CLINICAL TRIALS **TRANSFORMATION** INITIATIVE

September 30, 2022

CTTI's Digital Health Trials Hub

Recommendations and Resources to Run Your Digital Health Trial

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Disclaimer

- The views and opinions expressed in this presentation are those of the individual presenter and do not necessarily reflect the views of the Clinical Trials Transformation Initiative.

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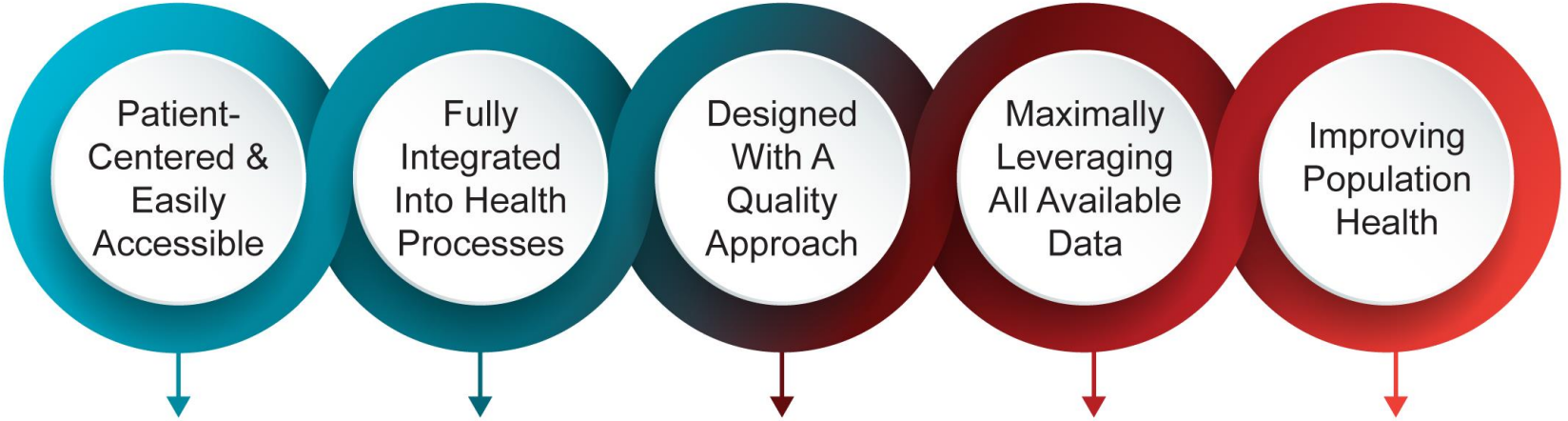
TRANSFORMING TRIALS 2030

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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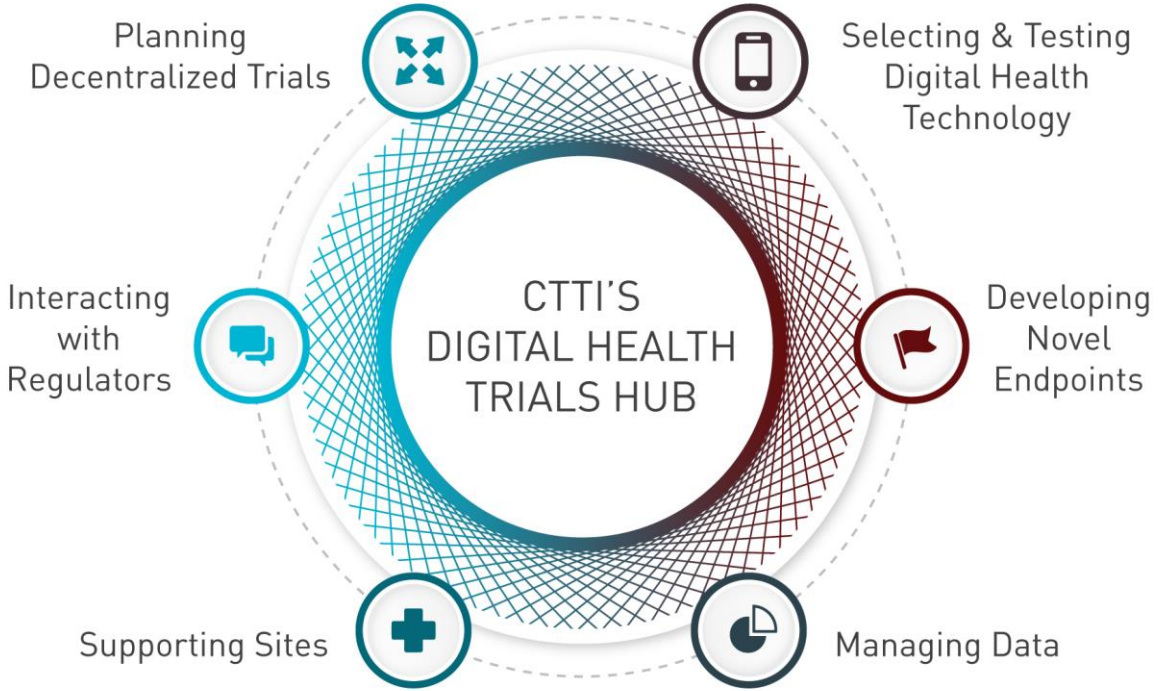
Six Sets of Recommendations & Resources



Decentralized Clinical Trials Update Project

1-Year Accelerated Project

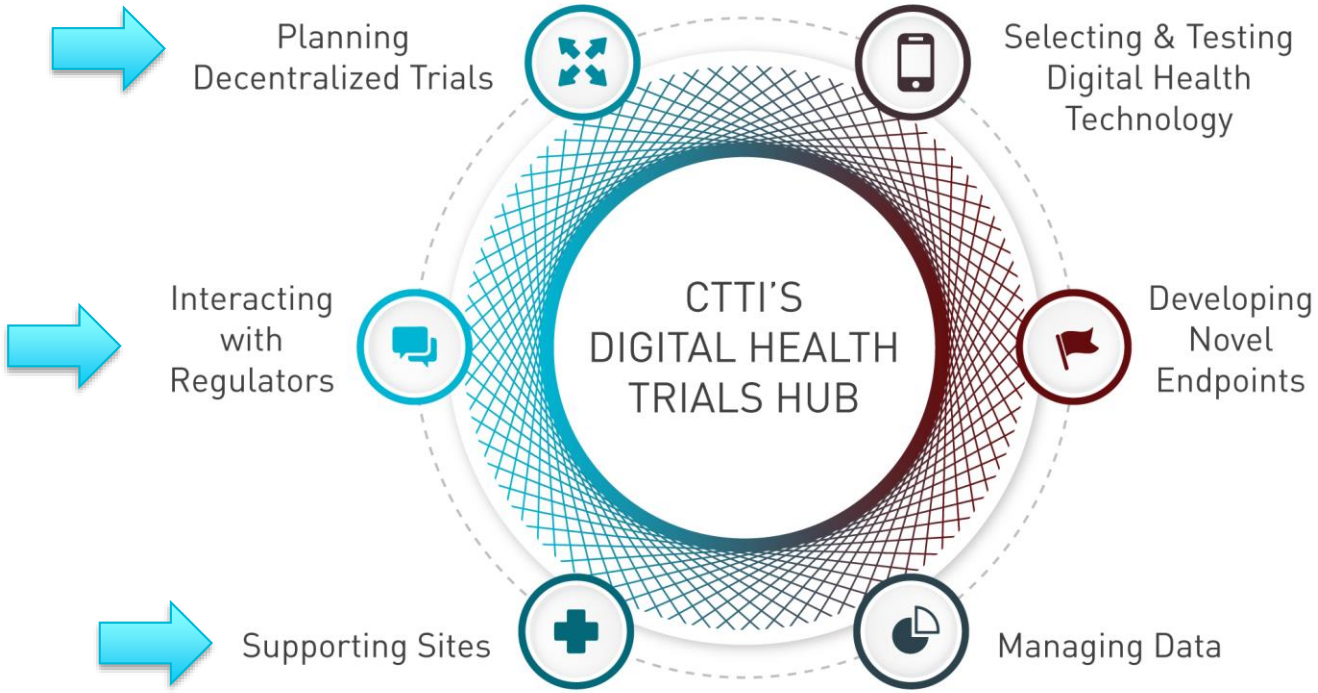
Purpose

- **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



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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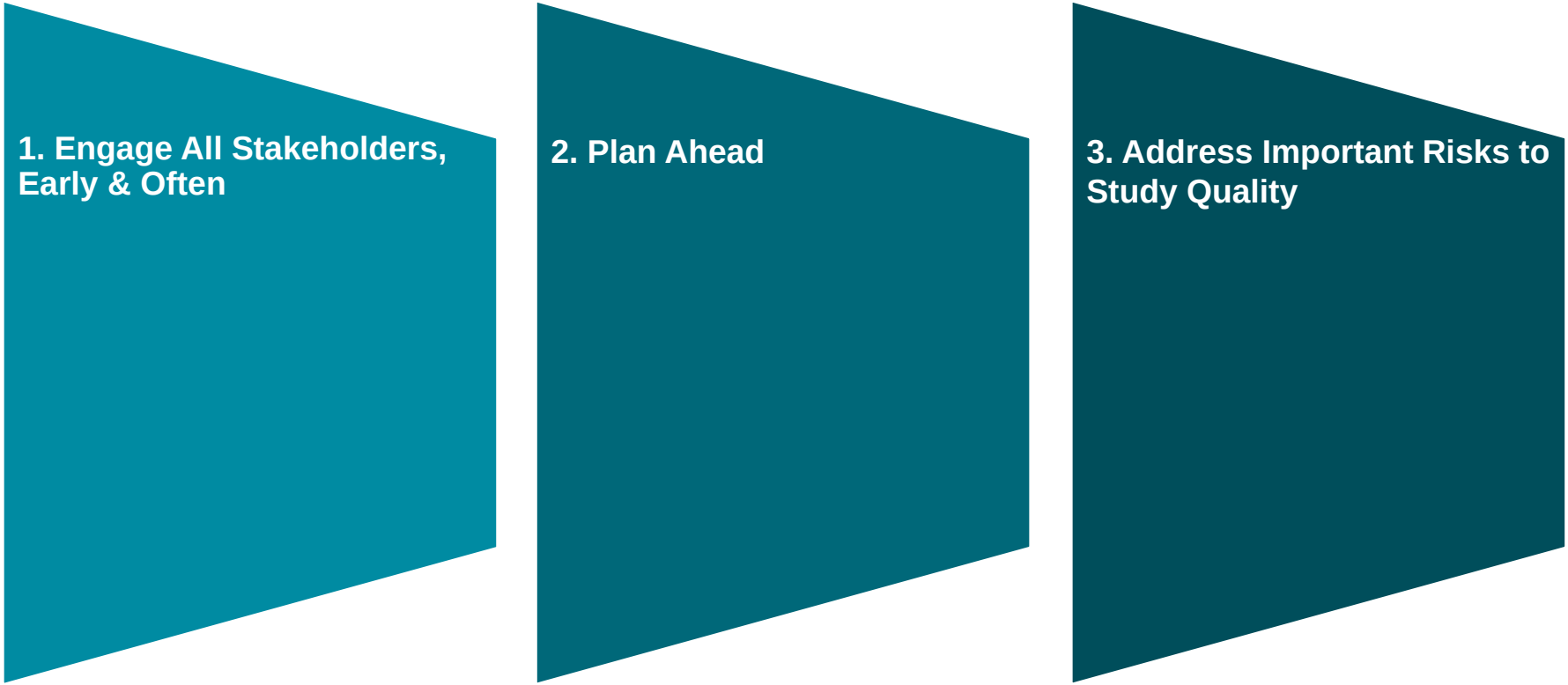
Recommendations for Planning DCTs*



*See full recommendations for details

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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

3. Address Important Risks to Study Quality

*See full recommendations for details

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Recommendations for Planning DCTs*

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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

*See full recommendations for details

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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

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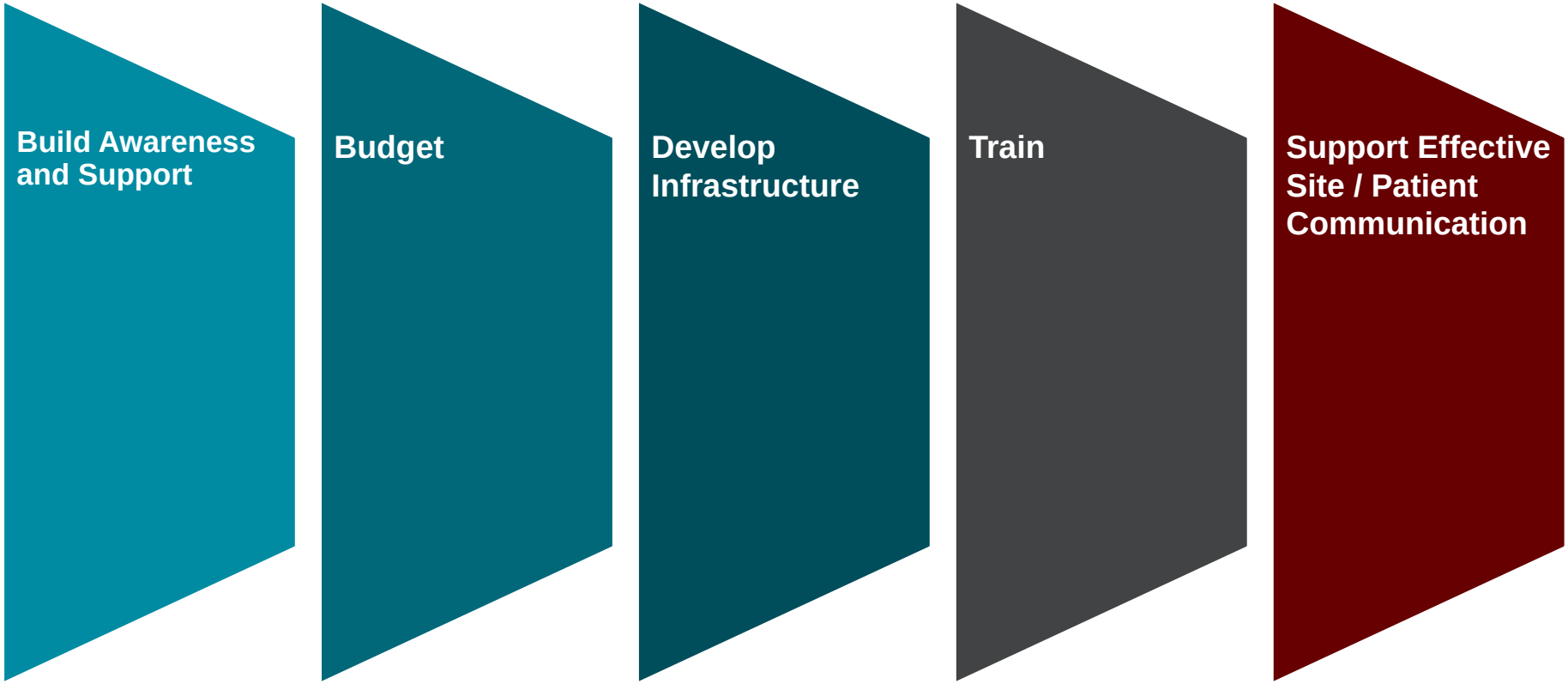
Recommendations to Sponsors for Supporting Sites*



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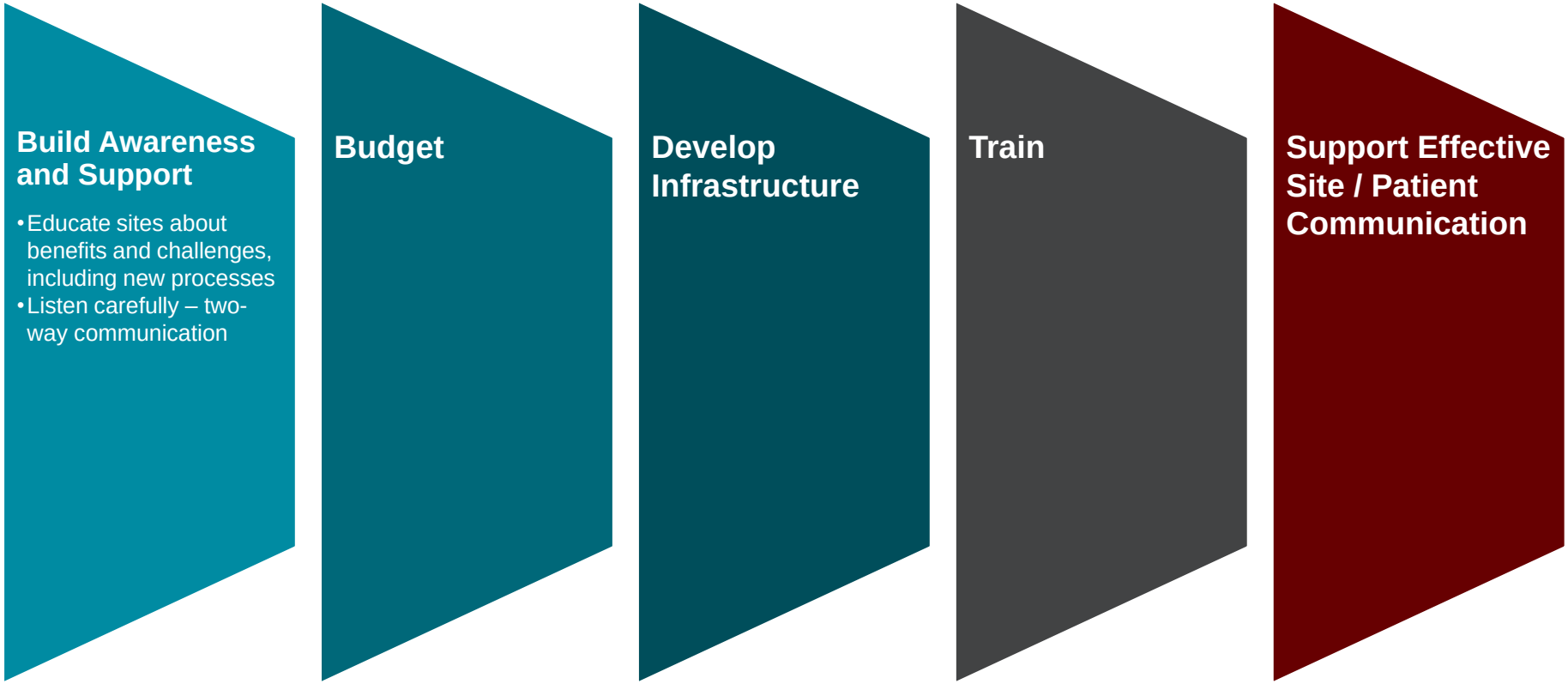

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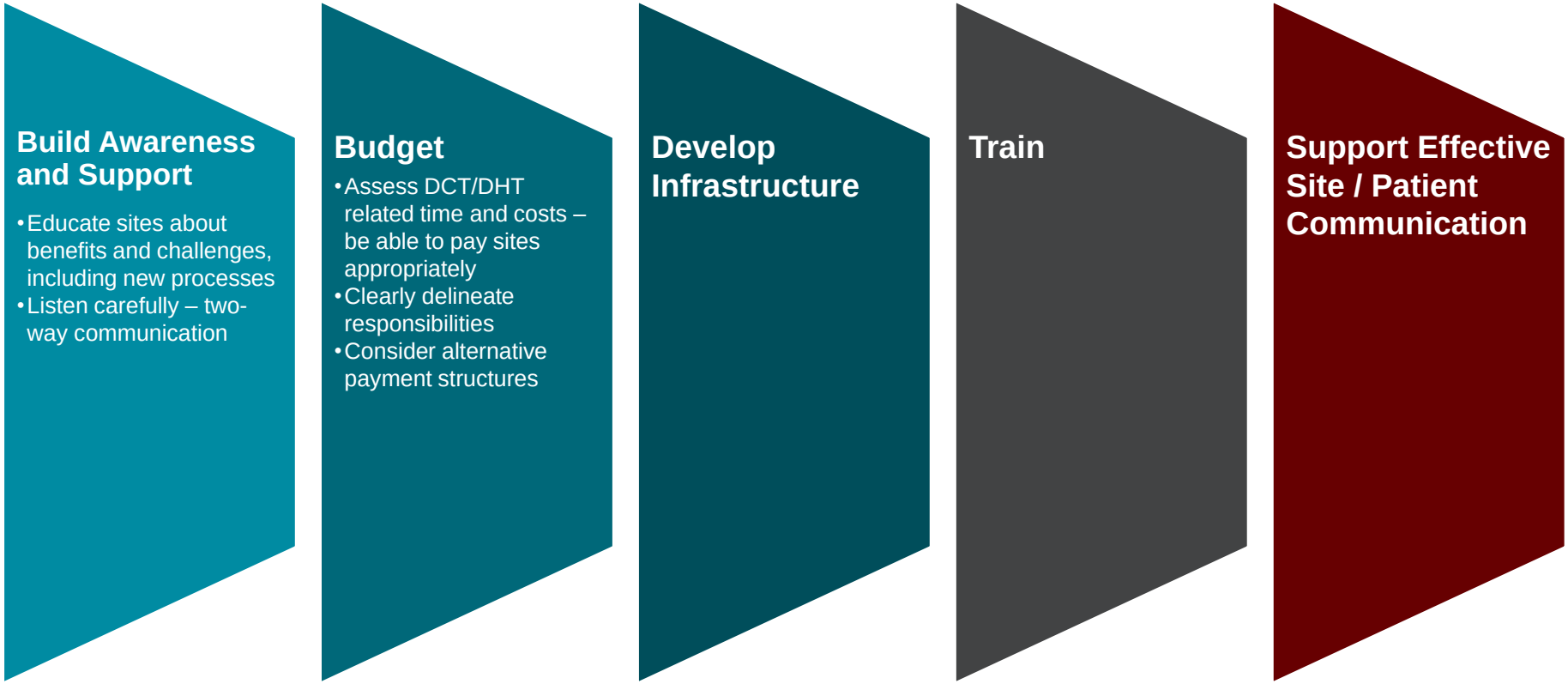

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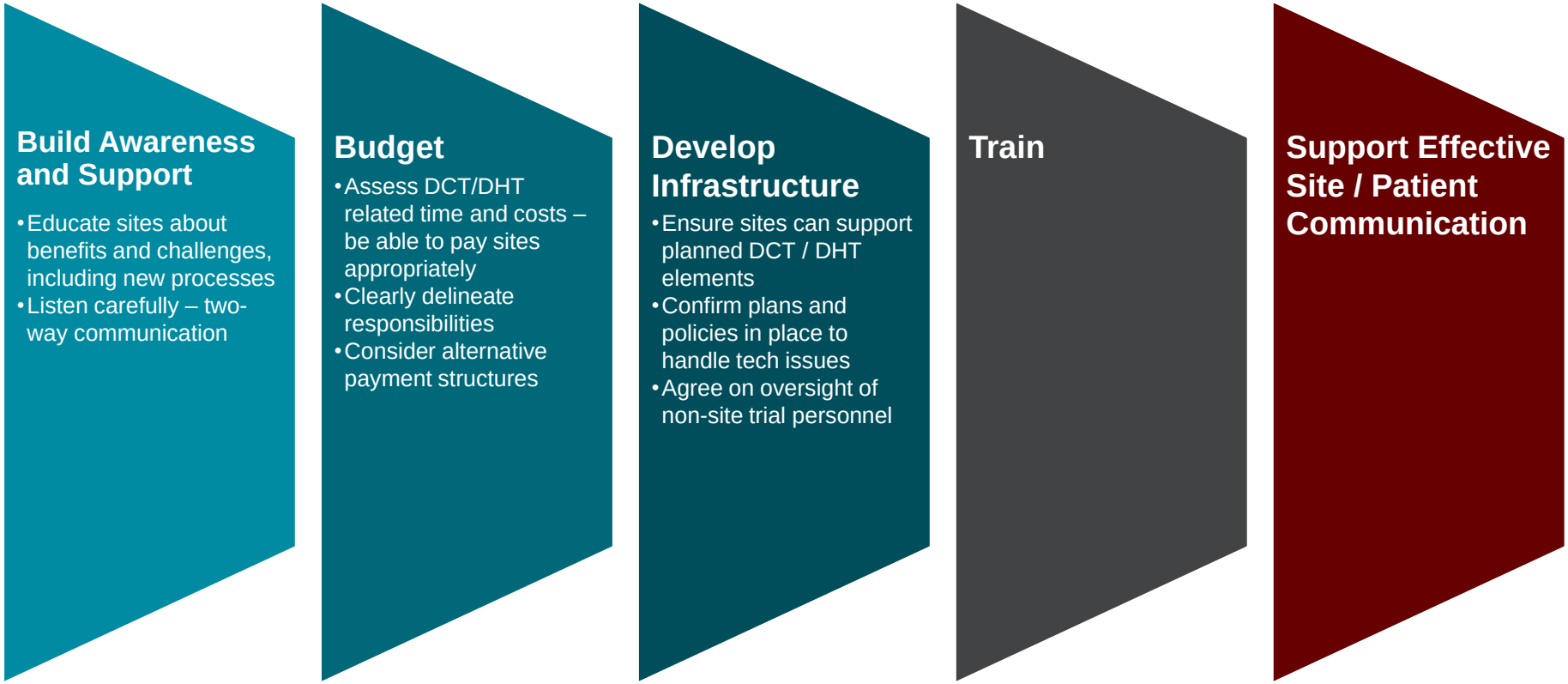

*See full recommendations for details

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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

*See full recommendations for details

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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

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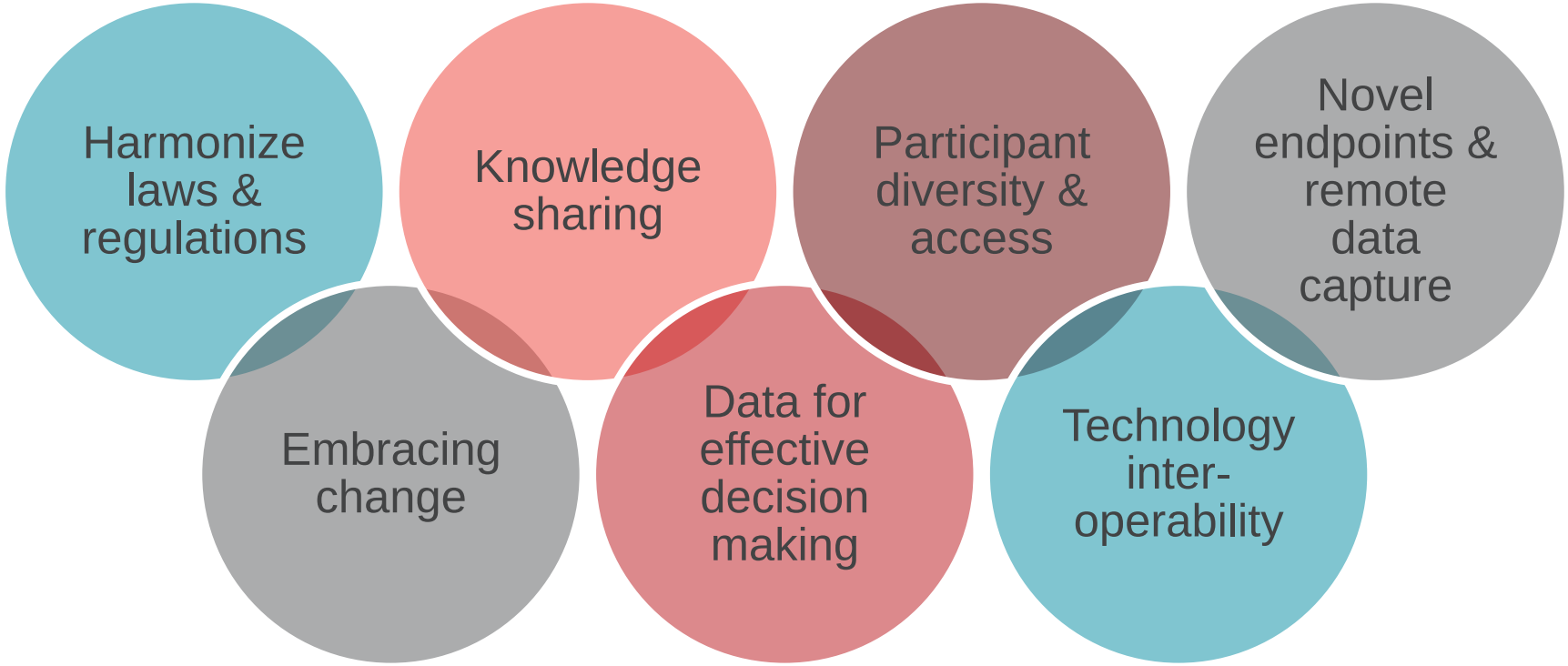
Clearing a Path for Broad Implementation



Novel Endpoints Project Update

Jörg Goldhahn, ETH Zurich

Novel Endpoints Project Update

Purpose

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

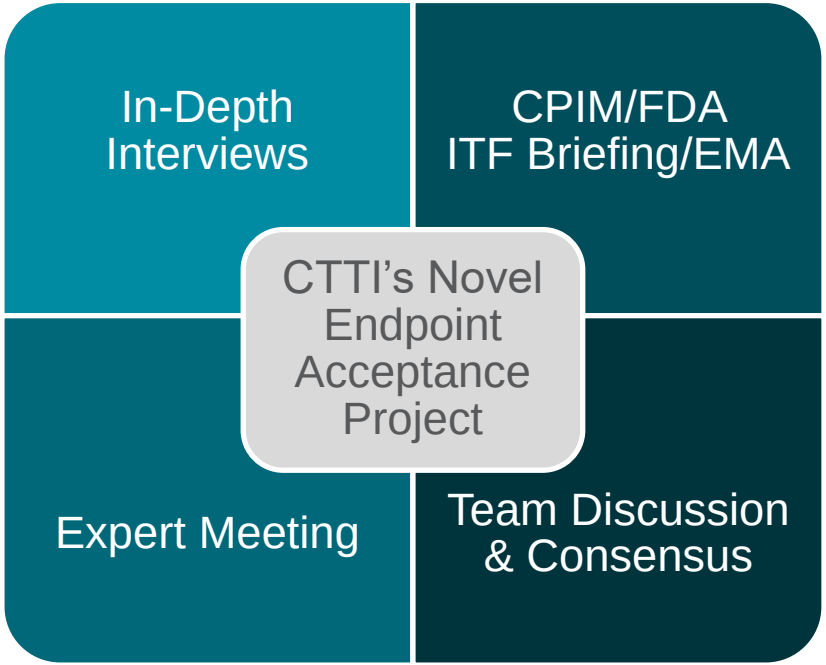
Anticipated Impact

- 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



- 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***

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Question Bank to Identify Meaningful Measures *(New)*

What

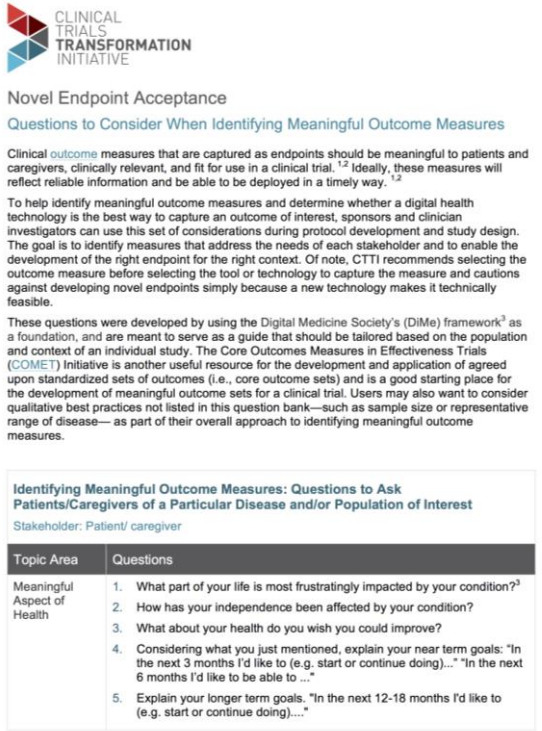
- A set of considerations to identify meaningful measures that are fit for use in a digital health trial
- Serves as an inspirational guide (to be tailored accordingly)

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)...."

Question Bank to Identify Meaningful Measures *(New)*

CLINICAL TRIALS TRANSFORMATION INITIATIVE

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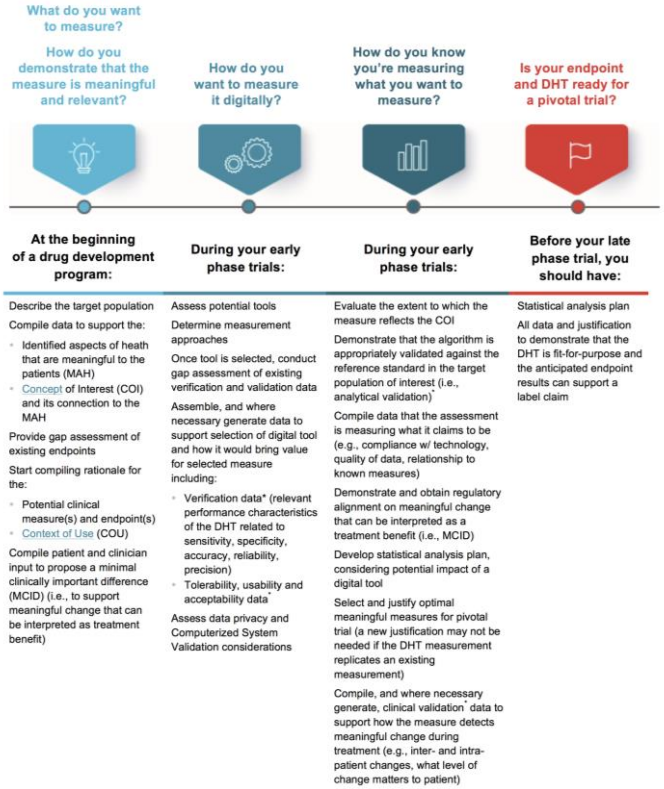
Process Map for an Individual Medical Product Development Track *(New)*

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



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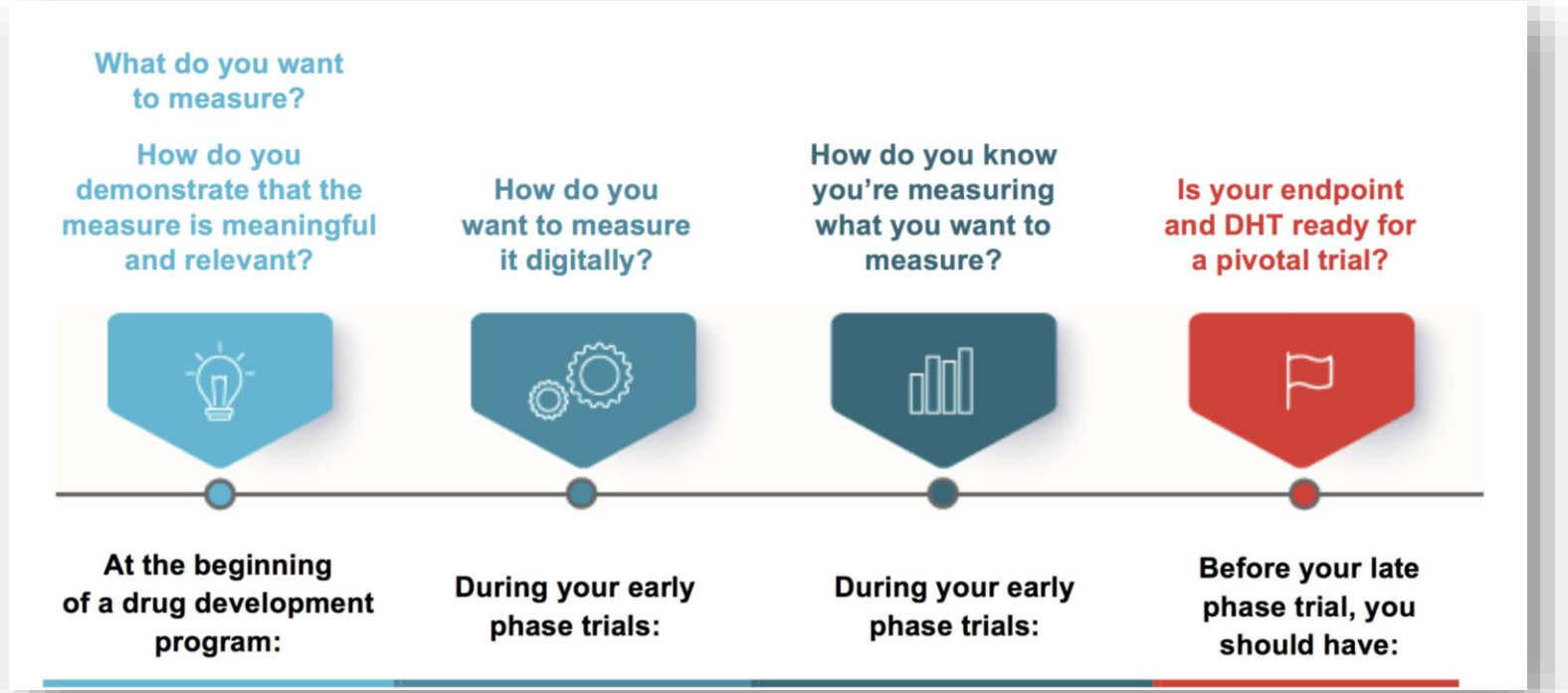


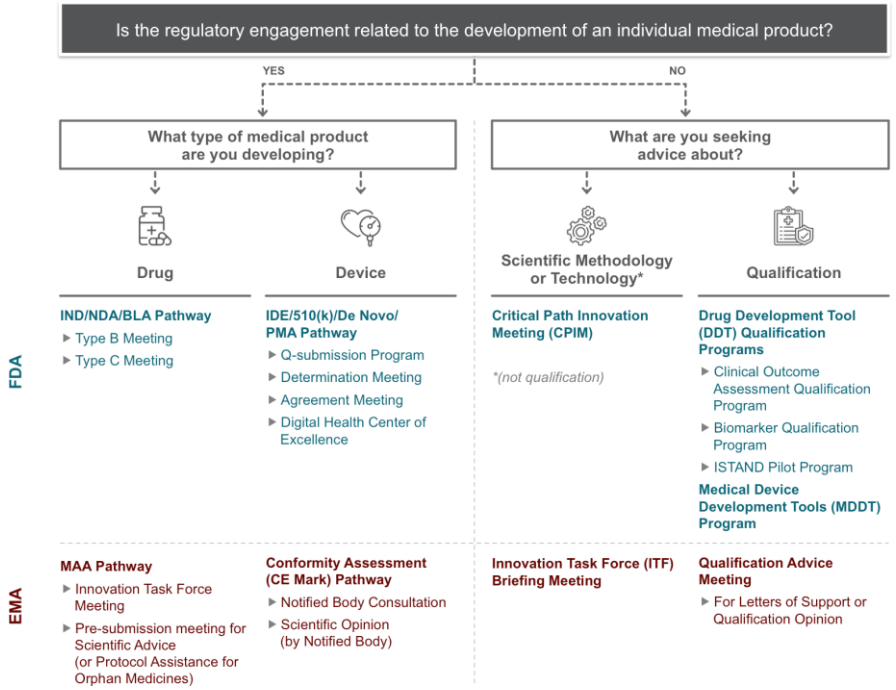
Regulatory Engagement Guide *(Revised)*

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



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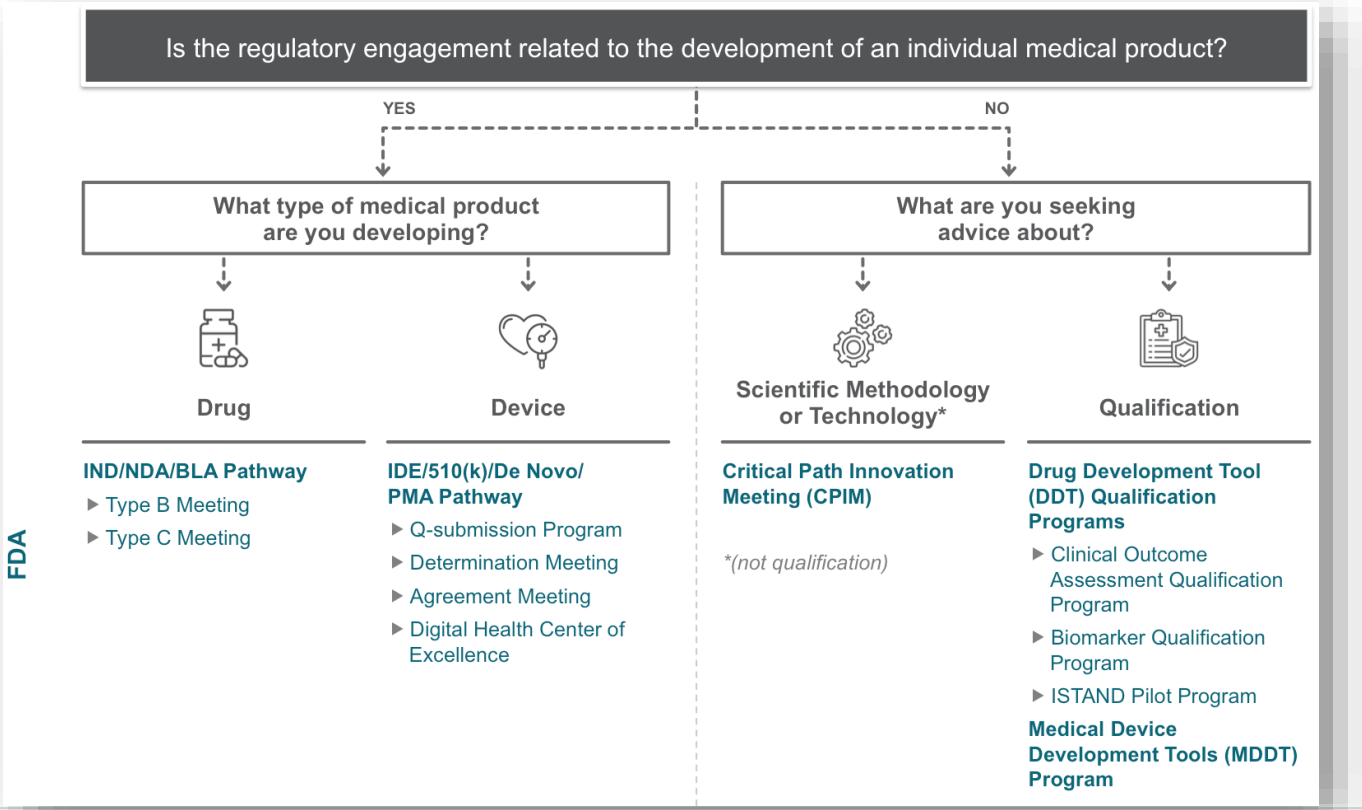


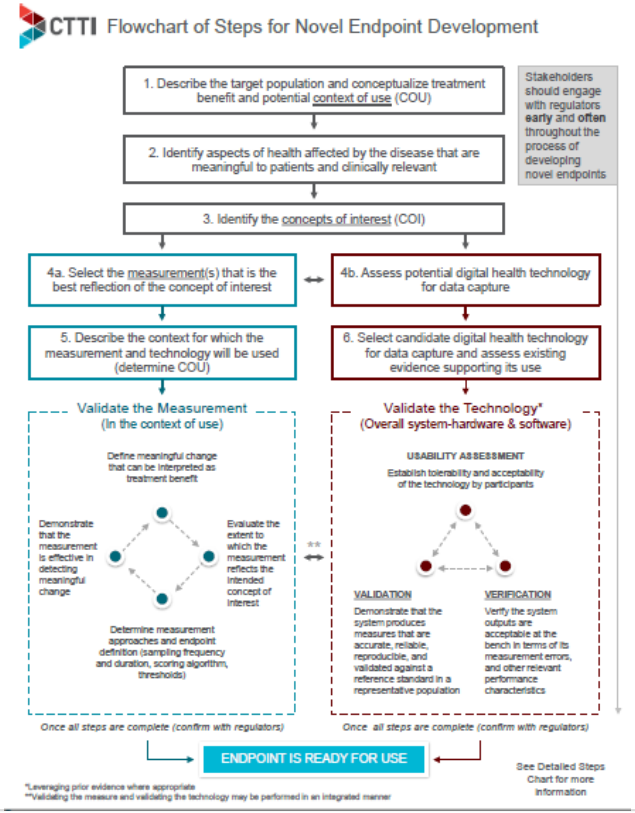
Flowchart of Steps for Novel Endpoint Development *(Revised)*

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

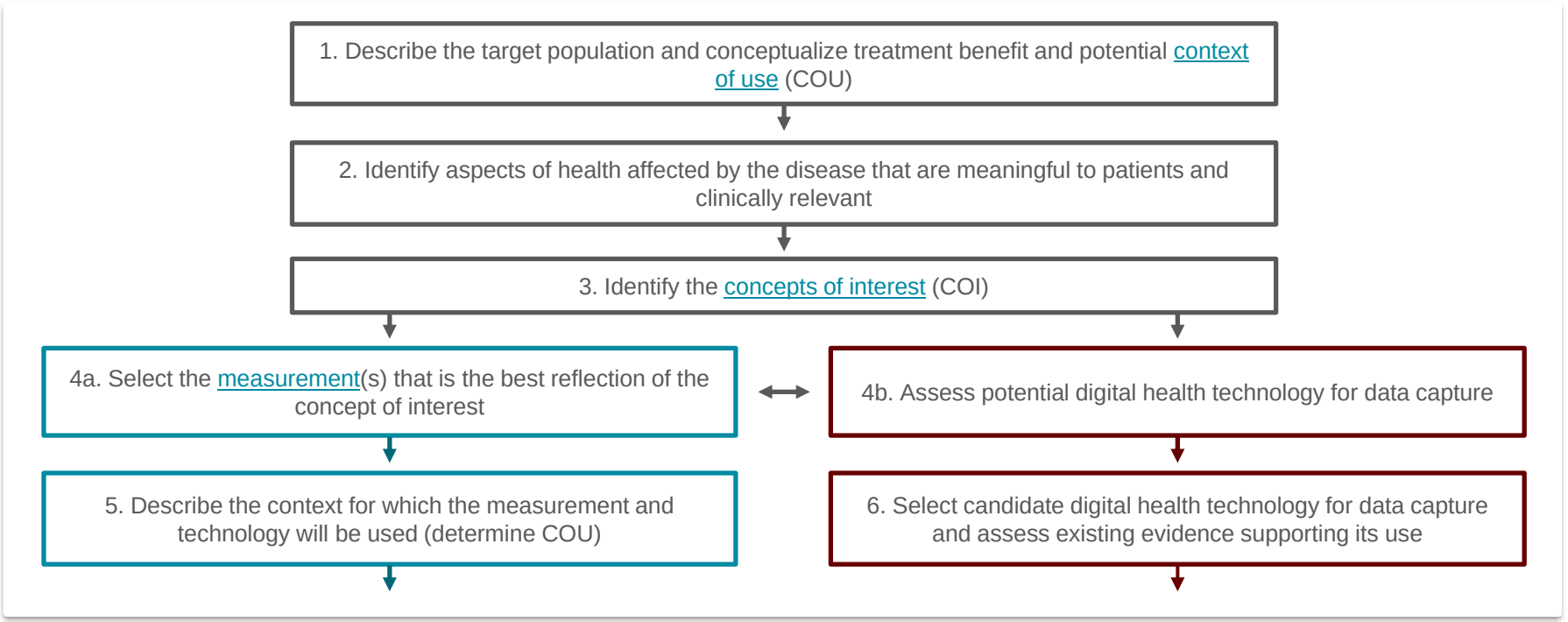
For Whom Sponsors, clinician investigators, and technology providers

When During program development and strategy

Why To provide clarity around how to develop an endpoint using a DHT

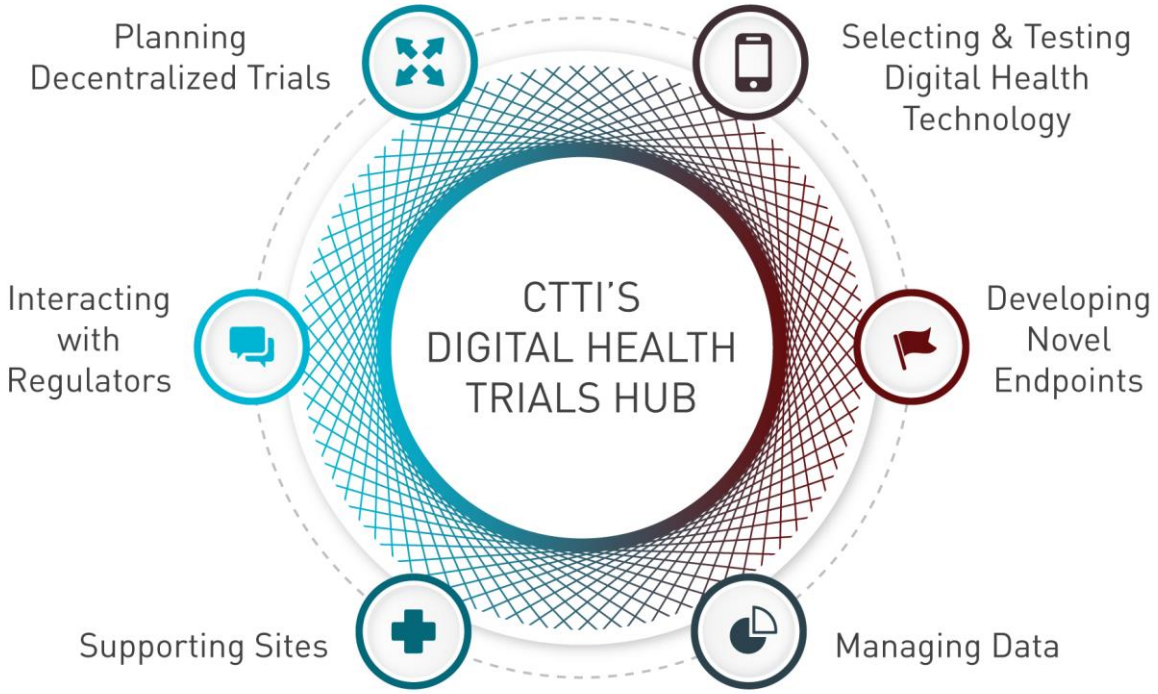


Flowchart of Steps for Novel Endpoint Development *(Revised)*

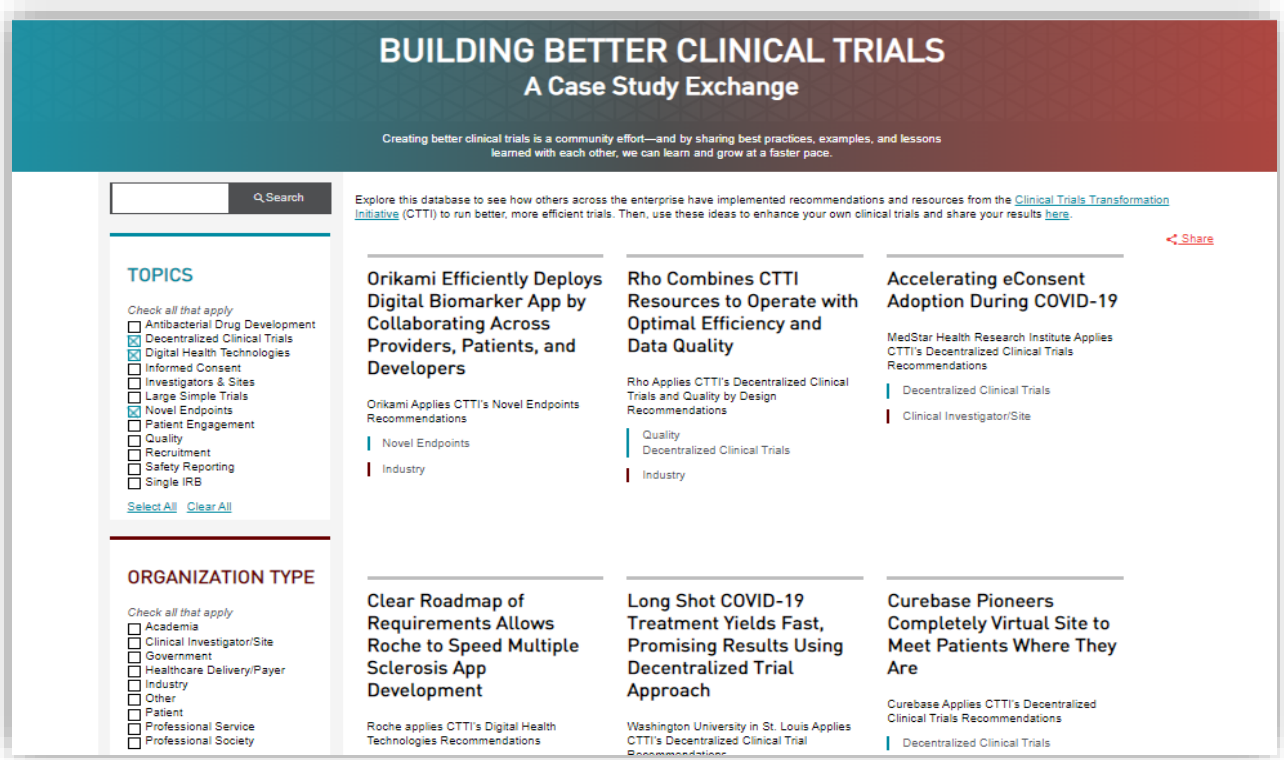


How do I implement these CTTI resources?

35 Tools to Help Implement CTTI Recommendations



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

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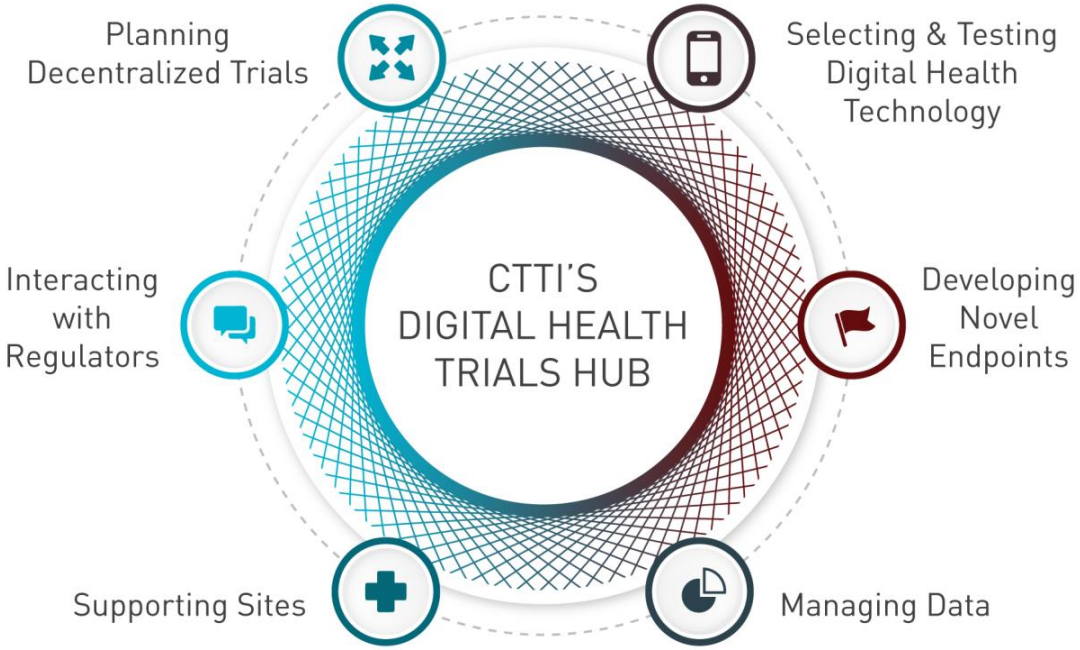
How do we advance digital health trials?

- 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

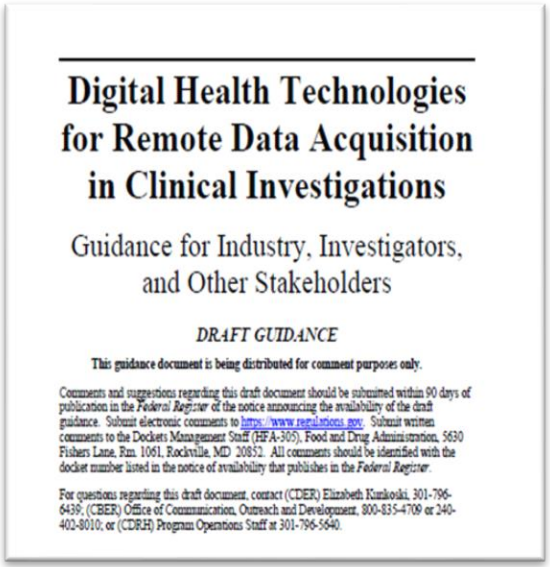
Take Away #1

- CTTI has multiple resources to support the design and execution of digital health trials.



Take Away #2

- Regulators are developing guidance to provide clarity.



Digital Health Technologies for Remote Data Acquisition in Clinical Investigations

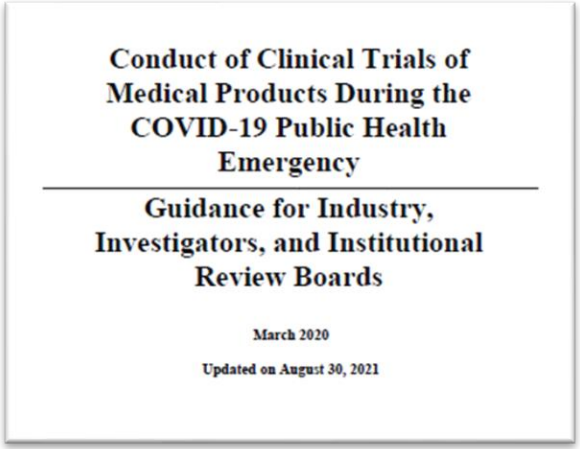
Guidance for Industry, Investigators, and Other Stakeholders

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 90 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact (CDER) Elizabeth Kunkoski, 301-796-6439; (CBER) Office of Communication, Outreach and Development, 800-835-4709 or 240-402-8010; or (CDRH) Program Operations Staff at 301-796-5640.



Conduct of Clinical Trials of Medical Products During the COVID-19 Public Health Emergency

Guidance for Industry, Investigators, and Institutional Review Boards

March 2020

Updated on August 30, 2021

GOV.UK

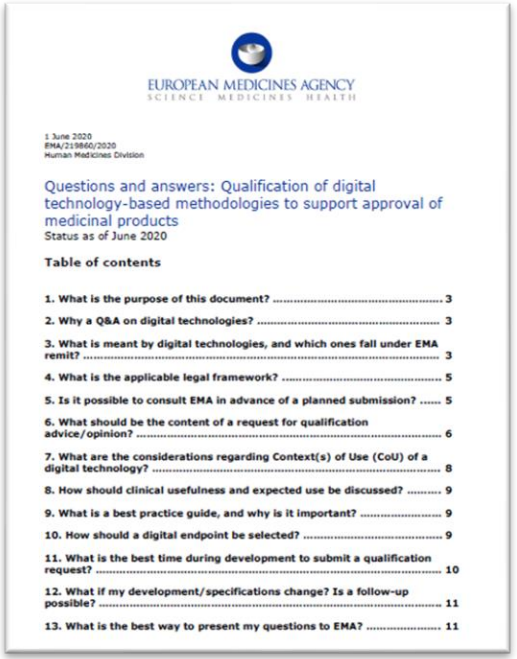
Topics

Home > Clinical trials and investigations

Guidance

Managing clinical trials during Coronavirus (COVID-19)

How investigators and sponsors should manage clinical trials during COVID-19



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

1 June 2020
EMA/219460/2020
Human Medicines Division

Questions and answers: Qualification of digital technology-based methodologies to support approval of medicinal products

Status as of June 2020

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Take Away #3

- Establishing collaborative relationships and sharing lessons learned can advance the digital health trial field.

Download the Recommendations

Available Now on the CTTI website:

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

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Q&A

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