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Strategy for scaling semi-continuous downstream and integration of process analytical tools for monoclonal antibody toxicology

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STRATEGY FOR SCALING SEMI-CONTINUOUS DOWNSTREAM AND INTEGRATION OF PROCESS ANALYTICAL TOOLS FOR MONOCLONAL ANTIBODY TOXICOLOGY

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Currently, continuous processing for biologics is being pursued from a technology perspective in order to increase productivity and decrease cost of manufacture. Disruptive technologies, such as PCC (Periodic Counter-current Chromatography), have been researched extensively in order to reduce the bottleneck for the downstream capture chromatography step. However, there is extremely limited knowledge in how to scale these disruptive technologies for clinical and commercial manufacturing. In this presentation, we demonstrate a strategy for scaling and integration of a PCC capture step into a semi-continuous downstream process (Protein A chromatography-Viral inactivation-Filtration-Anion exchange chromatography). Harvest cell culture fluid (HCCF) feed streams ranging from 0.5 – 1 kg of various subclasses of IgG antibodies was purified using this integration process to generate material for toxicology studies. The process parameters on PCC for each mAb is matched to the process parameters in batch mode except for loading. The productivity ($\text{g/L}^{-1} \text{hr}^{-1}$), product quality and yield are compared to the small scale semi-continuous operations and traditional batch mode operation. The use of PAT (Process Analytical Tools) for monitoring real time product quality and processing is also described.