

DELIVERY OF CONSISTENT AND HIGH-QUALITY ANTIBODY THERAPEUTICS BY ACTIVELY MONITORING AND CONTROLLING CRITICAL QUALITY ATTRIBUTES

J Madiha Khurshid, Process Development, Amgen Inc., USA
mblewis@amgen.com

ack Huang, Process Development, Amgen Inc., USA
Peter Schindler, Process Development, Amgen Inc., USA
Tony Wang, Process Development, Amgen Inc., USA
Richard Wu, Process Development, Amgen Inc., USA

Therapeutic recombinant monoclonal antibodies (mAbs) display a wide variety of critical quality attributes (CQAs) that are essential for achieving their safety and efficacy endpoint in patients. Traditionally, to ensure consistent product quality, manufacturing processes are designed to control CQAs by operating process parameters within defined ranges. This “process defines product” approach has produced many successes within the biopharmaceutical industry, albeit, with limited understanding of the underlying mechanisms between the process parameters and CQAs. Recently, with inclusion of biosimilars and novel modalities into Amgen’s pipeline, meeting tightly specified CQAs using this traditional approach has sometimes proven to be challenging. To better meet such challenges moving forward, we need to develop processes that are adaptable and yet offer robust CQAs control. One strategy for accomplishing this is to develop a product attribute control (PAC) platform that integrates process science with process model control to modulate the CQAs throughout the production processes. PAC is an attribute-focused method that starts by defining desired CQAs and further elucidating the process and attribute relationship (PAR). PAR provides mechanistic understanding of how process parameters (levers) impact CQAs and identifies effective levers that could modulate CQAs of interest within pre-determined ranges. One of the key elements of a PAC process is the integration of process analytical technology (PAT) elements to enact real-time sampling and analytics. Based on real-time process inputs and CQA responses generated by PAT, a mechanistic predictive control model (MPC) or an empirical multivariate statistical process control model (MSPC) for one or more CQAs can be created, and integrated into PAC. In addition, such an approach begins with initial clone selection, with the goal of identifying production cell lines that are responsive to process levers over a dynamic range that will enable adaptive control. This PAC strategy, by combining PAR, PAT, and MPC/MSPC, enables CQAs to be monitored, predicted, and controlled throughout the production process. A study demonstrating control of glycan CQAs incorporating aforementioned PAC strategy will be demonstrated in this presentation. This newly proposed strategy enables robust CQAs control to challenging molecules and ensures the delivery of high quality mAb therapeutics to our patients.