Success – Optimizing Bioburden Reduction in an Enzyme Solution

CRITICAL PROCESS FILTRATION, INC.

Description of the Filtration Challenge

A biopharmaceutical manufacturer was developing a process to create an enzyme product. The product was in development and a number of filter suppliers were asked to perform tests with an intermediate enzyme solution and recommend filtration steps for bioburden reduction in the solution. Testing was to be done at laboratory scale to support the scale-up of the process to full production volumes.

The challenges were:

- the solution had very high turbidity - high levels of particles
- bioburden levels were high
- the filters could not affect the protein levels or protein activity of the solution

Application Testing at the Customer Site

Our Technical Service team and similar teams from other filter suppliers visited the customer facility and conducted initial tests to screen possible filter media and membranes. Two different batches of an intermediate enzyme solution made on separate dates were provided by the customer for these field tests.

Because of the limited amount of solution available, media screening tests were done using disc filters. The solution was fed through the filter discs at a constant flow rate, and the volume filtered recorded once a terminal pressure drop value was reached.

Several filter media were tested in this field trial:

1. Polyethersulfone (PES) Membrane
2. Polypropylene Membrane
3. Three Fiberglass Depth Media options
4. Three Polypropylene Depth Media options

Field Test - Media Option Results:

The solution was passed through each media option individually, then filtrate from media showing promise as a prefilter was filtered through possible downstream bioburden reduction filter membrane options to test throughput. At the end of the field tests, the team recommended a filter train using:

- A high pore size pleated polypropylene depth media
- A small pore size pleated polypropylene depth media
- A submicron pore size polyethersulfone (PES) membrane

The customer compared lab scale performance data for the filter recommendations from Critical Process Filtration tests and the data from other competitors and found the performance of the Critical Process Filtration filters superior. The decision was made to send additional solution to Critical Process Filtration for application optimization testing.

Optimization Testing at the Critical Process Filtration Application Laboratory

The customer sent additional enzyme solution to Critical Process Filtration for further testing. However, the additional solutions were not the same as the solution tested in the field. One solution was very similar (an intermediate product). The other was a fully formulated product from further downstream in the process that was also to be tested for filterability and prefiltration options. The customer requested recommendations from Critical Process regarding which solution should be filtered for bioburden reduction. Neither had been created using filters in their facility. As in the field tests, the enzyme solutions were filtered through the filter discs at a constant flow rate, and the volume filtered recorded once a terminal pressure drop value was reached.

A slightly smaller group of filter media were tested in this laboratory test:

1. Three Polypropylene Depth Media options
2. Two Fiberglass Depth Media options
3. High Capacity Polyethersulfone (PES) membrane

Lab Test - Media Option Results:

Testing was done on the fully formulated product. The filtration results were not as expected based on the test results obtained during the field trial. All of the media options recommended after the field tests clogged much faster than the field tests. The filtration results for the formulated product clearly showed that it did not have the same filterability as the intermediate product tested in the field.

The media series that worked best for the fully formulated solution was:

- A high pore size pleated fiberglass depth media
- A small pore size pleated fiberglass depth media
- A submicron pore size high capacity polyethersulfone (PES) membrane

Testing on the intermediate product that was similar to the solution tested in the field returned results approximately the same as those of the field trials, leading the team to recommend the same filter media for the intermediate solution as they did after the field tests.

Discussion:
Comparison of results from the testing n the Critical Process Filtration laboratory with those obtained in the field showed that the filterability of the fully formulated product solution was very different than that of the intermediate product, but the end result could still be achieved. Though the filters that worked well with the intermediate product do not work well with the fully formulated version, an adjustment to the media allowed the fully formulated product to be filtered to the same level as the intermediate product. The team recommended filtering the fully formulated solution as a more efficient option than filtering the intermediate solution and not the fully formulated one.

Customer Confirmation Testing

The filtrates from the fully formulated solution tests were sent to the customer for QA testing. The solution showed very good clarification after the fiberglass filters, with the filters reducing turbidity (as measured by NTU) by nearly 90%.

The filtrate after the high capacity PES membrane showed levels of bioburden well below those specified by the customer for the product at that stage of production.

In addition to the bioburden tests, the customer also confirmed that all protein concentration and activity results were within the product specifications.

Conclusion
The customer implemented the filter train for the fully formulated solution using the media and membrane recommended after testing at the Critical Process Filtration application laboratory..

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