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EVOLUTION OF AN INTEGRATED CONTINUOUS ANTIBODY MANUFACTURING PROCESS

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Efforts continue to reduce the timeline and cost of progressing biologics from discovery through preclinical development to product launch. Integrated processes, those that link upstream and downstream processing with control of product quality are an attractive way to achieve meaningful reductions in the overall cost of ownership of a biologics manufacturing process.

To start along this path, an integrated continuous processing laboratory, the PROLab (Protein Refinery Operations Lab) was built to pilot the concepts of an integrated continuous antibody manufacturing process under automated control. A perfusion process was developed capable of operating for >30 days using either TFF (Spectrum KrosFlo® perfusion system) or alternating tangential flow (Repligen ATF system). The biomass in the perfusion process was controlled at constant density (~50 million cells per ml) via automated feedback loop using an online capacitance probe. The product containing permeate was depth filtered and continually fed into the purification unit operations; consisting of protein A via simulated moving bed, viral inactivation, a polishing step, viral filtration, and a concentration step. A PATROL UPLC system from Waters equipped with an online QDA mass spec was used to continually monitor, with the ultimate goal of controlling, product quality attributes at multiple points across the upstream and downstream process. In addition, the PATROL system was used to monitor key metabolites in the upstream process. Uniquely, both the upstream and downstream processes were coordinated and controlled using a DeltaV based automation system. The automation coordinated inter-stage adjustments and checks, as well as managing the speed of material flow through the purification process ensuring optimal operation. In summary, the PROLab environment will enable the evolution of the antibody manufacturing platform towards fully integrated and continuous by providing a proving ground for both processes and technologies; thereby building high quality and robust automated and continuous manufacturing platforms.