Introduction to CTTI
Clinical Trials in Crisis

Discovery's 'First In Human' Calls Much-Needed Attention To Clinical Trials
Addressing This Need

CLINICAL TRIALS TRANSFORMATION INITIATIVE

Public-Private Partnership
Co-founded by Duke University & FDA
Involves all stakeholders
80+ members

MISSION: To develop and drive adoption of practices that will increase the quality and efficiency of clinical trials
Multi-Stakeholder

Everyone must have a seat at the table

- Clinical Investigators
- Government & Regulatory Agencies
- Industry (pharma, bio, device, CRO, & tech)
- IRBs
- Trade & Professional Orgs
- Academia
- Patients, Caregivers & Patient Advocacy Groups
CTTI Membership
We use quantitative & qualitative research methods, selecting those best aligned with each project’s objectives, to:

- Identify/describe “what is going on” to gain a better understanding of a particular phenomenon
- Move beyond individual views to a more complete and objective understanding of the disincentives and motivators for change

Equipped with data, we then challenge assumptions, identify roadblocks, build tools and develop recommendations to change the way people think about and conduct clinical trials.
Real-World Impact within Organizations

CTTI’s Central IRB tools & recommendations are used by:
- Celgene Corporation
- National Institute of Neurological Disorders and Stroke (NIH)
- Northwell Health

CTTI’s Quality by Design framework is used by:
- AstraZeneca
- DCRI
- The Medicines Company
- PCORNET
- Pfizer
- Seattle Genetics
- Target Health Inc
- University of Oxford
CTTI and its work have been cited in:

- NIH Policy
- Several FDA guidance documents
- An EMA reflection paper
- HR 21st Century Cures & corresponding Senate effort
CTTI Projects
Project Methodology

- **State Problem**
  - Identify Research Impediments
  - Issue Statement & Project Plan

- **Gather Evidence**
  - Identify Gaps/Barriers
  - Literature Reviews, Surveys, & Interviews

- **Explore Results**
  - Analyze & Interpret Findings
  - Team Meetings

- **Finalize Solutions**
  - Develop Recommendations/Tools
  - Team, Expert, & Ad Hoc Committee Meetings

- **Drive Adoption**
  - Disseminate & Implement
  - Pilot Studies, Measure Impact, & Implementation

- **Multi-Stakeholder Engagement**

- **Communications**
# Project Portfolio

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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

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

**PLAN**
- Implement study risk management strategies

**DO**
- Monitor leading indicators of quality in the study

**CHECK**
- Systematically drive remediation and learning

**ACT**
- Implement study risk management strategies
QbD 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

- Focus effort on activities that are essential to the credibility of the study outcomes

- Involve the broad range of stakeholders in protocol development and discussions around study quality

- Prospectively identify and periodically review the critical to quality factors
Investigator Community: Characteristics of “One-and-Done” Investigators

Time to lead trial takes away from other necessary activities
- Long work hours
- Unpredictable work hours
- Trial time makes it difficult to devote time to:
  - Clinical and non-clinical activities
  - Activities fostering academic promotion

Too much time required to lead trial
- Amount of time to implement trial in general
- Time required by investigator to support trial and staff
- Amount of time required by staff to support trial
- Amount of time required to prepare for trial set up

Burden of data and safety reporting
- Amount
- Method
- Frequency

Dissatisfaction with trial finance
- Sponsor/site contract negotiations
- Sponsor/site budget negotiations
- Final contract
- Final site budget
- Schedule of site payments

Surprise Finding: 44% of “one and done” investigators wanted to conduct more trials
Investigator Community: Characteristics of Successful Active Investigators

- Sufficient and well-trained staff
- Strong commitment and work ethic
- Institutional support
- Ability to recruit patients

- Business knowledge and experience
- Strong reputation
- Ability to network
- Ability to be realistic when selecting protocols/recruitment
Investigator Community Recommendations Overview

- Develop site-based research infrastructure and staff
- Optimize trial execution and conduct
- Improve site budget and contract negotiations
- Identify additional trial opportunities for interested investigators
Investigator Qualification

Purpose

To critically evaluate current approaches to investigator qualification, including GCP training, and issue recommendations on efficient and effective methods for investigators to become qualified to conduct clinical trials.
Investigator Qualification

Quality by Design

Investigator Community
CTTI’s Approach to Expert Meetings

- Everyone participate, no one dominate
- Disagree without being disagreeable
- Stay open to new ways of doing things
- Respect each others’ thinking and value their contributions
- Articulate hidden assumptions
- Listen for the future to emerge
THANK YOU.