



Quality by Design: Strategies from the Real World

Note to reader: There is no one “right” way to implement Quality by Design (QbD), and readers are encouraged to explore the ideas presented in this case study with that understanding. In general, however, the likelihood of a successful, quality trial can be dramatically improved through proactive, cross-functional discussions and decision making about: (1) what aspects of a trial are critical to generating reliable data and providing appropriate protection of research participants (“critical to quality” factors, or CTQ factors); and, (2) what strategies and actions will effectively and efficiently support quality in these critical areas.

This document captures examples of strategies used by four organizations to integrate the Clinical Trial Transformation Initiative’s (CTTI) QbD thinking into their protocol development process. For more background on each strategy, please follow the link to explore the case studies in full.

Present QbD as logical thinking

When a large part of a study team is unfamiliar with QbD, there is a risk that formally introducing this concept and its associated technical language will seem overly bureaucratic. For that reason, a strategy to present QbD thinking as logic, rather than a formal paradigm, may be helpful. Learn more: [QbD Case Study: Duke Clinical Research Institute](#)

Use a ‘clean slate’ approach to trial design

When designing a trial, many organizations tend to simply copy and modify the protocol of the most recent similar trial. A better strategy may be to start each protocol from scratch, and ask, “What is the scientific question I am trying to answer?” This will ensure you build out only the essential elements needed in the protocol to answer that question reliably. Learn more: [QbD Case Study: University of Oxford CTSU](#)

Consider four core QbD questions

Regardless of whether the protocol being designed is for a small phase 1 or a large global trial, four core questions never change:

1. Why do we need this component (or do we)?
2. Can we do this in an easier way?
3. What are the drivers of this component?
4. Can we get this information elsewhere?

Continually going back to these questions during multi-stakeholder collaboration will help keep the protocol as streamlined and focused as possible. Learn More: [QbD Case Study: The Medicines Company](#)

Leverage an ABCD approach to Critical-to-Quality (CTQ) factor assessment

QbD emphasizes focusing limited resources on proactively addressing “errors that matter to decision making.” One DCRI team applied the same thinking with an ABCD model (below) that they developed, categorizing each element of the study as either critical (A), important (B), nice to have (C), or worthless (D), and allocating resources and effort accordingly. For example, although critical factors are likely to only represent around 5 percent of the project, these factors should command around 50 percent of the study team’s effort. Conversely, somewhere around 50 percent of activities can often be safely categorized as “nice to haves” that shouldn’t command more than a small fraction (perhaps 5 percent) of the team’s effort and resources. Learn more: [QbD Case Study: Duke Clinical Research Institute](#)



	% of Project	% of Effort*
A - Critical	5	50
B - Important	45	45
C - Nice to Have	50	5
D - Worthless	0	0

**Percentages are used as directional guidelines for the team; they are not intended to be literally or strictly applied.*

Allow for flexibility

It is critical that a specific QbD strategy is developed for each trial, reflecting its unique challenges—be it in design, operation, team structure and organization, resources, etc. Resisting the urge to heavily formalize the process across an organization can help QbD embed itself as a common sense, helpful approach rather than a bureaucratic to-do that unnecessarily burdens teams. *Learn More: [QbD Case Study: The Medicines Company](#)*

Don't use QbD as a gatekeeping strategy

There is nothing about QbD that needs to slow down the timelines. It should not be a rate-limiting step. For example, if a team does not fully identify CTQ factors at the protocol concept sheet stage as CTTI recommends, it is not too late. The team should still identify them with as much rigor and thought as possible, even if it is later than ideal. QbD is meant to help teams, not hinder them. *Learn More: [QbD Case Study: Alexion](#)*

Keep evolving the approach

For example, Alexion's product-specific QbD steering committees were disbanded in favor of portfolio-wide risk-based quality management steering committees that ensure the quality approach is calibrated across all products. These teams include development heads for therapeutic areas, as well as leaders from regulatory, clinical operations, quality, and data management. Each drug program in the company also has a quality steering committee, which includes the product team lead, quality operations leads, and more. *Learn More: [QbD Case Study: Alexion](#)*
