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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