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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Application-Specific Enhancements to Thermo Scientific™ HyPerforma™ Single-Use Bioreactor (S.U.B.)

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ABSTRACT
The rapid growth of bio-therapeutic manufacturing has created significant demand for workflow solutions featuring greater product yield, lower production costs, and accelerated development timelines. To address these demands, developers have moved away from ‘one-size-fits-all’ approaches and are increasingly focused on solutions that address the specific needs of diverse bioproduction processes. Given this shift toward process-specific solutions, Thermo Scientific has introduced a series of application-specific enhancements to the HyPerforma™ Single Use Bioreactor (S.U.B.) product platform. Each is tailored to the unique requirements of perfusion, intensified fed-batch, and adherent cell cultures (Table 1).

RESULTS

Enhanced S.U.B. for Perfusion
Perfusion cell culture conditions are especially demanding and require high mixing PIV, high mass transfer, and ATFF/TFF connectivity. To address the unique demands of perfusion cell culture, the enhanced Thermo Scientific HyPerforma™ S.U.B. features an upsized impeller, improved DHS design, and user-friendly port configuration for ATFF. These enhancements resulted in an up to a 4.3-fold increase in kₐ (Figure 3a). When used in perfusion cell culture, the enhanced S.U.B. was able to support a viable cell density (VCD) of greater than 50 M/mL, for more than 2 weeks, reaching a maximum VCD of nearly 264 M/mL on day 25 (Figure 3b). Figure 3. (a) Apparent kₐ plotted with respect to O₂ flow rate in vessel volumes per minute (VVM) for enhanced (solid) and legacy (dashed) S.U.B.s. (b) Performance of enhanced S.U.B. throughout 20-day perfusion cell culture.

Enhanced S.U.B. for Fed-Batch
Increasing demand for high-product yields and greater risk mitigation in bioproduction processes has pushed legacy S.U.B. performance to its technological limits. To address the growing interations of fed-batch bioproduction processes, the enhanced Thermo Scientific HyPerforma™ S.U.B. features an upsized impeller and improved DHS design, which sustains high cell viability in culture (Figure 4). In addition, the enhanced S.U.B. can operate at a 4.1 turnover ratio. The ability of the enhanced S.U.B. to operate at low fluid volumes reduces the number of vessels required to reach production scale culture (e.g., 300 L Fed-Batch vessels in a process used train reduces risks associated with transferring high-density cell cultures between vessels while simplifying bioprocess development.

Enhanced S.U.B. for Microcarriers
Adherent cell culture is an increasingly attractive strategy for producing vaccines and viral vectors for gene and cell therapies. However, reliable scale-up of adherent cell cultures with microcarriers is difficult due to the sensitivity of both the cells and microcarriers to shear (Figure 5a-b). To address this sensitivity limitation, we engineered an enhanced Thermo Scientific HyPerforma™ S.U.B., featuring the same upsized impeller and turnover ratio as the enhanced fed-batch, as well as optimized port configuration for media decantation, allowing high cell densities to be achieved on microcarriers (Figure 6).

CONCLUSIONS
To address the trend toward specialization in bioproduction, Thermo Scientific™ has upgraded the HyPerforma™ S.U.B. product platform to feature application-specific enhancements for: Perfusion Fed-Batch Adherent cell culture with microcarriers Thermo Fisher Scientific is committed to developing best-in-class solutions and is proud to introduce the enhanced HyPerforma™ S.U.B. line in this tradition.

REFERENCES
3. Chait, A. A Brief History of Adherent Cell Culture: Where We Came From and Where We Should Go. Bioprocess International. 2019

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