

Quality by Design in Preclinical: An Analysis

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The Food & Drug Administration’s Quality by Design initiative presents a difficult decision: expand your manufacturing-based compliance programs into your product development environs or adopt a more innovative, less process-driven strategy known as **lean design**.

At a May 2007 workshop in Bethesda, Maryland, hosted by the Parenteral Drug Association and the Food & Drug Administration (FDA), those two competing schools of thought—standardized process control into R&D and lean product design—became abundantly clear.

At stake is faster time-to-market approval, cheaper product development, and lighter regulatory burden. Early adopters with new products approved via the new FDA review “gates” of Quality by Design will set the tone and establish the playing rules for everyone else.

Quality by Design

The FDA has been exploring Quality by Design since 1998 as a means to speed time to market for new medicines while easing the regulatory burden.

Barry Cherney, Ph.D., of the FDA noted, “Quality by Design is *not* process capability; it’s about tying new product specifications to preclinical data literature surveys, prior clinical experiences, scientific judgments and risk assessments.” The genesis of successful Quality by Design begins in preclinical.

Lean Design

In the 1970’s Toyota Motor Company pioneered “lean” product development—incorporating significant input from the customer, limiting late stage design changes once final testing begins and mastering the design flow to focus on the most efficient, most effective quality and cost.

In biopharmaceutical development terms: **limit variability going into clinical trials.**

Recommendations

RECOMMENDATION #1: *Reduce Batch Sizes.*

Frequently, the cycle time from testing to report can be quite lengthy; consider breaking the final report into separate stages corresponding with specific tests. By asking your reviewers—lab supervisors, quality assurance, and so on—to receive, review and approve (or not) modular reports, you get three advantages:

1. Use of smaller batch sizes speeds preclinical testing;
2. Capturing the information in modular fashion allows you to apply it to other products in development; and
3. Near parallel testing gives you the opportunity to make changes early on.

RECOMMENDATION #2: *Customer Voice.*

Develop a slave-like devotion to the top 3-5 aspects of safety and efficacy important to your potential patients. This will help you define the product, its differences, its unique benefits, and its superior value, while clarifying critical quality attributes.

Draw upon “virtual customer” techniques (such as web-based surveys) to obtain insight on the most important safety and efficacy features (and side effects) most important to your intended users. Forcing survey takers to choose between two or more alternatives is a best practice to force ranking and prioritization.

RECOMMENDATION #3: *Learn from Others.*

Ask your development partners for access to previous research databases; use literature surveys to help isolate and identify your most critical safety and efficacy attributes—and where they do not; pull out your discovery notes and review dead-ends or discarded development paths for hidden insights and safety ranges.

Cherney noted that while such information is not perfect, “You can get good, reasonable information. This is data that can go into proving the range of safety and efficacy of the finished product to a reasonable level of expectation.”

For more suggestions, request our research report and workbook, *Is Quality by Design Right for My Organization...?*, from the resource library on the Cerulean website. (www.ceruleanllc.com).

About the Author

John Avellanet is a former *Fortune 50* subsidiary C-level medical device and biotechnology executive where he created, developed and ran his firm’s Records Management and IT departments. In 2006, he founded his independent consulting firm, Cerulean Associates LLC (www.ceruleanllc.com) and has since become one of the leading experts on Quality by Design.