CLINICAL TRIALS **TRANSFORMATION** INITIATIVE

April 6, 2022

CTTI's Digital Health Trials Hub

Revised Recommendations and New Resources for DCTs and Novel Endpoints

Agenda slide

Time (EST)	Content	Presenter
11:00 AM	Welcoming Remarks	Sally Okun (CTTI)
11:05 AM	Decentralized Clinical Trial Project Recommendations	Megan Doyle (Amgen)
11:15 AM	Novel Endpoints Acceptance Recommendations & Resources	Jörg Goldhahn (ETH Zurich)
11:30 AM	Stakeholder Perspectives	Beth Kunkoski (FDA), Phil Green (Patient), Reem Yunis (Medable), Jeremy Wyatt (ActiGraph) Moderator: Lindsay Kehoe (CTTI)
11:45 AM	Q&A	Lindsay Kehoe (CTTI)
11:57 AM	Final Comments & Adjourn	Lindsay Kehoe (CTTI)

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CLINICAL TRIALS **TRANSFORMATION** INITIATIVE

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

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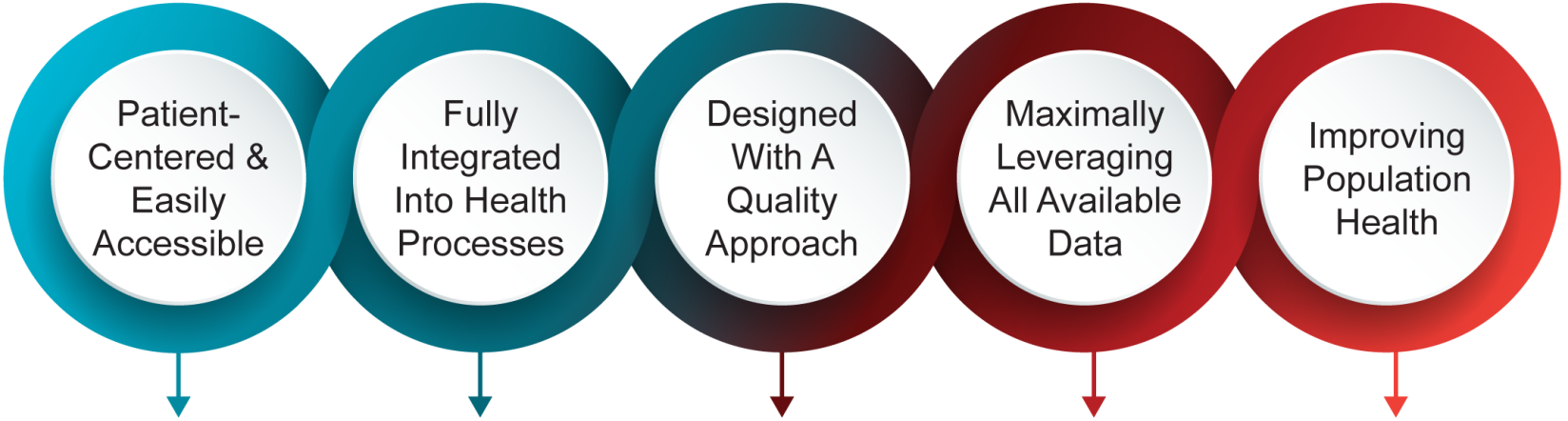
TRANSFORMING TRIALS 2030

By 2030, clinical trials need to be:



A critical part of the Evidence Generating System

https://ctti-clinicaltrials.org/who_we_are/strategic-vision/

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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

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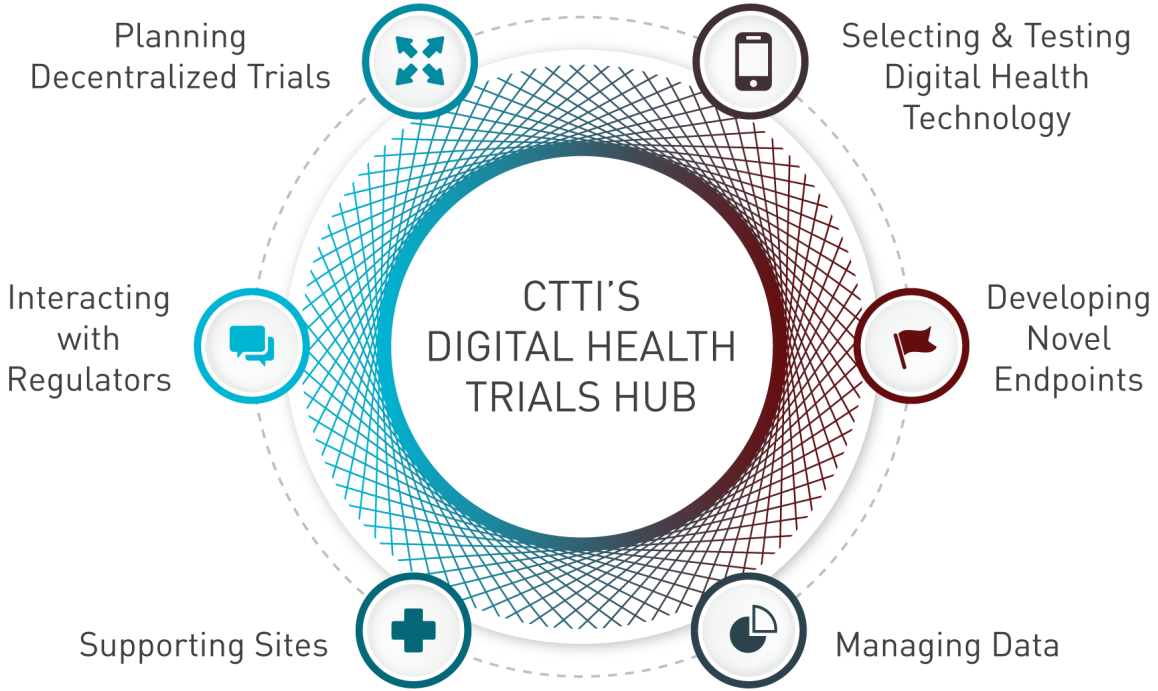
Six Sets of Recommendations & Resources



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Thank You to All DHT Project Team Members

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

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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

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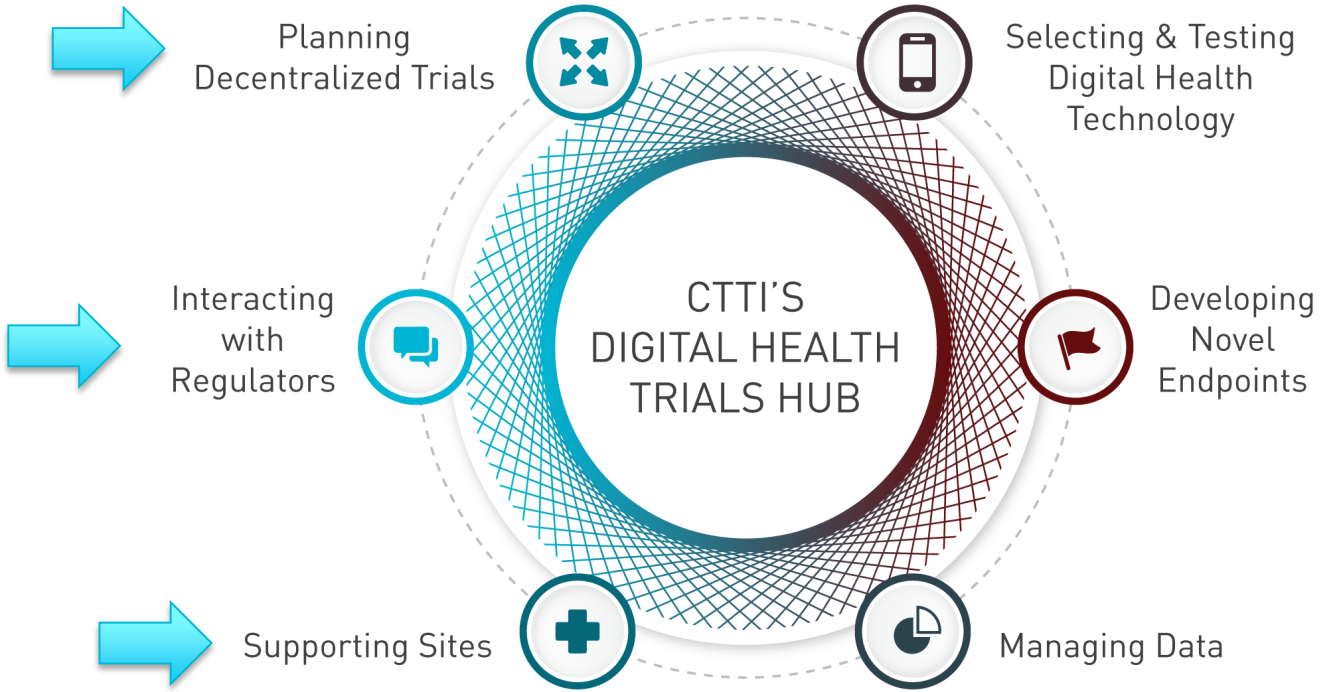
Three Updated Sets of Recommendations



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

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Decentralized Clinical Trials

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

Investigators connected to patient wherever they go

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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

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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

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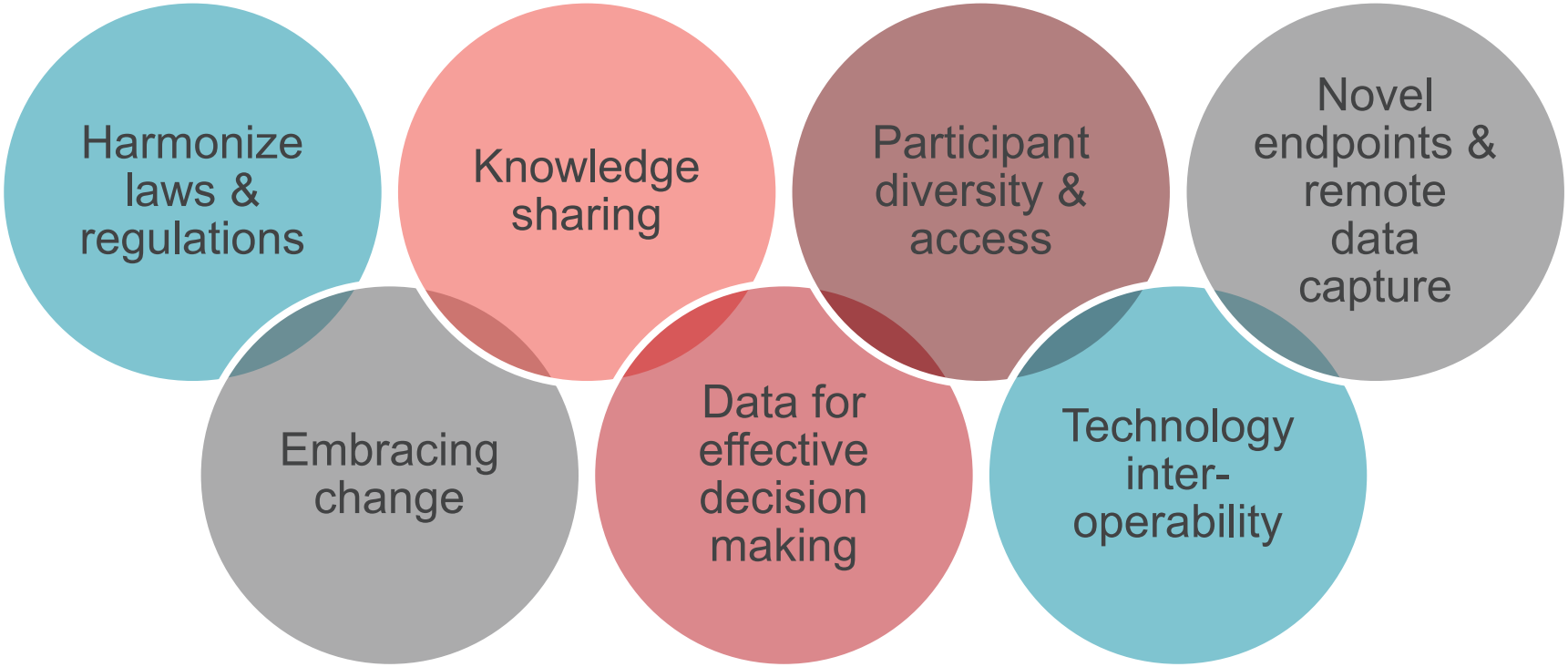
Clearing a Path for Broad Implementation



Novel Endpoint Acceptance

Jörg Goldhahn | ETH Zurich, CTTI Team Lead

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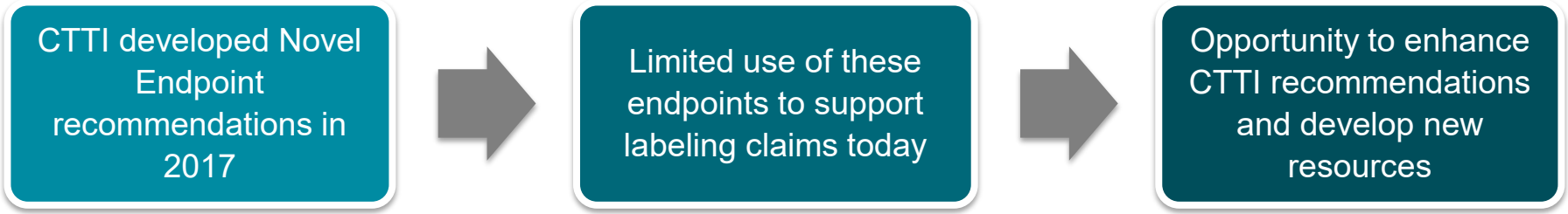
Novel Endpoint Acceptance Project

- **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



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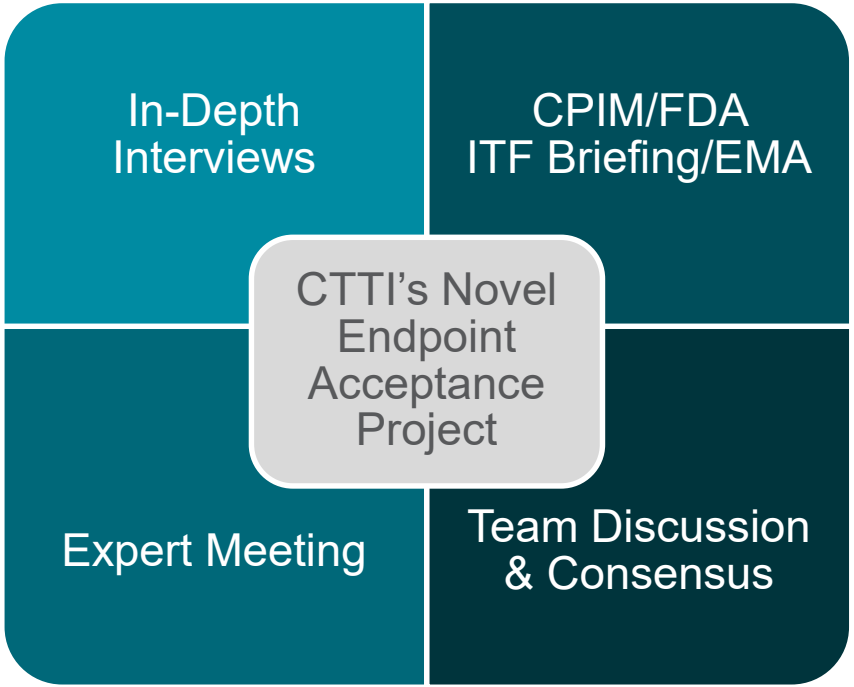
Novel Endpoint Acceptance



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

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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

CLINICAL TRIALS TRANSFORMATION INITIATIVE

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. [1,2] Ideally, these measures will reflect reliable information and be able to be deployed in a timely way. [1,2]

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[3] 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

Stakeholder: Patient/ caregiver

Topic Area	Questions
Meaningful Aspect of Health	1. What part of your life is most frustratingly impacted by your condition?[3] 2. How has your independence been affected by your condition? 3. What about your health do you wish you could improve? 4. Considering what you just mentioned, explain your near term goals: "In the next 3 months I'd like to (e.g. start or continue doing)..." "In the next 6 months I'd like to be able to ..." 5. Explain your longer term goals. "In the next 12-18 months I'd like to (e.g. start or continue doing)...."

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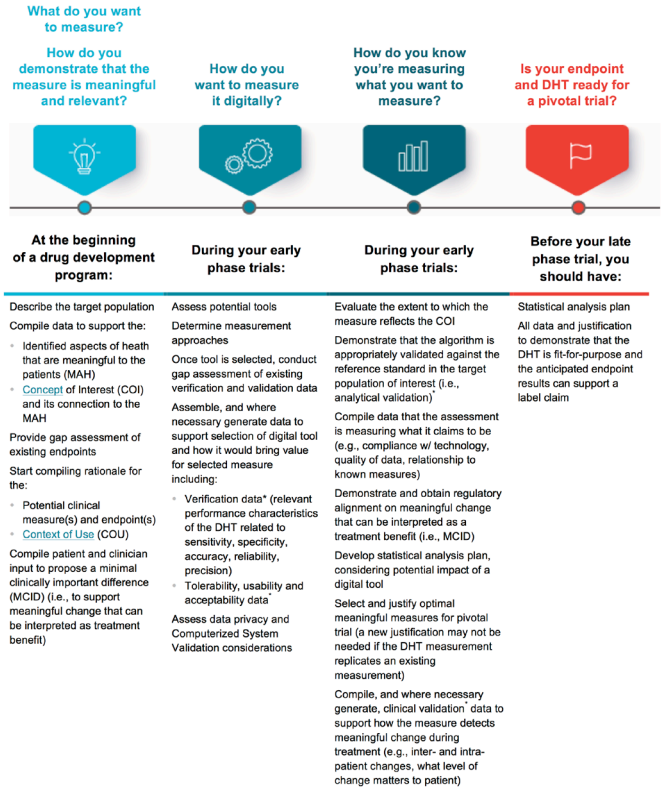
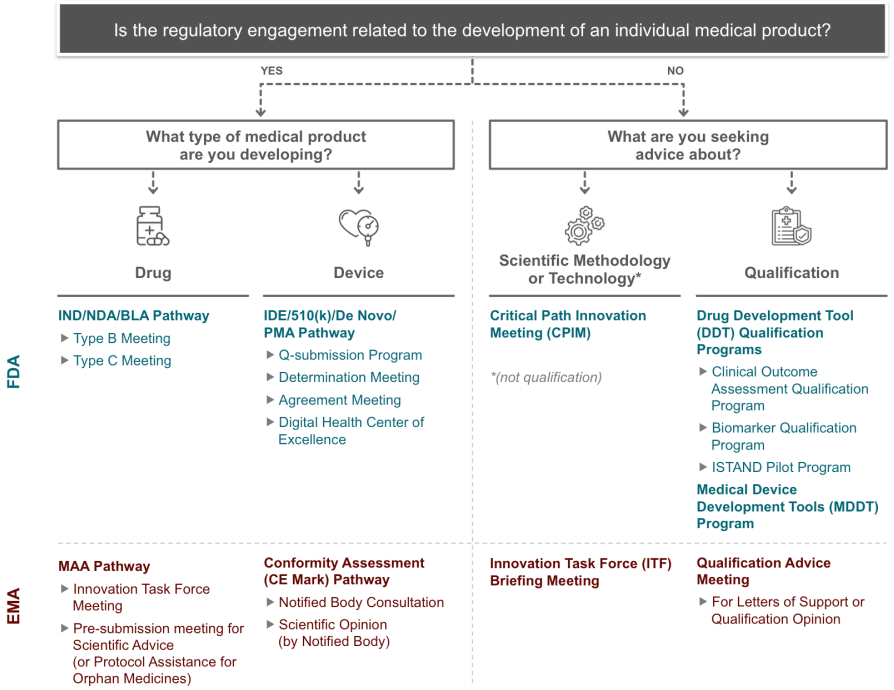
Process Map for an Individual Medical Product Development Track *(New)*

- **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



Regulatory Engagement Guide *(Revised)*

- **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



Why are these updates important and how can they advance CTTI's TT2030 vision?

Q&A

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Download the Recommendations

Available Now on the CTTI website:

https://ctti-clinicaltrials.org/our-work/digital-health-trials/

Learn How Others Implement CTTI Recs

CTTI CASE STUDY EXCHANGE

Available Now through the CTTI website:

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