

HYBRID FED-BATCH CULTURES USING XCELL ATF FOR BETTER YIELD AND ROBUST CLARIFICATION PROCESS

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Fed-batch cell culture processes require a clarification step to isolate the protein of interest from biomass which includes whole cells, lipids and cell debris. Selecting a suitable clarification technology is critical as it can rise concerns for bioburden, pose substantial risks to protein quality, and impact subsequent downstream purification process. The current technology of depth filtration demonstrates the limitation to perform the clarification process in a sterile manner. This process also often requires additional coupling with centrifugation turning it into a multi-stage process.

We report a scalable single-step novel clarification method, High Yield Harvest (HYH), for fed-batch bioreactors using the XCell ATF system. Unlike depth filtration, the HYH method allows for a sterile clarification process while maintaining cell viability to minimize protein degradation. As an added benefit, this method is shown to elevate the protein production compared to a traditional clarification process.

In the case study presented, the clarification process was initiated a few days prior to the end of fed-batch cultivation using an XCell ATF system. During this period, perfusion methodologies maintained the cell viability and increased the protein production due to the replacement of nutrients and removing toxins. The same ATF system was then used to harvest the remaining protein from the bioreactor on the final day of the cultivation. These results suggest that protein production can be increased by 40% without increasing the original fed-batch process time. The entire process is performed as a single step in a sterile manner, resulting in a clarified product ready for downstream purification.