Case Study

Improving Upstream Prefiltration and Converting Sterilizing Filters in New Process Design

Background

An animal serum processing company was experiencing low flow and extended processing times during upstream prefiltration of their product, which lead to multiple, mid-batch filter changes and product loss. To address these issues, the company chose to redesign their filtration process and desired to work with a single supplier to assure product consistency and provide qualification testing.

Upstream Prefiltration

Evaluation & Testing

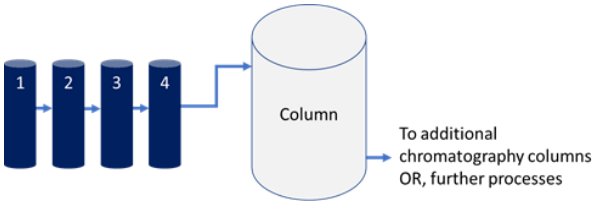
The CPF Technical Service team evaluated the current filtration process which consisted of four different steps using filters from various vendors. No formal research had been done before implementation on how these filters would interact. Long, unacceptable processing times were experienced, which took up to 48 hours to process a 30-liter batch. In addition, inconsistent amounts of gel were reappearing from batch to batch after filtration. Although pre-screening through a 100-micron strainer or decanting the serum from the gels would improve the process, neither option would be practical at full scale.

Customer samples of animal serum were then tested in the CPF Application lab. The primary step was to identify a first stage filter (particle filtration) that could process a 30-liter batch without prescreening or decanting. Three media were tested using 47 mm discs. Both constant flow and constant pressure tests were performed to predict the expected throughput for a 10" filter. The results are as follows:

Media	Pore Size	Projected Volume (for 10" filter)
Polypropylene Depth	1 µm	7 liters
Fiberglass Depth	1 µm	33 liters
Fiberglass Depth	10 µm	65 liters

Similar testing was performed using the serum to identify appropriate filters for clarification, prefiltration and bioburden reduction steps which would allow processing 30-liters through a single 10-inch filter. The optimized filters were identified as:

1) Particle Filtration: PGD Fiberglass filter (10 µm)
2) Clarification: PGD Fiberglass filter (1 µm)
3) Prefiltration: PPD Polypropylene Depth (1 µm)
4) Bioburden Reduction: BPS (0.22 µm or 0.45 µm) Polyethersulfone filters



Serum processing using the above filtration sequence showed no sign of gel reappearance after three weeks of

storage at 4°C. Although the data showed the PGD filter (1 µm) to be acceptable as the first filter in the series, a PGD (10 µm) was recommended due to the inconsistency of the gel content in the serum.

Post Installation Results

The CPF Technical team assisted with the installation of the new filtration process, provided training for personnel and verified the operation of the filter train. The customer benefitted from placing filters in a series as opposed to four separate steps. A batch was successfully processed with the 4 recommended filters listed. Throughput has increased more than 100%, while processing time for a 30-liter batch of serum was reduced to less than 24 hours (about 50% reduction).

An additional batch was also completed successfully without the PGD 10 µm filter on serum with a lower level of visual gels. As a result of this test, CPF developed a "filterability test" using 47 mm disks of the 1 µm Fiberglass media and a small volume of serum that the customer could use to determine whether or not the 10 µm filter would be required on future runs.

The Technical Service team provided written documentation on filter operation, reviewed the existing customer documentation with recommended revisions, and generated a written procedure for the filterability test.

The upstream issues were addressed and the new process design has reaped great benefits with Critical Process Filtration cartridge filters.

Transitioning Sterilizing Filters

The company's desire to work with a single supplier also meant qualifying CPF's sterilizing filters by means of competitive testing.

Filter Requirements

CPF's application engineers partnered with the customer's process team to establish a list of capsule filter design and performance characteristics that were critical to filter acceptance in the application. They included product specifications, membrane testing and regulatory compliance.

Filter Comparisons: CPF vs Another Vendor

The customer was using different size capsule filters from another supplier. All of the capsule filters were made with dual-layer polyethersulfone (PES) membrane. The following table shows the basic capsule configurations used by the customer (Comp 1 & 2) and CPF's equivalent filters (CPF/PPS1 & CPF/PPS2) used in the evaluation. The following charts show the comparison results.

Models Tested

Filter	Body Length	Membrane	Filtration Area
Comp 1	3.31"	Dual layer – PES 0.45/0.22 µm	0.1 m^2
CPF/PPS1	2.53"	Dual layer – High Capacity PES 0.45/0.22 µm	0.093 m^2
Comp 2	5.8"	Dual layer – PES 0.45/0.22 µm	0.2 m^2
CPF/PPS2	5.63"	Dual layer – High Capacity PES 0.45/0.22 µm	0.278 m^2

Integrity Test Values

Filter	Bubble Point	Diffusive Flow
Comp 1	≥ 46 psi	≤ 5 mL/min @ 36 psi
CPF/PPS1	≥ 50 psi	≤ 4.3 mL/min @ 35 psi
Comp 2	≥ 46 psi	≤ 7 mL/min @ 36 psi
CPF/PPS2	≥ 50 psi	≤ 12.9 mL/min @ 35 psi

Water Flow Rate

Filter	Clean Water Flow Rate (liters/min @ 1 psid)
Comp 1	1.5
CPF/PPS1	1.7
Comp 2	2
CPF/PPS2	6

Membrane Testing

The final sterilizing membrane was harvested from both the competitor's capsules and CPF capsules and cut into a 47 mm disc for membrane testing.

Integrity Test Verification

Membrane	Bubble Point Spec	Actual Bubble Point
Comp 0.22 µm	≥ 46 psi	56 psi
CPF PPS 0.22 µm	≥ 50 psi	58 psi

Membrane Water Flow Rate

Because each capsule filter design had a different amount of filter area, the membrane was tested for flow rate through a=the same area. The 47 mm discs from each capsule were tested and the flow rate measured for comparison.

Filter	Clean Water Flow Rate (mL/min/cm^2 @ 10 psid)
Comp 0.22 µm	17
CPF PPS 0.22 µm	≥ 24

Serum Throughput

The membrane from each capsule filter was throughput tested and compared. New serum, provided by the customer, was used as the test fluid. The serum was pumped through 47 mm discs (filtration area 13 cm^2) at a constant rate (25 mL/min) using a peristaltic pump. Pressure differential across the membrane was measured as a function of serum volume filtered.

Filter	Volume Filtered (L)	Ending Differential Pressure (psid)	Volume Filtered @ 15 psid (L)
Comp 0.22 µm	0.182	20	0.155
CPF PPS 0.22 µm	0.258	15	0.258

Serum Throughput Projections

The data from the 47 mm disc throughput test was used to create projections for serum throughput in capsule form. The volume filtered at an ending differential pressure of 15 PSID was used to create the projections based on the filtration area of each capsule design.

Filter	Filtration Area	Projected Volume @ 15 psid Ending Pressure
Comp 1	0.1 m^2	12 liters
CPF/PPS1	0.093 m^2	18 liters
Comp 2	0.2 m^2	24 liters
CPF/PPS2	0.278 m^2	55 liters

Regulatory Compliance

Both CPF filters and the competitor's products were found to be compliant in the following areas:

- Individually Integrity Tested Filters
- Integrity Test Correlated to Bacteria Retention (ASTM F838-05)
- Passes USP Class VI Plastics Test
- Non-Pyrogenic per USP <85>
- Non-Fiber Releasing (per 21 CFR 211.72)

In Conclusion

Based on comparative review and testing, Critical Process filters met customer specifications, exceeded competitive product performance and CPF was awarded the business.

Critical Process Filtration performs process evaluations, troubleshooting analyses, filter process development tests and application consulting every day. Contact us to discuss your filtration challenge.

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