

IMPLEMENTATION OF AN INTEGRATED CONTINUOUS DOWNSTREAM PROCESS FOR A MONOCLONAL ANTIBODY PRODUCTION

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The biopharmaceutical market is driving the revolution from batch to continuous manufacturing (CM) for higher productivity and lower cost. In this work, a bench-scale fully integrated continuous downstream process for monoclonal antibody production was established and successfully scaled up to 200 L scale. The process includes a continuous proteinA step, a viral inactivation step, a batch-wise cation exchange and anion exchange step, a batch-wise viral-filtration step, and a single-pass UF/DF step. An inline protein quantity monitoring system was designed to control protein loading mass on cation exchange column. All the steps were connected through surge tanks and integrated by DeltaV™ automatic control system. The setup was tested for the continuous production of a mAb, and the overall production process can be finished within 24 hours (Figure 1). Reproducible performances and product quality were observed over 3 lab batches (Figure 2). The process was then successfully scaled up to pilot plant (200 L, fed batch) with consistent results. The viral clearance study and lifetime study on Protein A step was designed with scale down model. This work demonstrates the feasibility and advantage of applying integrated continuous process in monoclonal antibody production and may provide a reference for large scale manufacturing.

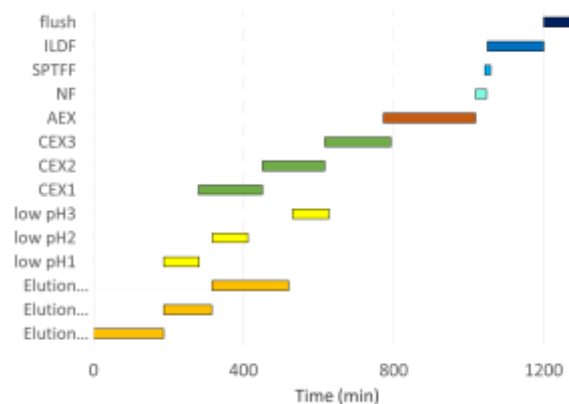


Figure 1. Unit operation time of continuous downstream process

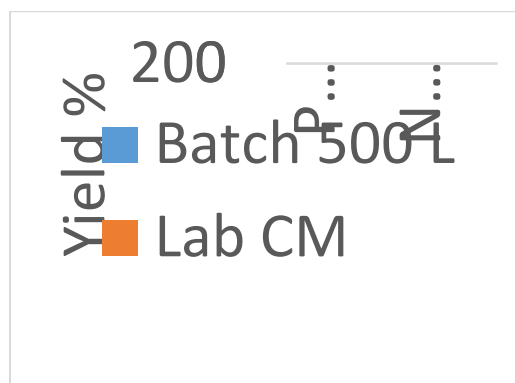


Figure 2. Comparison of recovery yields among 500 L scale batch, lab scale CM and 200 L scale CM