PROCESS AND COST MODELING APPROACHES FOR MANUFACTURING OPERATIONS UTILIZING MULTI-COLUMN CHROMATOGRAPHY APPLICATIONS

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Biologics manufacturing continues to remain dominated by batch operations, and as upstream titers continue to increase due to developments in higher producing cell lines and cell culture process optimization, the downstream purification process must adapt to meet the demands of productivity and processing cadence as to avoid becoming the bottleneck in manufacturing operations. There is also a significant drive to improve upon the cost performance index of well-established processes, such as those for monoclonal antibodies, to ultimately lower operating costs as material demands continue to rise. It has been demonstrated repeatedly that next generation technologies may be implemented in a manufacturing environment to help alleviate these issues . Nevertheless, the calculation of the possible benefits obtained from the implementation of these technologies is not always evident and is usually dependent on many factors and various production scenarios. In the present work, a framework has been developed for a technoeconomic feasibility analysis capable to assess the impact of changes in the operations of protein A capture and multi-column polishing chromatography on process performance. The simulation used in this analysis is based on fundamental knowledge of the process and it incorporates previously developed tools for the calculation of dynamic process variables. The parameters needed for material balances, time calculation, scheduling and cost modeling were obtained from literature, process descriptions, manufacturing batch records, facility fit reports and the empirical knowledge from process experts. This framework was adapted to simulate intensified production schedules, increases in feed titers, multi-column capture chromatography (MCC) and integrated batch polishing (IBP). These process alternatives were compared through key performance indicators (KPI), which were selected seeking to respond to specific questions on the suitability of these process intensification strategies in a particular context. Ultimately, the results of the analysis were presented graphically aiming for a decision maker to easily identify the best process alternatives given the necessities and prospects for a given production scenario. Additionally, other multi-column chromatography applications (such as multi-column countercurrent solvent gradient purification, or MCSGP) have been explored in a similar context to shed light on how this framework may be applied across differing modes of operation as well as differing modalities of products.

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