CASE STUDY

Enhancing nanofiltration efficiency in mAb production process

Syngene

Putting Science to Work

The context

Nanofiltration is a highly effective viral clearance method in mAb manufacturing, primarily based on size exclusion. An essential part of validating the efficacy of the nanofiltration step are virus spiking studies to ensure the nanofiltration process can reliably remove viruses and meet regulatory requirements for product safety.

The requirement

A major pharmaceutical company was facing challenges in the nanofiltration step of their mAb production process. During virus spiking at 1% - 0.5% of the load volume, they encountered reduced filtration efficiency and flux decay. These issues affected the overall performance of the nanofiltration step, including increasing operational costs due to the need for frequent filter changes.

The pharma company decided to partner with Syngene to address these problems. Their goal was to improve the efficiency of the nanofiltration process in order to achieve viral clearance and reduce operational costs

Challenges posed by the nanofiltration process

- Low protein concentration: Low protein concentration passing through the membrane resulting in reduced filtration efficiency.
- Filter flux decay: High flux decay during protein processing affecting filter performance.
- Low virus clearance efficiency: Need to ensure effective virus clearance while maintaining high throughput.
- Compatibility issues: Adapting the spike percentage so that it was compatible with the filter, protein matrix, and virus concentration.

The solution

Our team approached the problem by focusing on optimizing the nanofiltration process. The solution involved a multi-step methodology.

1. Optimization of viral load: Our Viral Testing team adjusted the viral load used in the spiking studies to a level that ensured high throughput while maintaining effective virus clearance. This was crucial for overcoming the limitations of low protein concentrations and improving filter performance.
2. Adjustment of spike percentage: By decreasing the spike percentage in the suspension, we enhanced compatibility with the filter and protein matrix. This adjustment was critical for minimizing flux decay and maintaining effective virus clearance.
3. Enhanced filter compatibility: We carefully matched the filter, protein matrix, and virus concentration to improve overall filtration efficiency. This included selecting filters with optimal characteristics for handling the adjusted spike percentage.
4. Implementation and monitoring: We implemented the process in a controlled manner with continuous monitoring to ensure the flux decay remained low and the virus aggregates also remained controlled. Real-time data was used to make necessary adjustments and optimize performance.

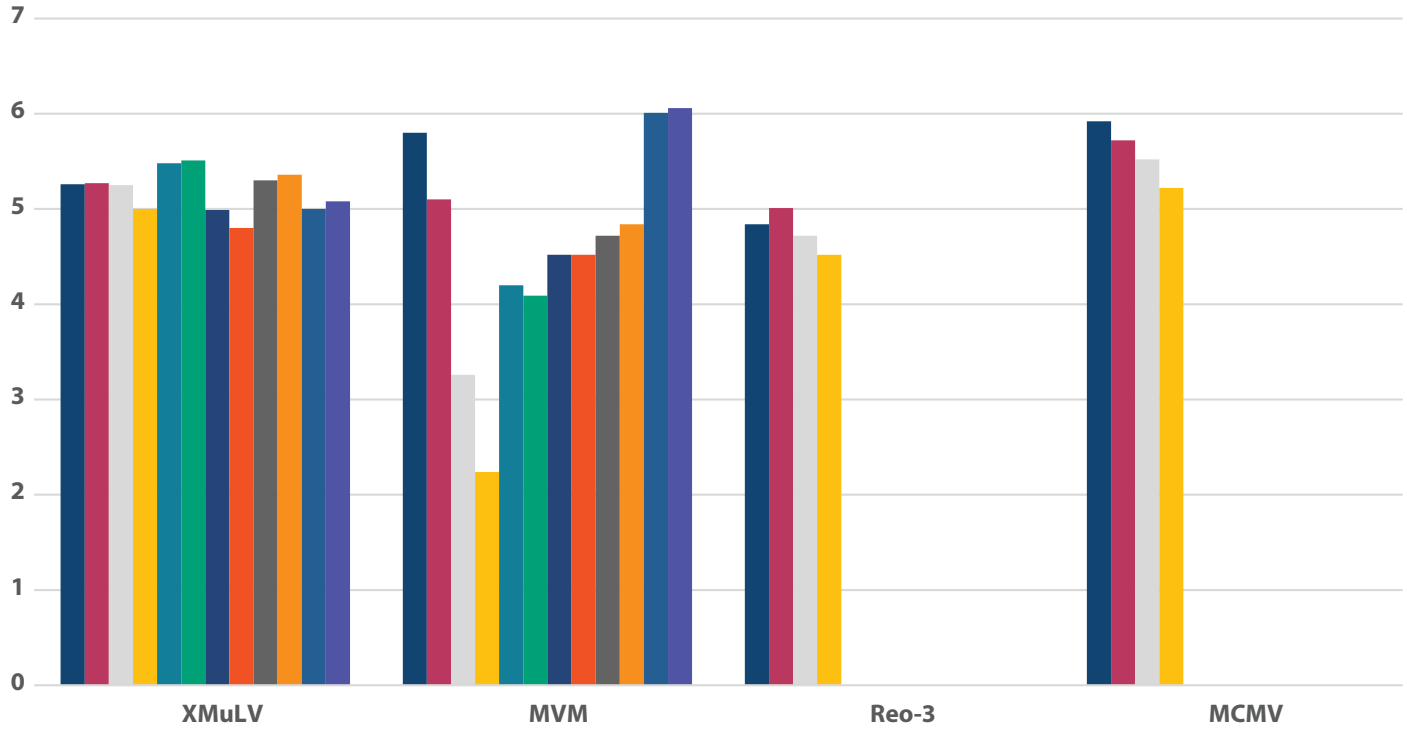

Figure 1: The graph shows virus clearance attained during the nanofiltration step across four different viruses. The Y axis depicts the log reduction value for each virus. Optimum virus clearance achieved is a combination of factors such as protein- virus interaction, virus spike concentration and filter fouling due to feed quality.

Impact and results

After implementing our solution, the client successfully achieved the desired target throughput with flux decay levels at under 40%. The virus aggregates were effectively controlled, resulting in a more efficient and cost-effective nanofiltration process. The optimized process enabled the client to operate at higher flow rates, while maintaining effective virus clearance throughout the process. The new process also required fewer filter changes, significantly reducing overall costs.

Future plans

The client is considering further collaboration with Syngene to explore additional optimizations and innovations in their manufacturing processes. Our expertise continues to be a key driver in advancing the client's production capabilities and ensuring continued success in drug manufacturing.

Our ongoing capability and capacity expansion in biologics have established Syngene as one of the largest CRDMOs in India. As a trusted biologics partner, we have delivered 100 commercial batches in the last two years. Our track record of over 250 GMP batches, 150+ projects, and support for over 25 INDs across biologics modalities is a testament to our expertise.

To know more about our Viral Testing and Clearance services, **contact our experts**

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