

Online/At-line Monitoring of Product Titer & Critical Product Quality Attributes (CQAs) During Process Development

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Abstract

Process analytical technology (PAT) has been defined by the Food and Drug Administration (FDA) as a system for designing, analyzing, and controlling manufacturing through timely measurements to ensure final product quality. Based on quality-by-design (QbD) principles, real-time data monitoring is essential for timely control of critical quality attributes (CQAs) to keep the process in a state of control. To facilitate next-generation continuous bioprocessing, deployment of PAT tools for real-time monitoring is integral for process understanding and control. Real-time monitoring and control of CQAs is essential to keep the process within the design space, which is in alignment with the guiding principles of QbD concepts. The contents of this manuscript are pertinent to the online/at-line monitoring of upstream titer and downstream product quality. We have demonstrated that Waters' PATROL system can be utilized to measure product titer and CQAs directly from bioreactors and downstream unit operations, respectively. We have established that online titer assay results from fed-batch and perfusion-based alternating tangential flow (ATF) bioreactors are comparable to at-line and conventional offline results. The utility of the PATROL system for online product quality measurements of down-stream unit operations for real-time peak pooling has been demonstrated.

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