Introduction to CTTI
Clinical Trials in Crisis

Discovery's 'First In Human' Calls Much-Needed Attention To Clinical Trials
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
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CTTI

MULTISTAKEHOLDER

EVIDENCE-BASED

REAL-WORLD IMPACT

TRANSFORMING CLINICAL TRIALS

TRANSFORMING CLINICAL TRIALS
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:

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

MULTI-STAKEHOLDER ENGAGEMENT

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

COMMUNICATIONS
## Project Portfolio

### Areas of Strategic Focus:

<table>
<thead>
<tr>
<th>SYSTEMATIC EVIDENCE GENERATION</th>
<th>PATIENTS AS EQUAL PARTNERS</th>
<th>EFFICIENT &amp; QUALITY TRIALS</th>
<th>PUBLIC HEALTH CONCERN</th>
<th>SAFE &amp; ETHICAL TRIALS</th>
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### Active Projects:

- MCT Legal & Regulatory
- MCT Mobile Devices
- MCT Stakeholder Perceptions
- Real World Evidence
- State of Clinical Trials

### Patient Groups & Clinical Trials

- Investigator Qualification

### Complete Projects:

- Large Simple Trials
- MCT Novel Endpoints
- Registry Trials

### GCP Training

- Investigator Community
- Monitoring
- Quality by Design
- Recruitment
- Site Metrics

### ABDD Peds Trials

- ABDD
- Streamlining HABP/VABP Trials
- ABDD Unmet Need
- Long-Term Opioid Data

### Central IRB, Central IRB Adv

- DMCs
- Informed Consent
- Pregnancy Testing
- IND Safety, IND Safety Adv
- SAE Reporting
CTTI Mobile Clinical Trials (MCT) Program

PURPOSE: Develop evidence-based recommendations that affect the widespread adoption and use of mobile technology in clinical trials for regulatory submission

SCOPE: FDA-regulated clinical trials after the time of initial volunteer consent

4 PROJECTS

- Novel Endpoints
- Mobile Devices
- Legal & Regulatory Issues
- Stakeholder Perceptions
  - Investigative Sites
  - Potential Participants
Novel Endpoints: Project Objective

Describe best practices for selecting, developing and including novel endpoints, generated using mobile technology, in clinical trials.

*Novel endpoints are defined as either 1) new endpoints that have not previously been possible to assess, or 2) existing endpoints that can now be measured in new and possibly better ways using mobile technology.
Novel Endpoints: Recommendations Summary

- Optimize novel endpoint selection
  - Focus on measures that are meaningful to patients
  - Select the device after selecting an outcome assessment
  - Use a systematic approach to identify key novel endpoints

- Approach novel endpoint development process practically
  - Foster collaboration among key stakeholders
  - Engage regulators throughout the development process
  - Create technical standards for mobile technology-derived assessments
  - Include novel endpoints as exploratory endpoints in existing clinical trials and observational cohort studies
  - Critically position novel endpoints in interventional trials
Novel Endpoints: Resources

Recommendations

Tools

- Novel endpoint development benefit framework
- Selection tool to support decisions between viable novel endpoints for development
- Guide to interacting with FDA regarding novel endpoint development
- Flowchart of steps for novel endpoint development
- Detailed description of steps for novel endpoint development, with suggested approaches and considerations
- Four use cases to provide tangible examples of novel endpoint development
  - Parkinson’s disease, diabetes, heart failure, Duchenne’s muscular dystrophy
Mobile Devices: Project Objectives

- **Identify solutions to the data challenges** associated with using mobile devices to capture objective data in clinical trials.

- **Identify and describe the scientific and technological considerations** associated with managing mobile devices for objective data capture in clinical trials and develop guiding principles to promote their inclusion.

*For the purposes of this project, mobile devices are defined as mobile applications and remote sensor devices that capture objective data, including both consumer and medical grade devices.*
Mobile Devices: Topics and Issues

<table>
<thead>
<tr>
<th>DATA CHALLENGES</th>
<th>SCIENTIFIC CONSIDERATIONS</th>
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<tr>
<td>- Data origins &amp; source data</td>
<td>- Providing real-time data to study participants</td>
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<td>- Data integrity</td>
<td>- Monitoring outcomes</td>
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<tr>
<td>- Data collection</td>
<td>- Real time safety signals</td>
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<td>- Data attribution</td>
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<td>- Study monitoring</td>
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<td>- Data security</td>
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<td>- Audit trail</td>
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<td>- Data reproducibility</td>
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<table>
<thead>
<tr>
<th>TECHNOLOGICAL CONSIDERATIONS</th>
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<tr>
<td>- Device validation</td>
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<tr>
<td>- Calibration</td>
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<tr>
<td>- Device management</td>
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<tr>
<td>- BYOD</td>
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<tr>
<td>- Device failure</td>
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<td>- Device reuse</td>
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Mobile Devices: Data Security Findings

Three points of risk when mobile devices are used for data capture
- Data collection
- Data transfer
- Data storage

Tool under development
A framework that would allow classification of data/device into risk categories, with minimally acceptable security standards for each risk level described
**Mobile Devices: Sharing Data in Real Time Findings**

- Overarching goal should always be the integrity of the study.
- Patient(s) should always be engaged in protocol development.
- Regardless of whether or not mobile devices are used for data capture, data should always be shared with participants at the end of the study.

*Tool under development*

A decision tree to support decisions around sharing data in real time with study participants during protocol development.
Legal & Regulatory Issues: Project Objectives

- Identify perceived and actual legal and regulatory barriers to conducting mobile clinical trials
- Identify opportunities to clarify and inform policies that affect the implementation of mobile clinical trials
Legal & Regulatory Issues: Example Questions to Consider

- How do we think differently about ‘sites’ in context of MCTs?
- How do issues regarding investigator delegation and oversight change?
- What adjustments to safety reporting SOPs and escalation plans may be necessary?

Tool under development

A considerations document to support legal and regulatory considerations regarding protocol development, investigator delegation and oversight, and safety monitoring and reporting issues.
Legal & Regulatory Issues: Recommendations Focus Areas

- Protocol design
- Telemedicine and state licensing issues
- Drug supply chain issues
- Use of mobile practitioners
- Considerations for investigator delegation and oversight
- Safety monitoring and reporting
Stakeholder Perceptions: Project Objectives

Among potential research participants:

- Determine familiarity and ease of use with mobile technologies.
- Identify perceived concerns of using mobile technologies to collect and share personal data in clinical trials.
- Identify preferred and undesirable attributes of mobile technologies when used in clinical trials.
- Determine the acceptability of and willingness to participate in clinical trials that use mobile technologies (and how those might be different from trials without use of mobile technology)
Stakeholder Perceptions: Project Objectives

Among site investigators who have been involved in mobile clinical trials:

- Describe site investigators’ insights on the advantages and disadvantages of mobile clinical trials.
- Explain site-level budgetary, training, and other support needs necessary to adequately prepare for and implement mobile clinical trials.
- Describe site investigators’ advice for other site investigators who are interested in participating in mobile clinical trials.
Stakeholder Perceptions Project

Methods

Products

Anticipate Impact

- High quality, efficient trials that successfully leverage the use of mobile technology in ways that incorporate the needs and expectations of potential research participants and investigative sites
Thank You To The MCT Stakeholder Perceptions Project Team

- Cindy Geoghegan, Patient and Partners
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- Kara Dennis, Medidata Solutions
- Sue Dubman, Individual Patient
- Guy Eakin, Arthritis Foundation*
- Terri Hinkley, ACRP*
- Guy Eakin, Arthritis Foundation*
- Les Jordan, Target Health
- Hassan Kadhim, Boehringer Ingelheim
- Kristine Nelson, EMMES*
- Amanda Niskar, Individual Patient
- Petros Okubagzi, MedStar Health Research Institute
- Ido Paz-Priel, Genentech
- Ken Skodacek, FDA
- Junyang Wang, FDA
- Immo Zadazensky, FDA*
- Amy Corneli, CTTI Social Science Lead
- Brian Perry, CTTI Associate Social Scientist
- Zachary Hallinan, CTTI Project Manager

*Former | Team Leader
Creating a Comprehensive Toolkit

www.ctti-clinicaltrials.org

- Novel Endpoint recommendations & tools are now available
- CTTI will issue additional project recommendations over next ~6 months
- Sign up to receive CTTI’s monthly e-newsletter for updates
Meeting Objectives

- Present findings from CTTI evidence gathering activities examining the perspectives of investigators and potential research participants on the use of mobile technology for objective data collection in clinical trials.

- Discuss how this and additional evidence presented may be used to provide direction to the research enterprise for the appropriate utilization of mobile technology in clinical trials.

- Identify products CTTI should develop to equip the clinical trials enterprise to address barriers, preferences and needs of investigative site personnel and potential research participants in regulatory submission trials using mobile technology for objective data collection.
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.