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Rapid development of a perfusion process with high productivity

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LATE STAGE DEVELOPMENT OF A FED-BATCH PROCESS: CHANGING EVERYTHING BUT PRODUCT QUALITY

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Continuous process improvement is required during a biologics process life cycle to increase process yield and reduce cost. In this poster, we will present a case study in late stage process development where everything was changed but the product quality. The following major changes were made when developing the new process:

- Production cell line – subclone of the original clone used.
- Media – from hydrolysate-containing feeds to fully chemically-defined feeds.
- Feeding strategy – from fixed volume/fixed schedule feeding to daily on-demand feeding.

Media components were optimized through spent media analysis and mechanistic understanding to accommodate the new feeding strategy. High-throughput bioreactor systems (ambr15™ and ambr250™) were used for rapid screening of experimental conditions, and the results were confirmed in 3 L bioreactors. As a result of the development effort, a 100% increase in peak cell density to 20-25e6 cells/mL, a 40% decrease in peak lactate level, and a 140% increase in antibody titer were achieved in the new process. Titer increase was attributed to the improved oxidative metabolism and significant increase in cumulative cell density. In the new process, final culture viability was still maintained at >90%, benefiting filtration primary recovery. The process was scaled-up to a 200 L SUB without losing productivity.

We show that product quality, especially N-linked glycosylation and charge variants, could be modulated by adjusting specific medium components and feeding strategy. The antibody quality attributes resulting from the new process are comparable with (or better than) those from the old process.