Advancing the Use of Mobile Technologies for Data Capture & Improved Clinical Trials

John Hubbard, Healthcare Strategic Advisory Board (SAB), Genstar Capital
Barry Peterson, Independent Consultant
Cheryl Grandinetti, FDA
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
## Project Portfolio

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<th>SYSTEMATIC EVIDENCE GENERATION</th>
<th>PATIENTS AS EQUAL PARTNERS</th>
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<td>SAE Reporting</td>
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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.

**ANTICIPATED IMPACT:**
Increased number of clinical trials leveraging mobile technology. More efficient trials generating better quality information.

*Scope: FDA-regulated clinical trials after the time of initial research volunteer consent*
# Project Team

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<tr>
<th>Team Leaders</th>
<th>Team Members</th>
<th>Project Manager</th>
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<tr>
<td>Marissa Bolognese (The Life Raft Group)</td>
<td>Adam Amdur (ASAA)</td>
<td>Jen Goldsack (CTTI)</td>
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<tr>
<td>Phil Coran (Medidata Solutions)</td>
<td>Jessie Bakker (Philips)</td>
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<td>Chris Dell (Pfizer)</td>
<td>Barry Peterson (Philips)</td>
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<td>Ray Dorsey (URMC)</td>
<td>Ernesto Ramirez (Fitabase)</td>
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<tr>
<td>Cheryl Grandinetti (FDA)</td>
<td>Drew Schiller (Validic)</td>
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<td>Kaveeta Vasisht (FDA)</td>
<td>Chris Miller (AstraZeneca)</td>
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<td>Tom Switzer (Genentech)</td>
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<td></td>
<td>Aiden Doherty (University of Oxford)</td>
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<td></td>
<td>Jonathan Helfgott (Stage 2 Innovations and Johns Hopkins)</td>
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<td></td>
<td>Ashish Naryan (Mount Sinai School of Medicine)</td>
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<td>Matt Kirchoff (NIH)</td>
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<td></td>
<td>Phillip Kronstein (FDA)</td>
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<td>Dharmesh Patel (FDA)</td>
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**Social Science Lead**

Amy Corneli (CTTI)

**EC Champion**

John Hubbard (Healthcare SAB, Genstar Capital)
Why Mobile Technologies?

**PATIENT CENTRICITY**
- High-quality, patient-centric endpoints
- Endpoints that matter to patients
- Reduced participation burden
- Fewer barriers to participation
- Better, more complete info

**EFFICACY**
- Improved predictability rates
- Increase in # of potentially successful treatments

**EFFICIENCY**
- Generation of data needed by payers to make coverage determinations
- Prevention of delays in coverage, payment, & use decisions
- Prevention of delays in patient access to meds

Potential Benefits of Using Mobile Technology in Clinical Trials
Topics to Discuss Today

- We’ll take a deep dive into certain aspects of
  - Mobile Technology Selection
  - Data Management

- Direct you to additional resources

- Discussion
MOBILE TECHNOLOGY SELECTION

Barry Peterson, PhD
Independent Consultant
Recommendations Overview

Know what you want to measure before selecting the mobile technology.

Mobile technology selection should be specification-driven and collaborative.

CTTI recommends that a technology’s regulatory status not be the sole driver in sponsors’ decisions about which mobile technology to use.

The appropriateness of the selected mobile technology should be justified through verification and validation processes.

Feasibility studies conducted before full implementation in a large study reduce risk.
Data Access Considerations Before Selecting a Mobile Technology

Sponsors should not assume that the technology manufacturer will provide them with all of the data collected by the mobile technology.

Prior to selecting a mobile technology for data capture, sponsors should consider:

- Whether they will have access to the raw data generated by the mobile technology,
- To what levels of processed data they will have access,
- Whether they will have access to the algorithm(s) used to process the data, and
- In what format the data will be provided.
Summary of Data Access Considerations

- How will the data generated by the mobile technology be accessed and used by the manufacturer?
- What data will be provided by the manufacturer to the sponsor?

CTTI Recommendation:
Ensure that access to data meets your needs prior to contacting an electronic service vendor.
Recommendations Overview

- Know what you want to measure before selecting the mobile technology
- Mobile technology selection should be specification-driven and collaborative
- CTTI recommends that a technology’s regulatory status not be the sole driver in sponsors’ decisions about which mobile technology to use
- The appropriateness of the selected mobile technology should be justified through verification and validation processes
- Feasibility studies conducted before full implementation in a large study reduce risk
Verification

Verification is an engineering assessment
Assessment of the basic sensors of the devices with respect to:

- Accuracy
- Precision
- Consistency across time, devices and environmental conditions

Lack of errors in firmware that processes the sensor data
Usually compared to a physical “bench” standard
Variances in sensor measurements are usually very small (<1%)
Verification data should be provided by device manufacturer/vendor
Validation

- Validation is a biological assessment
- Assessment of the accuracy and precision of the biological endpoints derived from the sensor data
  - Usually against an independent measurement standard.
- Variances in endpoint measurements may be large (5-15%) but may still be useful (statistical question)
- Validation data can be provided by:
  - device manufacturer
  - from an independent study by a user, or
  - from a new study for a specific patient population
Recommendations Overview

- Know what you want to measure before selecting the mobile technology
- Mobile technology selection should be specification-driven and collaborative
- CTTI recommends that a technology’s regulatory status not be the sole driver in sponsors’ decisions about which mobile technology to use
- The appropriateness of the selected mobile technology should be justified through verification and validation processes
- Feasibility studies conducted before full implementation in a large study reduce risk
Supporting Resources

- Mobile technology selection framework
- Two case studies:
  1. Verification and Validation Processes in Practice
  2. Feasibility Testing to Promote Successful Inclusion of Mobile Technologies for Data Capture
- Glossary defining key terms, including verification and validation
DATA MANAGEMENT

Cheryl Grandinetti, PharmD

FDA, CDER, OSI
Data Management

For mobile technology-derived outcomes data, sponsors should consider:

- Data integrity
- Data security
- Data usability and availability

Sponsors are ultimately responsible for data management, but processes are often carried out by, or in partnership with third parties, such as:

- CROs
- IT service providers
  - Mobile technology manufacturers
  - Third-party data platforms
CTTI Recommendations on Data Management

Guide sponsors on how to extend relevant regulations and guidance to management of data captured by mobile technologies in clinical trials.

Highlight specific data management tasks that should be internally reviewed or discussed with potential partners prior to entering into an outsourcing agreement.
Recommendations Summary

- Ensure the authenticity, integrity, and confidentiality of data over its entire lifecycle.
- Optimize data accessibility while preventing data access from unauthorized users.
- Ensure that access to data meets your needs prior to contracting an electronic service vendor.
- Apply an end-to-end, risk-based approach to data security.
- Monitor the quality of data captured by mobile technologies centrally through automated processes.
- Ensure that site investigators have access to data generated by their participants.
Data Flow Diagram

Study team has read only access to an appropriate level of data through an API

Mobile Technology  -->  Apps  -->  Manufacturer’s Servers  -->  Centralized Server(s)  -->  Filtering & Processing  -->  Dataset for Analysis

Typically subjects and sites  |  Typically CROS and/or other electronic service vendors  |  Typically study sponsors

Strategies for Promoting & Protecting Data Integrity

Critical Points in Data Lifecycle

- Data collection
- Generation of processed data
- Data during transmission
- Data at rest
- Data during filtering & processing for analysis

CTTI resources advises best practices for promoting trial integrity at these critical points in the trial lifecycle both:

- Pre-trial
- During trial
Data Security

CTTI recommends applying an end-to-end, risk-based approach to data security should be applied to protect participants’ privacy and the confidentiality and integrity of their data.

Mobile era creates new data security demands

- Data should be secured on both the technology itself and during transfer from the technology.
  - Transfer likely occurs over Wi-Fi, Bluetooth, cellular and networks beyond control of sponsors and ESPs
- Data should be secured during additional transfer steps (ex: app → server) and all processing steps.

CTTI recommends that data security solutions are developed with the entire infrastructure in mind.
Centralized Monitoring

- When mobile technologies are used for data capture, FDA’s existing monitoring guidance still applies.
  - Guidance for Industry, Oversight of Clinical Investigations – A Risk-Based Approach to Monitoring

- Centralized monitoring is well suited to check for completeness, consistency, and correctness.

- Develop monitoring plans and strive to correct technical issues earlier.

- Monitoring plans should articulate who should resolve potential issues as identified.
Applying the Recommendations

John Hubbard, PhD, FCP

Genstar Capital
Take Action

Access recommendations and resources


Contact us with questions!

- CTTI Project Manager [jennifer.Goldsack@duke.edu](mailto:jennifer.Goldsack@duke.edu)
- Barry Peterson [barry.t.peterson@gmail.com](mailto:barry.t.peterson@gmail.com)
- Cheryl Grandinetti [Cheryl.Grandinetti@fda.hhs.gov](mailto:Cheryl.Grandinetti@fda.hhs.gov)
THANK YOU.
## Illustrative Examples from CTTI Recs

### Verification and Validation

<table>
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<th>Description</th>
<th>Raw Data</th>
<th>Processed Data</th>
<th>Outcome Assessment</th>
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<tr>
<td><strong>VERIFICATION</strong></td>
<td><strong>VALIDATION</strong></td>
<td></td>
<td></td>
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<tr>
<td><strong>Description</strong></td>
<td><strong>Output from physical sensor</strong></td>
<td><strong>Output from mobile technology firmware</strong></td>
<td><strong>Output from analysis algorithm</strong></td>
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<tr>
<td><strong>Example: Accelerometry</strong></td>
<td>Acceleration (m/s²)</td>
<td>Activity counts (n)</td>
<td>Time spent active (min)</td>
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<td></td>
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<td>Total sleep time (min)</td>
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<td><strong>Example: ECG</strong></td>
<td>Electrical potential (mv)</td>
<td>Heart rate (beats/min)</td>
<td>Heart rate variability (e.g. pNN50)</td>
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The pNN50 statistic is a time domain measure of heart rate variability (HRV).