Cambrex

Case Study
Analytical Services

Method optimization: Assay development following compendial methods

Creating multiple efficiencies within USP<621> requirements.

Racing the regulatory clock: Overcoming multiple barriers in assay optimization

Chapter 621 of the USP explains the allowable adjustments to chromatography systems while staying within quality requirements. It is important to consider these criteria before beginning to optimize assays for APIs and related substances to ensure that methods meet requirements during regulatory filing.

In this case, Cambrex had a short time frame of only 7 weeks to complete assay optimization and conduct pre-validation studies within the confines of USP<621>. The additional challenges they faced from inherent properties of the API included a narrow pH window (± 0.05 of the pKa), and controlling reaction conditions to allow use of an ion pairing agent. In addition, the analysis time was lengthy (72 minutes), and required evaluation of multiple peaks and PDA spectral evaluation during system suitability.

In the 7 weeks allowed for this work, 183 sample sequences with 1,083 injections were processed using 4 Waters ARC UHPLCs in parallel by only 2 chemists – half the resourcing expected by the client.

Within the first 5 weeks, the team modified conditions to optimize screen columns, mobile phases, and column temperature according to limits in USP<621>. This allowed 2 weeks to execute full pre-validation and lead condition. During this stage, the API impurity accuracy, linearity and LOQ on primary condition were evaluated. The team also verified the specificity of mass balance in forced degradation across 3 additional conditions.

Performing these stress studies not only complies with FDA guidance, but also provides valuable information to improve the formulation and manufacturing process. Cambrex provides comprehensive summaries of available options for improving their methods, and generates reports on all method development studies to support clients' readiness for regulatory filing.

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Optimal efficiency.

On time delivery without over-spending on resources.

About Cambrex

Cambrex is a leading global contract development and manufacturing organization (CDMO) that provides drug substance, drug product, and analytical services across the entire drug lifecycle.

With over 40 years of experience and a growing team of over 2,200 experts servicing global clients from North America and Europe, Cambrex is a trusted partner in branded and generic markets for API and finished dosage form development and manufacturing.