IMPROVING DEVELOPMENTAL TIMELINES THROUGH THE GENERATION OF PREDICTIVE SCALE DOWN MODELS

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Key Words: Process Development, Scale Down Model Development

The importance of scale down models in biomanufacturing has increased with accelerating program timelines and desired efficiency improvements. To meet these demands, it is necessary not only to have a platform scale down model that can reliably perform across early programs, but to also understand the key aspects of the model so as to be able to adapt it to specific program needs and to different manufacturing equipment and scales. We are working to create this level of understanding by combining both traditional engineering principles with more detailed knowledge of how scale differences commonly impact cell culture behavior. As part of this process, we have systematically characterized the volumetric mass transfer coefficients ($k_L$as) for our laboratory and manufacturing bioreactors and have used this data to determine the scaling criteria that most accurately captures the differences between our systems. We then modified the setup of and general practices used for our laboratory scale bioreactors based on these results to better align with the predictions of the identified scaling criteria. Through this process we were able to rapidly establish scale down models for 3 early stage programs at 2 different manufacturing scales. These models were used to transfer these programs following a single clone selection run at the 3 L scale and without additional runs at intermediate scales. The identification of the critical scaling criteria for our manufacturing bioreactors also allowed for the direct transfer of a late stage program between suites without engineering runs. We are currently expanding this work to understand how changes to our scale down practices have impacted additional characteristics of our cultures apart from the standardly measured attributes, and how these characteristics can be used to drive more predictive models.