PROCESS SCALE UP AND CHARACTERIZATION OF AN INTENSIFIED PERFUSION PROCESS

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Continuous biomanufacturing provides many advantages for the production of therapeutic proteins through process integration, automation and intensification. Sanofi currently has developed a robust and integrated continuous biomanufacturing platform to achieve improved volumetric productivity and consistent product quality. Process intensification reduces the physical footprint as well as capital and operating expenses of manufacturing facilities. This presentation is a case study on the implementation of the intensified process for commercialization of a biotherapeutic product.

Using a QbD approach, we successfully implemented an intensified perfusion process coupled with continuous product capture for a commercial product. High cell densities have resulted in a significant increase in volumetric productivity, which allows a substantial footprint reduction and increases flexibility in the commercial facility. To understand the impact of process parameters on critical quality attributes (CQAs), univariate and multivariate studies were conducted in small scale bioreactors. Mix model repeated measurement was applied in the data analysis to incorporate time-dependent information into the predictive model. This was followed by Monte Carlo simulation to determine proven acceptable ranges (PARs) for critical process parameters in support of process control strategy (PCS). Facilitated by computational fluid dynamics (CFD) simulation, we successfully scaled up the process to commercial scale. In this presentation, challenges associated with application of QbD approach for a perfusion process and the advantages of an intensified perfusion process will be discussed.