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mAb product consistency in long duration microfiltration-based CHO perfusion process

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TITLE

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ABSTRACT

Perfusion processes have traditionally been used for the generation of unstable proteins in cell culture systems. The use of perfusion for production of stable proteins has been limited by low product concentration, media costs, and system complexity. However, with the advent of new single-use technology, cell culture media specifically formulated to support high density perfusion, and high-producing cell lines, perfusion processes are gaining widespread industry attention. Additionally, perfusion processes are considered an integral part of the "Factory of the Future" vision through enabling continuous processing while delivering a product effluent with consistent product quality and concentration.

In this study, we evaluate the ability of a long duration perfusion process to deliver a consistent product stream. Although rarely reported, a reduction in protein sieving/transport through the microfiltration-based cell retention device is associated with many perfusion processes. To better understand this observation, we have investigated the impact of membrane pore size, membrane area, cross-flow rate, and mode of operation on protein sieving through a microfiltration-based cell retention device connected to a 3L single-use bioreactor operated in a 30^{+} day perfusion process. It has also been reported that perfusion processes can be exploited to deliver a consistent product with more uniform product quality attributes. To support this observation, we will also present product quality data (i.e., glycosylation patterns, charge heterogeneity, product aggregation) for a long-duration mAb perfusion process and compare the results to a more traditional fed-batch process.