Cambrex

Case study
Analytical services

Successful control strategies – Part 1

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Building quality into the product through range finding studies.

Dual purpose: Supporting regulatory filing while optimizing design

Over the last decade, the FDA's initiative to improve product safety through principles of Quality by Design (QbD) has spurred a transformation in manufacturing processes. The concept of using a control strategy to ensure product quality was originally devised to increase consumer safety, but following these guidelines also offers benefits to drug producers.

The application of QbD methods to process design yields better understanding of each step in product synthesis. With a complete picture of the parameters that control each step during manufacturing, chemists can monitor and control individual reactions to optimize the overall production process.

A robust GMP manufacturing process can pay dividends in both time and cost efficiency, all while aligning the process to fulfil regulatory filing requirements. Done properly, range finding studies comply with QbD standards to document critical parameters in Sections 2.2 and 2.6 of the NDA.

Cambrex applies exceptional analytical methods to ensure that quality of your end product is designed at the front end of your process. The combination of our world-class facilities and the experience of our pharma-trained scientists give us a competitive edge in demonstrating complete control of a manufacturing process during regulatory filing.

Sharpen the focus: Uncovering critical quality attributes

Range finding studies explore the operational limits for individual Critical Process Parameters (CPPs) to determine the Proven Acceptable Range (PAR) for defining manufacturing specifications.

Our expert scientists begin these studies by identifying Critical Quality Attributes (CQAs) of the drug product and API, so that characteristics which impact product quality can be studied and controlled. For example, known impurities that arise during synthesis represent a common class of CQAs that may affect final quality of the product. Other CQAs might include crystal form or particle size. Cambrex identifies potential CQAs as early as possible to support timely development of the optimal manufacturing process.

Quality begins here.

Building quality into the product starts with firm control of critical process parameters.

About Cambrex

Cambrex is **the** small molecule company that provides drug substance, drug product and analytical services across the entire drug lifecycle. Enjoy working with our experts to accelerate your small molecule therapeutics into the market.

With over 35 years' experience and a growing team of over 2,000 experts servicing our global clients from our sites in North America and Europe, we are tried and trusted in branded and generic markets for API and dosage form development and manufacturing.

With increased understanding of CQAs, chemists can pinpoint areas of the process that need tighter control in order to maintain quality. Parameters that have a large impact over a small range are deemed critical processing parameters in Section 2.2 of an NDA. Our scientists apply this knowledge to avoid obstacles later in the process. In the case of impurities, modifications to the process to eliminate or reduce the impurity may avert a critical issue later with product purity or activity, as well as avoid the remediation effort to fix it.

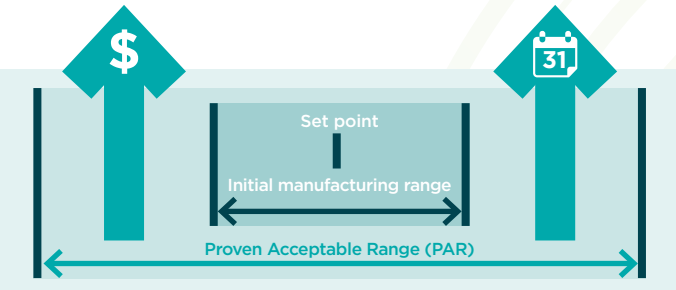
Pushing the limits: How far can parameters stray from center?

Once all potential CQAs are identified, they are mapped to the process to identify where each CQA can be assessed. Targeting the location of CQAs in the process allows chemists to uncover the parameters that control them. Further analysis can determine whether parameters are critical to drug attributes, and how far they can be stretched while maintaining specifications.

CPPs control any CQAs of the drug product or drug substance. During this phase of the range finding study, our experts design and conduct experiments to test the impact of variability in parameters, and modify specifications accordingly. Parameters can be critical to product quality, or critical to process performance, or both.

For instance, if formulation studies dictate a specific form as a requirement for correct dissolution, chemists can focus analysis on determining the specific parameters of the dissolution process affecting the desired form, including crystallization solvents, heating and cooling. With that knowledge in hand, the team can set the optimal specifications and define a range of deviation within the parameters that still yields acceptable quality.

These can be critical points of discovery in the development process, because they can translate to cost savings in manufacturing. In the same way the increased understanding reveals areas that require tighter control, it can also expose steps that can tolerate looser parameters. It might allow a manufacturer the flexibility to select less costly starting material, with the knowledge that each process will maintain an acceptable range of deviation, and the ultimate product quality will be uncompromised.



When the Proven Acceptable Range (PAR) allows looser control of a particular CQA, it may translate into cost savings in manufacturing, without compromising end product quality.

Trusting an outsider: Confidence in validated methods

Bringing a range finding project online is complex and requires multidisciplinary collaboration – and trust – between the client and the CDMO. Despite lacking the facilities to take on definitions studies of this magnitude, many large pharma companies choose to perform these studies in-house to avoid potential risk in using non-GMP studies to support regulatory filing. Cambrex has superior chemists to carry out a thorough tech transfer process in well-equipped facilities and routinely provides validated methods to stand up to the scientific rigor of regulatory standards.

Our scientists have vast experience with these late-stage studies and work closely with the client to gather required information to conduct thorough analysis. Before running CPP and PAR studies, we perform a full non-GMP tech transfer of the manufacturing process to demonstrate reproducibility of the process at smaller scale. Next, chemists conduct in-depth analysis to confirm analytical equivalency of the final material. Our process chemists and analytical chemists collaborate closely during the transfer of each step of the process, and customize the process according to the unique needs of each project.

Many contract organizations don't perform the extra steps to provide validated methods, but this inevitably leads to repeated work. At Cambrex, our scientists do it right the first time, rather than having to reproduce validated data. Our analytical group is accustomed to working with validated methods and designing them so that gathered data can go directly into regulatory filing.

The FDA implemented QbD to ensure that manufacturers have complete control over their process in order to guarantee product quality. Quality can't be added in at the end of your product development; it's a byproduct of the design. Cambrex provides the validated methods to demonstrate control of the process so that you can succeed in manufacturing high quality product.

Can your CDMO do this?

1. Reproduce your process
2. Demonstrate product equivalency
3. Scale appropriately
4. Deliver validated methods

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