BIOMANUFACTURING AND TESTBED DEVELOPMENT FOR THE CONTINUOUS PRODUCTION OF MONOCLONAL ANTIBODIES

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Monoclonal antibodies (mAbs) play a vital therapeutic role in the treatment of diseases ranging from autoimmune diseases to cancer. Continuous biomanufacturing of biologics is of growing importance due to its more efficient manufacturing processes. Continuous manufacturing today can also increase the quality of the product with increased manufacturing flexibility in a smaller production footprint.

We have built a continuous testbed for the manufacturing of mAbs, which is being used to experimentally validate data analytics-based modeling tools and control design methods for the manufacturing of biopharmaceuticals [1,2]. The testbed consists of four parallel upstream systems including four perfusion devices, and two reactor assemblies integrated within a fully continuous downstream system, including Protein A chromatography, an in-house designed viral inactivation skid, and ion exchange chromatography. The testbed is equipped with instrumentation to thoroughly characterize the processes, including in-reactor probes for Raman spectroscopy, viable cell density, and optical density. To provide further at-line process and product characterization, each upstream assembly is equipped for automated sampling for both the reactor contents and the perfusate. The autosampling system delivers samples to a cell culture analyzer for key metabolite quantification and to verify in-reactor sensor data, e.g., pH. For at-line characterization of critical quality attributes (CQAs), the cell-free perfusate samples are collected in an automated liquid handler, purified using at-line protein A chromatography, and delivered automatically via autosampler to either high-performance liquid chromatography (HPLC) for assessment of aggregation and titer or to liquid chromatography/quadrupole-time-of-flight (LC/QTOF) mass spectroscopy for characterization of glycosylation profiles.

The presentation discusses our team effort in continuous process development as well as the impact of processing modes on the product CQAs. The continuous biomanufacturing testbed is being used to obtain process data, develop and validate analytical methods for determination of the CQAs, and develop and validate process control strategies for assurance that CQA specification are satisfied. The presentation will feature observations, and conclusions for a series of runs from batch, semi-batch, and continuous – including for single runs lasting more than 50 days.

References

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