Cambrex

Case Study
Drug Substance

Route development: Designing synthesis for GMP production

Rapid development of readily scalable and robust synthesis.

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Planning early in the pipeline: Designing synthesis to suit later stages

The successful transition from initial synthesis of an API to a kilogram-scale route requires expert analysis and design. In addition to optimizing each intermediate reaction, chemists must balance economic, regulatory and time constraints. Furthermore, designing the best synthesis route for GLP and GMP production cannot begin without adequate knowledge of the compound, and it may require high-purity intermediates. Each API presents a unique set of challenges.

These barriers do not stall Cambrex from delivering on time. State-of-the-art facilities armed with world class experts and vast experience drive our success in designing the best synthetic route for each API. In this case study, our experts developed a robust, high-yield process to enable GMP production under tight time pressure for a first-in-human clinical trial.

It is not unusual for compounds to be received with very little chemical knowledge. Full characterization of the compound is required before beginning route development in order to ensure success. For this API, the team also had to address excessive levels of palladium (~10,000ppm) that were historically reduced during chromatography in the medicinal chemistry process.

Medicinal chemistry routes are not optimized to meet regulation standards for purity, and they often involve chromatography steps that must be eliminated in order to be scalable. Our experts developed a unique approach to remove palladium during two reaction steps without the use of expensive scavengers. The level of palladium in the final API was reduced to 10-20ppm without the use of chromatography.

Another component of optimal route design is controlling impurity formation in each step of synthesis while optimizing yield. Ideally, chemists seek to balance efficient chemistry with ease in purification and alignment with ICH guidelines. In this case, the redesigned route allowed control over impurities in both the process and starting material, and produced a yield of 87%. Moreover, our team exceeded expectations by developing the crystallization process for the final API salt in addition to the modifications to synthesis.

Don't let design be your limiting factor.

Cambrex applies the tools, experts, and experience to develop the best route.

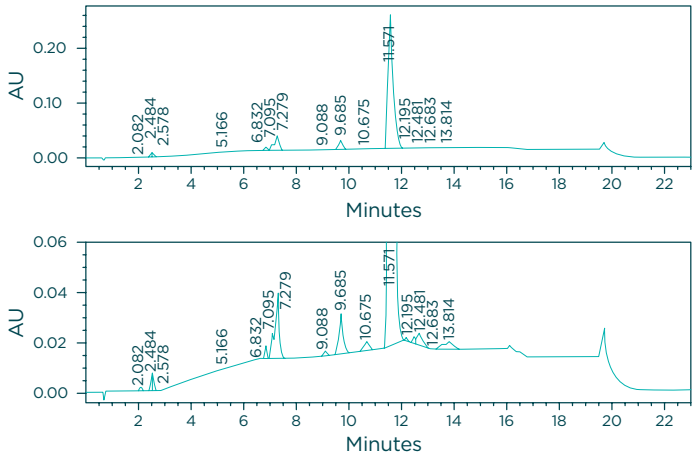
About Cambrex

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.

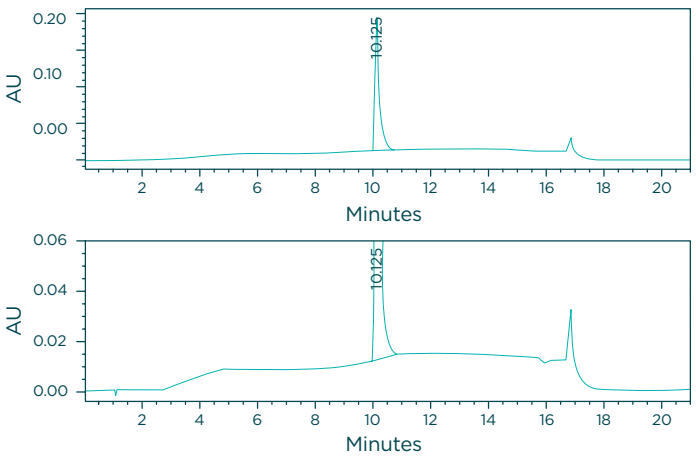
With over 40 years of experience and a growing team of over 2,200 experts servicing global clients from North America and Europe, Cambrex is a trusted partner in branded and generic markets for API and finished dosage form development and manufacturing.

Purity comparison

Purity profile: Med chem route



Purity profile: Final Cambrex procedures



Several improvements were made during development of the optimal synthesis route from the original medicinal chemistry route, resulting in a superior purity profile.

The design of an API synthesis route can be either a limiting factor or boost production, depending on how well it's done. By applying our expertise and innovation, Cambrex delivered a suitable route for GLP and GMP production along with high-purity intermediates and crystallization of the API under a tight timeline.