HIGH THROUGHPUT UPSTREAM RANGING STUDY USING AMBR® 250 MINI BIOREACTORS WITH DOE AND MULTIVARIATE DATA ANALYSIS (MVDA)

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Process ranging studies require screening numerous variables like seed density, temperature, dissolved oxygen, pH, raw material variability, etc. Due to the large number of variables that need to be studied as well as the interactions between them, it is prudent to use automated and high throughput bioreactor systems such as the ambr® 250 combined with Multivariate Data Analysis (MVDA) to monitor and analyze batches. The suitability of such methodology for determining process performance at not only standard conditions but also for excursions of variables at extreme values was evaluated. A fractional factorial design with four process parameters (pH, temperature, dissolved oxygen and seeding density) and using a CHO cell line expressing an IgG, was performed and compared in both 2-L glass bioreactors and an ambr® 250 system with 24 single-use vessels. Responses like peak viable cell density, viability and titer followed very similar trends in the 2-L and the ambr® 250 bioreactors. However, some quality attributes like charge variants were different between the two systems. MVDA analysis was performed using both online and offline post batch analysis with SIMCA software. It demonstrated that the process performance of 2-L and ambr® 250 for most variables were highly similar. Also, MVDA helped elucidate the potential sources for discrepancies between the AMBR and 2-L bioreactors quality attributes.