

Bristol Myers Squibb (BMS) Co-Hosts Quality by Design Workshop with CTTI to Achieve Quality Culture Aligned with ICH E8(R1)

BMS Leverages CTTI's Recommendations to Deliver Quality by Design Workshop

SUMMARY

A major clinical research event of 2022 was the publication of the final [E8\(R1\)](#) paper on "General Considerations for Clinical Studies" by the International Council for Harmonisation (ICH), a guidance document that had not been amended for over 20 years. One key takeaway from the updated guidance is that regulators consider the ability to identify and proactively manage risk in clinical trials as a key driver to trial quality. Translation: moving forward, proof of early, end-to-end proactive quality planning and sound trial execution is paramount. This case study details how Bristol Myers Squibb (BMS) worked with the Clinical Trials Transformation Initiative (CTTI) to better align its organization to the E8(R1) and impending release of E6(R3) guidelines by embedding Quality by Design thinking across its organization.

GOAL(S)

When the Head of BMS' R&D Quality Strategy and Business Operations (SBO) function took on her role, she had a vision to implement an effective Quality by Design (QbD) and risk-proportionate quality management approach in conducting trials across the company. Her vision marked a significant shift in thinking, which traditionally focused largely on the execution within individual phases of a clinical trial, rather than execution of the trial as a whole. However, a QbD approach that spans from study design through conduct, reporting and analysis had been gaining momentum across the industry for its ability to focus on the patient first, as well as ensure good quality, data integrity and reliability of trial results. The ICH publication of E8(R1) on "General Considerations for Clinical Studies," which emphasizes a proactive, risk-based approach to trial design and execution as a key driver to trial quality, was a tipping point that brought QbD thinking to the fore for many drug developers — including BMS. BMS' Head of R&D Quality SBO, wanted to harness momentum around E8(R1) to build an integrated and holistic strategy to drive an end-to-end risk management centered on QbD, clinical trial risk management, effective issue management, and continuous improvement.

CHALLENGES

A challenge that many organizations have with implementing QbD is taking an abstract concept that's at risk for sounding "buzz-wordy" and translating it to concrete actions that resonate with employees and meaningfully improve quality across the board. At its core, QbD is a common-sense concept that comes down to a handy habit of critical thinking applicable in many areas of life: "**Stop and Think**." It's about resisting the urge to rely on previous templated study designs and instead, bringing together multiple perspectives to determine early on what components are really needed in a trial, where risks exist, and how they can best be managed. But employees worried such actions would create an extra step and potentially delay timelines (a common concern that is unfounded — QbD thinking is intended to shorten trial delivery timelines and reduce downstream re-work).

SOLUTION(S)

BMS' Head of R&D Quality SBO, serves on the CTTI Steering Committee and has been involved in developing some of the QbD adoption tools including [recommendations for monitoring](#), [recommendations for QbD](#), [a principles document](#), and a [QbD toolkit](#) that outlines how to apply QbD principles in clinical trials. More recently, CTTI created additional resources—a [metrics framework](#), [maturity model](#), [implementation guide](#), and [documentation tool](#)—to help organizations and individual trial teams effectively implement a QbD approach for their trials. This suite of resources proved invaluable to BMS as it set out to host its first QbD workshop.

TAKING ACTION

As CTTI's recommendations note, gaining leadership support and buy-in is a crucial element of implementing QbD thinking across an organization. To that end, soon after E8(R1) was released (in 2021), BMS used CTTI's Maturity Model to perform an organizational maturity assessment that would help define the desired future state of QbD in the organization. The assessment included perspectives from 35-40 diverse stakeholders spanning a range of different functions across BMS. Results from that effort were presented to senior leaders in the BMS R&D Quality Council and three core areas of priority were agreed upon: 1) Adoption of QbD Principles, 2) Risk Management, and 3) Stakeholder Engagement.

With the desired outcome in hand and leaders aligned with QbD's value, BMS began planning the company's first QbD workshop (in 2022), with CTTI's support, for a novel respiratory compound. Key to this effort was bringing together the perspectives of multiple stakeholders that reach beyond Quality in the organization. BMS' workshop included clinical scientists, regulatory, commercial teams, disease-area advocates, members of BMS' Clinical Center of Excellence, quality teams, the project's vendor oversight manager, data management, and others. The Head of R&D Quality sponsored this first QbD pilot.

The workshop began with an overview of CTTI's principles document to establish the basics of QbD, followed by a CTTI-conducted survey to start identifying the study's "Critical to Quality" factors, or CTQs. In QbD, CTQs are those pivotal factors on which the trial's overall success (or failure) hinges — but CTQs are often captured differently depending on where an individual sits in an organization, making cross-functional stakeholder input and engagement essential. This is where healthy debate on what truly rises to the level of a CTQ, which is arguably the most value-add element of QbD, begins.

"The study was at the draft protocol stage when we identified CTQ factors, which was great timing. This allowed us wriggle room to make change to the protocol before it was finalized" said BMS' Head of R&D Quality SBO. "It was interesting to see cross-functional teams challenging one another's assumptions and how quickly some of those assumptions broke down with critical thinking. For example, when safety reporting was identified as a CTQ, we did a deep dive into what, how and where safety data points would be collected. We strategized to 'ring-fence' the process for collecting safety data to

minimize risk and therefore any potential impact to the primary objective."

The QbD workshop received positive feedback and sent a message to senior leaders that such collaborative critical thinking should be part of every trial design early on in the protocol development process. It was seen as a breath of fresh air, not just for saving time and cost, but also in its ability to generate a lean study design that is scientifically sound, operationally feasible, and most importantly, focused on trial participant feasibility.

IMPACT

"Since the initial workshop, BMS has been working to deeply embed a culture of quality across the organization to create a sort of 'QbD thought ecosystem' – focused on people, process, technology, and data," said BMS' Head of R&D Quality SBO. To continue the positive momentum from the workshop, BMS has held additional workshops, trainings, and a Protocol Simplification Championship.

While the Head of R&D Quality SBO firmly believes that cultural change is an important start, she also suggests that it has to be supported with process change (embedding QbD principles into procedural documents), technology (incorporating automation and emerging technologies to support risk identification and management), and data (having fit-for-purpose data and analytics).

ADVICE

BMS' Head of R&D Quality SBO, is pleased with her organization's journey to shift quality from a reactive mindset to a proactive mindset that is owned by all. Her vision is to continue to build a holistic quality-integrated capability and process model to enable critical thinking and drive accountability.

While BMS included patient partners (an important group many new to QbD miss), they did not include external vendors, like Contract Research Organizations (CROs), niche providers, and labs — a decision BMS plans to correct for upcoming workshops. Given so many trials rely on vendors to execute important elements of their research (including primary objectives), it is important their voice is included in cross-functional debate and aligned with the company's values as they relate to QbD thinking.

The BMS leader also notes the importance of flexing to the needs of your organization as it relates to QbD adoption:

"The ICH E8(R1) guidance applies across the board, but QbD implementation to support its aims is definitely not one-size-fits-all," she explains. "For example, QbD adoption in academia will likely look different than it does at a large pharma like BMS, and that's okay. Tailor the adoption as needed with the understanding that despite nuanced differences, all of us embracing QbD are working toward the same goal: to keep trial participants in the center of our efforts and speed new therapies to patients, who are at the heart of all that we do."

ORGANIZATION

Bristol Myers Squibb

CONTACT

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ORGANIZATION TYPE

Industry

IMPLEMENTATION DATE

2022

TOPIC

Quality

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