CTTI’s Digital Health Trials Hub
Revised Recommendations and New Resources for DCTs and Novel Endpoints
<table>
<thead>
<tr>
<th>Time (EST)</th>
<th>Content</th>
<th>Presenter</th>
</tr>
</thead>
<tbody>
<tr>
<td>11:00 AM</td>
<td>Welcoming Remarks</td>
<td>Sally Okun (CTTI)</td>
</tr>
<tr>
<td>11:05 AM</td>
<td>Decentralized Clinical Trial Project Recommendations</td>
<td>Megan Doyle (Amgen)</td>
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<tr>
<td>11:15 AM</td>
<td>Novel Endpoints Acceptance Recommendations &amp; Resources</td>
<td>Jörg Goldhahn (ETH Zurich)</td>
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<tr>
<td>11:30 AM</td>
<td>Stakeholder Perspectives</td>
<td>Beth Kunkoski (FDA), Phil Green (Patient), Reem Yunis (Medable), Jeremy Wyatt (ActiGraph) Moderator: Lindsay Kehoe (CTTI)</td>
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<tr>
<td>11:45 AM</td>
<td>Q&amp;A</td>
<td>Lindsay Kehoe (CTTI)</td>
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<tr>
<td>11:57 AM</td>
<td>Final Comments &amp; Adjourn</td>
<td>Lindsay Kehoe (CTTI)</td>
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Multi-stakeholder, public-private partnership co-founded by Duke University & FDA

Participation of 500+ more orgs and + 80 member organizations

MISSION: To develop and drive adoption of practices that will increase the quality and efficiency of clinical trials
By 2030, clinical trials need to be:

- Patient-Centered & Easily Accessible
- Fully Integrated Into Health Processes
- Designed With A Quality Approach
- Maximally Leveraging All Available Data
- Improving Population Health

A critical part of the Evidence Generating System

https://ctti-clinicaltrials.org/who_we_are стратегическое видение
Potential Benefits of Digital Health Trials

**OBTAINING BETTER, MORE RELIABLE INFORMATION**
- Provides a broader picture of treatment effects and how patients function
- Enables more inclusive & generalizable trials
- Supports better regulatory & subsequent reimbursement decision making

**CONDUCTING MORE PATIENT-CENTRIC RESEARCH**
- Healthcare can be near or in the patient’s home
- Endpoints that matter and are meaningful to patients are used in clinical trials
- Burden on the participant is reduced, which increases trial participation & retention

**MOVING AT HIGHER EFFICIENCY & SPEED**
- Recruitment is faster and retention is better
- Data collection is more frequent, continuous, and/or useful
- Burden on site and staff resources is decreased
Six Sets of Recommendations & Resources

CTTI’s Digital Health Trials Hub

- Planning Decentralized Trials
- Interacting with Regulators
- Supporting Sites
- Managing Data
- Selecting & Testing Digital Health Technology
- Developing Novel Endpoints
Thank You to All DHT Project Team Members

AbbVie Inc  Curebase  Harvard University  Mt Sinai Health System
ActiGraph  Department of Veterans Affairs  HumanFirst  NIH
Advarra  Department of Veterans Affairs  Individual Consultant  Northumbria University
Alpha-1 Foundation  DiMe  Individual  Northwell Health
American Association of Kidney Patients  Duke University  Patient/Caregiver  Novartis
American Society of Clinical Oncology  Elektra Labs  IQVIA  Orikami
Amgen Inc  Eli Lilly and Company  Johns Hopkins University  Parent Project Muscular Dystrophy
ASAA  EMD Serono  Johnson & Johnson/Janssen  Patient and Partners LLC
AstraZeneca  ETH Zurich  Lilly  PFF
Pharmaceuticals LP  Evidation Health  Massachusetts General Hospital  Pfizer, Inc.
Bioclinica Inc  FDA/CBER  MC10  Phillips Respironics
Biogen  FDA/CDER  McMaster University  PhRMA
Boehringer Ingelheim  FDA/CDRH  Medable  Pulmonary Fibrosis Foundation
Bristol-Myers Squibb  FDA/OC  Medidata Solutions  Queen's
CCF  Feinstein  MedStar Health  Quorum Review IRB
Cleveland Clinic Coordinating Center for Clinical Research  Fitabase  MicroMedicine  Science37
Clinical Trials Transformation Initiative  FPWR  MJFF  Society for Clinical Research Sites
Curebase-a member of the Roche Group  Genentech-a member of the Roche Group  MonARCH Bionetworks
Cleveland Clinic Coordinating Center for Clinical Research  Mt Sinai Health System  NIH
Mt Sinai Health System  NIH  Northumbria University
National Institutes of Health  Northwell Health  Novartis
Novartis  Orikami  Parent Project Muscular Dystrophy
Parent Project Muscular Dystrophy  Patient and Partners LLC  Pfizer, Inc.
Patient and Partners LLC  Phillips Respironics  PhRMA
PhRMA  Pulmonary Fibrosis Foundation  Queen's
Queen's  Quorum Review IRB  Science37
Science37  Society for Clinical Research Sites  Susan G Komen
Susan G Komen  Syneos Health  Target Health, LLC
Syneos Health  Target Health, LLC  The George Institute
Target Health, LLC  The George Institute  The Life Raft Group
The Life Raft Group  UCB  UNC NC TraCS
UNC NC TraCS  University of California, San Francisco  University of Kansas
University of California, San Francisco  University of Kansas  University of Michigan
University of Kansas  University of Michigan  University of Rochester
University of Rochester  VA  Yale University
University of Rochester  VA  Yale University
Yale University  Yale University  Yale University
DCT Update Project

Megan Doyle | Amgen, CTTI Team Lead
Decentralized Clinical Trials Update Project

1-Year Accelerated Project

Purpose

- **Deliver updated recommendations** that reflect the learnings and best practices emerging since CTTI’s Decentralized Clinical Trials (DCT) recommendations were released

Anticipated Impact

- **Increase adoption** of DCT solutions in the development of new trials going forward.

Background

- CTTI produced DCT recommendations in 2018
- One of the most downloaded CTTI resources in 2020
- Pandemic substantially expanded experience with DCTs across stakeholder groups
Three Updated Sets of Recommendations

Planning Decentralized Trials

Selecting & Testing Digital Health Technology

Developing Novel Endpoints

CTTI’S DIGITAL HEALTH TRIALS HUB

Interacting with Regulators

Supporting Sites

Managing Data
Defining DCTs

CTTI defines decentralized clinical trials (DCTs) as those in which some or all study assessments or visits are conducted at locations other than the investigator site via any or all of the following DCT elements:

- tele-visits;
- mobile or local healthcare providers, including local labs and imaging centers;
- and home delivery of investigational products.

Decentralized clinical trials can be completely remote or partially decentralized with hybrid approaches.

Hybrid trials are those that require some visits to be conducted on site, while other visits or assessments can be performed at a participant’s home or within their local care community.

Fully remote trials have no required site visits.

Key Points

- Visits / assessments conducted away from site
- Use “DCT elements”: tele-visits, mobile/local HCPs, and/or home delivery of investigational products
- Range from nearly-traditional to hybrid to fully remote
Decentralized Clinical Trials

DESIGNING TRIALS TO FIT INTO THE PATIENT’S LIFE, INSTEAD OF THE OTHER WAY AROUND

Flexibility
Optionality
Patient-centricity

Data collected remotely

Drugs sent to patients

Community sites

Mobile clinical sites

Local diagnostics

Investigators connected to patient wherever they go
Recommendations for Planning DCTs*

1. Engage All Stakeholders, Early & Often
   Including…
   • Internal stakeholders (e.g. biostatisticians, PV)
   • Patient and site needs for each DCT element
   • Early consultation with regulators on novel elements
   • In-country experts on local laws and regulations
   • Technology providers on operational considerations

2. Plan Ahead
   • Assess feasibility of remote activities as early as possible in clinical development plan
   • Incorporate DCT elements that provide overall benefit
   • Incorporate flexibility at all levels
   • Plan budgets holistically
   • Assess capabilities of operational partners

3. Address Important Risks to Study Quality
   • Monitor for consistency and comparability of data collection
   • Understand and address impact on access, participation, diversity
   • Evaluate and address risks to privacy, confidentiality, and study data
   • Define responsibilities for evaluating data
   • User-test tech and platforms

*See full recommendations for details
Recommendations to Sponsors for Supporting Sites*

**Build Awareness and Support**
- Educate sites about benefits and challenges, including new processes
- Listen carefully – two-way communication

**Budget**
- Assess DCT/DHT related time and costs – be able to pay sites appropriately
- Clearly delineate responsibilities
- Consider alternative payment structures

**Develop Infrastructure**
- Ensure sites can support planned DCT / DHT elements
- Confirm plans and policies in place to handle tech issues
- Agree on oversight of non-site trial personnel

**Train**
- Focus on new or unique elements for the trial
- Support sites in training involved local HCPs

**Support Effective Site / Patient Communication**
- Provide materials to train and support participants
- Be transparent about safety monitoring
- Account for health and tech. literacy
- Provide easy access to tech support
- Ensure investigators have timely, appropriate access to participant data

*See full recommendations for details*
Clearing a Path for Broad Implementation

- Harmonize laws & regulations
- Knowledge sharing
- Participant diversity & access
- Novel endpoints & remote data capture
- Embracing change
- Data for effective decision making
- Technology interoperability
Novel Endpoint Acceptance

Jörg Goldhahn | ETH Zurich, CTTI Team Lead
Purpose  Obtain reliability & acceptance of meaningful, digitally-derived novel endpoints

Expected Impact  Increase the use of meaningful, digitally-derived novel endpoints as key endpoints in clinical trials for labeling claims

Scope  Functional measures and/or other clinical outcome assessments that use digital health technologies (DHTs) for data capture (not ePROs, biomarkers, digital therapeutics)

PROJECT CONTEXT

CTTI developed Novel Endpoint recommendations in 2017

Limited use of these endpoints to support labeling claims today

Opportunity to enhance CTTI recommendations and develop new resources
Novel Endpoint Acceptance

- In-Depth Interviews
- CPIM/FDA ITF Briefing/EMA
- CTTI’s Novel Endpoint Acceptance Project
- Expert Meeting
- Team Discussion & Consensus

Recommendations on Developing Novel Endpoints
Evidentiary Considerations/Process Map (New)
Regulatory Engagement Guide (Revised)
Question Bank to Identify Meaningful Measures (New)
Updated Recommendations

1. Focus on measures that are meaningful to patients and are clinically relevant
2. Identify key endpoints by assessing and meeting the needs of each stakeholder
3. Select the technology after selecting an outcome
4. Engage with regulators early and often
5. Include digitally-derived endpoints in early phase clinical trials and observational cohort studies to demonstrate they are fit-for-purpose
6. Think critically about how to optimally position novel, digitally-derived endpoints in interventional trials
7. Promote the sharing of knowledge and lessons learned regarding the development of digitally-derived endpoints
Question Bank to Identify Meaningful Measures (New)

What

- A set of considerations to identify meaningful measures that are fit for use in a digital health trial
- Serves as an inspirational guide (to be tailored accordingly)

For Whom

Sponsors and clinician investigators

When

Protocol development and study design

Why

To enable:

- Widely accepted and agreed upon measures
- The development of the right endpoint for the right context
Process Map for an Individual Medical Product Development Track (New)

**What** A map of evidentiary considerations for a digitally-derived endpoint supporting an individual medical product development

**For Whom** Sponsors, operational partners, clinician investigators

**When** Strategizing product development

**Why** To provide clarity around what steps in digitally-derived endpoint development to take and when during the development of a specific medical product

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### What do you want to measure?

- **Describe the target population**
- **Identified aspects of health that are meaningful to the patient (MAH)**
- **Concept of interest (COI)**
- **Evidence for a digital tool or endpoint**
- **Potential clinical measure(s) and endpoint(s)**
- **Center of use (COU)**

### How do you demonstrate that the measure is meaningful and relevant?

- **Clinically meaningful change (CMC)**
- **Statistical significance**
- **Sensitivity and specificity**
- **Reliability**
- **Validity**

### How do you know you’re measuring what you want to measure?

- **Assess potential tools**
- **Determine measurement approaches**
- **Select the tool or endpoint**
- **Evaluate the extent to which the measure reflects the COI**

### Process Map for an Individual Medical Product Development Track (New)

- **At the beginning of the drug development program:**
  - **Sponsors, operational partners, clinician investigators**
- **During your early phase trials:**
  - **Describe the target population**
  - **Identified aspects of health that are meaningful to the patient (MAH)**
  - **Concept of interest (COI)**
  - **Evidence for a digital tool or endpoint**
  - **Potential clinical measure(s) and endpoint(s)**
  - **Center of use (COU)**
- **Before your late phase trial, you should have:**
  - **Statistical analysis plan**
  - **All data and justification to demonstrate that the DHT is fit-for-purpose and the anticipated endpoint results can support a label claim**
**What** A guide for how sponsors might engage with the FDA and/or EMA when developing a digitally derived endpoint

**For Whom** Sponsors and clinician investigators

**When** Varies, dependent on the engagement reason

**Why** To provide clarity around when and how to engage with regulators

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### Regulatory Engagement Guide (Revised)

**Is the regulatory engagement related to the development of an individual medical product?**

<table>
<thead>
<tr>
<th>YES</th>
<th>NO</th>
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<tbody>
<tr>
<td><strong>What type of medical product are you developing?</strong></td>
<td><strong>What are you seeking advice about?</strong></td>
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<tr>
<td><strong>Drug</strong></td>
<td><strong>Scientific Methodology or Technology</strong></td>
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</table>
| IND/INDA/BLA Pathway  
  - Type B Meeting  
  - Type C Meeting | IDE/FDA/De Novo Pathway  
  - Q-submission Program  
  - Determination Meeting  
  - Agreement Meeting  
  - Digital Health Center of Excellence |
| **Device** | **Qualification** |

**For the FDA**

- **MAA Pathway**
  - Innovation Task Force Meeting
  - Pre-submission meeting for Scientific Advice (or Protocol Assistance for Orphan Medicines)

**For the EMA**

- **Conformity Assessment (CE Mark) Pathway**
  - Notified Body Consultation
  - Scientific Opinion (by Notified Body)

**For the CTTI**

- **Innovation Task Force (TF) Briefing Meeting**
  - For Letters of Support or Qualification Opinion

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***CPTI***
Why are these updates important and how can they advance CTTI’s TT2030 vision?
Decentralized Clinical Trials Update Project Team

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* Formerly Rodrigo Garcia (EMD Serono)  ** Formerly Elektra Papadopoulos (FDA)
Download the Recommendations

Available Now on the CTTI website:

Learn How Others Implement CTTI Recs

Available Now through the CTTI website:
https://connects.ctti-clinicaltrials.org/case_study_exchange
THANK YOU

www.ctti-clinicaltrials.org