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## On-Line Ion Exchange Liquid Chromatography as a Process Analytical Technology for Monoclonal Antibody Characterization in Continuous Bioprocessing

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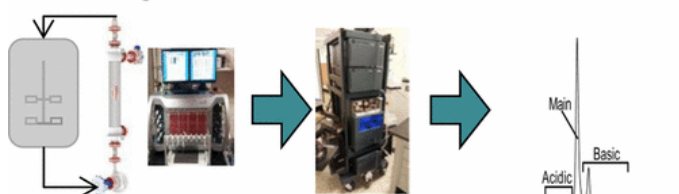
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## Abstract

### Combining PAT Tools with Continuous Production



Combining process analytical technology (PAT) with continuous production provides a powerful tool to observe and control monoclonal antibody (mAb) fermentation and purification processes. This work demonstrates on-line liquid chromatography (on-line LC) as a PAT tool for monitoring a continuous biologics process and forced degradation studies. Specifically, this work focused on ion exchange chromatography (IEX), which is a critical separation technique to detect charge variants. Product-related impurities, including charge variants, that impact function are classified as critical quality attributes (CQAs). First, we confirmed no significant differences were observed in the charge heterogeneity profile of a mAb through both at-line and on-line sampling and that the on-line method has the ability to rapidly detect changes in protein quality over time. The robustness and versatility of the PAT methods were tested by sampling from two purification locations in a continuous mAb process. The PAT IEX methods used with on-line LC were a weak cation exchange (WCX) separation and a newly developed shorter strong cation exchange (SCX) assay. Both methods provided similar results with the distribution of percent acidic, main, and basic species remaining unchanged over a 2 week period. Second, a forced degradation study showed an increase in acidic species and a decrease in basic species when sampled on-line over 7 days. These applications further strengthen the use of on-line LC to monitor CQAs of a mAb continuously with various PAT IEX analytical methods. Implementation of on-line IEX will enable

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