Clinical Quality by Design: From Supervision to Collaboration and Beyond

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The views and opinions expressed in this presentation are those of the individual presenter and do not necessarily reflect the views of the Clinical Trials Transformation Initiative.
Origins of the Quality by Design Project
Key Driver for Clinical QbD

If you are in a shipwreck and all the boats are gone, a piano top buoyant enough to keep you afloat that comes along makes a fortuitous life preserver. But this is not to say that the best way to design a life preserver is in the form of a piano top.

I think that we are clinging to a great many piano tops in accepting yesterday's fortuitous contriving as constituting the only means for solving a given problem.....

Operating Manual for Spaceship Earth, Buckminster Fuller; 1968

Clinical trials are essential to the evaluation of promising scientific discoveries, but they are becoming unsustainably burdensome, threatening to deprive patients and health-care providers of new therapies and new evidence to guide the use of existing treatments.

Impediments to Clinical Research in the United States; J M Kramer, P B Smith, R M Califf, Clinical Pharmacology & Therapeutics (2012); 91 3, 535–541
Key Considerations: Quality

- Simply advocating the “highest level” of quality has little practical meaning in itself.
- The cost associated with incremental improvements in quality becomes ever higher as perfection is approached and becomes disproportionate to any additional benefit achieved.
Quality by Design: QbD Defined

“Quality” in clinical trials is defined as the absence of errors that matter

Prospectively examining the objectives of a trial and defining factors critical to meeting these objectives

... focusing effort on those “errors that matter” for the success of the clinical trial

... taking action to prevent important risks to these critical factors from negatively impacting outcomes

Understanding what data and processes underpin a successful trial is essential to subsequently identifying and managing important and likely risks to improve quality and outcomes for clinical trials.

“Quality” in clinical trials is defined as the absence of errors that matter.
QbD Implementation: Plan, Do, Check, Act

**PLAN**
Build/plan quality into clinical trials from the beginning, focusing on what matters most

**DO**
Implement study risk management strategies

**CHECK**
Monitor leading indicators of quality in the study

**ACT**
Systematically drive remediation and learning
CTTI QbD Project Plan

- Produce a draft document outlining:
  - High-level principles for building quality into the design and operations of trials
  - One potential approach to prospective quality planning

- Test and refine the document through a series of workshops
  - Different therapeutic areas and product types
  - Model prospective, cross-functional dialogue, including input from investigators, patients, health authorities, and others with a stake in trial conduct

- Evaluate the workshops’ impact and disseminate the initial results

- Encourage and support further development and implementation
Project Recommendations
“Quality” is defined as the absence of errors that matter to decision making—that is, errors which have a meaningful impact on the safety of trial participants or credibility of the results (and thereby the care of future patients)
Create a culture that values and rewards critical thinking and open dialogue about quality, and that goes beyond sole reliance on tools and checklists.

- Encourage proactive dialogue about what is critical to quality for a particular trial or development program and, when needed, the development of innovative methods for ensuring quality.

- Discourage overreliance on checklists and inflexible “one size fits all” approaches that undermine creation of specific strategies and actions intended to effectively and efficiently support quality in a given study.

- Verify that quality and performance measures are aligned with incentives driving a culture that rewards critical thinking.
Focus effort on activities that are essential to the credibility of the study outcomes

- Rigorously evaluate study design to verify that planned activities and data collection are essential.
- Streamline trial design wherever feasible.
- Deploy resources to identify and prevent or control errors that matter in the study.
- Consider whether nonessential activities may be eliminated from the study to simplify conduct, improve trial efficiency, and target resources to most critical areas.
THINK about the protocol

What is the rationale for…
- Choice of study population
- Sample size
- Inclusion/exclusion criteria
- Data items collected
- Practical procedures and assessments
- Biochemical assays
- Study endpoints

Just because you can…doesn’t mean you should…

Louise Bowman, University of Oxford,
Operationalizing QbD in Clinical Trials, April 2015
Involve the broad range of stakeholders in protocol development and discussions around study quality

- Engaging all stakeholders with study development is an important feature of quality by design.

- The process of building quality into the study plan may be informed not only by the sponsor organization but also by participation of those directly involved in successful completion of the study such as clinical investigators, study coordinators and other site staff, and patients.

- Clinical investigators and potential trial participants have valuable insights into the feasibility of enrolling patients who meet proposed eligibility criteria, whether scheduled study visits and procedures may be overly burdensome and lead to early dropouts, and the general relevance of study endpoints to the targeted patient population.

- When a study has novel features in elements considered critical to quality (e.g., defining patient populations, procedures, or endpoints), early engagement with regulators should also be considered.
Prospectively identify and periodically review the critical to quality factors

The CTTI Quality by Design Principles can be used to identify those aspects in each study that are critical to generating reliable data and providing appropriate protections for research participants, and to develop strategies and actions to effectively and efficiently support quality in these critical areas.

Periodically review critical to quality factors to determine whether adjustments to risk control mechanisms are needed.
Thank you!

- Team leaders
- Team members
- Principles Document expert working group members
- Workshop attendees
- Interviewees
THANK YOU.

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