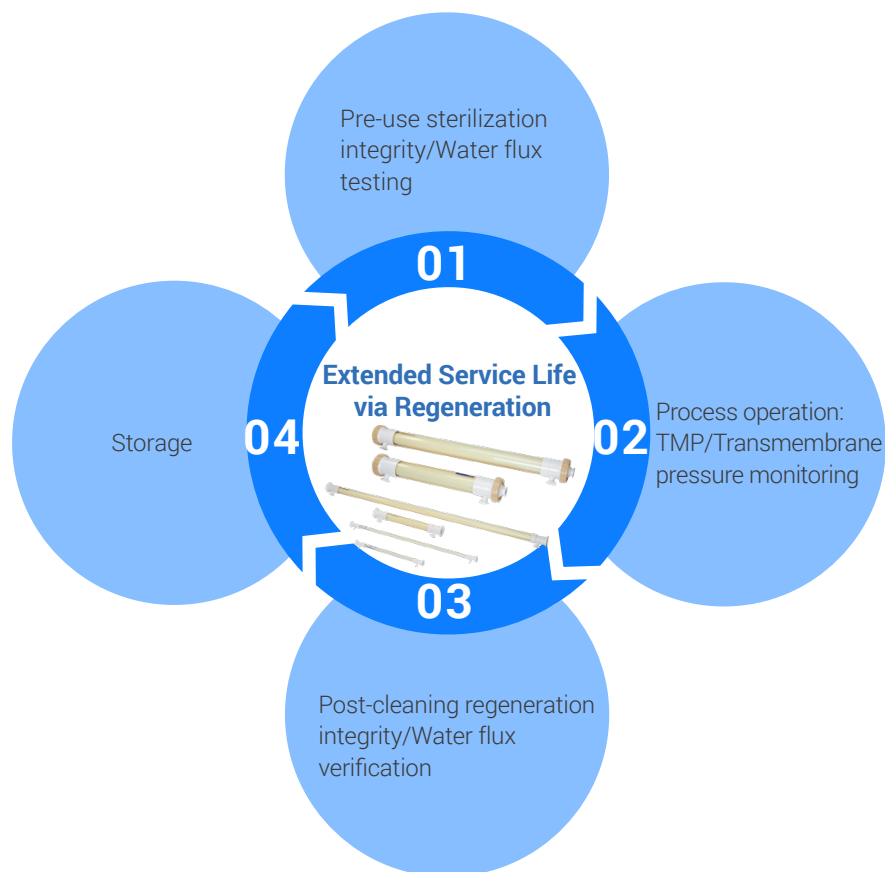




Biophsep™ Hollow Fiber Cleaning and Reuse Guidelines





Hollow fiber membranes, characterized by their unique porous structure, high separation efficiency, and low shear stress properties, are widely employed in pharmaceutical production and serve as key materials in drug separation and purification processes.

During operation, hollow fiber membranes are susceptible to contamination and fouling, which can result in diminished membrane flux and separation efficiency. Physical or chemical cleaning methods can be utilized to remove contaminants from the membrane surface and pores, thereby restoring their initial filtration performance.

It can also effectively prevent cross-contamination between batches, eliminate contaminants and residual residues, prevent microbial and pyrogenic contamination, maintain process flux and production efficiency, ensure stable yield and product quality, and maximize service life through thorough cleaning.

Recommended Cleaning Agents and Temperature Parameters

The LRV results determined by plaque assay showed that under low pressure, recommended pressure, and high pressure conditions, the MVM levels were reduced below the quantitation limit, demonstrating the robust viral removal performance of the filter under all three pressure conditions and during process pauses.

Cleaning agents must:

- Be compatible with hollow fiber modules and hardware systems
- Be fully removable post-cleaning
- Have verifiable removal efficacy
- Utilize commonly available chemical types

Contaminant Examples	Cleaning Agent Type	Concentration	pH	Operating Temperature	Time	Residue Validation
Protein hydrolysates, Saponified lipids	NaOH	0.1-0.5M	>13	25-45 °C	30-60min	pH Test
Most organic compounds & cellular debris	NaClO Available Chlorine	300-500ppm	9-10	25-45 °C	30-60min	Colorimetry/ Conductometry
Nucleic acid hydrolysates, inorganic salts (Fe/Mn)	Citric acid	1.0%	3	25-45 °C	30-60min	pH Test
Nucleic acid hydrolysates, inorganic salts (Fe/Mn)	Phosphoric acid/Nitric acid	0.1M	1	25-45 °C	60-90min	pH Test
Liposome/LNP	Ethanol	50-70%	6-7	25-45 °C	30-60min	UV/Conductometry
Lipopolysaccharide	SDS	0.1%	5-8	25-45 °C	30-60min	UV/Conductometry
Protein/Protein precipitation	Urea	7M	8	25-45 °C	30-60min	UV/Conductometry

Table 1: Commonly Used Cleaning Agents and Temperature Recommendations

Cleaning Process Development Methodology

To evaluate the cleaning effectiveness of hollow fiber membranes, we can test the recovery rate of the normalized water flux before and after cleaning.

- **Normalized Water Permeability**

$$\text{NWP} = \frac{\text{Permeate flow}}{\text{Area} \times \text{TMP}}$$

- **Water Flux Recovery Rate**

$$\text{Water Flux Recovery Rate} = \frac{\text{NWP (after CIP)}}{\text{NWP (before use)}}$$

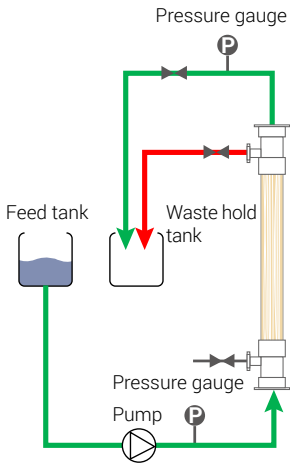
Recommended Ceaning Strategies:

- Implement NaClO treatment followed by acidic cleaning agents, with post-storage testing
- Evaluate comprehensively through process flux, product quality, and NWP recovery metrics
- Cleaning efficacy enhancement hierarchy: Temperature elevation > Extended cleaning duration > Increased tangential flow velocity
- For initial use, develop CIP methods achieving $\geq 70\%$ NWP recovery
- Conduct pre-/post-use NWP comparisons under identical test parameters (tangential flow velocity, TMP)
- Monitor post-storage NWP for slow-release contaminants

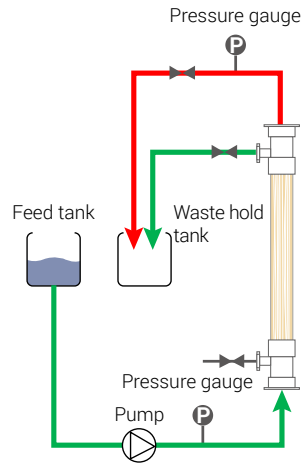
Parameter	Typical Recommendation	Development guideline
Cleaning agent type	NaOH	Select based on contaminant types.
Cleaning agent type	0.5M	Apply at suggested concentration levels.
Temperature	25-45°C	Elevating temperature improves efficacy.
Time	30-120min	Optimize protocols through process-specific parameter refinement.
Tangential flow velocity (TFV)	6000-10000S-1 Shearing	Avoid employing excessively low flow rates during operation.

Table 2 : Recommendations of Cleaning Process Development

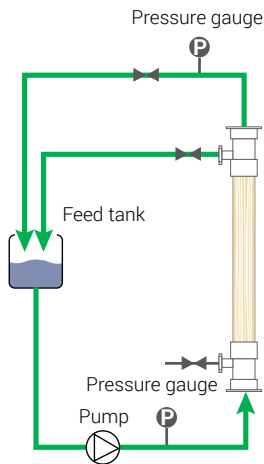
Hollow Fiber Membrane Cleaning Sequence



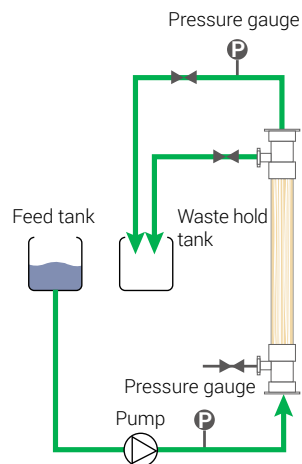
Feed Port Flushing:
Remove residual feed solution



Permeate Port Flushing:
Remove residual feed solution



Recirculation Flushing for Regeneration

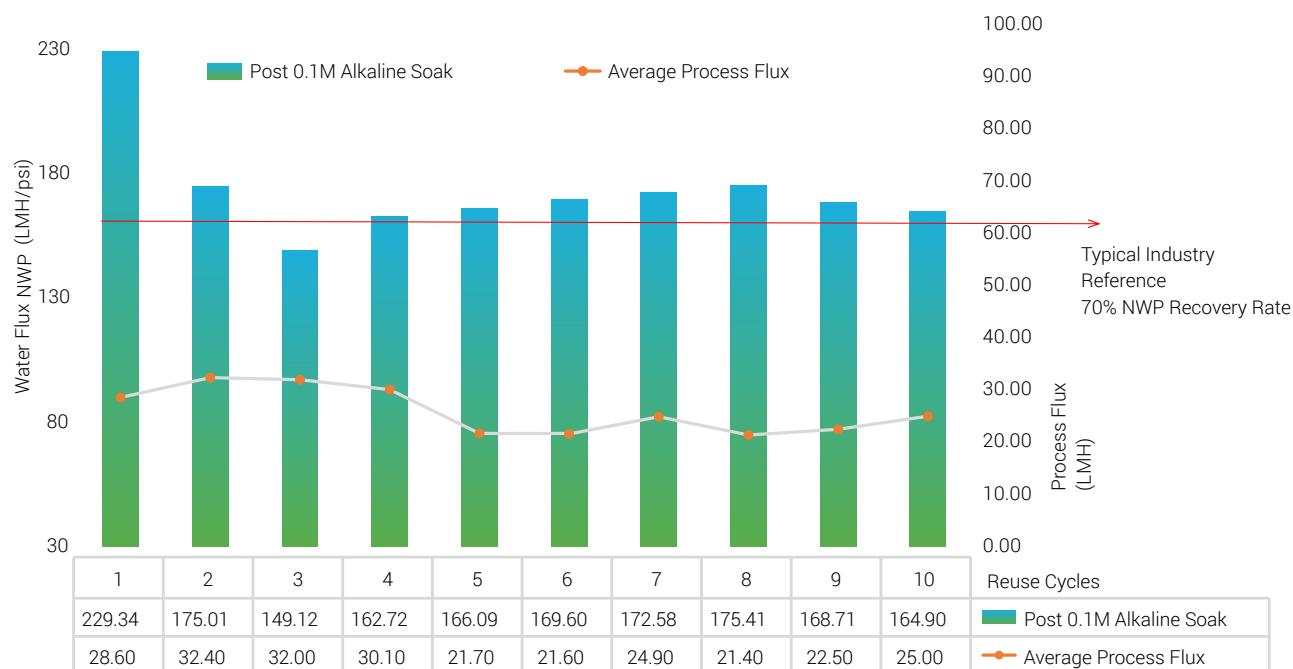


Water flushing:
Remove residual cleaning solvent

Tips

Keep cleaning records and record relevant test processes and parameters

Cleaning Efficacy Demonstration



Typical NWP recovery rates: 70-80% post-cleaning

Process flux averages: ~30 LMH for first 4 cycles, ~23 LMH for subsequent 6 cycles
(varies with material batches)

Cleaning Efficacy Demonstration

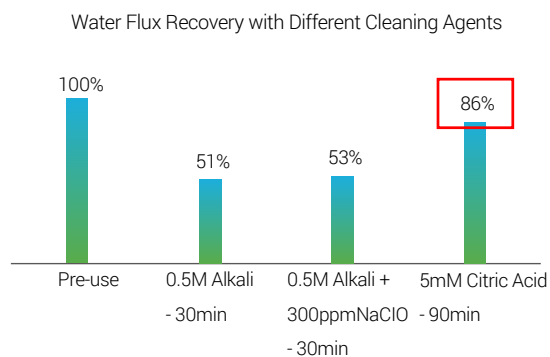
Study 1: Insulin Project, 100kDa Clarification

Materials

36 pcs of Cobetter Hollow Fiber (Part No.: HFEU501000810),
filtration area 468 m²

Results

Optimized from retaining 50% of the feed to retaining only 2%.



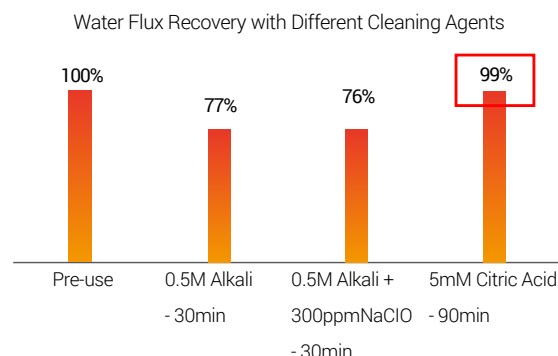
Study 2: Collagen Project, 50/100kDa Clarification

Materials

Cobetter Hollow Fiber

Results

The water flux recovered to 100% after cleaning. The second test indicated no gel permeated.



Summary of Case Study 1 and 2

Optimized cleaning protocols significantly improved yield retention during second reuse cycle. For nucleic acid-based contaminants resistant to alkaline cleaning, acid washing is recommended.

Post-Cleaning Storage Recommendations

Hollow Fiber Membrane	Storage Time	Recommended Storage Solvent	Recommended Storage Temp
Biophsep™ Hollow Fiber mPES	≤3 days	WFI	25°C
	≤1 month	0.1M NaOH	25°C
	≤12 months	0.05-0.1M NaOH	4°C

Tips

- Never store dried or frozen
- Maintain storage solution sealed within hollow fiber cartridges
- Optimal storage: 4°C refrigeration (≤25°C maximum), protected from direct sunlight
- Replace storage solution monthly initially; adjust replacement frequency based on validation studies

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Specifications subject to change without notice.