

REDUCED SCALE MODEL QUALIFICATION OF A 5-L BIOREACTOR USING MULTIVARIATE VISUALIZATION & BAYESIAN INFERENCE METHODS

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A 5-L bioreactor reduced scale model (RSM) was qualified for 2000-L manufacturing scale for a CHO cell line producing a recombinant monoclonal antibody. The study identified process performance and product quality attributes that capture important aspects of the production bioreactor process. The qualification of the smaller scale bioreactors – showing that the attributes are comparable across scales – was performed using two novel statistical approaches: multivariate dimension reduction and data visualization techniques, via PLS-DA, and Bayesian multivariate linear modeling for inferential analysis. Bayesian linear modeling results comparing individual probability distributions of the differences and ratios of the mean of each attribute for each scale, as well as joint probability statements on the differences and ratios of the means for multiple attributes, are presented. After analysis by PLS-DA, adjustments to the operating conditions of the 5-L bioreactors were identified so that performance more closely resembles that of the 2000-L manufacturing scale. The results of the analyses facilitate iterative and risk-based decision making with regards to the continuous improvement of the reduced scale bioreactor models. Using Bayesian Multivariate Linear Modeling to assess equivalence between scales and PLS-DA to determine potential improvements to the RSM allows for a continuous and iterative approach to RSM qualification and model improvement.