CONTINUOUS PROCESS PERFORMANCE ENHANCEMENTS FOR 50 L TO 500 L SINGLE-USE BIOREACTORS: A TECHNICAL COMPARISON OF PERFORMANCE CHARACTERIZATION, CELL CULTURE, AND SCALE-UP MODELING

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Improvements in single-use systems have allowed implementation of high-density cultures in emerging bioprocess work flows. Specifically, advantages of single-use bioreactors have been realized in perfusion applications in high-density seed train intensification or as a compact production-scale bioreactor system. Due to this and additional progressive advances in media optimization and improved clone genetic selection have increased stress on the perceived performance limitations of single-use bioreactors. This study shows integration of the Thermo Scientific™ HyPerforma™ Single-Use Bioreactor (S.U.B.) and how strategic enhancements to the sparger and agitation systems have revealed the potential for 3-4X improvement of mixing and mass transfer performance compared to legacy SUB designs. This work includes:

1) Bioreactor characterization and scalability analysis of the S.U.B. when targeting perfusion applications from 50 L pilot scale to 500 L production scale working volumes.

2) High-density culture results (>200E06 cells/mL) while maintaining proper operating parameters using a TruBioTM DeltaV controller and online process analytics. New data reveals specifically how a 50 L S.U.B. equipped with a specialized precision drilled hole sparger (DHS), single use foam probe, and oversized impeller is able to improve overall SUB operating efficiency. Coupled with best practices and the desirable process benefits achieved through automation and control of vital process parameters, evidence is provided as to the advantages of continuous processing in single-use systems.