PROCESS SIMULATION BASED DECISIONAL TOOL TO EVALUATE STRATEGIES FOR CONTINUOUS DOWNSTREAM BIOPROCESS IMPLEMENTATION – A CDMO PERSPECTIVE

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To maintain a competitive space in the rapidly expanding and highly competitive market, many biopharmaceutical companies are outsourcing to contract development and manufacturing organizations (CDMOs) to accelerate research and development, shorten the time to market, alleviate internal capacity and technical constraints, and reduce risks associated with production [1]. To acquire new and maintain current clients, CDMOs must have strong, diverse technical offerings for development, manufacture, and testing of products with competitive pricing and timelines [2]. Adopting innovative technologies like continuous downstream processing can help debottleneck the process and reduce processing time, which is the most appealing to CDMOs as it translates to an increased number of batches per year. The majority of continuous processing assessments to date have focused on cost of goods and not on the time reduction potential [3-7]. End-to-end continuous downstream processing is not always practical as CDMOs must accommodate a wide range of molecules and processes. Hence, it is imperative to evaluate and customize continuous production based on client needs. Application of process simulation as a decisional tool to select an appropriate downstream processing strategy was evaluated. Two modelling programs were evaluated: BioSolve Process and SuperPro Designer®. Fully continuous and hybrid (continuous Protein A operation only) downstream processing were assessed for a 2000 L fed-batch bioreactor producing 1, 5, and 10 g/L of monoclonal antibody at 40 and 200 kg production demands. Hybrid and continuous processing decreased batch duration by 20% and 60%, respectively. Continuous processing was more favorable for higher titer processes (≥ 5 g/L). The largest cost reductions were observed for 5 and 10 g/L titer processes during 40 kg production. The results highlight the business case for continuous downstream bioprocessing especially at a CDMO. Selection of a processing method will be influenced by a range of factors and the impact can easily be assessed using process simulation. Therefore, it is recommended that CDMOs use process simulation to ensure the most favorable processing strategy is selected.

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