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USE OF QUALITY BY DESIGN PRINCIPLES FOR DEVELOPMENT OF UPSTREAM PROCESS CONTROL STRATEGY

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A systematic approach was developed using the QbD (Quality by Design) principles to study and characterize monoclonal antibody upstream production processes. This approach comprises of risk assessment of upstream process parameters, small scale model development and qualification, process characterization as well as the determination of CPPs (Critical Process Parameters) and PARs (Proven Acceptable Ranges). A high throughout analytical method to measure N-linked glycans and a Chemometric method to calibrate the results were developed in order to overcome the analytical bottleneck. These studies improved the process understanding, explored the multivariate interactions, and established the relationship between CPPs and CQAs (Critical Quality Attributes). The outcome of the studies was used to develop the integrated control strategy for supporting GMP manufacturing. This approach has been successfully implemented on multiple late stage pipeline molecules including one recently approved monoclonal antibody. In this presentation, the experimental design and relevant statistical analysis methods will be presented using various case studies.