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Laboratory Ultrafiltration Troubleshooting Guide

Quickly find solutions to problems that may arise during ultrafiltration and diafiltration processes.

Problem	Cause	Solution
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 properties of the feed, choose a MWCO around 1/6 the size of the target and re-assess recovery.
	Feed composition	Chemical incompatibilities can lead to membrane or housing material damage. Check chemical compatibility in the instruction manual and adjust the feed composition or chosen ultrafilter accordingly.
	Membrane integrity	Membrane discrepancies may occasionally become apparent, since relatively small areas are used in lab ultrafilters. In case multiple ultrafilters are affected with no other cause, contact Sartorius 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. Ensure the MWCO is not too high, use a buffer rinse to desorb weakly-bound material, try a different membrane material, adjust the feed composition, or minimize contact time.
	Feed preparation	Analyze samples before and after ultrafiltration, to check whether an issue has occurred during feed preparation. Confirm that the method used for quantification or analysis is appropriate for the target molecule.
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 properties of the feed, 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. Ensure the MWCO is not too high, use a buffer rinse to desorb weakly-bound material, try a different membrane material, adjust the feed composition, minimize contact time.
	Molecule precipitation	High feed concentrations, over-concentration or changing ionic strength may cause target aggregation or precipitation. Dilute the feed, add solubilizing agents, implement continuous diafiltration, reduce RCF, or pre-define final retentate volumes.
Molecule fractionation or removal is unsuccessful	Insufficient size difference	For reliable separation by ultrafiltration, at least a 10-fold size difference is recommended. Try diafiltration to increase separation efficiency, or an alternative method, such as size exclusion chromatography.
	Similar molecule properties	Shared properties, such as size, conformation or pI may affect retention and passage. Try adjusting the feed buffer composition to encourage charge differences or aggregation, or test an alternative method.
	Co-concentration	Low MW molecules can remain in the retentate of complex samples, even with high MWCO membranes. Implement a purification step before ultrafiltration, use diafiltration to encourage passage.
Target molecule degrades during ultrafiltration	Molecule precipitation	High initial concentrations, over-concentration or changing ionic strength may cause target aggregation or precipitation. Dilute the feed, 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 or tangential flow ultrafiltration..
Ultrafiltration | diafiltration 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 an ultrafilter with larger membrane area or advanced design.
	Membrane area	Refilling ultrafilters will extend processing times, and particle loaded feeds or viscous solutions take significantly longer to process. Choose an ultrafilter with sufficient capacity for the feed, try an ultrafilter with excess capacity relative to the feed, minimize the number of refills.
	Feed composition	Particle loaded feeds or viscous solutions take significantly longer to process. Clarify the feed by microfiltration, try pressure-fugation, pressure-shake, counterflow or tangential flow ultrafiltration.
	Temperature	Lower temperatures reduce membrane passage dynamics. Where possible, increase process temperatures, or try a higher MWCO, pressure-fugation or pressure-shake ulrafiltration.
Target molecule is contaminated after ultrafiltration	Microbial contamination	Most ultrafilters are supplied non-sterile and may have low levels of bioburden. Sanitize ultrafilters with 70% ethanol or ethylene oxide before use. Note: do not allow the membranes to dry out after sanitizing.
	Other organic contamination	Contamination by endotoxins, nucleases, nucleic acids or carry-over from previous runs may be possible. De-pyrogenate ultrafilters with NaOH (for those with appropriate chemical compatibility) or pre-wash with WFI before use. If residual DNA must be avoided, use PCR grade ultrafilters. Do not re-use single use ultrafilters. 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-wash ultrafilters with water or buffer before use. Note: do not allow the membranes to dry out after pre-treatment.
Ultrafilter is damaged or defective	Production or shipping	If damage or defects are identified upon delivery, contact Sartorius for support.
	Crazing	The appearance of fine lines within the plastic housing of some ultrafilters is normal, especially during longer-term storage. Ultrafiltration | diafiltration performance will not be affected. The product can still be used.
	Handling or storage	Damage or faults may be identified some time after delivery. Confirm the product was correctly stored and used, according to the instruction manual, and that the expiration date has not passed.
Ultrafiltration membranes have dark spots or patches	Moisture	In rare environmental conditions during shipping or storage, moisture may condense on ultrafiltration membranes. Allow membranes to dry within the recommended storage temperature range. The product can still be used.
	Contamination	Dark spots on dry membranes are usually cosmetic and have no negative impact on performance. In case issues are detected with feeds concentrated with these membranes, contact Sartorius for support.

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

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