

Instructions for Use

Sartobind STIC[®] PA

Void Volume Optimized Capsules and Cassettes
With 4 mm Bed Height



1000032238



SARTORIUS

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1 About these Instructions

1.1 Validity

These instructions are part of the product; they must be read in full and retained. These instructions apply to the following versions of the product:



4 mm: Nano 1 mL



Mini 10 mL



75 mL



200 mL



400 mL



600 mL



Jumbo 2.5 L



Cassette 0.8 L

1.2 Related Documents

In addition to these instructions, please observe the following documents:

- Operating instructions of the device in which the product is used
- Pilot Filter Holder Instructions for Use
- Process | Double Process Filter Holder Instructions for Use
- Validation Guide of the respective product

1.3 Target Groups

These instructions are addressed to the following target groups. The target groups must possess the knowledge specified below.

Target Group	Knowledge and Qualifications
Operator	The operator is familiar with the product and the associated work processes. The operator understands the hazards which may arise when working with the product, and knows how to prevent them.

1.4 Symbols Used

1.4.1 Warnings in Operation Descriptions

CAUTION

Denotes a hazard that may result in moderate or minor injury if it is **not** avoided.

NOTICE




Denotes a hazard that may result in property damage if it is **not** avoided.

1.4.2 Other Symbols

- ▶ Required action: Describes activities that must be carried out. The actions in the sequence must be carried out in succession.

- ▷ Result: Describes the result of the activities carried out.

2 Safety

-  Use of the products in applications not specified or not described in this manual, may result in improper function, personal injury, or damage of the product or material. The products are supplied as non-sterile unless otherwise expressly described. The membrane is dried from glycerol.
-  Die Verwendung dieser Produkte für Anwendungen, für die sie nicht bestimmt oder nicht in dieser Anleitung beschrieben sind, können zu einer schlechteren Funktion, Zerstörung der Produkte oder sogar zu Verletzungen von Mensch und Material führen. Die Produkte sind nicht steril sofern dies nicht ausdrücklich anders beschrieben ist. Die enthaltene Membran wird aus Glycerin getrocknet.
-  L'utilisation des produits pour des applications non-spécifiées ou décrites dans ce manuel peut causer un dysfonctionnement, une destruction du produit, des dommages matériels ou même corporels. Les produits sont fournis non-stériles, sauf indication contraire expressément mentionnée. La membrane est séchée avec de la Glycérine.

- ⚠ La utilización de este producto en aplicaciones ajenas o no establecidas en el manual de operación, puede provocar un mal funcionamiento del producto, del material, así como daños personales. Los productos suministrados no son estériles a menos que se describa lo contrario. La membrana ha sido secada de glicerina.

- ⚠ 把产品用于手册中没指定或描述的应用, 可能导致产品失效, 人员受伤, 或使产品及物料受损。囊式膜柱以非灭菌的形式供应。膜用甘油脱水。

- ⚠ 当製品を該当しない用途、あるいは当製品取扱説明書に記載されていない応用分野において使用した場合、当製品の機能上の不具合や損傷、人体への危害、あるいは他の物品の損傷を招く恐れがあります。特に明記のない場合、当製品は滅菌処理されていません。当メンブレンはグリセリンを用いて乾燥させてあります。

2.1 Intended Use

The product is intended exclusively for use in accordance with these instructions. Any other use is considered improper.

The membrane chromatography products – also described as membrane adsorbers – should be used only once for flowthrough (negative) chromatography applications to avoid carryover as well as tedious and costly cleaning validation procedure.

Sartobind STIC® PA Nano 1 mL has been developed as a scouting product for working with small sample volumes while retaining the cylindrical design of the large scale membrane adsorbers.

Sartobind® Mini 10 capsules have been developed for first scale up trials and preclinical production. This product size closes the gap between the Nano and the 75 mL size.

Sartobind STIC® PA 75 mL up to Jumbo 2.5 L have been developed for intermediate and pilot scale up to production scale in the biopharmaceutical industry.

Sartobind® 0.8 L cassettes are used in the Pilot Scale Filter Holder of up to 10.4 L membrane volume for the biopharmaceutical production.

2.2 Modifications to the Product

If the product is modified: Personnel may be put at risk. Product-specific documents and product approvals may lose their validity. If you have any queries regarding modifications to the product, contact Sartorius.

2.3 Qualifications of Personnel

Personnel who do **not** possess adequate knowledge about how to use the product safely may injure themselves and other personnel.

2.4 Personal Protective Equipment

Personal protective equipment protects against risks arising from the product. If the personal protective equipment is missing or is unsuitable for the work processes on the product: Personnel may be injured. The following personal protective equipment must be worn:

- Protective work clothing
- Safety gloves
- Safety glasses

2.5 Leaking Liquids from the Product

If the product is damaged or incorrectly installed:
Liquids can leak from the product.

- ▶ Do **not** exceed the maximum pressure (see chapter “8 Technical Data”, page 50).
- ▶ Perform a visual inspection before use.
- ▶ Ensure correct installation.

3 Product Overview

3.1 Operating Principle

The capsules and cassettes with 4 mm bed height are salt tolerant weak anion exchange chromatography products based on macroporous membranes. They can be used for chromatographic separation in downstream processing of viruses and proteins. The ligand is coupled to the membrane which is fitted into a plastic housing ready to use. The products are constructed with optimized fluid channels.

The capsules contain a central core and the cassettes a spacer element to minimize void volume. To set up and operate the Sartobind® Jumbo (2.5 L membrane volume) we recommend the Jumbo trolley (see chapter “10.2 Accessories”, page 58). These products are intended for single use to avoid carryover as well as tedious and costly cleaning validation procedures (see also section “5.13 Regeneration and Storage”, page 36). They are applied for contaminant removal from proteins and viral | virus like particles (VLP) vaccines in flow-through mode (negative chromatography) to bind DNA, residual protein, host cell proteins (HCP), endotoxins and viruses.

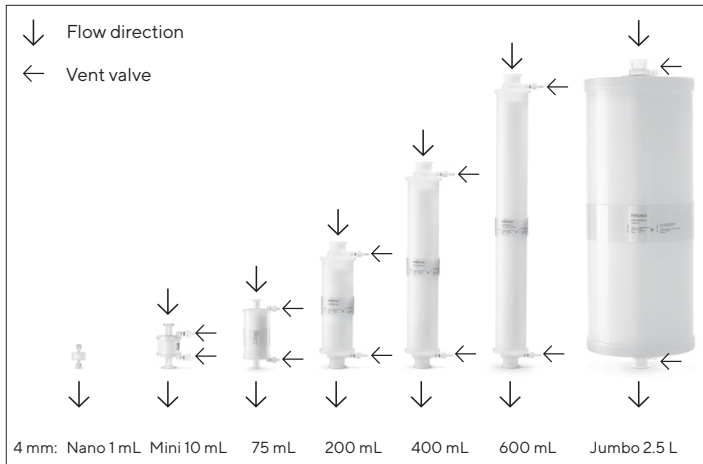


Fig. 1: Flow direction and position of vent valves of 4 mm capsules



Fig. 2: Flow direction and position of vent valve connection of 4 mm cassettes

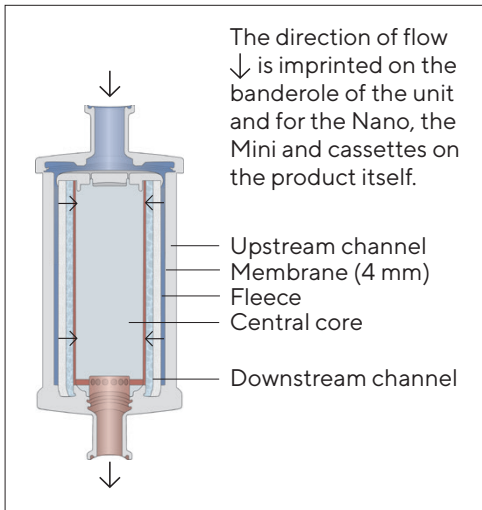


Fig. 3: Construction and flow path inside of the capsules

For Nano, Mini and 75 mL products the central core is made from a solid polypropylene cylinder. For the larger capsules it is made from a self-contained air filled polypropylene cylinder. The interior of the core is inaccessible for gases and fluids. The 2 flat membrane stacks of the cassettes are separated by a central spacer element.

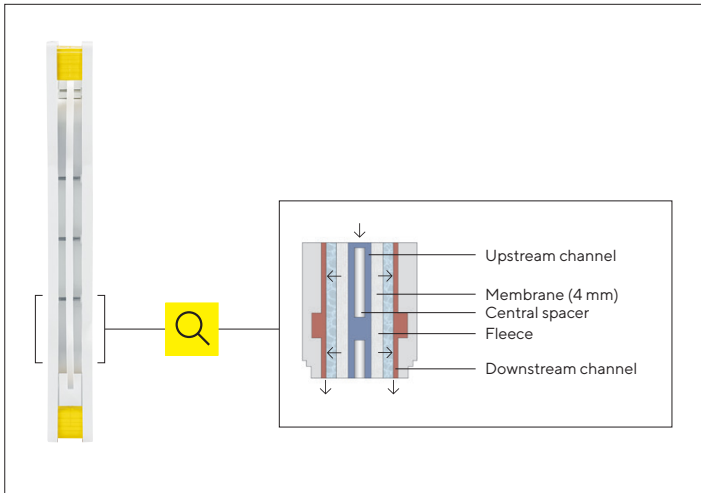


Fig. 4: Side view cassette;
highlighted section
see Fig. 5

Fig. 5: Construction and flow path inside
the 4 mm cassette

4 Installation

NOTICE

Malfunctions due to damaged products. A damaged product can cause malfunctions.

- ▶ Visually inspect the product before use.
 - ▶ Close vent valve before use by screwing the valve clockwise.
 - ▶ For the cassettes close the clamps at the manifold set.
 - ▶ Do **not** keep or place the products with the connector directly on the floor.
 - ▶ In case of damage: Replace the product.
-

Sartobind® Phenyl Jumbo 2.5 L

- ▶ Take the capsule including the styrene foam end protectors out of the box and place it upright on the end protectors.
- ▶ Move the Jumbo trolley (see chapter “10.2 Accessories”, page 58) in place.
- ▶ Remove upper foam protection and transparent bag.
- ▶ Lift the Jumbo directly onto the trolley (inlet is up and the arrow imprinted on the banderole is pointing down).

- ▷ It is recommended to connect the Jumbo with the trolley by the 3 screws delivered with the trolley.
- ▷ The protective caps on inlet and outlet should stay until you use the unit.
- ▶ Store the caps when you plan to autoclave (see chapter “5.4 Autoclaving”, page 29).
- ▶ Remove before venting.

Sartobind® Phenyl Capsules | Cassettes

- ▶ Protect inlet and outlet connectors when unpacking.
- ▶ Install the product in an upright position according to the process flow.
- ▷ The inlet is up.
- ▷ The flow is guided to an external channel passing through the membrane layers to an internal channel and to the outlet of the capsule (see Fig. 3).
- ▶ Install the capsule in-line with a prefilter (0.2 µm or 0.45 µm) in front of the product to prevent blockage or pressure build-up.
- ▶ For Sartobind® cassettes you need an appropriate cassette holder and one Manifold Set (see chapter “10.2 Accessories”, page 58).
- ▶ If you plan to use a different filter holder from other manufacturers, please contact Sartorius for technical advice.

Installing Sartobind® Phenyl Cassettes

- ▶ Unpack the Manifold Set containing one inlet and one outlet plate.
 - ▶ Place the “INLET” marked plate at one end of the holder.
 - ▷ “THIS SIDE UP” mark on the manifold should be readable on the top.
 - ▶ Place the manifold marked with “OUTLET” at the other end of the holder, so that “THIS SIDE UP” is readable from the top.
 - ▷ The fluid channels of both plates are oriented to the same direction.
-

CAUTION

Leaking liquids due to incorrect installation!

- ▶ Place the cassettes (4, see Fig. 5) in the lowest possible position in the holder.
 - ▶ The cassettes (4) used for chromatographic separation must originate from the same lot.
-

- ▶ Put the desired number of Sartobind® cassettes (4) between the manifolds (see Fig. 5).
- ▷ “THIS SIDE UP” is readable on top.
- ▶ Adjust the clamping force for cassettes in Pilot and Process holders to a minimum of 25 kN (optimal range: 25–30 kN).
- ▷ In the Pilot holder up to 13 cassettes and a manifold set can be installed.
- ▶ Close all DRAIN and VENT valves (1) of the manifold plates manually using the pinch clamp.

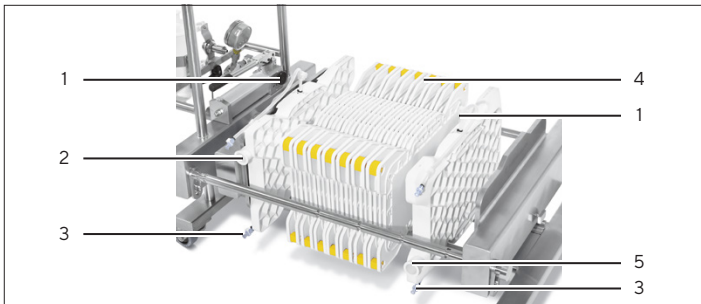


Fig. 6: Insert cassette(s) between the manifold inlet and outlet plates on the Pilot Filter Holder.

Pos.	Name
1	Vent valve
2	Inlet manifold
3	Drain valve
4	Cassettes
5	Outlet manifold

- ▶ Connect the inlet and outlet plates with 1½ inch tri-clamp to the process solution.
- ▷ Maximum pressure for the set-up of 1 to 13 cassette(s) is 2 bar (0.2 MPa, 29 psig).
- ▷ During flushing the clamping force may reduce.
- ▶ In order to avoid dripping during operation, it is recommended to re-adjust the clamping force to a minimum of 25 kN before you continue with equilibration.
- ▶ Make sure that the pump peak pressure caused by pulsation stays below this limit.

5 Operation

5.1 Venting the Capsule

All capsules except Nano have vent valves (see Fig. 1).

Procedure

- ▶ Remove the entire air from the unit before use.
- ▷ The vent valves are equipped with hose barb connectors for the fluid spilled out during venting.
- ▶ Check vent valve position.
- ▷ When turning anticlockwise, the valve is open, when turning clockwise, the valve is closed.
- ▶ Before opening the vent valve, connect the valves with flexible tubing (inner diameter 6 mm) to waste.
- ▶ **NOTICE** Insufficient closing of the valve due to excessive pressure! During venting of capsules do **not** exceed 0.05 MPa (0.5 bar | 7.3 psi).

- ▶ Open the vent valve screw $\frac{1}{3}$ turn to left until all air is replaced by fluid.
- ▶ For venting the cassettes, tubes with quick connectors are attached to the inlet and outlet manifolds and closed with a pinch clamp.

5.2 Venting the Nano mL Capsule

- ▶ Fill a 10–20 mL Luer syringe with equilibration buffer and connect to the capsule, then hold capsule upright (outlet is up) and expel air as shown in Fig. 7.
- ▶ If you still detect any air in the filled unit, close it at the outlet, hold the syringe up and move the plunger slightly up and down that air bubbles can ascend into the syringe.
- ▶ Alternatively, connect a second empty syringe to the top of the Nano and expel air and buffer into that syringe, disconnect the upper syringe to push out air and reconnect to the Nano, turn it and purge the solvent back and forth.
- ▷ Very small air bubbles observed directly below the inlet of the Nano do **not** disturb performance.
- ▷ The capsule function will **not** be influenced as long as the small air bubbles remain outside of the membrane bed.

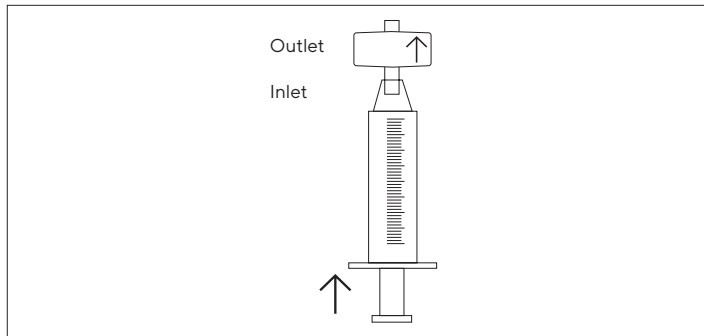


Fig. 7: Filling the Sartobind[®] Nano with a Luer syringe for air removal

5.3 Cleaning and Equilibration

The products have to be cleaned in place directly before use with 1 N NaOH for 30 min at 20°C. Preferentially, work at room temperature as low temperature increases viscosity of solvents. Also cold NaOH can cause swelling of the cellulose matrix and significantly reduce flow rate.

- ▶ For sanitization, use 30 membrane volumes (MV) of 1 N NaOH solution at a flow rate of 1 MV/min.
- ▶ Flush with 100 MV of equilibration buffer (e.g. 20 mM Tris/HCl, 150 mM NaCl, pH 7.5) at 5 MV/min.

5.4 Autoclaving

CAUTION

The cassette material is not compatible to autoclaving.









- ▶ The capsules can be autoclaved once at 121°C for 30 minutes at 1 bar (0.1 MPa | 14.5 psi).
- ▶ Pre-wet the capsule with equilibration buffer.
- ▷ When using water you may detect a lower flow rate which is due to swelling.
- ▶ The protective caps enclosed in the Jumbo delivery must be reinstalled on inlet and outlet connectors of the Jumbo.
- ▶ Close valves immediately after sterilisation.
- ▶ For autoclaving of Sartobind® Jumbo refer to separate autoclaving instructions enclosed in delivery.

5.5 Recommended Flow Rates and Equilibration Volumes

Membrane adsorbers can be run at much higher flow rate per volume than resin columns. The recommended flow rates for membrane adsorbers with 4 mm bed height are between 10 to 30 membrane volumes per minute. This recommendation is only a guideline as buffers and samples have different compositions and viscosities. Please test your respective flow rates with a small scale product to ensure that the flow rate fits with your pump capacities and the pressure limits. Lower flow rates than the recommended ones can also be used but will typically **not** improve binding capacity or overall performance. Cold room temperature increases buffer viscosity and possibly back pressure.

The equilibration volume is 100 membrane volumes.

For the cassettes, flow rate and equilibration volumes have to be multiplied with the number of cassettes in use.

								
Membrane volume (MV)	1 mL	10 mL	75 mL	200 mL	400 mL	600 mL	2.5 L	800 mL
Rec. flow rate (L/min)	0.02	0.2	1.5	4	8	12	50	16**
Rec. equilibration volume* (L)	0.1	1	7.5	20	40	60	250	80**

* Refer to 7.2 Cleaning and equilibration

** Multiply with number of used cassettes

5.6 Buffer Conditions

The ionic strength of buffers used during loading on Sartobind STIC® PA can be higher than for conventional anion exchange membrane adsorbers. Up to 20 mS/cm are possible for Sartobind STIC® PA. The pKa of the chosen buffer should **not** exceed ± 0.5 pH units of the operation pH. It should be filtered with 0.2 μm or 0.45 μm filters before use and the quality of water and chemicals should be of high purity.

NOTICE

It is recommended to use monovalent buffers e.g. TRIS or Acetate. Multivalent buffers like phosphate or citrate will reduce the binding capacity for proteins. Contaminants such as DNA and endotoxin can still bind depending on character of multivalent buffer. Up to ~150 mM salt can be used to achieve better separation of target molecules from contaminants. Application of pure water may lead to a reversible swelling of the membrane and may reduce permeability.

5.7 Selection of pH and Salt Conditions

In ion exchange chromatography a charged molecule is bound to oppositely charged groups attached to the insoluble matrix. This binding is reversible and induced by an increase of the salt concentration in the elution buffer. The pH value at which a biomolecule has no net charge is the isoelectric point: pI . If the pH of the buffer is below the isoelectric point (rule of the thumb at least 1 pH unit) a protein has a positive net charge and will bind to a cation exchanger (e.g. Sartobind[®] S). If the pH of the buffer is above its isoelectric point (at least 1 pH unit), it will bind to anion exchangers (e.g. Sartobind[®] Q or Sartobind STIC[®] PA).

The amine ligand used for Sartobind STIC® PA is a weak anion exchanger. This means the positive charge is reduced at higher pH. To optimize the binding capacity and load volume, multiple pH values should be tested (e.g. on 96 well plates).

Conventional ion exchangers are loaded at low conductivity. Proteins are easily eluted by adding e.g. 1 M NaCl. Sartobind STIC® PA binding is also influenced by salt but higher levels of salt are needed to elute the molecules. At a level of e.g. 150 mM NaCl where conventional anion exchanges do **not** bind, the salt tolerant membrane shows good binding capacity. To remove protein from the membrane, higher salt concentration than for conventional ion exchanger are required.

5.8 Contaminant Removal From Therapeutic Proteins and Other Sources in Flow-Through Mode

For contaminant removal from products such as monoclonal antibodies, pH conditions in the range of pH 6 to 8 should be used. Contaminants include highly negatively charged DNA, endotoxins, protein contaminants, some host cell proteins and viruses. The product of interest, the monoclonal antibody with

isoelectric points (pI) of 8–9.5 for example, will **not** bind and pass through the Sartobind STIC® PA. The influence of the flow rate on the performance is very low.

5.9 Sample Preparation

Procedure

- ▶ Adjust the sample to the starting buffer and prefilter it through a 0.2 µm membrane, e. g. Sartopore® XLG capsule.
- ▶ For small volumes in the mL range, use a 0.2 µm Minisart® filter with Luer outlet (order number 16532-K for polyether-sulfone or 16534-K for cellulose acetate membrane).

NOTICE

Unfiltered feed will block the Membrane Adsorber and lead to capacity loss and increased back pressure.

- ▶ We recommend inline filtering during operation.
 - ▶ When the pressure increases replace the prefilter.
-

5.10 Washing

Procedure

- ▶ When using capsules in bind & elute mode, wash with equilibration buffer after sample loading.

5.11 Elution

Procedure

- ▶ To elute the target protein use buffer with appropriate salt concentration.
- ▶ Take into account that Sartobind STIC® PA has been developed for single-use and that the original binding capacity typically **cannot** be restored due to strong binding of the primary amine ligand to the negatively charged species.

5.12 Draining

A dual air regulator system is recommended to prevent over-pressure of the Sartobind® products. The first regulator should reduce line air pressure to 2 bar.

The second regulator, positioned immediately upstream of the Sartobind[®], should reduce the 2 bar regulated supply pressure to the <1 bar (14.5 psi) for a capsule and 0.5 bar (7.3 psi) for 1 to 13 cassettes draining pressure.

Procedure

- ▶ Drain the capsules by application of air or nitrogen pressure (<1 bar | 14.5 psi) to the inlet of the product.

5.13 Regeneration and Storage

After elution and wash with equilibration buffer a regeneration step with 1 N NaOH for 1 hour can be used to clean Sartobind STIC[®] PA.

However, binding capacity **cannot** be completely restored. Sartobind STIC[®] PA can be stored in equilibration buffer with 20% ethanol.

5.14 Operation of the Sartobind® Nano with Peristaltic Pumps or Liquid Chromatography (LC) Systems

Procedure

- ▶ After the unit is filled completely with equilibration buffer, close the outlet of the Sartobind® Nano and remove the syringe.
- ▶ Start the LC system or peristaltic pump at a low flow rate.
- ▶ When fluid emerges, stop the pump, connect the tubing to the inlet of the Sartobind® Nano.
- ▶ Make sure that no air is introduced.
- ▶ Remove the cap from outlet.
- ▶ Run the pump until fluid emerges from the outlet of the unit and stop it.
- ▶ Then connect the outlet of the unit via Luer adapter to the LC detector and proceed with loading.
- ▶ If your system pressure is too high, refer to your LC system manual to remove any flow restrictor after the UV cell, as the system may generate a pressure above the allowed maximum pressure.
- ▷ As membrane adsorbers are typically run at much higher flow rates than columns, there is no risk of bubble formation in the UV cell when removing the flow restrictor.

5.15 Scaling Up

Run break through experiments for the target compound (contaminants) to be bound on the membrane matrix. After optimisation of the binding conditions for the contaminants, the purification step can be scaled up to a larger capsule.

Recommendations:

Maintain

- Bed height (stay within the same bed height when scaling up)
- Linear flow (when using capsules with same bed height, the flow rate will scale up linear when keeping MV/min constant)
- Sample concentration

Increase (see scaling factors in the following table)

- Sample load volume
- Volumetric flow rate
- Membrane volume

Scale up is done preferably by keeping the bed height constant and adjusting the membrane volume. This will make the calculation simple. Other methods for scale up via residence time will lead to same results. Residence time is calculated by the membrane volume divided by the flow rate.

When using Sartobind® Nano 1 mL, the scale up factor for flow rate and binding capacity is equal to the multiplication factor of the membrane volumes for the listed scale up products:

Size	Membrane volume [mL]	Factor to increase* (from Nano)
Nano	1 mL	-
Mini	10 mL	10
5"	75 mL	75
10"	200 mL	200
20"	400 mL	400
30"	600 mL	600
Jumbo	2.5 L	2500
Cassette	800 mL	800
Cassettes**	10.4 L	10,400

* Flow rate and binding capacity;

** 13 Cassettes as example

Example: After breakthrough experiments with the Nano you determined that a 500 fold higher binding capacity is needed. Then you choose the 600 mL capsule. Then adjust the flow rate by a factor of 600.

NOTICE

Keep sample concentration constant in lab and production scale.

- ▶ Adjustments might be required due to additional volumes from tubing and the system.
-

6 Integrity Test by Diffusion

The integrity of the membrane adsorber can be tested by a diffusion test.

The testing procedure describes the diffusion test for pre and post use. The test is intended to discriminate between defective and intact products and to detect major bypasses, large holes and faulty assembly.

6.1 Installation

Procedure

- ▶ Install capsule as shown in Fig. 8.

The test procedure has been developed and checked with the Sartochek[®] instrument family e.g. Sartochek[®] 4 Plus (26288) or 4 (16288). The use of Sartochek[®] instruments older than Sartochek[®] 4 will generate faulty data.

- ▶ Note that the test procedure with other vendor's integrity testers can require a different set up.

6.2 Operation Procedure

6.2.1 Pre-washing of Device

- ▶ Pre-wash the product with 30 membrane volumes (MV) of buffer or 0.9% NaCl in water at recommended flow rate.

NOTICE

The capsule needs to be pre-washed with the testing solvent, to remove any glycerol.

- ▶ The washing solution should have room temperature.
 - ▶ Keep the unit in an upright position for proper venting and open the vent screw on top of the product until all air is replaced by the testing solvent.
-

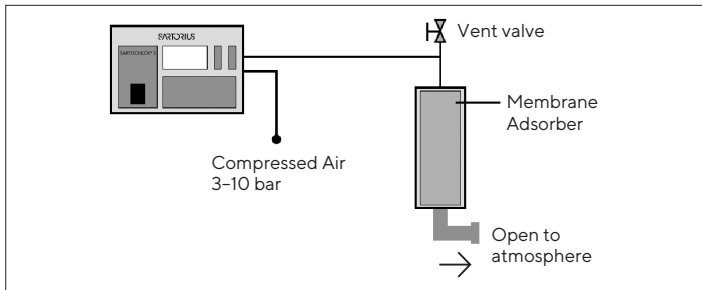


Fig. 8: Set up of diffusion test with Sartochek®.

6.2.2 Diffusion measurement with Sartochek®

- Choose “Programming” in the main menu
- Choose “Diffusion Test”
- ▶ Choose the test pressure, stabilization and testing time for your product from the table (next page).
- ▶ If you set the Net Volume to zero, Sartochek® automatically measures the upstream void volume including tubing.

Test Parameters

Size	Bed height (mm)	Membrane volume (MV)	Test pressure mbar (psi)	Stabilization time (min)	Testing time (min)	Diffusion max. mL/min
Nano	4 mm	1 mL	100 (1.45)	3	1	15
Mini	4 mm	10 mL	100 (1.45)	2	1	15
5"	4 mm	75 mL	100 (1.45)	2	1	75
10"	4 mm	200 mL	100 (1.45)	3	1	75
20"	4 mm	400 mL	100 (1.45)	3	1	75
30"	4 mm	600 mL	100 (1.45)	3	1	75
Jumbo	4 mm	2.5 L	100 (1.45)	3	1	150
Cassette(s)*	4 mm	0.8–10.4 L	100 (1.45)	5	1	15–195

* Diffusion max. per 4 mm cassette is 15 mL/min multiplied by number of cassettes

6.2.3 Results and Evaluation for One Device

- Diffusion \leq Diffusion max.:
Test passed (diffusion value on the print out)
- Diffusion $>$ Diffusion max.:
Test failed (red text on the print out)

7 Troubleshooting

Problem	Possible cause	Action
Air bubbles can be seen	Incomplete air removal	Small air bubbles seen in the top of the unit do not interfere with the purification as long as they do not touch the membrane bed. If too much air is enclosed, repeat removal as described in chapter "5.1 Venting the Capsule", page 26.
I installed the capsule upside down	Installation of capsule may be easier in the process flow	Validation has been done with a process flow from top to bottom. Thus it is clearly recommended to use capsules in the described flow direction (Feed enters capsule on top and leaves it on bottom).
I deviated from the CIP and flushing equilibration procedure		The capsules have been qualified and validated according to the given procedure. If a deviation is necessary, the results may also deviate from the given validation data.
High back pressure	Material has not been filtered	Prefilter with 0.2 μm or 0.45 μm filter before processing through the unit (preferentially inline).

Problem	Possible cause	Action
High back pressure	Material has been filtered but was stored before purification	Proteins can form aggregates within hours or during operation. Thus we recommend to prefilter inline by attaching a 0.2 µm filter in front of the adsorber. When you observe again pressure built up, replace the filter.
	LC system generates high pressure	Remove restrictor after the UV cell.
	The adsorber is clogged membrane fouling	Replace unit. You may backflush within given flow and pressure limits, perform a regeneration cycle.
	Viscosity swelling effects	Work at room temperature, avoid lower temperatures
	Pure water leads to swelling of membrane	Add sodium chloride or use ionic buffers
I have to use water for wetting the capsules	Economic considerations; easier usage	You may use pure water but you have to expect a decreased flow rate which may lead to a higher backpressure. The use of water will not change diffusion testing values. The flow rate returns to normal after using buffer again.

Problem	Possible cause	Action
Target molecule is not bound	Conditions for binding are insufficient	Process conditions, e.g. prefiltration, pH, conductivity, multivalent buffers etc. have to be checked and optimized. Sartobind STIC® membrane is salt tolerant.
Binding capacity is not sufficient	Process conditions not optimized	Use larger adsorber product, or: connect two adsorbers (same size) in series (i.e connect outlet of first adsorber to inlet of second) to achieve higher binding capacity. As a rule of thumb the pressure doubles when the flow rate is kept constant and the number of membrane layers is doubled.
Incomplete elution	Strong binding	Use capsule only for polishing in flowthrough mode.
I want to reuse the STIC capsules	Economic reasons	The ligand strongly binds the contaminants and cleaning with 1 N NaOH does typically not restore 100% of the binding capacity depending on the character of your sample and the contaminants. Sartobind STIC® has been developed for mainly single-use application to avoid the revalidation.

Problem	Possible cause	Action
I need to remove DNA endotoxins but I have to use PBS	I heard PBS is a multivalent buffer which reduces binding capacity	Go ahead with the PBS as DNA is a high negatively charged species and will bind to STIC. The same accounts for endotoxins. You may even work at pH conditions which normally would not be accessible as target protein could be bound.
A vertical line is seen on one capsule side when filled	Membrane edge visible	No action necessary. It can be visible the edge of the fleece touching the inner tube.
I purged with air or nitrogen and lost flow and binding capability.	Air has entered into the pores	See troubleshooting “Applied bubble point instead of diffusion test” below.
Accidentally a bubble point test instead of diffusion test has been run	Operation error	The membrane has then to be purged extensively to remove all the air which has been pressed into the pores. If properly purged, the diffusion test can be run successfully and the product works as expected.

8 Technical Data

8.1 Technical Information

Membrane volume (MV)	1 mL	10 mL	75 mL
Nominal membrane area	36.4 cm ²	364 cm ²	2,700 cm ²
Bed height	4 mm	4 mm	4 mm
Design	Cylindrical	Cylindrical	Cylindrical
Sartobind STIC® PA typical 10% dynamic binding capacity*	50 mg	500 mg	3.75 g
Maximum pressure bar (MPa, psig) at 20°C	4 (0.4, 58)	4 (0.4, 58)	4 (0.4, 58)
Maximum pressure during venting bar (MPa, psig) at 20°C	-	0.5 (0.05, 7)	0.5 (0.05, 7)
Nominal void volume (mL)	3.5	32	200
Nominal void volume (MV)	3.5	3.2	2.7
Approximate weight	10 g	65 g	400 g

1 mL membrane = 36.4 cm² membrane

Ion capacity per cm² of membranes: 18–22 µeq

Short term pH stability 2–14 refers to cleaning in place procedure described in section “5.3 Cleaning and Equilibration”, page 28

200 mL	400 mL	600 mL	2.5 L	0.8 L
7,300 cm ²	14,600 cm ²	22,000 cm ²	91,000 cm ²	29,000 cm ²
4 mm	4 mm	4 mm	4 mm	4 mm
Cylindrical	Cylindrical	Cylindrical	Cylindrical	Flat sheet
10 g	20 g	30 g	127 g	40
4 (0.4, 58)	4 (0.4, 58)	4 (0.4, 58)	3 (0.3, 43,5)	2 (0.2, 29)
0.5 (0.05, 7)	0.5 (0.05, 7)	0.5 (0.05, 7)	0.5 (0.05, 7)	0.5
540	1,080	1,600	7,000	2500
2.7	2.7	2.7	2.8	3.1
760 g	1.3 kg	1.9 kg	16 kg 20 kg wet 23 kg filled	4.9 kg 6.0 kg wet

* See section "8.3 Binding Capacity", page 53

8.2 Materials

Membrane materials

Matrix	Stabilized reinforced cellulose
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Membrane thickness membrane volume = membrane area	275 μm 1 mL = 36.4 cm^2
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Nominal pore size	> 3 μm
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Ion exchanger ligand STIC PA	Weak anion STIC PA; primary amine (R-NH ₂)
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Capsule materials

Outer cage, inner core, end caps, capsule housing, nonwoven, fleece	Polypropylene
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O-ring in vent valve (except Nano)	EPDM (ethylene propylene diene monomer)
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Cassette materials

Outer cage, seal, nonwoven, fleece	ABS, silicone, polyethylene, stable to gamma irradiation
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8.3 Binding Capacity

Data are based on dynamic binding capacity measurements at 10% breakthrough using 3 layers of 5 cm² membrane discs (15 cm² total area membrane thickness of 275 μm) arranged in a holder and run at 10 mL/min.

Typical dynamic binding capacity 10%	Reference protein and buffer
1.4 mg/cm ² (50 mg/mL)	BSA (bovine serum albumin) in 20 mM Tris/HCl 150 mM NaCl, pH 7.5

8.4 Storage Conditions

Clean, dry place in closed bag and box at room temperature

Protected from direct sunlight

8.5 Chemical Stability

Stable for all commonly used buffers in chromatography

No oxidizing agents

9 Quality Assurance

The final Sartobind® products are tested for protein dynamic binding capacity and flow rate. Sartobind® membranes are tested for protein dynamic binding capacity, flow rate, thickness, and evenness.

Capsules, cassettes and membranes are manufactured in a controlled environment. The product meets all Sartorius standards for traceability, production and specifications as given here or exceeded them as certified in the quality assurance certificate enclosed. A validation and an extractables guide are available on request.

10 Ordering Information

10.1 Products

Order number	Description and type of connectors	Quantity
96STPA42DN-11-A	Sartobind STIC® PA Nano 1 mL, 4 mm, Luer female connectors, 2 PEEK adapters Luer male to UNF 10-32 female, manual, certificate	4
96STPA42D4R11--A	Sartobind STIC® PA Mini 10 mL, 4 mm, Luer female connectors, 8 PEEK adapters Luer male to UNF 10-32 female, manual, certificate	4
96STPA42D4RFF--A	Sartobind STIC® PA Mini 10 mL, 4 mm, 3/4" sanitary clamp, manual, certificate	4
96STPA42D4ROO--A	Sartobind STIC® PA Mini 10 mL, 4 mm, hose barb connectors, manual, certificate	4
96STPA42D9MFF--A	Sartobind STIC® PA 75 mL, 4 mm, 3/4" sanitary clamp, manual, certificate	4
96STPA42D1GSS	Sartobind STIC® PA 200 mL, 4 mm, 1 1/2" sanitary clamp, manual, certificate	1




Order number	Description and type of connectors	Quantity
96STPA42D2HSS	Sartobind STIC® PA 400 mL, 4 mm 1½" sanitary clamp, manual, certificate	1
96STPA42D3KSS	Sartobind STIC® PA 600 mL, 4 mm, 1½" sanitary clamp, manual, certificate	1
96STPA42D3NSS	Sartobind STIC® PA Jumbo 2.5 L, 4 mm 1½" sanitary clamp, 2 protective caps, manual, autoclaving instructions, certificate	1
98STPA42D-L	Sartobind STIC® PA Cassette 0.8 L, 4 mm, 1½" sanitary clamp via manifold set (accessory), manual, certificate	1

10.2 Accessories

Order number	Description	Quantity
1ZA---0004	Adapter Luer male to UNF 10 - 32 female, PEEK	1
1ZAOGV0003	Adapter UNF 10 - 32 female to sanitary ¾", 25 mm, polyoxymethylene	2
5ZGI--0001	Holder for 1 × 200 to 1,200 mL (10 - 30") capsule, stainless steel, 3 legs	1
5ZALB-0002	Distribution adapter for 3 × 200 (10 - 30") to 1200 mL capsules, 1 × 2", 3 × 1½", sanitary, stainless steel	1
7ZAL-V0013	Reducing adapter 1½" (50.5 mm) to ¾" (25 mm), sanitary	1
7ZAL-V0010	Reducing adapter 2" (64 mm) to 1½" (50.5 mm), sanitary	1
9ZGL--0102	Trolley for Jumbo 2.5 or 5 L, stainless steel	1
16288	Sartocheck® 4 Plus Integrity Tester	1
26288---FT	Sartocheck® 4 Plus Filter Integrity Tester	1
29Z-S00001	Manifold set for Sartoclear® Sartobind®, 1½" sanitary clamp	2

Order number	Description	Quantity
2ZGL--0005	Pilot filter holder for Sartoclear® Sartobind®	1
2ZGL--0006	Process filter holder for Sartoclear® Sartobind®	1
2ZGL--0007	Double process filter holder for Sartoclear® Sartobind®	1
2ZGL--0008	Drip pan for Pilot Filter holder	1
2ZGL--0015	Drip pan for Process and double Process Filter Holder	1

11 Dimensions and Connections

Membrane volume 4 mm bed height			
	1 mL	10 mL	75 mL
Size	Nano	Mini	5"
Dimensions in mm	37 × 31 H × Ø	Luer: 70 × 54.5 Sanitary: 100 × 54.5 Hose barb: 110 × 54.5 H × Ø	190 × 77 H × Ø
Connectors	Luer female	- Luer female - Sanitary 3/4", 25 mm outer, 14 mm inner Ø - Hose barb 1/2", 12.7 mm*	Sanitary 3/4" 25 mm outer, 14 mm inner Ø
Gaskets	n.a.	3/4", inner Ø 16 mm	3/4", inner Ø 16 mm

n.a. = not available | * Recommended internal diameter of flexible tube: 1/2", 12.7 mm



200 mL

10"

350 × 100
H × Ø

Sanitary 1½"
50.5 mm outer,
36 mm inner Ø

1½",
inner Ø
35.8 mm



400 mL

20"

570 × 100
H × Ø

Sanitary 1½"
50.5 mm outer,
36 mm inner Ø

1½",
inner Ø
35.8 mm



600 mL

30"

810 × 100
H × Ø

Sanitary 1½"
50.5 mm outer,
36 mm inner Ø

1½",
inner Ø
35.8 mm



2.5 L

Jumbo

850 × 302
H × Ø

Sanitary 1½"
50.5 mm outer,
36 mm inner Ø

1½",
inner Ø
35.8 mm



0.8 L

Cassette

634 × 387 × 49
W × L × Ø

Via manifold:
Sanitary 1½"
50.5 mm outer,
36 mm inner Ø

For manifold:
1½",
inner Ø
35.8 mm

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List of Sartorius material numbers applying to EPA-FIFRA

96STPA42D1GSS

96STPA42D2HSS

96STPA42D3KSS

96STPA42D3NSS

96STPA42D9MFF--A

96STPA42DN-11--A

98STPA42D-L
