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Process intensification through integration of upstream perfusion cell culture with downstream continuous chromatography in monoclonal antibody production

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Process intensification is gaining interest as a strategy to reduce production costs, while improving product quality and throughput in the manufacturing of biopharmaceuticals. For a competitive production process, continuous or semi-continuous upstream and downstream processing can be employed. Compared with a process performed in batch runs, continuous processing allows for increased capacity utilization and eliminates or minimized the need for intermediate hold-up steps. Here, we describe the integration of a high-performing upstream cell culture process with downstream purification utilizing new emerging technologies such as periodic counter-current (PCC) chromatography and straight-through processing (STP).

A high-cell density perfusion process based on commercially available ActiCHO™ cell culture media was developed for a MAb-producing Chinese hamster ovary (CHO) cell line. Medium prototypes were evaluated in small scale using the single-use ReadyToProcess WAVE™ 25 bioreactor system. Medium optimization resulted in a final process with a cell-specific perfusion rate (CSPR) of less than 50 pL/cell/d. Process performance was verified at laboratory scale using single-use stirred-tank bioreactor systems. Productivity and product quality of the developed perfusion process were compared with a standard fed-batch process.

MAb capture on MabSelect SuRe™ LX protein A chromatography medium (resin) was performed in a three-column PCC (3C PCC) setup. The capture step was followed by two polishing steps using Capto™ S ImpAct ion exchange and Capto adhere multimodal ion exchange media in serially connected columns in a STP setup. MAb purity and yield of the developed continuous processes were compared with traditional setups performed in batch runs.

In this case study, we demonstrate the feasibility of integrated upstream and downstream MAb processing performed in a continuous manner. The developed process shows a performance equivalent to traditional processing performed in batch runs.