

STEP-WISE STRATEGY TO ADDRESS PROCESS CHARACTERIZATION – TOWARD THE DEFINITION OF A STANDARDIZED APPROACH

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Drivers for process characterization and late phase development include improving process understanding, achieving process robustness, and assurance that the process delivers consistent product quality within all PAR (Proven Acceptable Ranges). In addition, regulatory expectations for biologic submissions have imposed the need for a strategy that includes the application of statistical methods to improve the confidence of the PARs and lead to the definition of Design Space. Different methodologies have been reported for Process Characterization which contain common elements such as risk assessment, scale-down model qualification, and statistical experimental approach. However, there is not a consensus on criteria for the selection of a unique or multiple experimental designs for the evaluation of CPP (Critical Process Parameters) at every stage. The purpose of this work is to propose a stepwise approach for the definition and execution of Process Characterization for the production of a monoclonal antibody. This approach will improve the efficiency and effectiveness of the process by targeting the right design and number of experiments. An overview of the stepwise approach is presented in Figure 1. Simulation data will be presented to support the soundness of the approach using selected stages in a typical process for the production of monoclonal antibodies. The results support the importance of clear definition of the objectives to better utilize and understand statistical tools. The application of this strategy allows the completion of Process Characterization work within the usually challenging timelines imposed by the rapid progression from Phase 3 to filing.

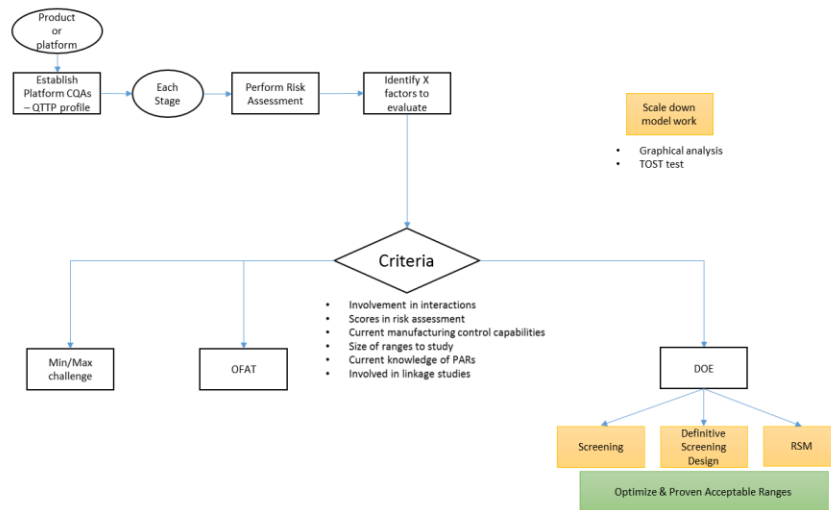


Figure 1. Flow chart for the definition of experimental approach for Process Characterization