SUCCESSFUL TRANSITION FROM FED-BATCH TO CONTINUOUS MANUFACTURING WITHIN A mAb PROCESS DEVELOPMENT CYCLE

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Process development for biologics is fraught with numerous challenges and opportunities. One prominent challenge is the uncertainty in future commercial demand for assets in early clinical trials due to unknown dosage, market size, competitive landscape and/or launch strategy. To enable rapid commercialization, commercial process development is often initiated while clinical PoC is still pending. Continuous manufacturing affords the opportunity to overcome this challenge by allowing development of highly productive, flexible manufacturing processes that require minimal upfront capital investment. In this case study, we demonstrate the successful transition of a biologics process from fed-batch in early development to continuous manufacturing for late clinical and commercial launch. Cell culture volumetric productivity was improved by over ~5x fold through perfusion process development which included experimentation to increase media depth, parameter optimization, and various adaptations to fit the manufacturing floor including development of media concentrates. A majority of the upstream process development was performed in ambr© 250 bioreactors run in perfusion mode. For the purification process, the protein A capture step was adapted to multi-column configuration, while changes were made to the viral filtration step to accommodate low flow rates. Single pass TFF was developed for the final UFDF step. PAT tools for real time process monitoring were concurrently developed to improve process robustness and control. The process change did not entail a new cell line, and resulted in substantially comparable product quality, thereby minimizing regulatory risks. Pilot scale runs demonstrated robust process scalability from ambr© 250 and 2-L scales. Taken together, the strategies and considerations established in this work serve as a framework for future programs considering a similar transition.