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A quality by design (QbD) approach to cell culture process characterization

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A QUALITY BY DESIGN APPROACH TO CELL CULTURE PROCESS CHARACTERIZATION

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Quality by Design (QbD) is a science- and risk-based approach to development that begins with predefined objectives and emphasizes product and process understanding as well as process control. This case study will describe a QbD approach to characterizing a monoclonal antibody (MAb) cell culture process. Process parameters to study were selected through a risk ranking and filtering assessment based on historical development data, manufacturing history, and scientific understanding. Statistically designed, multifactor process characterization studies were performed in scale-down bioreactors to build understanding of parameter impacts on critical quality attributes (CQAs) and key performance indicators (KPIs). Production culture process characterization studies, which are the primary focus of this presentation, were comprised of an initial screening design of experiments (DOE) study followed by higher resolution DOEs to resolve interactions between process parameters and refine the acceptable operating ranges. Model-predicted worst-case conditions were subsequently tested to verify the statistical models. Challenges associated with wide observed process output ranges and limited model predictability for several CQAs will be discussed.

The drivers and considerations for a design space claim for this MAb process will also be discussed. As defined by ICH guidance Q8(R2) and Q11, movement of parameters within a design space is not considered a change. Although a 'process-wide' design space comprised of all unit operations may provide maximum flexibility, there may be rationale for unit operation-specific design spaces that only include a subset of process parameters. In determining an appropriate design space strategy, the process capability of each unit operation and desired flexibility to move process targets to modulate CQA levels or meet facility transfer requirements in the future should be considered.