

Reduce the Level of Host Cell Proteins in the Bioreactor Harvest

Host cell proteins (HCPs) are an inevitable byproduct of biologics manufacturing and can have an impact on product quality and efficacy as well as patient safety. Processes designed to remove HCPs from the bioreactor harvest must be both successful in achieving acceptable limits and scalable.

The combination of our innovative, custom solutions and decades of expertise in biologics manufacturing allows us to conceptualize and implement effective approaches to address process development challenges such as HCP removal, in an accelerated timeframe.



The Challenge

Our customer had one month to reduce the level of HCPs in the bioreactor harvest prior to a production run to supply drug substance for a scheduled Phase 1 clinical trial. The high level of HCPs (1,000,000 in the harvest and 700 ppm at the end of purification) unfavorably impacted the planned clarification process and subsequent downstream steps. The goal was to reduce the level of HCPs to maximum of 300 ppm at the end of process purification and ensure clarification of the entire 2,000 L harvest.



Our Approach

HCP levels can be reduced using mixed-mode and hydrophobic interaction columns, but these approaches are more complex and would not have allowed us to deliver an optimized solution within the compressed timeframe. Further, these options would not solve the problem of clarification filter filterability of the 2,000 L. A reduction in bioreactor size to 1,000 L, which would allow for clarification, was not feasible due to the amount of drug substance needed for the trial. The approach selected to drastically reduce HCPs and increase filterability was caprylic acid precipitation followed by filtration using Clarisolve® filters. Design of experiments (DOE) was used to identify the optimal conditions for precipitation with a focus on two key parameters, the concentration of caprylic acid and temperature. Use of DOE enabled us to reduce the number of experiments required to evaluate these parameters, which was crucial as we had a limited number of time and cells available for the study.



The Outcome

The combination of caprylic acid precipitation and Clarisolve® filters enabled a reduction of 80% of harvest HCPs to reach a target of less than 100ppm at the end of process purification and clarification of the entire 2,000 L harvest. Incorporation of the Clarisolve® filters also had a positive impact on downstream steps including reducing the number of filters needed, the volume of water needed to wash the filter and the dilution of the material after the wash. With a reduced dilution, the capture step following the filtration required less time.

For clients seeking an outsourcing partner, we provide a streamlined experience to cover the entire value chain from pre-clinical to commercial phases. Our integrated Millipore® CTDMO Services offering combines our expertise in contract testing, development, and manufacturing to accelerate solutions for clients and patients. Our technical leadership, regulatory know-how, testing services, and manufacturing expertise are tightly aligned with our supply network to offer total solutions for our clients. We leverage 30+ years of global success with dedicated sites around the world. We are the industry's experienced choice, built to serve pioneers.

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