Process Analytical Technology (PAT) approaches for monitoring and control of excipients in formulation of biotherapeutics

ABSTRACT

Excipient concentrations are critical quality attributes of monoclonal antibody (mAb) drug products and affect their safety and efficacy. In manufacturing processes, mAb products are formulated into the buffer containing the desired excipients using ultrafiltration (UF) and diafiltration (DF). Excipient concentrations are critical quality attributes (CQA) of the final drug product. The development of process analytical technology (PAT) approaches for monitoring and control of excipient concentrations is critical to establish a robust continuous manufacturing train. We present a series of different PAT strategies for this purpose. First, a series of rapid simultaneous at-line HPLC methods are developed for quantification of a range of excipients, well-suited as a gold standard for in-process measurements in near real time. Second, a model-based strategy is developed to predict the excipient drift in UF processes at high concentration and compensate for it by adjusting the formulation of the DF buffer using a model predictive approach. Thirdly, near infrared spectroscopy (NIRS) is used to develop multivariate calibration models for some common excipients, and a control strategy is demonstrated for excipient drift. The strategies are suited to both batch and continuous processing and together form a robust framework for monitoring and control of excipient concentrations in the formulation step for manufacturing of mAbs.

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