CTTI’s Digital Health Trials Hub
Recommendations and Resources to Run Your Digital Health Trial

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Disclaimer

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## Created by Multi-Stakeholder Project Teams

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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/strategic-vision/
# Potential Benefits of Digital Health Trials

<table>
<thead>
<tr>
<th>Obtaining Better, More Reliable Information</th>
<th>Conducting More Patient-Centric Research</th>
<th>Moving at Higher Efficiency &amp; Speed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Provides a broader picture of treatment effects and how patients function</td>
<td>Healthcare can be near or in the patient’s home</td>
<td>Recruitment is faster and retention is better</td>
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<tr>
<td>Enables more inclusive &amp; generalizable trials</td>
<td>Endpoints that matter and are meaningful to patients are used in clinical trials</td>
<td>Data collection is more frequent, continuous, and/or useful</td>
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<tr>
<td>Supports better regulatory &amp; subsequent reimbursement decision making</td>
<td>Burden on the participant is reduced, which increases trial participation &amp; retention</td>
<td>Burden on site and staff resources is decreased</td>
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CTTI
Six Sets of Recommendations & Resources

CTTI’S DIGITAL HEALTH TRIALS HUB

Planning Decentralized Trials
Selecting & Testing Digital Health Technology
Interacting with Regulators
Developing Novel Endpoints
Supporting Sites
Managing Data
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.
Three Updated Sets of Recommendations

CTTI’S DIGITAL HEALTH TRIALS HUB

- Planning Decentralized Trials
- Selecting & Testing Digital Health Technology
- Developing Novel Endpoints
- 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...
   - Patient and site needs for each DCT element (and all aspects of trial)
   - Early consultation with regulators on novel elements
   - In-country experts on local laws and regulations
   - Technology providers on capabilities and operational considerations

2. Plan Ahead
   - Assess feasibility of remote activities as early as 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

*See full recommendations for details
Recommendations for Planning DCTs*

1. Engage All Stakeholders, Early & Often
   
   Including…
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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
- Budget
- Develop Infrastructure
- Train
- Support Effective Site / Patient Communication

*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

Develop Infrastructure

Train

Support Effective Site / Patient Communication

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

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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

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

Support Effective Site / Patient Communication

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**Build Awareness and Support**
- Educate sites about benefits and challenges, including new processes
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**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 Endpoints Project Update

Jörg Goldhahn, ETH Zurich
Novel Endpoints Project Update

Purpose

- Obtain reliability & acceptance of meaningful, digitally-derived novel endpoints

Anticipated 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)
Novel Endpoints Acceptance Project

- 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)
- Flowchart of Steps for Novel Endpoint Development (Revised)
Updated Novel Endpoint 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
Question Bank to Identify Meaningful Measures (New)

Novel Endpoint Acceptance

Questions to Consider When Identifying Meaningful Outcome Measures

Clinical outcome measures that are captured as endpoints should be meaningful to patients and caregivers, clinically relevant, and fit for use in a clinical trial. Ideally, these measures will reflect reliable information and be able to be deployed in a timely way.

To help identify meaningful outcome measures and determine whether a digital health technology is the best way to capture an outcome of interest, sponsors and clinician investigators can use this set of considerations during protocol development and study design. The goal is to identify measures that address the needs of each stakeholder and to enable the development of the right endpoint for the right context. Of note, CTTI recommends selecting the outcome measure before selecting the tool or technology to capture the measure and cautions against developing novel endpoints simply because a new technology makes it technically feasible.

These questions were developed by using the Digital Medicine Society’s (DiMe) framework as a foundation, and are meant to serve as a guide that should be tailored based on the population and context of an individual study. The Core Outcomes Measures in Effectiveness Trials (COMET) Initiative is another useful resource for the development and application of agreed upon standardized sets of outcomes (i.e., core outcome sets) and is a good starting place for the development of meaningful outcome sets for a clinical trial. Users may also want to consider qualitative best practices not listed in this question bank—such as sample size or representative range of disease—as part of their overall approach to identifying meaningful outcome measures.

### Identifying Meaningful Outcome Measures: Questions to Ask Patients/Caregivers of a Particular Disease and/or Population of Interest

<table>
<thead>
<tr>
<th>Stakeholder: Patient/caregiver</th>
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<table>
<thead>
<tr>
<th>Topic Area</th>
<th>Questions</th>
</tr>
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<tbody>
<tr>
<td>Meaningful Aspect of Health</td>
<td>1. What part of your life is most frustratingly impacted by your condition?</td>
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<tr>
<td></td>
<td>2. How has your independence been affected by your condition?</td>
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<tr>
<td></td>
<td>3. What about your health do you wish you could improve?</td>
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<tr>
<td></td>
<td>4. Considering what you just mentioned, explain your near term goals:</td>
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<tr>
<td></td>
<td>&quot;In the next 3 months I’d like to (e.g. start or continue doing)...&quot;</td>
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<td>&quot;In the next 6 months I’d like to be able to ...&quot;</td>
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<tr>
<td></td>
<td>5. Explain your longer term goals. &quot;In the next 12-18 months I’d like to</td>
</tr>
<tr>
<td></td>
<td>(e.g. start or continue doing)....&quot;</td>
</tr>
</tbody>
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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
Process Map for an Individual Medical Product Development Track *(New)*

- **What do you want to measure?**
  - How do you demonstrate that the measure is meaningful and relevant?

- **How do you want to measure it digitally?**

- **How do you know you're measuring what you want to measure?**

- **Is your endpoint and DHT ready for a pivotal trial?**

**At the beginning of a drug development program:**

**During your early phase trials:**

**During your early phase trials:**

**Before your late phase trial, you should have:**
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
Is the regulatory engagement related to the development of an individual medical product?

**YES**
- **What type of medical product are you developing?**
  - **Drug**
    - IND/NDA/BLA Pathway
      - Type B Meeting
      - Type C Meeting
  - **Device**
    - IDE/510(k)/De Novo/ PMA Pathway
      - Q-submission Program
      - Determination Meeting
      - Agreement Meeting
      - Digital Health Center of Excellence

**NO**
- **What are you seeking advice about?**
  - **Scientific Methodology or Technology**
    - Critical Path Innovation Meeting (CPIM)
      - *(not qualification)*
  - **Qualification**
    - Drug Development Tool (DDT) Qualification Programs
      - Clinical Outcome AssessmentQualification Program
      - Biomarker Qualification Program
      - IStand Pilot Program
    - Medical Device Development Tools (MDDT) Program
Flowchart of Steps for Novel Endpoint Development (Revised)

What  A stepwise approach for developing an endpoint using a DHT for data capture

For Whom  Sponsors, clinician investigators, and technology providers

When  During program development and strategy

Why  To provide clarity around how to develop an endpoint using a DHT
Flowchart of Steps for Novel Endpoint Development (Revised)

1. Describe the target population and conceptualize treatment benefit and potential context of use (COU)

2. Identify aspects of health affected by the disease that are meaningful to patients and clinically relevant

3. Identify the concepts of interest (COI)

4a. Select the measurement(s) that is the best reflection of the concept of interest

4b. Assess potential digital health technology for data capture

5. Describe the context for which the measurement and technology will be used (determine COU)

6. Select candidate digital health technology for data capture and assess existing evidence supporting its use
How do I implement these CTTI resources?
35 Tools to Help Implement CTTI Recommendations

CTTI’S DIGITAL HEALTH TRIALS HUB

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- Developing Novel Endpoints
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Learn from CTTI’s Case Study Exchange
Does using a digital tool in my trial make sense?

CTTI Recommendations:

- Focus [first] on measures that are meaningful to patients and are clinically relevant
- Engage stakeholders early and often
- Address important risks to study quality

Resources:

- Question Bank to Identify Meaningful Measures
- Planning Trials Using Mobile Technologies: Gathering Patient & Site Input
- Checklist for Sponsors: Considerations in Selecting & Equipping Sites for Clinical Trials with Digital Health Technologies
How do I select & validate the fit-for-purpose digital tool?

CTTI Recommendations:
- Select the technology *after* selecting an outcome
- Ensure that all technologies and associated platforms have been thoroughly tested by the end users.
- Plan how to handle system failures at any level

Resources:
- Framework: Specifications to Consider During Digital Health Technology Selection
- Digital Health Trials: Recommendations for Selecting and Testing a Digital Health Technology
- Flowchart: Steps For Novel Endpoint Development
- Case Study: Verification & Validation Processes in Practice
How do we advance digital health trials?

CTTI Recommendations:

- Plan Ahead
- Incorporate flexibility, where feasible, at all levels of the trial
- Engage with regulators early and often
- Promote the sharing of knowledge and lessons learned

Resources:

- Clearing a Path for Broad Implementation of DCTs
- Publication: A systematic review of feasibility studies promoting the use of mobile technologies in clinical research
- Regulatory Engagement Opportunities when Developing Digitally Derived Endpoints
CTTI has multiple resources to support the design and execution of digital health trials.

Take Away #1

- Planning Decentralized Trials
- Selecting & Testing Digital Health Technology
- Interacting with Regulators
- Developing Novel Endpoints
- Supporting Sites
- Managing Data
Take Away #2

Regulators are developing guidance to provide clarity.
Establishing collaborative relationships and sharing lessons learned can advance the digital health trial field.
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
Q&A