

## CONTINUOUS PROCESS PERFORMANCE ENHANCEMENTS FOR 50-500 L S.U.B.S

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Improvements in single-use systems have allowed implementation of high-density cultures in emerging bioprocess workflows while progressive advances in media optimization and improved clone genetic selection have underscored the perceived performance limitations of single-use bioreactors (S.U.B.s). This study presents how strategic enhancements to the sparge and agitation systems of Thermo Scientific™ HyPerforma™ S.U.B.s have revealed the potential for a three- to four-fold improvement of mixing and mass transfer performance compared to legacy SUB designs. This study investigates the following:

- Bioreactor characterization, TruBio™ DeltaV™ controller optimization, online process analytics, and scalability analysis of the S.U.B. when targeting perfusion applications from 50 L pilot scale to 500 L production scale working volumes.
- High-density culture results (>260E06 cells/mL) while maintaining proper operating parameters. New data reveal 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 S.U.B. operating efficiency. Results also include specific suggestions on how to maintain a nearly ideal dissolved carbon dioxide environment, reduce headspace foam generation, and produce lower overall shear levels, thus yielding excellent cell viability.
- The work also demonstrates best practices and the desirable process benefits that can be achieved through reduced technical risk, lower labor, and simplified technical transfer of a completely disposable processing assembly. Further evidence is presented on the advantages of continuous processing when used in high-density seed train intensification or as a compact production-scale bioreactor system operating at reasonable media exchange rates of one to two vessel volumes per day (VVD).

