University of California Irvine's Multidisciplinary Trial Design Studios Yield Streamlined, Considered Protocols

University of California Irvine Applies CTTI's Quality by Design Recommendations

SUMMARY

University of California (UC) Irvine, an academic health center, used CTTI'sQuality by Design (QbD) principles and resources to conduct multi-stakeholder "design studios" where investigator-initiated protocols are assessed early in the development process by experts on clinical trial informatics, statistical design, recruitment, ethics and more to ensure quality and feasibility. UC Irvine ultimately intends to quantify the value of QbD in these settings via a "clinical trial of clinical trials" comparatively assessing traditional trials and QbD-focused trials across factors like enrollment, adverse events, and more.

GOAL(S)

Looking back on the research response to the COVID-19 crisis, Janet Woodcock, MD, acting commissioner of the Food and Drug Administration (FDA), recently noted something extraordinary: Only five percent of clinical trial arms launched for COVID-19 therapies will actually yield generalizable information on safety and efficacy. These issues are the result of both low enrollment and lack of trial-design focus on assessment of clinical benefits and risks. The result is that a significant amount of time and funding are being spent on research that, in the end, may not help the public navigate the pandemic in the real world. The challenge of trial design isn't COVID-specific, either; developing thoughtful, proactively considered protocols in today's complex environment marked by siloes, competing priorities among stakeholders, and inefficiencies has been a struggle for decades. In this setting, many trials fail to enroll participants, are plagued with adverse events, and are never published.

UC Irvine wanted to address these challenges head-on within its academic health center. After learning about QbD, UC Irvine sought to create a formalized pathway for implementing its principles into the design and conduct of clinical research directed at its institution. Specifically, it wanted to create Critical-to-Quality Design Studios to review the feasibility and acceptability of protocols through the lens of QbD and, ultimately, glean data to prove the value of the approach to fellow academics pursuing investigator-initiated trials.

CHALLENGES

While industry sponsors may secure buy-in for novel approaches to trial design like QbD in a top-down fashion, research in academic centers is less centralized, making change implementation a different process. UC Irvine needed to convince skeptical investigators to agree to invest their time in the approach and not reflexively dismiss it. That meant finding ways to appeal to academia's data-driven nature and elevating the QbD approach as a true driver of value to investigators' studies.

SOLUTION(S)

CTTI's suite of recommendations and resources help the clinical research community understand the value of QbD and apply its principles. A particularly popular resource is CTTI's QbD Critical-to-Quality (CTQ) Factors Principles Document, which walks study teams through a crucial part of the QbD process: proactively identifying the elements of a study that are key to the integrity of data and/or patient safety. Once a CTQ is defined for a particular study, CTTI also offers resources for the subsequent tailoring of the protocol design to eliminate unnecessary complexity and avoid predictable errors, as well as devise a focused, efficient, and streamlined monitoring and auditing plan for oversight. UC Irvine used these resources as the starting point to bring investigators on board and begin its Design Studio development.

TAKING ACTION

UC Irvine's process was multistep: 1) Engage institutions through an informative workshop; 2) Develop a QbD Working Group; and 3) Plan and structure the Design Studio:

Engaging Institutions
As the first step, UC Irvine made key stakeholders involved in clinical research aware of QbD concepts. UC Irvine accomplished this through a one-day workshop sponsored jointly by its Institute for Clinical and Translational Science and CTTI. Attendees included organizational leaders in the School of Medicine, as well as key personnel involved in clinical research development and administration. The workshop not only described QbD concepts and key components of the CTQ Principles Document, it also involved case studies of previous and prospective trials at UC Irvine to demonstrate the QbD approach. Two important points UC Irvine noted as critical to engagement were 1) illustrating that QbD was not a regulatory barrier, but rather a resource for investigators to build better studies and 2) using key influencers in the community to elevate and champion the approach. In UC Irvine's case, their chair of the Department of Medicine served as that influencing resource.

Developing a Working Group
To effectively conduct Design Studios at the earliest stages of UC Irvine's protocols, it needed a core Working Group of people to bring together collaborative expertise. The group UC Irvine selected was made up of core members who were chosen based on their expertise in areas of critical importance shared by all clinical trials, including experts on clinical trial informatics, statistical design, recruitment and retention, and research ethics. The core group also included experienced study coordinators, research nurses, and seasoned clinical trial investigators who provided practical guidance on trial design and conduct. Additionally, there was an ad hoc group that included the Principal Investigator (PI) and the study team as well as content experts who were tailored to the needs of the study being discussed and included investigators with scientific expertise (including preclinical experts) in the particular field of study. Importantly, the ad hoc group also included a patient/participant representative who was selected based on the condition being studied. According to UC Irvine, the voice of the patient is consistently among the most powerful for the investigator in its Design Studios, sharing

key insights that trialists and other experts simply are not privy to.

Planning & Structuring the Design Studio
Once a Design Studio is scheduled, the investigator provides a 3-4 page description of the study, its aims, rationale and implementation plan. On the day of the Design Studio, the Working Group opens dialogue around the study and begins the process of identifying CTQs based on areas considered high-risk with potential to disrupt the study. Post-meeting, a survey is used to prioritize the proposed CTQs, with those scores emailed to the investigator and the research team. A written summary includes rationale and helpful references for the team to consider. UC Irvine also solicits feedback from investigators to help continuously improve the Design Studio process.

IMPACT

Over the past 2 years, the UC Irvine Design Studio team has reviewed eight separate clinical research protocols, including five during the COVID-19 pandemic. The studies that underwent the QbD process via Design Studios included a wide range of clinical research designs, and the CTQs identified helped clarify the resources needed that would otherwise not have been addressed. For instance, insights from the Design Studio helped a study team proactively anticipate that an international COVID-therapy trial would require significant resource development and staff training for successful site initiation.

The experience with Design Studios is also creating a cultural shift across UC Irvine investigators, who have reported on average that they modified their study protocol to address 59% of the CTQ factors identified in their report. In comments entered on the survey, investigators reported specific benefits such as, "We modified our approach to both data collection and oversight/data integrity based on the feedback" and, "There were a number of things I had not yet begun to think about with respect to clinical needs."

ADVICE

UC Irvine's study teams are reporting smoother, better-designed trials as a result of the QbD approach. Far from being a pie-in-the-sky theoretical concept, QbD appeals to the very nature of academics who are compelled by numbers and specific ideas. Once embraced, CTQ identification and a QbD mindset becomes a logical part of the protocol design process that delivers true value to the scientific community.

ORGANIZATION

University of California, Irvine

CONTACT

Dan Cooper

ORGANIZATION TYPE

Academia

IMPLEMENTATION DATE

2019

TOPIC

Quality

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