Automated calibration and in-line measurement of product quality during therapeutic monoclonal antibody purification using Raman spectroscopy

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Abstract

Current manufacturing and development processes for therapeutic monoclonal antibodies demand increasing volumes of analytical testing for both real-time process controls and high-throughput process development. The feasibility of using Raman spectroscopy as an in-line product quality measuring tool has been recently demonstrated and promises to relieve this analytical bottleneck. Here, we resolve manual calibration effort by engineering an automation system capable of collecting Raman spectra on the order of hundreds of calibration points from two to three stock seed solutions using controlled mixing. We used this automated system to calibrate multi-product quality attribute models that accurately measured product concentration and aggregation every 9.3 seconds using an in-line flow-cell. We demonstrate the application of a non-linear calibration model for monitoring product quality in real-time during a biopharmaceutical purification process intended for clinical and commercial manufacturing. These results demonstrate potential feasibility to implement quality monitoring during GMP manufacturing as well as to increase CMC understanding during process development, ultimately leading to more robust and controlled manufacturing processes.

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