ADVANCED CONTROL STRATEGIES FOR THE CONTINUOUS PRODUCTION OF MONOCLONAL ANTIBODIES

Markus Kampmann, Sartorius, Corporate Research, Germany
Markus.Kampmann@Sartorius.com
Thomas Kruse, Sartorius, Corporate Research, Germany
Jonas Austerjost, Sartorius, Corporate Research, Germany
Johannes Lemke, Sartorius, Corporate Research, Germany
David Pollard, Sartorius, Corporate Research, Germany

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The ability to support disease therapeutic areas by the application of monoclonal antibodies (mAbs) therapies continue to expand. The vision for the continuous manufacturing of mAbs is to provide a flexible solution, to meet the rapidly changing market demands, by providing a 'turn key' supply on demand solution. Whilst the feasibility of integrating intensified single use unit operations have been demonstrated, the challenges remain to achieve a robust and adaptive process to control deviations and changing demands
In this study, various concepts will be provided to demonstrate the overarching control of an integrated Upstream (USP) and Downstream process (DSP) for the production of mAbs. The use of mechanistic modeling to support the process control including perfusion will be presented. An advanced control strategy across units operations was implemented by interfacing the involved USP/DSP equipment as well as novel process analytical technologies with an overarching custom software component. This approach incorporated a novel approach to incorporate visual programming tools to rapidly establish equipment integration and process control strategies. This approach was used to trigger and control specific equipment actions based on real time monitored process data. Starting from a perfusion process with automated cell bleed control and an alternating tangential flow module for cell retention, the mAb was captured from the permeate by a simulating moving bed (SMB) affinity chromatography prior to a continuous virus inactivation (VI). Setpoint changes and variations throughout the USP were addressed by a dynamic flow control as well as a dynamic loading of the SMB resulting in an optimized resin utilization while simultaneously avoiding product losses. Continuous low pH VI was connected to a sterile filtration step, with flowrates adjusted by the overarching control component.
The establishment of this novel overarching control component, with a high yield and purity of the mAb offers great potential for the establishment of adaptive continuous manufacturing of biopharmaceuticals.