Vivaspin® and Vivapore® Devices for General Laboratory Use

Pre-Validation Guide

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1. Introduction

Proteins are critical to many biological processes. Therefore, the measurement of proteins in various human body fluids is important for the diagnosis and monitoring of a variety of diseases and disorders. To enable accurate and early diagnosis, it is often necessary to concentrate or filter the protein content of human specimens prior to analysis. Sartorius Vivaspin® and Vivapore® ultrafiltration devices are the ideal starting point for the qualitative concentration | filtration of proteins and macromolecules from human body fluids, to reach the sensitivity required for accurate detection in subsequent (semi-)quantitative analysis.

These devices are intended for general laboratory use and can be applied in a broad range of scientific research or diagnostic sample preparation workflows.

1.1 Applications for Ultrafiltration

Ultrafiltration is a convective process using anisotropic semi-permeable membranes to separate proteins and other macromolecules from solvents and micromolecules – primarily on the basis of size. It is particularly appropriate for the concentration or filtration of proteins and other macromolecules, and can also be used for purification or solvent exchange. Ultrafiltration is a gentle, non-denaturing method that is more efficient and flexible than alternative processes.

Solute Concentration | Filtration in Clinical Setting

Ultrafiltration devices are commonly used in general laboratory settings for the concentration and filtration of proteins and macromolecules from biological samples, including human specimens such as blood, serum, urine, and cerebrospinal fluid. These devices can also be used in clinical settings for sample preparation prior to the detection of disease markers, such as Bence Jones protein.

The use of ultrafiltration devices in clinical settings can provide a rapid and efficient method for preparing samples for diagnostic testing by improving sensitivity and specificity of diagnostic assays.

Principle

Vivaspin® 500 | 2 | 6 | 20, Vivaspin® Turbo 4 | 15 and Vivapore® 5 | 10 devices are used for the initial preparation step to reduce the volume of human specimens to a volume that contains a higher concentration of the protein and | or other macromolecule in question, if it is present in the specimen. When the protein or other macromolecule of interest is in a high concentration, a higher confidence level of the test results from subsequent semiquantitative or quantitative analysis is given. These devices do not provide specific information on physiological or pathological states, or treatment predictions.

Vivaspin® Filtrate is used for the initial preparation step of filtering human urine specimens to separate the protein or other macromolecule in question, if it is present in the specimen, from larger proteins and macromolecules. When the protein or macromolecule of interest is separated from larger proteins and macromolecules, a higher confidence level of the test results from subsequent semiquantitative or quantitative analysis is given. These devices do not provide specific information on physiological or pathological states, or treatment predictions.

Qualitative claims for Vivaspin®, Vivaspin® Turbo and Vivapore® are based solely on the ability of the devices to reduce human specimens to specific volumes, while retaining and concentrating molecules above a certain molecular weight. These claims have been determined based on the typical performance of a sample of test devices.

Qualitative claims of Vivaspin® Filtrate are based solely on the ability of the devices to filter human specimens, while enabling molecules above or below a certain molecular weight to be retained by or permeate the membrane, respectively. These claims have been determined based on the typical performance of a sample of test devices.

The device does not provide specific information on physiological or pathological states, or treatment predictions, but provides a specimen preparation step to enable subsequent semi-quantitative or quantitative analytical methods by increasing the concentration of macromolecules in the specimen and thus increasing the chance of detection in IVD procedures.

Subsequent diagnostic results may come from instruments and systems such as enzyme linked immunosorbent assay (ELISA), urine protein electrophoresis (UPE), immunofixation electrophoresis (IFE), sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) and | or mass spectrometry (MS), among others.

These analyses are performed after using the devices. Vivaspin® and Vivapore® devices do not offer test results.

1.2 Regulatory Information

European *In Vitro* Diagnostic Regulation ((EU) IVDR 2017/746)

The (EU) IVD Regulation (IVDR) 2017/746 replaced the IVD Directive (IVDD) 98/79/EC in May 2022. The IVDR provides the regulatory framework for manufacturers and for authorized representatives which place *in vitro* diagnostic products on the EU market. Products that satisfy the regulatory requirements and classification rules are permitted to carry the CE IVD mark.

Classification

The IVDR specifies the conditions under which general laboratory products must carry a CE IVD mark. Products that do not fall under the classification rules of IVDR may not carry CE IVD mark, not even for marketing purposes.

Following the issued guidelines from the European Commission Directorate General for Health and Consumers and after conducting a thorough review of the IVDR classification rules, Sartorius has determined that the Vivaspin® and Vivapore® product families do not meet the classification criteria for an IVD product (classification rule 5 of IVDR) and will be classified as general laboratory use (GLU) products.

Since products for GLU do not provide diagnostic results for an individual (e.g., patient) and are not intended specifically for diagnostic applications, they do not require classification as *in vitro* diagnostic devices according to the IVDR and can be applied in a broad range of scientific research or diagnostic sample preparation[1] workflows.

In the context of diagnostic sample preparation, this refers to the use of a product for a variety of procedures associated with preparing samples, prior to semi-quantitative or quantitative analysis by a diagnostic method(s). For example, the Vivaspin® or Vivapore® devices may be used to increase the concentration of disease protein markers from human specimens prior to diagnostic methods such as: enzyme-linked immunosorbent assay (ELISA), urine protein electrophoresis (UPE), immunofixation electrophoresis (IFE), sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) and mass spectrometry (MS).

[1] Final validation and confirmation of GLU product applicability in diagnostic procedures is the responsibility of the diagnostic laboratory.

2. Pre-Validation Guide

This pre-validation guide was specifically created for diagnostic applications where Vivaspin® | Vivapore® products will be used for sample preparation of human specimens. This guide demonstrates how the products should be validated to ensure accurate and reliable diagnostic sample preparation, avoiding technical errors.

2.1 Process Requirements

Specimen Collection and Handling

The human specimen used for the test shall be collected by standard laboratory procedures and based on the requirements related to the specific IVD procedure which will be used.

Vivaspin® and Vivapore® devices are not considered specimen collection devices, although specimens requiring concentration will be placed into the devices. Before and after concentration, the specimen should be transferred to a dedicated storage vessel.

Users operating the device should wear suitable personal protective equipment (PPE) needed for the specimen being handled and as laid out by the clinical laboratory standards and risk assessments. Typically, this includes laboratory gloves, laboratory coat and safety glasses.

To allow for concentration, the specimen will typically be transferred from storage vessel to device and vice versa, using a suitable air displacement pipette, fitted with pipette tip if appropriate.

Pre-analytical Procedure and Quality Control

To our knowledge, no pre-analytical procedure is essential | required for the concentration step with Vivaspin® or Vivapore®. The devices are used in a pre-analytical procedure themselves.

The time required to concentrate a specimen may be affected by several parameters, including MWCO, porosity, specimen protein concentration, viscosity, and temperature.

The use of standard operating procedures is considered good laboratory practice and may contribute to reduced performance variability between devices and human specimens. The user operating the device may choose to use specimens of similar volume and type, and apply fixed system settings, including the same centrifugal force*, duration in the centrifuge*, and processing temperature, for standardized operation of the device.

*not applicable to Vivapore® devices

Use Environment

Vivaspin® or Vivapore® devices are intended for general laboratory use and should therefore only be used in a laboratory setting. The devices are not intended to be used for point of care testing, or by patients, or in a home environment.

Instructions for Use

The guidelines on how to operate the devices can be found in the instructions provided with the product. The instructions contain important information on the correct usage and handling of the device, including any precautions, warnings and steps for proper operation. It is important to read and follow the instructions carefully to ensure that the device is used correctly and to reduce the risk of any potential hazards.

Physical Parameters

During storage, the devices must be protected from exposure to direct light and extremes of temperature and moisture (Table 1). Direct contact of any fluid with the membrane may affect the device performance when used.

Table 1: Physical Parameters of Vivaspin® and Vivapore® devices

	Vivaspin® 6 | 20	Vivaspin® Turbo 4 | 15	Vivaspin® Filtrate	Vivapore® 5 | 10|20
Light	Protect from direct light.			
Storage temperature ranges	15 – 30°C	15 – 30°C	15 – 30°C	4 – 40°C
Operatingtemperature ranges	15 – 25°C	15 – 25°C	15 – 25°C	15 – 25°C
Humidity, fluids	Protect from high humidity (>50%). Keep dry before use.			
Maximum shelf life	2 years	2 years	3 years	1 year

2.2 Validation Procedures

First, the initial total protein (TP) of the collected human specimen sample should be measured using colorimetric dye binding or a similar method. To increase the sensitivity required in subsequent (semi-)quantitative analysis, the specimen must be concentrated | filtered prior to analysis. Laboratories will normally use the initial TP to determine the desired concentration factor (CF). The CF calculation is dependent on the minimum TP recommended for the subsequent analytical method that will be used.

After determining the target CF, most labs will first fill the sample reservoir to its rated capacity and stop the concentration process at the appropriate final volume. With Vivaspin®, the centrifugation time is adjusted to yield the correct final volume but this can be a trial and error process. If a sample is concentrated too much, filtrate or purified water | buffer can be added back to adjust the sample to the desired volume. Other labs will reduce the starting volume to achieve a lower CF. This method has been used for Vivaspin® and has the added benefit of reducing the centrifugation time since a lower volume of sample has to be filtered.

Laboratories will usually generate a chart showing the target CF as a function of the initial TP concentration. Examples of these charts are shown in Tables 1 and 2. The values shown in these tables depend on: (1) the type of concentrator, (2) choice of analytical method, (3) the final desired TP, and (4) the choice of constant or variable sample volume. Note that the CF values are only suggestions and increased concentration may be needed to increase sensitivity in certain analytical methods. Following concentration, the final TP concentration may be calculated by multiplying the starting TP concentration by CF.

Table 1: Concentration Chart

Values using a Vivaspin® 4 with variable sample volume and desired final TP of 1.0 g/dL

Initial TP Conc. [mg/dL]	Sample Volume [mL]	Conc. Volume [µL]	CF	Final TP Conc. [g/dL]
< 25	8	100	80	< 2.0
25 – 50	4	100	40	1.0 – 2.0
51 - 100	2	100	20	1.0 – 2.0
101 – 250	1	100	10	1.0 – 2.5
> 250	0.4	100	4	> 1.0

Table 2: Concentration Chart

Values using a Vivaspin® 6 with constant sample volume and desired final TP of 2.0 g/dL

Initial TP Conc. [mg/dL]	Sample Volume [mL]	Conc. Volume [µL]	CF	Final TP Conc. [g/dL]
< 17	6	30	200	< 3.4
17 - 40	6	50	120	2.0 – 4.8
41 – 70	6	100	60	2.5 – 4.2
71 – 170	6	200	30	2.1 – 5.1
171 – 340	6	500	12	2.1 – 4.1
> 340	6	1000	6	> 2.0

Validation Methods

Concentration procedures should be validated on a regular basis to comply with quality inspections. Measuring TP recovery after human specimen concentration by one of the following methods is a popular way to do this:

I. Protein Recovery by Concentration Factor Test

1. Prepare the specimen as described previously and determine the initial TP (TP1).
2. Fill the concentrator with a defined specimen volume (V1) and perform the concentration (according to the instructions).
3. Measure the final concentrate volume (V2) accurately and then measure final TP (TP2).
4. Calculate the CF according to the equation: $$CF = \frac{V1}{V2}$$
5. Calculate the recovery (R) according to the equation:

$$R\ (\%) = \{\frac{1{,}000 \times TP2}{CF \times TP1}\}$$

The 1,000 factor is used to convert TP2 from g/dL to mg/dL.

Example:
TP1 = 80 mg/dL and V1 = 5 mL
V2 = 100 µL (0.1 mL) and TP2 = 3.4 g/dL (3400 mg/dL)
CF= 5 / 0.1 = 50x.
R = 3400 mg/dL / (50 x 80 mg/dL) = 3400 / 4000 = 0.85 = 85%

II. Protein Recovery by Sample Dilution Test

1. Prepare the specimen as described previously and determine the initial TP (TP1).
2. Fill the concentrator with a defined specimen volume (V1) and perform the concentration (according to the instructions).
3. Add water to dilute the specimen back to the starting volume, mix well and then immediately withdraw the entire specimen from the device.
4. Determine the final TP (TP2) of the re-diluted solution from the concentrator.
5. Calculate the Recovery (R) according to the equation:

$$R\ (\%) = \frac{TP2}{TP1} \times 100$$

Example:
TP1 = 80 mg/dL
TP2 = 70 mg/dL
R= 70 mg/dL / 80 mg/dL = 0.875 = 87.5%

Note

Using TP is not a completely accurate method to measure protein recovery. For example, it is not unexpected to observe loss of small urine proteins through the filter membranes that are measured by clinical analyzers. Some decreased recovery can be attributed to the loss of these proteins, which are not clinically significant. Therefore, samples from patients with known disease are generally better for validation. To minimize the effect of small protein loss, it is also recommended to use samples with an initial TP of 50 mg/dL or higher.

General Considerations

Total protein concentrations, specimen volumes and concentration factors may be entered into a spreadsheet to calculate the average TP recovery (see example in Table 3). Labs should define their own quality criteria but 70 – 80% is usually acceptable.

Table 3: Validation Chart

Values for TP readings using Vivaspin® 4 devices with various patient samples.

Sample number	TP1 Starting Conc. [mg/dL]	V1 Sample Volume [mL]	V2 Conc. Volume [µL]	CF	TP2 Final Conc. [g/dL]	Recovery R
1	30	4	50	80	2.0	83%
2	120	4	200	20	2.2	92%
3	18	4	20	200	2.9	81%
4	60	4	100	40	2.1	88%
Average						86%

To ensure reproducibility, laboratories usually determine the average TP recovery on 20 different human specimens. To ensure precision, laboratories determine the average TP recovery 5 times with the same human specimen. Some laboratories determine these values for each batch of ultrafiltration devices used.

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Laboratory Ultrafiltration
How to Choose the Optimal Device & Method

A Qualification Guide to Aid Device Selection Based on Sample Characteristics

This guide below is designed to help research and process development scientists select the best Sartorius ultrafiltration product for each application. It focuses on the three critical aspects of selection: target molecule type, target size and sample volume, to highlight the most suitable product ranges. Various treatments, process controls and application examples are also provided. This guide is based upon typical ultrafiltration models and selected data. Due to the variations within protein, membrane and inorganic chemistry, we always recommend establishing the most suitable device for your application as part of a robust process optimization strategy.

How to use this guide:

Sample Characteristic

Guidance includes information on the **membrane angle, material** and **MWCO**, the **products available**, and **process methods and controls**.

Some typical recommendations are also provided, based on application testing and data.

Target Type

Proteins (neutral or negatively charged)

Membranes:
Vertical PES, RC or CTA
Products Available:
Vivaspin® 500, 2, 6, 20, 100
Vivaspin® Turbo 4, 15
Vivaflow® 50, 200

Proteins (positively charged)

Membranes:
Vertical HY or RC
Products Available:
Vivaspin® 2, Filtrate
Vivaspin® Turbo 15
Vivaflow® 50R, 200
Vivacon® 500, 2

Viruses

Membranes:
Vertical HY, PES or RC
Products Available:
Vivaspin® 500, 2, 6, 15R, 20, 100
Vivaspin® Turbo 4, 15
Vivaflow® 50, 50R, 200

Extracellular Vesicles

Membranes:
Vertical HY, PES or RC
Products Available:
Vivaspin® 500, 2, 6, 15R, 20, 100
Vivaspin® Turbo 4, 15
Vivaflow® 50, 50R, 200

Nucleic Acids

Membranes:
Horizontal HY or CTA
Products Available:
Vivaspin® Filtrate
Vivacon® 500, 2

Inorganics

Membranes:
Vertical HY, PES or RC
Products Available:
Vivaspin® 500, 2, 6, 15R, 20, 100
Vivaspin® Turbo 4, 15
Vivaflow® 50, 50R, 200

Target Size*

<10 kDa

MCWOs:
2 or 3 kDa
Products Available:
Vivaspin® 500, 2, 6, 15R, 20
Vivaspin® Turbo 4, 15
Vivaflow® 50, 200
Vivacon® 500, 2

10 – 30 kDa

MCWOs:
3 or 5 kDa
Products Available:
Vivaspin® 500, 2, 6, 15R, 20, 100
Vivaspin® Filtrate, Turbo 4, 15
Vivaflow® 50, 50R, 200

30 – 150 kDa

MCWOs:
10, 20, 30 or 50 kDa
Products Available:
Vivaspin® 500, 2, 6, 15R, 20, 100
Vivaspin® Filtrate, Turbo 4, 15
Vivaflow® 50, 50R, 200
Vivacon® 500, 2

150 – 500 kDa

MCWOs:
50, 100 or 125 kDa
Products Available:
Vivaspin® 500, 2, 6, 20, 100
Vivaspin® Filtrate, Turbo 4, 15
Vivaflow® 50, 50R, 200
Vivacon® 500, 2

500 – 1000 kDa

MCWOs:
100, 125 or 300 kDa
Products Available:
Vivaspin® 500, 2, 6, 20, 100
Vivaspin® Filtrate, Turbo 4, 15
Vivaflow® 50, 50R, 200
Vivacon® 500, 2

>1000 kDa

MCWOs:
300 or 1,000 kDa, 0.2 µm
Products Available:
Vivaspin® 500, 2, 6, 20, 100
Vivaspin® Filtrate
Vivaflow® 50, 200

Sample Volume

0.1 – 2.5 mL

Process Method:
Centrifuge
Products Available:
Vivaspin® 500, 2, Filtrate
Vivacon® 500, 2

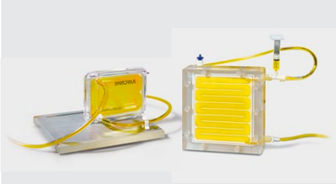
2.5 – 20 mL

Process Method:
Centrifuge, pressure or pressure-fuge
Products Available:
Vivaspin® 6, 15R, 20, Filtrate
Vivaspin® Turbo 4, 15

20 – 100 mL

Process Method:
Centrifuge, pressure or pressure-shake
Products Available:
Vivaspin®100

100 - 5,000



Process Method:
Crossflow
Products Available:
Vivaflow® 50, 50R, 200

Treatment and Control

Buffer Exchange

Key Points:
Replacing the original buffer or desalting a sample to, e.g., ensure target molecule stability by preventing precipitation. Diafiltration allows for simultaneous buffer exchange and concentration
Process Control:
Diafiltration available to all products, especially with **Vivaspin® 20 diafiltration cups and Vivaflow® diafiltration reservoir.**

Application Note: ☑

Low Concentrations

Key Points:
Samples with low concentrations rely on near 100% recovery, preventing non-specific adsorption is key for this
Process Control:
Passivation by rinsing with non-interfering protein and buffer solutions (e.g. BSA, Tween 20, SDS). Available to **all products.**

Application Note: ☑

Depyrogenation

Key Points:
Removal of endotoxins (lipopolysaccharides) from devices before sample concentration.
Process Control:
NaOH treatment prior to concentration and buffer exchange. Available in products resistant to NaOH; **Vivaspin® Turbo 4 and 15, Vivaflow® 50R and 200**

Application Note: ☑

Device Sanitization

Key Points:
Reduction of bioburden and contaminating microbes. Level of reduction to be determined by user testing.
Process Control:
Pre-rinse with 70% ethanol or apply an EtO gas treatment process. Available to **all products excluding Vivaspin® 100 and Vivaflow®** (separate cleaning processes)

Application Note: TBA

Final Volume

Key Points:
Varying speeds of concentration make it hard to judge time to reach the desired final volume.
Process Control:
Pre-filling the filtrate tube limits the maximum concentration factor, thereby defining the final concentrated volume.
Available to **Vivaspin® 500, Vivaspin® Turbo 4 and 15**

Application Note: ☑

Sensitive Samples

Key Points:
Changing transmembrane pressures can result in varied shear stresses, degrading sensitive target molecules.
Process Method:
Pressurization and TFF provide more stable transmembrane pressure and flux compared to centrifugation. Available in **Vivaspin® 100 and Vivaflow®**

Application Note: ☑

Example Applications

1. Monoclonal Antibodies

Application: Concentration for purification
Target: IgG1, IgG2a, IgG2b, IgG3
Target Size: 160 kDa
Sample Volume: 3 L
Product Used: Vivaflow® 200, 30 kDa MWCO PES
Process Control: Pre-rinsing with 2 L DI water to remove storage buffer and perform integrity check.
Result: 98% recovery from 3 L Hybridoma cell culture supernatant concentrated 10-fold, from 30 to >300 mg/L, with an average flux of 20 - 25 mL/min (2 hour total processing time).

2. Extracellular Vesicles

Application: Concentration and purification of EVs
Target: Exosomes, microvesicles, apoptotic bodies
Target Size: 50 - 5,000 nm
Sample Volume: 2 mL
Product Used: Vivaspin® 2, 6, Turbo 4 or Filtrate, 10 kDa MWCO PES, HY or CTA
Process Method: Device benchmarking for optimal concentration of EVs from cell culture media.
Results: 7 to 9-fold conc. factor in ≤ 8 min. Highest recovery and purity of EVs with mean particle size of 150 nm (NTA) was observed when using Vivaspin® 2 with 10 kDa MWCO PES membranes.

3. Lentivirus

Application: Polishing after AEX chromatography
Target Type: Lentiviral vector
Target Size: ~100 nm
Sample Volume: 20 mL
Product Used: Vivaspin® 20, 100 kDa MWCO PES
Process Control: Parallel desalting and concentration with diafiltration cup
Results: 78 to 143-fold concentrations of 20 mL samples within 34 – 40 minutes, increasing particle concentration from 6.1×10^7 to 3.0×10^9 per mL after purification.

4. DNA PCR Primers

Application: Concentration and purification of DNA
Target: dsDNA
Target Size: 300 bp
Sample Volume: 1.8 mL
Product Used: Vivacon® 2, 30 kDa MWCO HY
Process Control: Separation of amplified DNA from PCR primers.
Results: Near total removal (> 95%) of primers and near total retention and recovery of 300 bp target DNA, within a 20 minute spin time and a total 40 minute procedure time.

Find further details of all tips, tricks, applications and products by contacting your local Sartorius representative.
www.sartorius.com

*To convert from diameter or nucleic acid length to molecular weight, please refer to the table in the Laboratory Ultrafiltration Selection Guide

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Laboratory Ultrafiltration Troubleshooting Guide

Find solutions to issues which may be encountered when using lab ultrafiltration devices and processes.

Issue Description	Root Cause	Resolution
Target molecule permeates the membrane	MWCO	Ensure the MWCO is a maximum 1/2 the size of the target. If the issue persists, consider the sample properties, choose a MWCO around 1/6 the size of the target and re-assess recovery.
	Sample composition	Chemical incompatibilities can lead to membrane or housing material damage. Check chemical compatibility in the Instructions for Use and adjust the sample composition or device choice accordingly.
	Membrane integrity	Membrane discrepancies may occasionally become apparent, since relatively small areas are used in lab ultrafiltration devices. In case multiple devices are affected with no other cause, reach out to your local Sartorius contact for support.
Target molecule not detectable in retentate or permeate	Membrane adsorption	High surface areas within the membrane matrix may contribute to non-specific binding, especially with “sticky” targets. Use a buffer rinse to desorb weakly-bound material, try a different membrane material, adjust the sample composition, or minimize contact time.
	Sample preparation	Analyze samples before and after ultrafiltration, to check whether an issue has occurred during sample preparation. Confirm that the method used for quantification or analysis is appropriate for the sample type.
Target molecule recovery is too low	MWCO	Ensure the MWCO is a maximum 1/2 the size of the target. If the issue persists, consider the sample properties, choose a MWCO around 1/6 the size of the target and re-assess recovery.
	Membrane adsorption	High surface areas within the membrane matrix may contribute to non-specific binding, especially with “sticky” targets. Use a buffer rinse to desorb weakly-bound material, try a different membrane material, adjust the sample composition, or minimize contact time.
	Sample precipitation	High initial concentrations, over-concentration or changing salt concentrations may cause target aggregation or precipitation. Dilute the sample, add solubilizing agents, implement continuous diafiltration, reduce RCF, or pre-define final retentate volumes.
Fractionation of target molecules is unsuccessful	Insufficient size difference	For reliable separation by ultrafiltration, at least a 10-fold size difference is recommended. With smaller size differences, consider diafiltration to increase separation efficiency, or an alternative method, such as size exclusion chromatography.
	Similar molecule properties	Shared properties, such as structural dimensions, foothold or PI may affect retention and passage. Try adjusting the sample buffer composition to encourage charge differences or aggregation, or test an alternative method.
Target molecule degrades during ultrafiltration	Sample precipitation	High initial concentrations, over-concentration or changing salt concentrations may cause target aggregation or precipitation. Dilute the sample, add solubilizing agents, implement continuous diafiltration, reduce RCF, or pre-define final retentate volumes.
	Shear stress	Changing pressures may cause degradation of sensitive targets, such as enveloped viruses or membrane proteins. Ensure consistent, lower transmembrane pressures by reducing RCF, or using pressure cells or tangential flow devices.
Ultrafiltration takes too long	MWCO	Lower MWCOs may increase target recoveries but increase processing time and retention of low MW contaminants. Test a higher MWCO, or try using a device with a larger active membrane area and | or optimized design, which may be better suited to the sample type.
	Sample composition	Particle loaded samples or viscous solutions take significantly longer to process. Clarify samples by microfiltration, try pressure-fugation or pressure-shake methods.
	Temperature	Lower temperatures reduce membrane passage dynamics. Where possible, process samples at higher temperatures, or try a higher MWCO, pressure-fugation or pressure-shake methods.
Target molecule is contaminated after ultrafiltration	Microbial contamination	Most lab ultrafiltration devices are supplied non-sterile and may have low levels of bioburden. Treat devices with 70% ethanol or ethylene oxide gas before use. Note: do not allow the membranes to dry out after sanitizing.
	Other organic contamination	Contamination by endotoxins or nucleases may be possible. De-pyrogenate devices with NaOH (for devices with appropriate chemical compatibility) or pre-rinse with WFI before use. If residual DNA must be avoided, use ethylene oxide-treated PCR grade devices. Note: do not allow the membranes to dry out after pre-treatment.
	Inorganic contaminants	Ultrafiltration membranes contain trace amounts of glycerine for stability during storage, which may interfere in downstream analyses. Pre-rinse the device with water or buffer before use. Note: do not allow the membranes to dry out after pre-rinsing.
Ultrafiltration device is damaged or defective	Production or shipping	If damage or defects are identified upon delivery, reach out to your local Sartorius contact for support.
	Crazing	The appearance of fine lines within the plastic housing of some ultrafiltration devices can be expected, especially during longer-term storage. Device performance will not be affected, and the product can still be used as normal.
	Handling or storage	Damage or faults may be identified some time after delivery of the devices. Check that the devices have been stored and handled correctly, according to the Instructions for Use, and that they are still within the expiry date printed on the packaging label.
Ultrafiltration membranes have dark spots or patches	Moisture	In rare environmental conditions during shipping or storage, moisture may accumulate on the membrane by condensation. Allow the membrane to dry within the recommended storage temperature ranges. There is no negative impact on performance.
	Contamination	Dark spots on dry membranes are usually cosmetic and have no negative impact on performance. In case issues are detected with samples concentrated with these membranes, reach out to your local Sartorius contact for support.

For more information and support, speak with your local Sartorius contact or visit: www.sartorius.com

Contacts

Germany
Sartorius Lab Instruments GmbH & Co. KG
Otto-Brenner-Straße 20
37079 Göttingen
Phone +49 551 308 0

USA
Sartorius Corporation
565 Johnson Avenue
Bohemia, NY 11716
Phone +1 631 254 4249
Toll-free +1 800 635 2906

UK
Sartorius Stedim Lab Ltd.
Sperry Way, Stonehouse Park
GL10 3UT Stonehouse, Gloucestershire
Phone: +44 1453 821972

For further information, visit
www.sartorius.com

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