst Pressure of Sartolab® P [bar]

Type Lot	18052 80134113	18052 80108113	18053 80136113	18056 80161113	18058 80161113	18058 080598	18068 071185	18075 080023	18075 80123113
1	> 8.0	> 8.0	> 8.0	> 8.0	> 8.0	> 7.0	> 7.0	> 7.0	> 8.0
2	> 8.0	> 8.0	> 8.0	> 8.0	> 8.0	> 7.0	> 7.0	> 7.0	> 8.0
3	> 8.0	> 8.0	> 8.0	> 8.0	> 8.0	> 7.0	> 7.0	> 7.0	> 8.0
4	> 8.0	> 8.0	> 8.0	> 8.0	> 8.0	> 7.0	> 7.0	> 7.0	> 8.0
5	> 8.0	> 8.0	> 8.0	> 8.0	> 8.0	> 7.0	> 7.0	> 7.0	> 8.0
6	> 8.0	> 8.0	> 8.0	> 8.0	> 8.0	> 7.0	> 7.0	> 7.0	> 8.0
7	> 8.0	> 8.0	> 8.0	> 8.0	> 8.0	> 7.0	> 7.0	> 7.0	> 8.0
8	> 8.0	> 8.0	> 8.0	> 8.0	> 8.0	> 7.0	> 7.0	> 7.0	> 8.0
9	> 8.0	> 8.0	> 8.0	> 8.0	> 8.0	> 7.0	> 7.0	> 7.0	> 8.0
10	> 8.0	> 8.0	> 8.0	> 8.0	> 8.0	> 7.0	> 7.0	> 7.0	> 8.0

Conclusion
The minimum burst pressure determined was 5 bar|72.5 psi. The recommended maximum operating pressure was set at 3 bar|43.5 psi to allow for a safety margin.

6.2 Pressure Hold Test

Background
This test assures that Sartolab® P20 filters maintain their integrity and do not leak during usage when the system is subject to the mechanical stress of constant pressure.

Method
A sufficient number of Sartolab® P20 filters from numerous production lots were sampled. Positive pressure was applied to the top of the Sartolab® P20 and Sartolab® P20 Plus filters containing a water-wetted membrane filter. For performing the pressure hold test for Sartolab® P20 or Sartolab® P20 Plus units, the integrity test holder 18099 is required. The pressure is set to a constant pressure of 2.0 bar|29.0 psi for Sartolab® P20 and Sartolab® P20 Plus. During the 1-minute test period, no air may pass through the membrane, which would be indicated by air bubbles at the outlet of the Sartolab® P20 and Sartolab® P20 Plus filters.

Results
Ten samples of each lot were tested. The results of these tests are summarized in the table below.

Lot Number	Type 18052	18053	18056	18058	18068	18075
80134113	No air passage					
80108113	No air passage					
80136113		No air passage				
80161113			No air passage			
80161113				No air passage		
080598				No air passage		
071185					No air passage	
080023						No air passage
80123113						No air passage

Conclusion
All Sartolab® P20 and Sartolab® P20 Plus filters hold positive pressure on the upstream side and no air passed through the membrane.

6.3 Flow Rate Performance Test

Background
This test assures that the membrane is in accordance with its specifications.

Method
Ten samples of Sartolab® P20 filters from numerous production lots were sampled. Each of the units were connected to a pressure vessel containing water. At a constant pressure of 1 bar|14.5 psi, water is filtered through the Sartolab® P20 and Sartolab® P20 Plus filters. The volume of water capable of being filtered within one minute is determined. The flow rate is strongly influenced by the viscosity of the medium being filtered. For this reason, all flow rate measurements are taken at 20 °C so that the influence of temperature on viscosity is not a factor.

Results
Ten samples of each lot were tested. The results of these tests were summarized in table below.

Table 6.3 – Results of the Flow Rate Performance Test for Sartolab® at 1.0 bar|14.5 psi [ml/min Sartolab®]

Membrane	SFCA						PES		
Type	18052		18053		18056	18058	18068		18075
Lot	80134113	80108113	80136113	80161113	80161113	80598	71185	80023	80123113
1	275.4	306.2	281.5	269.9	313.9	263.8	589.4	616.2	634.5
2	283.8	306.7	288.2	272.5	315.3	269.1	594.5	617.5	643.5
3	289.3	313.4	297.1	282.7	317.1	275.8	596.8	620.6	643.5
4	293.8	313.8	299.4	284.9	321.1	278.5	601.6	621.9	646.0
5	295.6	314.4	302.1	286.2	326.8	285.0	602.1	623.5	647.7
6	297.5	317.0	311.4	289.0	327.5	292.6	604.5	627.5	648.8
7	298.2	319.6	311.7	290.1	328.4	294.7	604.5	628.2	667.1
8	300.3	328.5	313.9	293.9	328.8	297.7	611.3	639.1	714.7
9	302.6	334.9	316.2	294.2	333.2	299.1	618.5	646.1	719.8
10	303.0	352.1	316.3	295.7	334.5	319.8	621.9	646.3	720.8
Mean	294.0	320.7	303.8	285.9	324.7	287.6	604.5	628.7	668.6

Conclusion
The values of the flow rates for Sartolab® P20 and Sartolab® P20 Plus filters with surfactant-free cellulose acetate membranes vary between 263 ml/min and 334 ml/min. For filters with polyethersulfone membranes, these lie in the range of 589 ml/min and 668 ml/min. The minimum flow rate per Sartolab® with an SFCA membrane to 250 ml/min, and for PES membrane 400 ml/min.

6.4 Air Flow Rate Performance Test of the Vent Filter

Background
The purpose of this test is to assure that the Sartolab® P20 filters maintain their integrity and do not have coarse pores or and to ensure that sufficient venting can take place.

Method
Ten samples of Sartolab® P20 filters from numerous production lots were sampled. Each unit was connected to a pressure source and the outlet was closed with a plug. At a constant pressure of 0.1 bar|1.5 psi air is filtered through the Sartolab® P20 and Sartolab® P20 Plus filters and measured with a Rotameter.

Table 6.4 – Results of the Air Flow Rate Performance Test for Sartolab® at 0.1 bar|1.5 psi [l/min Sartolab®]

Type	18052		18053	18056	18058	
Lot	80134113	80108113	80136113	80161113	80163113	80598
1	0.410	0.452	0.418	0.418	0.418	0.433
2	0.418	0.440	0.422	0.418	0.410	0.452
3	0.407	0.425	0.415	0.422	0.402	0.437
4	0.398	0.428	0.410	0.410	0.398	0.445
5	0.415	0.470	0.418	0.398	0.418	0.480
6	0.410	0.458	0.402	0.418	0.415	0.448
7	0.410	0.458	0.415	0.418	0.398	0.440
8	0.415	0.455	0.415	0.410	0.415	0.448
9	0.410	0.455	0.407	0.418	0.418	0.443
10	0.410	0.458	0.410	0.415	0.422	0.455
Mean	0.410	0.450	0.413	0.415	0.411	0.448

6.5 PTFE Leakage Test

Background
This test assures that the PTFE air filter membrane of Sartolab® P maintains its integrity and does not leak during usage when the system is subject to the mechanical stress of constant pressure.

Method
A sufficient number of Sartolab® P20 and Sartolab® P20 Plus filters from production lots were sampled. The outlet of each unit was closed, and their inlet was connected to a pressure vessel containing water. At a constant pressure of 2 bar|29 psi, water was pumped into the Sartolab® P20 and Sartolab® P20 Plus filters. No water was to pass through the vent holes.

Results
Ten samples of each lot of were tested. The results of these tests are summarized in table below.

Table 6.5 - Results of PTFE Leakage Test at 2.0 bar|29.0 psi

Lot Number	Type 18052	18053	18056	18058	18068
80134113	No water passage				
80108113	No water passage				
80136113		No water passage			
80161113			No water passage		
80161113				No water passage	
080598				No water passage	
071185					No water passage

Conclusion
The results confirmed that each of tested polytetrafluoroethylene membranes contained in the Sartolab® P20 and P20 Plus did not leak when water was fed into the device at a pressure of 2 bar|29 psi with the outlet closed.

7. Chemical Compatibility – Sartolab® P20 and Sartolab® P20 Plus Filters

Table 7.1 –
Chemical Compatibility

Reagents	Sartolab® P20 18052|53 18056|58	Sartolab® P20 18068 18075
Solvents		
Acetone	– –	– –
Acetonitrile	– –	– –
Gasoline	▭	▭
Benzene	– –	– –
Benzyl alcohol	– –	– –
n-Butyl acetate	– –	– –
n-Butanol	▭	▭
Cellosolve	– –	– –
Chloroform	– –	– –
Cyclohexane	– –	▭
Cyclohexanone	– –	– –
Diethylacetamide	– –	– –
Diethyl ether	– –	– –
Dimethyl formamide	– –	– –
Dimethylsulfoxide	– –	– –
Dioxane	– –	– –
Ethanol, 98 %	– –	– –
Ethyl acetate	– –	– –
Ethylene glycol	■	▭
Formamide	■	– –
Glycerin	▭	▭
n-Heptane	▭	▭
n-Hexane	▭	▭
Isobutanol	■	▭
Isopropanol	– –	– –
Isopropyl acetate	– –	– –
Methanol, 98 %	▭	– –
Methyl acetate	– –	– –
Methylene chloride	– –	– –
Methyl ethyl ketone	– –	– –
Methyl isobutyl ketone	– –	– –
Monochlorobenzene	– –	– –
Nitrobenzene	– –	– –
n-Pentane	▭	▭
Perchloroethylene	– –	– –
Pyridine	– –	– –
Carbon tetrachloride	– –	– –
Tetrahydrofuran	– –	– –
Toluene	– –	– –
Trichloroethane	– –	– –
Trichloroethylene	– –	– –
Xylene	– –	– –

Legend:
■ = Compatible
▭ = Limited compatibility
– – = Not compatible

Contact time:
24 hours at 20 °C

Chemical compatibilities can be influenced by various factors. Therefore, we recommend that you confirm compatibility with the liquid you wish to filter by performing a trial filtration run before you start actual filtration. This information was compiled from technical literature.

Reagents	Sartolab® P20 18052|53 18056|58	Sartolab® P20 18068 18075
Acids		
Acetic acid, 25 %	– –	– –
Acetic acid, 96 %	– –	– –
Hydrofluoric acid, 25 %	▭	– –
Hydrofluoric acid, 50 %	▭	– –
Perchloric acid, 25 %	– –	– –
Phosphoric acid, 25 %	▭	▭
Phosphoric acid, 86 %	▭	▭
Nitric acid, 30 %	▭	– –
Nitric acid, 65 %	– –	– –
Hydrochloric acid, 15 %	▭	▭
Hydrochloric acid, 20 %	▭	▭
Sulfuric acid, 25 %	▭	– –
Sulfuric acid, 98 %	– –	– –
Trichloroacetic acid, 25 %	– –	– –
Bases		
Ammonia, 1N	– –	– –
Ammonium hydroxide, 25 %	– –	– –
Potassium hydroxide, 32 %	– –	– –
Sodium hydroxide, 32 %	– –	– –
Sodium hydroxide, 1N	– –	– –
Aqueous Solutions		
Formalin, 30 %	▭	▭
Sodium hypochlorite, 5 %	▭	– –
Hydrogen peroxide, 35 %	▭	– –
pH Range		
pH 1-14	– –	– –
pH 1-13	– –	– –
pH 3-14	– –	– –
pH 3-12	– –	▭
pH 4-8	■	■

Legend:
■ = Compatible
▭ = Limited compatibility
– – = Not compatible

Contact time:
24 hours at 20 °C

Chemical compatibilities can be influenced by various factors. Therefore, we recommend that you confirm compatibility with the liquid you wish to filter by performing a trial filtration run before you start actual filtration. This information was compiled from technical literature.

8. Analytical Tests

8.1 Endotoxin Test

Background
The goal of this test is to determine that the amount of endotoxins released in the effluent of three Sartolab® P20 filters is less than 0.06 EU/ml according to the USP Bacterial Endotoxin Test Chapter <85>.

Method
Sartolab® P20 and Sartolab® P20 Plus filters from a variety of production lots were tested under the following conditions for endotoxins utilizing a kinetic turbid metric method based on the LAL test. Twenty ml of endotoxin-free water are filtered through three Sartolab® P20 or Sartolab® P20 Plus filters. The filtrates are collected in a test tube. The endotoxin test is performed with the filtrates together with a positive and a negative control according to the kinetic turbid metric method with an automatic reader, which determines the actual concentration of endotoxins.

Table 8.1 – Results of the Endotoxin Test for Sartolab® P20, Sartolab® P20 Plus [EU/ml]

Type	18052	18052	18053	18056	18058	18058	18068	18075	18075
Lot	80134113	80108113	80136113	80161113	80161113	080598	071185	080023	80123113
1	< 0.025	< 0.025	< 0.025	< 0.025	< 0.025	< 0.025	< 0.025	< 0.025	< 0.025
2	< 0.025	< 0.025	< 0.025	< 0.025	< 0.025	< 0.025	< 0.025	< 0.025	< 0.025
3	< 0.025	< 0.025	< 0.025	< 0.025	< 0.025	< 0.025	< 0.025	< 0.025	< 0.025

Conclusion
All Sartolab® P20 and Sartolab® P20 Plus filters tested under the conditions of the endotoxin test described above yielded results below 0.025 EU/ml bacterial endotoxin.

8.2 Biocompatibility Test

Background
These tests are to determine that all components used in the manufacture of Sartolab® P20 and Sartolab® P20 Plus filters are biosafe and meet or exceed the requirements for the current USP Class VI–121 °C Plastics Tests.

Method
Sartolab® P20 and Sartolab® P20 Plus filters were supplied to an independent testing facility for evaluation under the requirements of the USP Class VI Plastics Tests. The complete test report is available upon request.

Result
All material used in the construction of the Sartolab® P20 and Sartolab® P20 Plus filters units meet or exceed the requirements of the USP Class VI–121 °C Plastics Tests.

8.3 Extractables Analysis

Background
These tests are to determine that Sartolab® P20 and Sartolab® P20 Plus filters do not release heavy metal and ammonium ions.

Method
Sartolab® P20 and Sartolab® P20 Plus filters were supplied to an independent testing facility for extraction and evaluation.
120 g ultrapure water (supplied by arium®) was filtered through 10 Sartolab® units and, in addition, un-sealed membrane material was shaken in ultrapure water. The water extracts were analyzed.

Table 8.2 – Results for Sartolab® P20 Filters with SFCA Membrane [acc. to DIN EN 11885 (Hg acc. to DIN EN 1483)]

Element	Detection Limit [mg/l]	Ultrapure Water (blank value) [mg/l]	Sartolab® P20 and Sartolab® P20 Plus [mg/l]	SFCA Membrane [mg/l]
Pb	0.005	< 0.005	< 0.005	< 0.005
Cd	0.001	< 0.001	< 0.001	< 0.001
Ca	0.5	< 0.5	< 0.5	< 0.5
Cr	0.005	< 0.005	< 0.005	< 0.005
Fe, total	0.01	< 0.01	< 0.01	< 0.01
K	0.5	< 0.5	1.0	< 0.5
Cu	0.005	< 0.005	< 0.005	< 0.005
Mg	0.05	< 0.05	< 0.05	< 0.05
Na	0.5	< 0.5	1.1	< 0.5
Ni	0.005	< 0.005	< 0.005	< 0.005
P, total	0.05	< 0.05	< 0.05	< 0.05
Hg	0.0002	< 0.0002	< 0.0002	< 0.0002
Zn	0.01	< 0.01	< 0.01	< 0.01
Sn	0.01	< 0.01	< 0.01	< 0.01
NH4+	0.04	< 0.04	0.18	0.00

Table 8.3 – Results for Sartolab® P20 Filters with PES Membrane [acc. to DIN EN 11885 (Hg acc. to DIN EN 1483)]

Element	Detection Limit [mg/l]	Ultrapure Water (blank value) [mg/l]	Sartolab® [mg/l]	PES Membrane [mg/l]
Pb	0.005	< 0.005	< 0.005	< 0.005
Cd	0.001	< 0.001	< 0.002	< 0.002
Ca	0.5	< 0.5	< 0.05	< 0.05
Cr	0.005	< 0.005	< 0.001	< 0.00
Fe, total	0.01	< 0.01	< 0.01	< 0.01
K	0.5	< 0.5	1.0	< 0.5
Cu	0.005	< 0.005	< 0.005	< 0.005
Mg	0.05	< 0.05	< 0.05	< 0.05
Na	0.5	< 0.5	1.1	< 0.5
Ni	0.005	< 0.005	< 0.001	< 0.001
P, total	0.05	< 0.05	< 0.02	< 0.02
Hg	0.0002	< 0.0002	< 0.0001	< 0.0001
Zn	0.01	< 0.01	< 0.005	< 0.005
Sn	0.01	< 0.01	< 0.01	< 0.01
NH4+	0.04	< 0.04	0.18	0.00

Conclusion
It can be concluded that only a few ions are eluted from the Sartolab® P20 and Sartolab® P20 Plus filters. The Sartolab® P20 and Sartolab® P20 Plus filters are usually rinsed prior utilization (such as for integrity testing, etc.) and during this flush procedure the extractables are reduced to insignificant amounts.

8.4 Visual Inspections

Background

Sartolab® P20 and Sartolab® P20 Plus filters are manufactured under clean-room conditions. The plastic parts are treated with care; their dimensions should be within the specifications and they may have no structural damage, which might affect the manufacture or the usage.

Method

The parts were inspected visually for:

- Injection molded particles > 0.1 mm
- Loose particles or fibers > 0.1 mm
- Membrane sealing
- Injection molding defects
- Residues of the molding process
- Entrapped air bubbles
- Discoloration
- Cracks or other damage

Table 8.4 – Results of Visual Inspections for Sartolab®

Type Lot	18052 80134113	18052 80108113	18053 80136113	18056 80161113	18058 80161113	18058 080598	18068 071185	18075 080023	18075 80123113
1	OK	OK	OK	OK	OK	OK	OK	OK	OK
2	OK	OK	OK	OK	OK	OK	OK	OK	OK
3	OK	OK	OK	OK	OK	OK	OK	OK	OK
4	OK	OK	OK	OK	OK	OK	OK	OK	OK
5	OK	OK	OK	OK	OK	OK	OK	OK	OK
6	OK	OK	OK	OK	OK	OK	OK	OK	OK
7	OK	OK	OK	OK	OK	OK	OK	OK	OK
8	OK	OK	OK	OK	OK	OK	OK	OK	OK
9	OK	OK	OK	OK	OK	OK	OK	OK	OK
10	OK	OK	OK	OK	OK	OK	OK	OK	OK

Conclusion

When Sartolab® P20 and Sartolab® P20 Plus filters are manufactured under defined parameters, the percentage of visually rejected devices is less than 0.1 %.

Sales and Service Contacts

For further contacts, visit www.sartorius-stedim.com

Europe

Germany
Sartorius Stedim Biotech GmbH
August-Spindler-Strasse 11
37079 Goettingen

Phone +49.551.308.0
Fax +49.551.308.3289

www.sartorius-stedim.com

Sartorius Stedim Systems GmbH
Schwarzenberger Weg 73–79
34212 Melsungen

Phone +49.5661.71.3400
Fax +49.5661.71.3702

www.sartorius-stedim.com

France
Sartorius Stedim Biotech S.A.
Z.I. Les Paluds
Avenue de Jouques – BP 1051
13781 Aubagne Cedex

Phone +33.442.845600
Fax +33.442.845619

Sartorius Stedim France S.A.S
Z.I. Les Paluds
Avenue de Jouques – CS 71058
13781 Aubagne Cedex

Phone +33.442.845600
Fax +33.442.846545

Austria
Sartorius Stedim Austria GmbH
Franzosengraben 12
A-1030 Vienna

Phone +43.1.7965763.18
Fax +43.1.796576344

Belgium
Sartorius Stedim Belgium N.V.
Leuvensesteenweg, 248/B
1800 Vilvoorde

Phone +32.2.756.06.80
Fax +32.2.756.06.81

Denmark
Sartorius Stedim Nordic A/S
Hoerskaetten 6D, 1.
DK-2630 Taastrup

Phone +45.7023.4400
Fax +45.4630.4030

Italy
Sartorius Stedim Italy S.p.A.
Via dell'Antella, 76/A
50012 Antella-Bagno a Ripoli (FI)

Phone +39.055.63.40.41
Fax +39.055.63.40.526

Netherlands
Sartorius Stedim Netherlands B.V.
Edisonbaan 24
3439 MN Nieuwegein

Phone +31.30.6025080
Fax +31.30.6025099

Spain
Sartorius Stedim Spain SA
C/Isabel Colbrand 10–12,
Planta 4, Oficina 121
Polígono Industrial de Fuencarral
28050 Madrid

Phone +34.91.3586102
Fax +34.91.3588804

Switzerland
Sartorius Stedim Switzerland GmbH
Lerzenstrasse 21
8953 Dietikon

Phone +41.44.741.05.00
Fax +41.44.741.05.09

U.K.
Sartorius Stedim UK Limited
Longmead Business Park
Blenheim Road, Epsom
Surrey KT19 9 QQ

Phone +44.1372.737159
Fax +44.1372.726171

America

USA
Sartorius Stedim North America Inc.
5 Orville Drive
Bohemia, NY 11716

Toll-Free +1.800.368.7178
Fax +1.631.254.4253

Sartorius Stedim SUS Inc.
1910 Mark Court
Concord, CA 94520

Phone +1.925.689.6650
Toll-Free +1.800.914.6644
Fax +1.925.689.6988

Sartorius Stedim Systems Inc.
201 South Ingram Mill Road
Springfield, MO 65802

Phone +1.417.873.9636
Fax +1.417.873.9275

Argentina
Sartorius Argentina S.A.
Int. A. Avalos 4251
B1605ECS Munro
Buenos Aires

Phone +54.11.4721.0505
Fax +54.11.4762.2333

Brazil
Sartorius do Brasil Ltda
Av. Dom Pedro I, 241
Bairro Vila Pires
Santo André
São Paulo
Cep 09110-001

Phone +55.11.4451.6226
Fax +55.11.4451.4369

Mexico
Sartorius de México S.A. de C.V.
Circuito Circunvalación Poniente No. 149
Ciudad Satélite
53100 Naucalpan, Estado de México

Phone +52.5555.62.1102
Fax +52.5555.62.2942

Asia|Pacific

China
Sartorius Stedim Beijing
Representative Office
No. 33, Yu'an Road,
Airport Industrial Zone B, Shunyi District
Beijing 101300

Phone +86.10.80426516
Fax +86.10.80426580

Sartorius Stedim Shanghai
Represantative Office
Room 618, Tower 1, German Centre,
Shanghai, PRC., 201203

Phone +86.21.28986393
Fax +86.21.28986392.11

Sartorius Stedim Guangzhou Office
Room 704, Broadway Plaza,
No. 233–234 Dong Feng West Road
Guangzhou 510180

Phone +86.20.8351.7921
Fax +86.20.8351.7931

India
Sartorius Stedim India Pvt. Ltd.
10, 6th Main, 3rd Phase Peenya
KIADB Industrial Area
Bangalore – 560 058

Phone +91.80.2839.1963|0461
Fax +91.80.2839.8262

Japan
Sartorius Stedim Japan K.K.
KY Building, 8–11
Kita Shinagawa 1-chome
Shinagawa-ku
Tokyo 140-0001

Phone +81.3.3740.5407
Fax +81.3.3740.5406

Malaysia
Sartorius Stedim Malaysia Sdn. Bhd.
Lot L3-E-3B, Enterprise 4
Technology Park Malaysia
Bukit Jalil
57000 Kuala Lumpur

Phone +60.3.8996.0622
Fax +60.3.8996.0755

Singapore
Sartorius Stedim Singapore Pte. Ltd.
10, Science Park Road, The Alpha
#02-25, Singapore Science Park 2
Singapore 117684

Phone +65.6872.3966
Fax +65.6778.2494

Australia
Sartorius Stedim Australia Pty. Ltd.
Unit 5, 7-11 Rodeo Drive
Dandenong South Vic 3175

Phone +61.3.8762.1800
Fax +61.3.8762.1828

DuPont™ and Tyvek® are trademarks or registered trademarks of E.I. du Pont de Nemours and Company.

Specifications subject to change without notice. Printed in Germany on paper that has been bleached without any use of chlorine.
Publication No.: SL-5711-e12122 · Order No.: 85032-535-35|Ver. 12/2012