sartorius

Sartobind®
Membrane Adsorbers for Rapid Purification of Proteins

Sartobind – the pace maker in Membrane Adsorber technology

Unique microporous structure
Sartobind Membrane Adsorbers display a macroporous structure with a pore size of 0.45 or > 3 µm. That's orders of magnitudes larger than conventional chromatographic gel matrices. Molecules are transported by convective flow to ligands.

Characteristics of Membrane Adsorbers (MA)
: Ready-to-use units
: Simple handling
: Pore sizes > 3 and 0.45 µm
: Negligible diffusion limitation
: Low bed heights with 0.3 up to 16 mm
: Scalable to process dimension with Sartobind SingleSep disposable capsules and Sartobind System reusable modules
: Robust high performance separations
: No bed cracking, channeling, air entrapment
: Flow rate of ion exchange membranes > 80 ml/min 100 kPa (linear flow rate: > 4,800 cm/h)
: Chemistries: strong and weak ion exchange, coupling, affinity and metal chelate ligands

Low unspecific adsorption
The basis for all Sartobind membranes is a stabilized reinforced cellulose. It is made from regenerated cellulose and during the production to Sartobind it runs through a number of stabilization and grafting steps until a chromatographic matrix is formed on the cellulose backbone. In principle any ligands known from conventional chromatography can be bound covalently on the matrix.

Speed up 100 times
In a simple experiment using a Sartobind ion exchange unit with 5 cm^2 membrane area and a Luer Lock syringe you can achieve a flow rate of about 10 ml per 0.5 second by hand which corresponds to a linear flow rate of more than 14,000 cm/h. Even under these conditions you'll attain capture of your protein. Just try it (sample: cytochrome c, buffer: 10 mM sodium phosphate pH 7.0, unit: Sartobind S 5). In production scale (more than 10,000 liters), a typical speed up factor is about 25 measured in direct comparison to conventional column technology (reference: Walter, J. K. in: Bioseparation and Bioprocessing, Strategies and Considerations for Advanced Economy in Downstream Processing of Biopharmaceutical Proteins. G. Subramanian (ed.) Wiley VCH, Vol. II p. 447–460 (1998). Flow rate does not affect break through performance (see fig. 2).

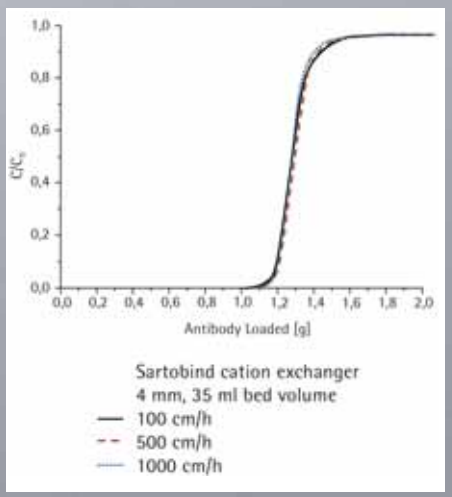


Fig. 2: Break through performance of a Sartobind MultiSep 35 ml cation exchange module at monoclonal antibody purification with various flow rates. For other published data see also: H.L. Knudsen et al., Genentech Inc., J. Chromatogr. A 907 (2001) 145–154 .

Sartobind membrane types
: Sartobind S, Q, C and D ion exchange
: Sartobind IDA (iminodiacetic acid) metal chelate
: Sartobind Aldehyde
: Sartobind Epoxy
: Sartobind Protein A (recombinant)
: Other ligands on request

Sartobind applications
Purification and Concentration
: Proteins, viruses, viral particles, monoclonal antibodies, oligonucleotides
Contaminant removal
: DNA, endotoxins, viruses, host cell proteins

◀ Fig. 1: Cytochrome c is eluted from a Sartobind S 75 Membrane Adsorber

... for robust separations

Chemical compatibility
The housing of Sartobind SingleSep capsules is polypropylene. The housing of Sartobind MA 15, 75 and 100 is polysulfone which is stable to many standard solvents applied in chromatography. Sartobind ion exchange membranes are compatible with alcohols such as ethanol, isopropanol, glycerol, and denaturing solvents such as 8 M urea and 8 M guanidine HCl and can be cleaned with 1 N sodium hydroxide.

Constant capacity
The robustness of Sartobind Membrane Adsorbers in ion exchange and affinity chromatography has been tested in consecutive runs of 1000 chromatographic cycles, (Fig. 3). Sartobind can be reused many times, and affinity membranes maintain their binding capacity over many cycles reflecting the chemical stability of the ligands.

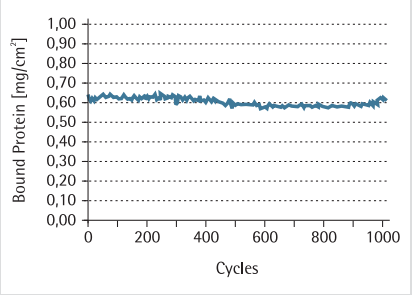


Fig. 3: Purification cycles of bovine serum albumin on Sartobind Q 75 strong anion exchanger repeated 1000 times. Flow rate: 120 cm/h, cycle time: 10 min, equilibration buffer: 20 mM phosphate buffer pH 7.0, sample: 5 ml bovine serum diluted 1:20 with equilibratioin buffer, elution buffer: 20 mM phosphate buffer pH 7.0 + 1 N NaCl, regeneration after each 100 cycles with 1 N NaOH

Formats from lab to process

Fig. 4: The Demo kit for the demonstration of the high speed and selectivity of Sartobind contains everything for an ion exchange chromatography purification

Fig. 5: Sartobind MAs may be used by hand or with a chromatographic system via Luer Lock adapters.

Demo kit
A demonstration kit for educational purposes is available to demonstrate a protein purification by hand in two minutes. Everything needed is included in the box: Buffer, colored protein | impurity solution, buffers, syringe and recipe for reuse.

Laboratory: Sartobind MA units
You may use Sartobind Membrane Adsorbers for any ion exchange or affinity chromatography which require high speed and simple operation. Four sizes of laboratory units can be chosen. Sartobind MA 5 (1 membrane layer) are for principle tests and should be disposed after use. If you have to work with larger mg quantities, please choose Sartobind MA 15 (3 layers), MA 75 (15 layers) or MA 100 (5 layers). These may be reused hundreds of times.

Fig. 6: Sartobind membrane

Fig. 7: Vivapure centrifugal units

Laboratory: Sartobind A4 sheets
The sheet (624 cm^2) format allows you to design your own Membrane Adsorber formats. An application for Sartobind A4 sheet is e.g. DNA fragment isolation from agarose gels.

Centrifugal format
If you don't need flow control but you have to screen a large number of proteins in parallel, use the Vivapure® centrifugal units.

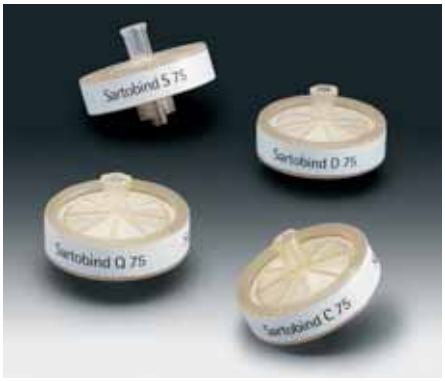


Fig. 8: Sartobind MA units for laboratory applications

Fig. 9: Sartobind System products: housings, storage containers, modules and cores for bind and elute applications

Fig. 10: Sartobind Direct for capturing

Starting with Sartobind MA 75 for further scale-up
The Sartobind MA 75 format with 4 mm bed height is available in all membrane types. It can be scaled straightly to the production format with the same bed height. For polishing application start with Sartobind Q SingleSep nano (4 mm bed height).

Production: Sartobind System, reusable modules
The modules represent a unique modular system for any chromatographic application with Membrane Adsorbers. Modules are available in 15 sizes and with protein capacities between 1 and 60 g (IEX). Module can be run in series and parallel for further scale-up.

Sartobind Direct
This new and unique format allows the capturing of proteins without prefiltration. The flow pattern of e.g. fermentation broth is routed tangentially over the membrane. Particles can pass through the system without retardation.

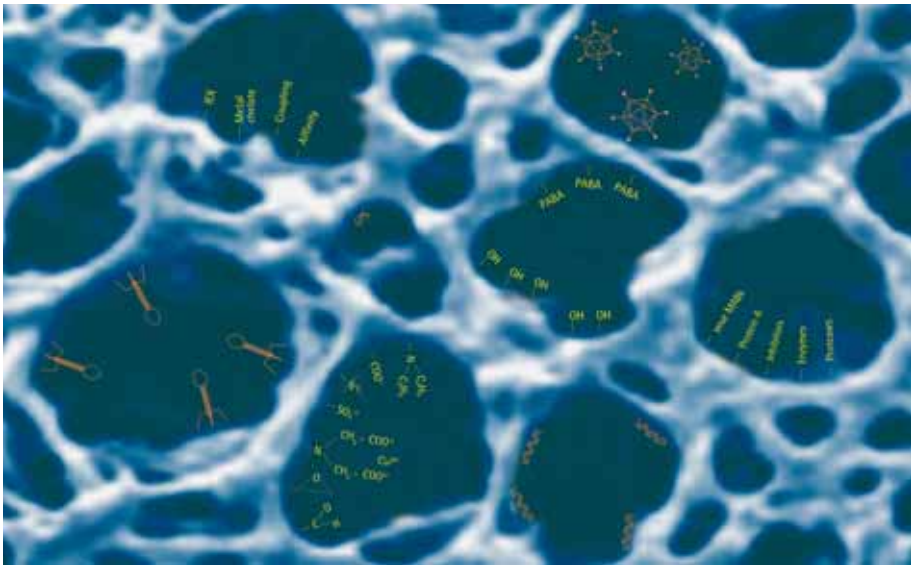


Fig. 11: There are no restrictions regarding ligands and applications.

Quality assurance
Membranes are tested for protein binding capacity, thickness, evenness, smoothness and flow rate. Sartobind MA laboratory units are tested for protein binding capacity and flow rate. Capsules are tested for dynamic binding capacity and flow rate, and modules are tested for small ion capacity and flow rate.

Validated technology
Sartobind System modules and SingleSep capsules (see p. 6) have met the requirements of current USP Plastic Class V and VI, respectively. Validation guides are available for System modules and SingleSep with detailed technical data and test results according to USP. Additionally, extractables guide is available for modules with data of GC-MS, HPLC and FT-IR analysis from aqueous, ethanolic and sodium hydroxide extraction.

FDA approved
Sartobind is the first Membrane Adsorber applied in approved pharmaceutical production (approval of CAMPATH-1H® by Food and Drug Administration, March 2001).

SingleSep™ the tool for contaminant removal

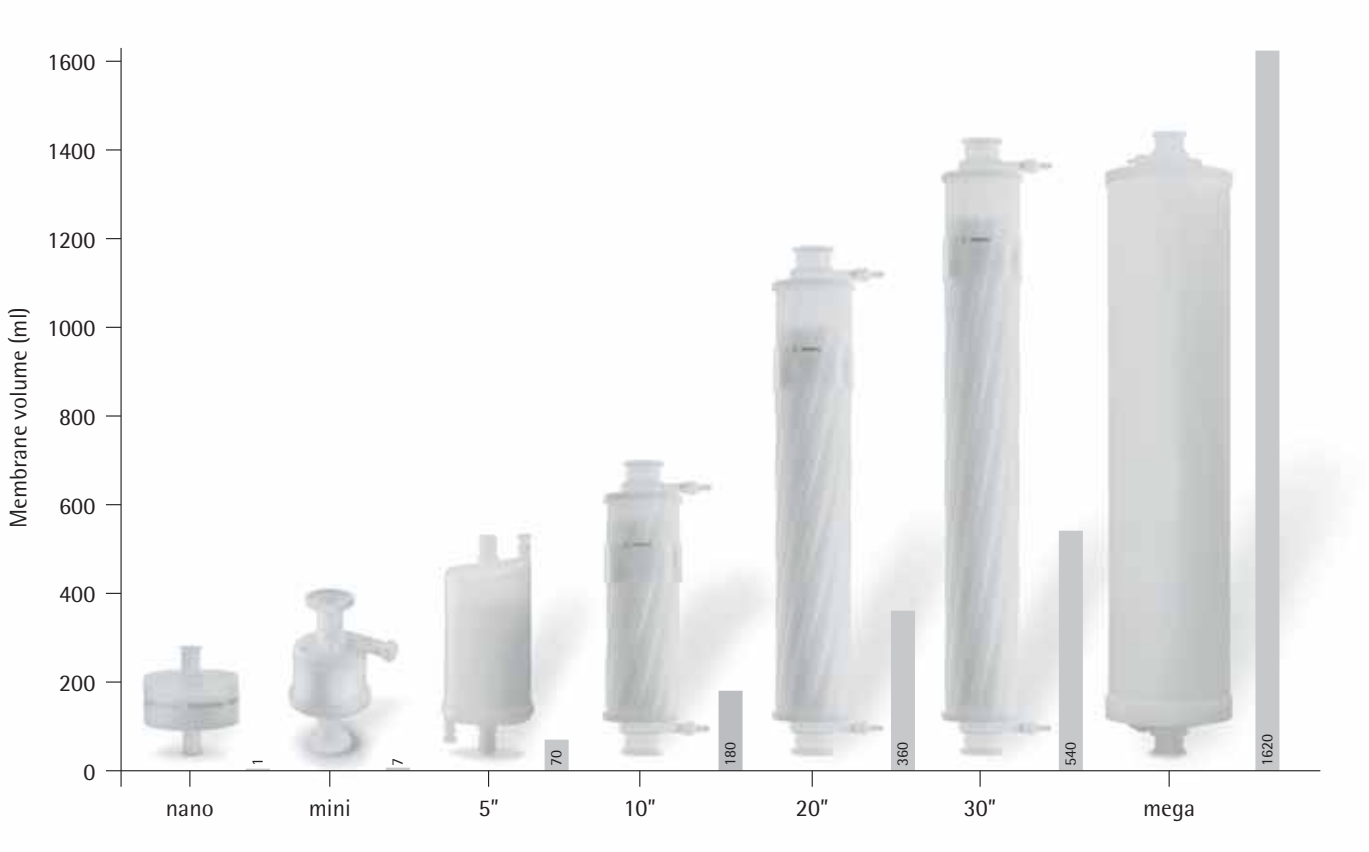


Fig. 12: Sartobind SingleSep Scale up from ml to 10000 liter scale

High speed polishing
Sartobind SingleSep capsules are designed to remove charged contaminants from therapeutic proteins at accelerated flow rates by ion exchange membrane chromatography. The high throughput is a direct result of negligible mass transfer effects and is made possible by the >3 µm macroporous membrane with 4 mm (15 layer) bed height.

Capsule design
The Sartobind SingleSep looks like a standard filter capsule except that the adsorbing membrane is reeled on a core to form a cylinder. The flow is from top into the outside channel and then perpendicular through the membrane layers to the center of the cylinder and leaves the capsule at the outlet.

Efficient
- Higher throughput (g/h) for trace impurity removal

Economical
- Saves capital
- No hardware investment & maintenance
- No column packing, testing, regeneration
- No re-use validation
- Less unspecific binding – higher yield
- Less labor
- Buffer consumption may be decreased 95%

Easy to use
- Disposable
- Simple and fast set up
- Handling like a filter capsule

A standard for virus purification

Unique for large proteins, DNA and viruses

Sartobind membranes are unique for purification of large proteins and virus particles. Conventional gel beads possess 95% of the binding capacity within the bead and large particles cannot enter their small pores. In contrast Sartobind membranes display huge capacities for large molecules. E.g. for DNA 10 times more dynamic capacity than conventional beads (reference: Sartobind Application Note DNA removal) and for virus purifications gels cannot compete at all. Sartobind membranes have been successfully applied for the purification of alphaherpesvirus, adenovirus and adenoassociated virus. The Vivapure AdenoPACK adenovirus purification and concentration kits offer researchers a convenient way to clean up within 1–2 hours. The system is scalable to production format.

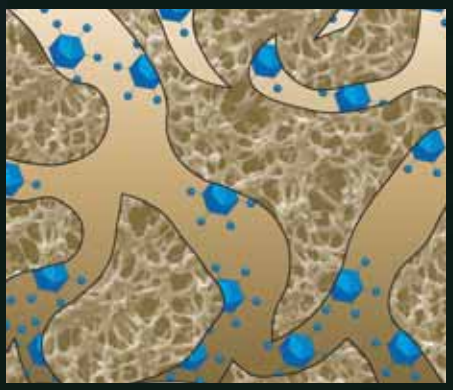


Fig. 13: Viruses can bind to the internal membrane structure

Fig. 14: Adeno PACK for convenient adenovirus purification and concentration

Technical Data

For liquid chromatography systems or Luer Lock syringe

	MA 5	MA 15	MA 75	MA 100
Application	Screening, disposable	Screening, application optimization, reusable	Down-scale trial, screening, application optimization, reusable	Screening, application optimization, reusable
Membrane material	Stabilized reinforced cellulose			
Adsorption area [cm^2]	5	15	75	100
Number of layers	1	3	15	5
Bed height [mm]	0.275	0.8	4.0	1.4
Bed volume* [ml]	0.14	0.41	2.1	2.8
Menbrane diameter [mm]	25	25	25	50
Housing material	MBS copolymer	Polysulfone	Polysulfone	Polysulfone
Inlet connector	Female Luer Lock	Female Luer Lock	Female Luer Lock	Female Luer Lock
Outlet connector	Male Luer Lock	Male Luer Lock	Male Luer Lock	Male Luer Lock
Minimum static binding capacity* [mg/unit]	4 / S 5 4 / Q 5 3 / D 5	12 / S 15 12 / Q 15 9 / D 15	60 / S 75 60 / Q 75 45 / C 75 45 / D 75 7.5 / IDA 75 2.2 / Epoxy 75 6 / Protein A 75	80 / S 100 80 / Q 100 60 / D 100
Flow rate** at 0.1 MPa (1 bar | 14.5 psi) [ml/min]	>150	>50	>20	>75
Dead volume [ml]	0.8	1.0	1.3	4.2
Maximum pressure [MPa]	0.4	0.6	0.6	0.6
Storage before use at	Room temperature	Room temperature	Room temperature Protein A 75 at +4°C	Room temperature

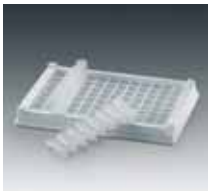
1 ml membrane volume is equal to 36.4 cm^2 membrane area
* Reference proteins ion exchange: S, C: lysozyme, Q, D: BSA, IDA: cytochrome C, epoxy. IgG, Protein A: IgG
** Ion exchange

Overview Membrane Types and Formats

Membrane Type	Description	Pore size (µm)	Capacity* (mg/ml)	Sartobind Lab Scale		Sartobind Process Scale			Sartobind Direct
				A4 sheet	MA 5, 15, 100	MA 75	SingleSep	System	
S	Sulfonic acid	>3	29	•	•	•	•	•	(•)
Q	Quaternary ammonium	>3	29	•	•	•	•	•	(•)
C	Carboxylic acid	>3	22	•		•		•	
D	Diethylamine	>3	22	•	•	•		•	
IDA	Iminodiacetic acid	>3	3.6	•		•		(•)	(•)
Epoxy	Epoxy	0.45	1.1	•		•		(•)	
Aldehyde	Aldehyde	0.45	1	•					
Protein A	Recombinant Protein A	0.45	3			•		(•)	(•)

* Minimum static binding capacity for reference protein, • available, (•) Sartobind Special

For centrifuge

	96 IEX	8 Strip	Mini	Maxi
Application	Screening, disposable	Screening, disposable	Screening, application optimization, disposable	Screening, application optimization, disposable
Membrane material	Stabilized reinforced cellulose			
Membrane diameter [mm]	5	5.5	6.4	22.5
Housing material	Polypropylene	Polypropylene	Polypropylene	Polypropylene
Minimum static binding capacity* [mg/unit]	0.2	IEX: 1 IDA: 130	M: 1 H: 4	M: 12–16 H: 48–64
Maximum volume [ml] (device inner volume)	0.8	0.3	M: 0.5 H: 0.4	M: 20 H: 19
Spin speed [g]	1000	IEX: 1000 IDA: 500	M: 500 H: 2000	M: 500 H: 500
Storage before use at	Room temperature	Room temperature	Room temperature Protein A at +4°C	Room temperature

IEX: ion exchange (S, Q, C, D), IDA: iminodiacetic acid
M: medium, H: high
* Reference proteins ion exchange: S, C: lysozyme, Q, D: BSA, IDA: cytochrome C

Ordering Information

Luer Lock units | sheets | kits

Order No.	Sartobind MA	Quantity
S5F	Sartobind S 5	15
Q5F	Sartobind Q 5	15
D5F	Sartobind D 5	15
S15X	Sartobind S 15	2
Q15X	Sartobind Q 15	2
D15X	Sartobind D 15	2
S75X	Sartobind S 75,	2
Q75X	Sartobind Q 75,	2
C75X	Sartobind C 75,	2
D75X	Sartobind D 75,	2
S100X	Sartobind S 100	1
Q100X	Sartobind Q 100	1
D100X	Sartobind S 100	1
93IDA426DB-12--V	Sartobind IDA 75	2
93EPOX06DB-12--V	Sartobind Epoxy 75	2
93PR-A06DB-12--V	Sartobind Protein A 75	2

Order No.	Sartobind A4 Sheet	Quantity
94IEXS42-001	Sartobind S A4 Sheet	1
94IEXQ42-001	Sartobind Q A4 Sheet	1
94IEXC42-001	Sartobind C A4 Sheet	1
94IEXD42-001	Sartobind D A4 Sheet	1
94IDA-42-001	Sartobind IDA A4 Sheet	1
94EPOX06-001	Sartobind Epoxy A4 Sheet	1
94ALD-06-001	Sartobind Aldehyde A4 Sheet	1

Order No.	Sartobind SingleSep	Quantity
92IEXQ42DN-11	Sartobind Q SingleSep nano 2.5 ml	1
92IEXQ42DN-11--A	Sartobind Q SingleSep nano 2.5 ml	4
92IEXQ42D4-SS--A	Sartobind Q SingleSep mini 7 ml	4
92IEXS42D4-SS--A	Sartobind S SingleSep mini 7 ml	4

Order No.	Accessories	Quantity
VS-AVPQ102	Vivapure Adeno PACK 100 RT*	
VS-AVPQ501	Vivapure Adeno PACK 500	
90-KIT-01	Sartobind Demo Kit	
17002---140	Pair of Luer Lock adapters, black Tefzel to connect Sartobind MA units to a liquid chromatography system with M6 thread	2
16517----------E	Syringe filter holders, 25 mm diameter, polycarbonate for filter or adsorber membrane	12
16214	Syringe filter holder 25 mm diameter, stainless steel for filter or adsorber membrane	1

Related products for production
Sartobind SingleSep capsules
Sartobind System modules
Sartobind Direct

* Vivapure Adeno PACK 100 RT does not contain Benzonase®

96 well plates | 8 strips | spin columns

Order No.	Vivawell	Quantity
VW96IS02	Vivawell-96 S-IEX purification plate	2 plates
VW96IQ02	Vivawell-96 Q-IEX purification plate	2 plates
VW96IC02	Vivawell-96 C-IEX purification plate	2 plates
VW96ID02	Vivawell-96 D-IEX purification plate	2 plates
VW08IS02	Vivawell 8 Strip S-IEX centrifugal purification strips	24 strips (2 plates)
VW08IQ02	Vivawell 8 Strip Q-IEX centrifugal purification strips	24 strips (2 plates)
VW08IC02	Vivawell 8 Strip C-IEX centrifugal purification strips	24 strips (2 plates)
VW08ID02	Vivawell 8 Strip D-IEX centrifugal purification strips	24 strips (2 plates)

Order No.	Vivapure Mini Spin Columns	Spin columns/ Centrifuge tubes
VS-IX01SM24	Vivapure S Mini M	24/48
VS-IX01SH24	Vivapure S Mini H	24/48
VS-IX01QM24	Vivapure Q Mini M	24/48
VS-IX01QH24	Vivapure Q Mini H	24/48
VS-IX01CM24	Vivapure C Mini M	24/48
VS-IX01CH24	Vivapure C Mini H	24/48
VS-IX01DM24	Vivapure D Mini M	24/48
VS-IX01DH24	Vivapure D Mini H	24/48

Order No.	Vivapure Maxi Spin Columns	Spin columns/ Centrifuge tubes
VS-IX20SM08	Vivapure S Maxi M	8/16
VS-IX20SH08	Vivapure S Maxi H	8/16
VS-IX20QM08	Vivapure Q Maxi M	8/16
VS-IX20QH08	Vivapure Q Maxi H	8/16
VS-IX20CM08	Vivapure C Maxi M	8/16
VS-IX20CH08	Vivapure C Maxi H	8/16
VS-IX20DM08	Vivapure D Maxi M	8/16
VS-IX20DH08	Vivapure D Maxi H	8/16

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