Scientific and Technological Issues Surrounding the Use of Mobile Devices in Clinical Trials

Multi-Stakeholder Expert Meeting

Summary of the Meeting held June 15-16, 2017

DoubleTree by Hilton Hotel Crystal City
300 Army Navy Drive | Arlington, VA

CTTI MISSION: To develop and drive adoption of practices that will increase the quality and efficiency of clinical trials

Meeting materials—including agenda, participant list, and presentations—are available on the Clinical Trials Transformation Initiative (CTTI) website at: http://www.ctti-clinicaltrials.org/projects/mobile-devices

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EXECUTIVE SUMMARY

The Clinical Trials Transformation Initiative (CTTI) MCT Mobile Devices project team convened a broad group of stakeholders to discuss the scientific and technological challenges inhibiting the widespread use of mobile devices in clinical trials, and to propose potential solutions and strategies to mitigate the key data challenges identified. Participants included individuals knowledgeable about clinical trials, as well as those with expertise in mobile devices and data issues.

Recurring themes throughout the meeting included:

- The recommended best practices for studies using mobile devices for data capture do not differ significantly from many of the best practices that we already apply to clinical trials.
- Studies using mobile devices for data capture should not be held to higher standards than traditional trials.
- This effort should strive to engage patients in study design.
- The existence of the technology should not drive the decision to incorporate a mobile device for data capture. Rather, that decision should follow the identification of a technology-derived measure that is better than the existing alternative(s).
- The device should be able to collect data to support the endpoint for the particular patient population.
- Perfect should not be the enemy of the good; rapid, incremental progress will be made by the willingness to include these mobile devices and learn as we go.

These themes and more specific solutions identified during discussions will drive the development of recommendations and tools to support the appropriate adoption of mobile devices for data capture in clinical trials.

MEETING OBJECTIVES

The goal of this meeting was to address the scientific and technological challenges inhibiting the widespread use of mobile devices in clinical trials through the following activities:

- Present findings from evidence-gathering activities.
- Discuss how this evidence may be used to provide direction for the appropriate utilization of mobile devices for objective data capture in clinical trials. Specifically,
  - Possible solutions to key data challenges
  - Scientific and technological considerations
- Identify the change agents who will drive adoption of mobile devices for capturing objective data in clinical trials, including for the purposes of regulatory submission.

- Describe what products CTTI should develop to equip change agents to include mobile devices for data capture in clinical trials, including for the purposes of regulatory submission.

MEETING BACKGROUND

Mobile technology offers a powerful tool to improve the quality and efficiency of clinical trials. Technology has the advantage that data can be acquired continuously, rather than at discrete time points, which should provide greater insight into disease progression. Moreover, as data are gathered in the "real world", they should more closely reflect patients' daily lives. By gathering data outside of the clinic, mobile technology can also decrease patient and investigator burden by reducing clinic visits, which may lead to increased patient recruitment and decreased loss to follow up. In addition, mobile technology offers a method to potentially reduce the overall costs of performing clinical trials.

Although many successful pilot studies utilizing mobile devices have been completed, they have yet to be widely used in clinical trials. The goal of the CTTI Mobile Clinical Trials (MCT) Program is to increase the adoption and appropriate use of mobile technology in clinical trials, including for the purposes of regulatory submission. The MCT Program includes four projects dedicated to identifying and addressing legal/regulatory, stakeholder perception, and device issues, as well as the opportunity for novel endpoint.

This meeting was convened by the CTTI MCT Mobile Devices project team, whose goal is to develop materials that support the appropriate adoption of mobile devices for capturing objective data in clinical trials. The project addresses critical issues regarding device selection, as well as operational and protocol issues that follow the decision to use a technology-derived endpoint. Recommendations have already been issued for identifying and developing technology-based novel endpoints and incorporating them into clinical trials. For the purposes of this project, mobile devices are defined as mobile applications and remote sensor devices that capture objective data, including both consumer and medical grade devices.

This meeting focused on the incorporation of mobile devices into FDA-regulated clinical trials after the stage of consent, highlighting the use of devices intended specifically for data capture, and not for the purposes of recruitment, retention, or as the study intervention.

The foundational assumption for this project is that the decision to use a mobile device for data capture is driven by a compelling unmet patient or scientific need, which is often accompanied by opportunities for efficiency gains.

MEETING SUMMARY

The purpose of the meeting was to engage stakeholders in discussion, grounded in data as opposed to hypothetical scenarios, to address the scientific and technological challenges inhibiting the widespread use of mobile devices in clinical trials. Also to propose potential solutions and strategies to mitigate the key data challenges identified. The meeting agenda may be found in Appendix 1 and the complete listing of meeting attendees is included in Appendix 2.

The meeting began with discussion of the next revolution in healthcare and clinical trials being driven by the digital transformation of patient health information. Several considerations were highlighted to successfully transform the way we conduct clinical trials. First, scalable, standardized tools are necessary to overcome the challenges facing the integration of multiple datasets for discovery and implementation. Also, mobile technologies offer a unique opportunity to create exciting experiences for patients by promoting participation and engagement. Finally, data sharing and collaboration are essential.

Additional dialogs considered how the FDA may regulate technologies used for data capture in clinical trials. Meeting participants were reminded that FDA clearance or approval of a technology grants authorization for marketing and sales of medical devices, which are associated with specific label claims related to use as a medical device. This underscored that while many mobile technologies are marketed and sold as consumer devices, they may still be useful in clinical investigations. Furthermore, that the use of a mobile device in a clinical trial does not mean that the technology must be regulated as a medical device.

Members of the MCT Mobile Devices project team presented results of interviews with sponsors, investigators, and technical experts (in device manufacturing, data management, biostatisticians, and data security).[1] They also shared data on specific topics that were delved into more deeply during breakout sessions.

Data Challenges (Sessions I-III)

These sessions reported evidence gathered from expert interviews with sponsors, investigators, and technical experts regarding solutions to the data challenges associated with using mobile devices to capture objective data in clinical trials.

Key lessons learned from investigators and sponsors with experience conducting studies using mobile devices for data capture included the need to incorporate

[1] Patient representatives participate in the CTTI MCT Mobile Devices project team and were well-represented at this meeting, but the patient perspective was not directly included in the evidence gathering activities. The MCT Stakeholder Perceptions project is devoted to the patient perspective, and all pertinent evidence will be encompassed in the associated materials for this project.

mobile devices into clinical trials early—beginning with small patient populations and low-risk data collection opportunities—to gain experience and knowledge prior to incorporation into a larger study. Technical experts agreed that it is best to understand the type, frequency of collection, and relative quantity of data needed at the onset of the study. The evidence also highlighted the need to reduce patient burden through, for example, selecting patient-friendly interfaces and reducing the total number of devices needed per patient. Other considerations included the capacity of data storage, uploading frequency of the device, and best practices to protect patient identity with appropriate data security measures. A synopsis of the evidence gathered from these expert interviews can be found here.

Scientific and Technological Issues (Sessions IV-VI)

These sessions described evidence on the scientific and technological considerations associated with managing mobile devices for objective data capture in clinical trials, as well as the development of guiding principles to promote their inclusion.

In discussing best practices, sponsors and investigators recommended due diligence with the vendor at the onset of device selection to ensure proper understanding of the device technology and data processing outputs. Knowledge of the verification, validation, and mobile device calibration measures allows sponsors and investigators to ensure that the device is "fit for purpose", and may allow earlier detection of irregular data. Device manufacturers who were interviewed agreed that understanding device performance and function was critical to ensure reliable, comparable, and accurate data across the patient population. A synopsis of the evidence gathered from these expert interviews can be found here.

Breakout Group Discussions

Following the presentation of evidence for each topic area, the meeting attendees split into three different breakout sessions, each focused on a subset of the key issues. Specific topics covered in the break-out groups on each of day 1 and day 2 are outlined in **Table 1** and **Table 2,** respectively.

Table 1. Day 1 Break-out Discussion on Data Challenges by Group

Group 1	Group 2	Group 3
Data attribution	Data collection	Audit trails
Data management	Data analysis & interpretation	Data integrity
Data access	Making data available to FDA	Data origins & source data
Data security		Study monitoring

Table 2. Day 2 Break-out Discussions on Scientific and Technological Issues by Group

Group 4	Group 5	Group 6
Monitoring outcomes	Device calibration	Device management
Real time safety signals	Device validation	Device failure
Providing real-time data to study participants	Device selection	Device selection
Bring your own device (BYOD)	BYOD	BYOD

Each break-out group was composed of participants who had experience using mobile devices in clinical trials, and who are passionate about determining the best path forward to promote more efficient, patient-centric trials with high-quality data captured by mobile devices. The multi-stakeholder groups evaluated current practices and identified solutions to inform pending recommendations and tools to support the appropriate use of mobile devices in clinical trials.

Common themes emerged from these sessions:

- The recommended best practices for studies using mobile devices for data capture often do not differ significantly from many of the best practices that we already apply to clinical trials.
- Studies using mobile devices for data capture should not be held to higher standards than traditional trials.
- Trials that leverage mobile devices for data capture should engage patients in endpoint selection and study design.

Ultimately, the high-quality discussions at this meeting greatly enriched the evidence gathered by the project team. Participants provided suggestions for recommendations and tools that will bring the field closer to reaping the benefits of incorporating mobile devices in clinical trials. Following this meeting, the project team is developing a suite of recommendations and tools that are expected to be released in early 2018.

FUNDING STATEMENT

Funding for this meeting was made possible, in part, by the Food and Drug Administration through grant R18FD005292. Views expressed in written materials or publications and by moderators or speakers do not necessarily reflect the official policies of the Department of Health and Human Services; nor does any mention of trade names, commercial practices, or organizations imply endorsement by the United States Government. Partial funding was also provided by pooled membership fees from CTTI's member organizations.

ABOUT CTTI

The Clinical Trials Transformation Initiative (CTTI)—co-founded by Duke University and FDA—is a public-private partnership whose mission is to develop and drive adoption of practices that will increase the quality and efficiency of clinical trials. The CTTI vision is a high quality clinical trial system that is patient-centered and efficient, enabling reliable and timely access to evidence-based therapeutic prevention and treatment options.

Appendix A. Meeting Agenda

AGENDA

Scientific and Technological Issues Surrounding the Use of Mobile Devices in Clinical Trials

June 15-16, 2017

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MEETING OBJECTIVES:

- Present findings from evidence-gathering activities
- Discuss how this evidence may be used to provide direction for the appropriate utilization of mobile devices for objective data capture in clinical trials. Specifically,
    - Possible solutions to key data challenges
    - Scientific and technological considerations
- Identify the change agents who will drive adoption of mobile devices for capturing objective data in clinical trials, including for the purposes of regulatory submission
- Describe what products CTTI should develop to equip change agents to include mobile devices for data capture in clinical trials, including for the purposes of regulatory submission

Mobile Devices defined as:
Mobile applications and remote sensor devices that capture objective data, including both consumer and medical grade devices.

THURSDAY, JUNE 15, 2017

9:00 AM — Welcome and Opening Remarks

9:00 AM — Welcome
Annemarie Forrest, CTTI

9:15 AM — The CTTI MCT Mobile Devices Project and Meeting Goals
Jen Goldsack, CTTI

9:30 AM — Keynote
Robert Califf, Duke University

10:15 AM — Mobile Clinical Trials and CDRH's Regulation of Devices
Dharmesh Patel, FDA

10:30 AM — Recommendations from CTTI's MCT Novel Endpoints Project
Jen Goldsack, CTTI

10:45 AM — Break

11:00 AM — SESSION I: Presentation of Evidence on Data Challenges

Session I Moderator: Jen Goldsack, CTTI
Session I Objective:

- Present and discuss findings from evidence gathering activities

11:00 AM — Session I Presenters:

Ray Dorsey, University of Rochester
Brian Perry, Duke University
Phil Coran, Medidata
Chris Miller, AstraZeneca
Cheryl Grandinetti, FDA

12:45 PM — Lunch

1:30 PM — SESSION II: Breakout Group Discussions – Data Challenges

Session II Objectives:

- Identify key themes from the data and meeting discussions that we should take forward into our recommendations
- Determine the tools required by experts to support the implementation of these recommendations and the appropriate adoption of mobile devices for data capture in clinical trials

1:45 PM Break-Out Group Discussions

Breakout Group Facilitators:
Group 1: Phil Coran, Medidata; Jen Goldsack, CTTI
Group 2: Chris Miller, AstraZeneca; Brian Perry, CTTI
Group 3: Jonathan Helfgott, Johns Hopkins; Annemarie Forrest, CTTI

Group 1	Group 2	Group 3
Data attribution Data management Data access Data security	Data collection Data analysis & interpretation Making data available to FDA	Audit trails Data integrity Data origins & source data Study monitoring

4:00 PM SESSION III: Addressing Data Challenges

Session III Objectives:

- Breakout teams present and engage all attendees in discussion on consensus approaches / recommendations / best practices / guiding principles for their assigned topics
- Discuss how attendees would like to see this information reported in CTTI recommendations, and tools and how they will use them

5:00 PM Adjourn Day One

FRIDAY, JUNE 16, 2017

8:15 AM Opening Remarks
Jen Goldsack, CTTI

8:30 AM SESSION IV: Presentation of Evidence on Scientific and Technological Issues

Session IV Moderator: Jen Goldsack, CTTI
Session IV Objective:

- Present and discuss findings from evidence gathering activities

8:30 AM Session IV Presenters:
Aiden Doherty, University of Oxford
Barry Peterson, Philips Respironics
Brian Perry, Duke University
Ashish Narayan, Northwell Health
Kaveeta Vasisht, FDA

10:15 AM SESSION V: Break-Out Group Discussions, Scientific and Technological Considerations

Session V Objectives:

- Identify key themes from the data and meeting discussions that we should take forward into our recommendations
- Determine the tools required by experts to support the implementation of these recommendations and the appropriate adoption of mobile devices for data capture in clinical trials

Break-Out Group Facilitators:
Group 4: Marisa Bolognese, Life Raft Group; Jen Goldsack, CTTI
Group 5: Barry Peterson, Philips & Brian Perry, CTTI
Group 6: Tom Switzer, Genentech & Annemarie Forrest, CTTI

Group 4	Group 5	Group 6
Monitoring outcomes Real time safety signals Providing real-time data to study participants BYOD	Device calibration Device validation Device selection BYOD	Device management Device failure Device selection BYOD

12:00 PM Working Lunch

12:15 PM SESSION VI: Addressing Scientific and Technological Considerations

Session VI Objectives:

- Break-Out teams present and engage all attendees in discussion on consensus approaches / recommendations / best practices / guiding principles for their assigned topics
- Discuss how attendees would like to see this information reported in CTTI recommendations, and tools and how they will use them

1:30 PM Wrap up and Close

1:30 PM An Overview of Next Steps

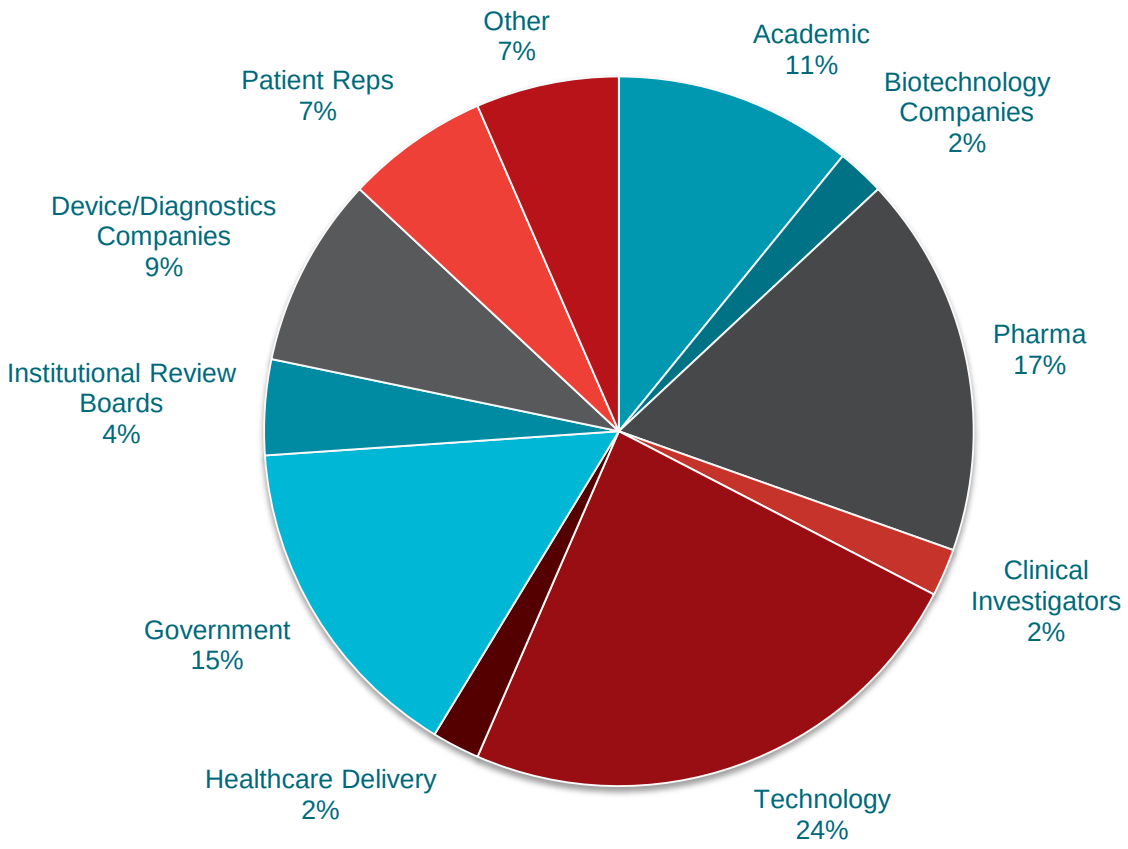
1:45 PM Closing Comments

2:00 PM Adjourn and Departures

Appendix B. Meeting Participants

Expert meeting participants represent a broad cross-section of the clinical trial enterprise. Participants are expected to be actively engaged in dialogue both days.

Stakeholders Represented



Meeting Participants

Name	Participant Affiliation
Adam Amdur	American Sleep Apnea Association
Stephen Arneric	C-Path Institute
Kassa Ayalew	Food & Drug Administration (CDER)
Jessie Bakker	Philips Respironics
Bill Bates	Validic
Marisa Bolognese	The Life Raft Group
Abby Bronson	Parent Project Muscular Dystrophy
Phil Coran	Medidata Solutions
Nirav Dalal	Abbott
Chris Dell	Pfizer Inc.
Aiden Doherty	University of Oxford
Ray Dorsey	University of Rochester
Sonya Eremenco	C-Path Institute
Karen Erickson	Alpha-1 Foundation
Luca Foschini	Evidation Health
Joy Graham	PMG Research
Cheryl Grandinetti	Food & Drug Administration (CDER)
Daniel Grant	Novartis
Matthew Heasley	GlaxoSmithKline
Jonathan Helfgott	Johns Hopkins University
Elena Izmailova	Takeda Pharmaceuticals
Travis Johnson	Garmin
Les Jordan	Target Health
Jeff Lee	mProve Health
Sean McNamara	Garmin
Claire Meunier	Evidation Health
Chris Miller	AstraZeneca
Polly Moore	Intra-Cellular Therapies
Ashish Narayan	Northwell Health
Ashley Needham	Validic
Dharmesh Patel	Food & Drug Administration (CDRH)
Barry Peterson	Philips Respironics
Maria Picone	Formed, Inc.

Meeting Participants *(Continued)*

Name	Participant Affiliation
Linda Reuter	Biomedical Research Alliance of NY
Jane Rhodes	Biogen
Peter Ridgway	Philips
Dan Rose	Pulmonary Fibrosis Foundation
Michelle Russell-Einhorn	Schulman IRB
Leonard Sacks	Food & Drug Administration (CDER)
Lita Sands	InVentiv Health
Ted Scott	Hamilton Health Sciences
Rav Sheth	Micro-Medicine
Brad Smith	FasterCures
Thomas Switzer	Genentech
Kaveeta Vasisht	Food & Drug Administration (CDER)
Evan Wearne	Food & Drug Administration (CDER)
Nicole Wolanski	Food & Drug Administration (OC)
Jeremy Wyatt	ActiGraph
Anne Zielinski	Bioclinica

CTTI and Meeting Staff

Annemarie Forrest, CTTI
Jennifer Goldsack, CTTI
Julie Hurt, Whitsell Innovations
Pamela Tenaerts, CTTI
Brian Perry, CTTI

For more information, contact the MCT Mobile Devices Project Manager, Jen Goldsack (jennifer.goldsack@duke.edu) or visit http://www.ctti-clinicaltrials.org/projects/mobile-devices.