IRB / EC Considerations for DCT Review

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With the assistance of Evan Sohn, MEd, Harvard Catalyst
Ethical Review of Decentralized Clinical Trials (DCTs): Tools, Resources and Best Practices
Results of a multi-stakeholder task force

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Taskforce Overview

• Definitions
• Problem Statement
• Task Force
• Work process
Definitions

- **Decentralized clinical trials (DCTs)** refer to clinical trials where some or all of the trial-related activities occur at locations other than traditional clinical trial sites.
- Trials are executed through mobile technologies and/or local healthcare providers with a decreased reliance on specialized research facilities and/or intermediaries for data collection and vary in location, methods, and procedures from traditional trials.
- Also termed remote, digital, virtual, tele-trials

Be aware of DCT exceptionalism:
What elements, if any, of DCTs differ from traditional clinical trials
DCTs

- Laboratory tests at local facility
- Clinical follow-up visit by telemedicine
- Telehealth and digital health (DHTs)
  - Activity trackers
  - Smart watches
  - Spirometers

Why DCTs?

- Enhanced convenience for trial participants
- Reduce burden on caregivers
- Expand access to more diverse populations and increase retention
- Improve trial efficiencies and decrease delays (and costs)
- Facilitate research on rare diseases and on diseases affecting populations with limited mobility

From

Site-based
Location of investigator’s site
In-person interactions
Lab/imaging on-site

To

Participant-based
Clinic/Hospital
Community-based site
Local lab, pharmacy
Visiting nurse
Tele-/video- visits

Wearables
Remote Monitoring
Activity Tracker
ePROs
Biomarker Lab Data

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Problem Statement

• Variety of ethical, regulatory, and legal challenges to the greater adoption of DCTs
  • In part due to a variety of kinds of trials that are called “decentralized” and “hybrid”
  • Rapidly changing field: evolving technologies
  • Lack of familiarity, common understanding, or education

• Many groups, academic centers, and companies are working on aspects of DCTs, and the effort was intended to be complementary.
• Task force: IRB review and approval of DCTs
• IRBs differ in their review:
  • Requirements for submission
  • Processes for review
  • Criteria for approval
Larger Questions

- What are the ethical issues the IRB should be concerned about in reviewing/approving a DCT in the first place?
  - Of all technology iterations, when should the IRB review and approve changes as a “formal amendment” prior to deployment?
- What is different about a DCT than a traditional study?
- What should not be considered as different in ethical review and removal?
  - E.g., Is a local lab different than a central lab at a performance site?
- Should we consider international issues, and if so, how?
Task Force Leadership and Process

**Leadership**
- Barbara Bierer, MD, MRCT Center
- Andrei Chiriac, Medable
- Leanne Madre, Medable
- Evan Sohn, Harvard Catalyst
- Pamela Tenaerts, MD, Medable

**Past:**
- Andrew Johnson, formerly Medable
- Lisa Murray, MRCT Center

**Medable Subject Matter Experts**
- Andrew MacKinnon
- Carl Franzetti
- Flo Mowlem

**Process**
- Start with the patient journey
- Identify IRB questions and best practices at each point
- What is unique about DCT as it relates to IRB / ethics review?
- Address 2 – 4 topics per meeting
- Seek 2-3 volunteers to help solidify key points for each topic post-meeting
- Define and develop deliverables
Task Force Members

Darin Achilles, US Food and Drug Administration
Alison Bond, Amgen
Megan Doyle, Amgen
Michelle Feige, Association for the Accreditation of Human Research Protection Programs, Inc
Jonathan Green, National Institutes of Health
Zachary Hallinan, Clinical Trials Transformation Initiative
Tara Isherwood, Syneos Health
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Jane Perlmutter, Gemini Group
Jennifer Ribeiro, Bristol-Myers Squibb
Robert Romanchuk, Advarra
Leonard Sacks, Food and Drug Administration
Sana Shakour, University of Michigan
Megan Kasmatis Singleton, Johns Hopkins Medical Institute
Joan Venticinque, Patient Advocate
Participant Journey

Digital Recruitment
- Find new opportunities to participate in research
- Understand trial activities anytime
- Specialist assistance

Local Visits
- Visit with a local provider or lab
- In home provider visits

In Home Visits
- In home provider visits

TeleVisits
- Meet with your provider virtually

Devices
- Use provisioned or BYOD

Direct to Participant Shipping
- Receive devices, sensors, and IMPs at home

Notifications & Reminders
- Reminders to complete your trial tasks

Rewards
- Rewards to keep motivated during your trial

Study Closeout
- Device return and retention of study data

Study Management
- View your study progress in real-time

Data Capture
- Capture outcomes in real time without paper

Digital Enablement
- Resources, education, and training to participants

ePro & eCOA
- Capture how you respond to treatment throughout the trial

Connected Sensors
- Capture how your body is feeling

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IRB/EC Considerations for DCT review

Participants & Technology >
- DTP Shipping
- eConsent
- Recruitment
- Study close out
- Real-time data monitoring

Connected sensors
- Helpdesk
- Rewards
- Remote visits

Quality
Privacy
Security

Devices >
- Notifications & Reminders
- People
- Remote data collection
- Data Oversight

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Complexities of Ethical Review of DCTs

Bob Romanchuk, BSHS, CIP
Spotting a DCT:

Is it decentralized?
- Not a binary determination
  - Better question: What DCT features does the study have?
    - What is the subject impact of those features?

How is it recognized?
- Most intake forms do not ask: Is this a DCT?
- Protocols are often silent on DCT features.
- What features deserve close attention?
Areas of focus and discussion:

- Technology
- Safety
- Oversight
## DCT Challenges: Technology

<table>
<thead>
<tr>
<th>The Promise</th>
<th>The Challenge</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remote technologies make clinical visits unnecessary</td>
<td>Remote technologies can be hard to understand and to operate</td>
</tr>
<tr>
<td>Connected devices allow collection of wide-ranging, real-world data</td>
<td>Connected device can be hacked, stolen or lost. The volume of data may be superfluous</td>
</tr>
<tr>
<td>Remote technologies allow increased access to underserved populations</td>
<td>Remote technologies require a connection that comes with a cost and a level of technical savvy.</td>
</tr>
<tr>
<td>eConsent facilitates and simplifies the consent process</td>
<td>Part 11 compliance. PI communication/interaction during the consent process.</td>
</tr>
</tbody>
</table>
DCT Technology: IRB Response

- **Subject Burden:** Weigh the real “cost” to the subject in time and resources. Assure clear disclosure in ICF.

- **Examine the range of data.** Does it contain sensitive PII? Is it secure? Does it actually contribute to study endpoints?

- **Examine TOU/PP for exculpatory text.**
# DCT Challenges; Safety

<table>
<thead>
<tr>
<th>Traditional Clinical Trials</th>
<th>DCTs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects attend a clinic visit where they are examined by HCPs and systematically queried regarding adverse events.</td>
<td>Subjects report research activity and adverse events through an eDiary or ePRO device. Contact with study team may be available via virtual technology.</td>
</tr>
<tr>
<td>Research procedures are conducted by trained research team members</td>
<td>Research procedures are performed by the participant using mobile/connected technology or by contracted (non-research) HCPs.</td>
</tr>
<tr>
<td>Clinical protocol procedures carried out by study team members in direct contact with PI.</td>
<td>Clinical protocol procedures carried out by contracted, non-research personnel that may not have direct line to PI.</td>
</tr>
</tbody>
</table>
DCT Safety: IRB response

- Identifying and reporting adverse events: Assure timely monitoring and follow up of incoming ePro data.

- Technology for AE collection/reporting: Assure adequate technology support and training when AE reporting depends on their use.

- If non-research, contracted HCPs carry out protocol requirements: Assure adequate training and PI oversight.
## DCT Challenges; PI Oversight

<table>
<thead>
<tr>
<th>The Promise</th>
<th>The Challenge</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moving protocol-driven activities to the home allows previously underserved populations to participate in clinical research. The classic “clinical site-based” research is obsolete.</td>
<td>The participant’s home becomes the research site. The research facility or site exists primarily for maintenance and retention of records.</td>
</tr>
<tr>
<td>Use of contracted HCPs proximal to the subject allows greater convenience to the participant increasing reach and ease of participation. “Patient centricity” is achieved.</td>
<td>The need for the PI to oversee multiple HCPs not under his/her direct supervision stretches the ability to provide adequate supervision.</td>
</tr>
<tr>
<td>The patient centric model increases convenience by tailoring research activities to the subject’s needs and schedule.</td>
<td>The “distance” between the investigator and the subject increases.</td>
</tr>
</tbody>
</table>
DCT Extension with “Clinical Research as a Care Option” (CRAACO) model

<table>
<thead>
<tr>
<th>The Promise</th>
<th>The Challenge</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>The Model:</strong></td>
<td>• The distinction between clinical research and clinical care (aka “the therapeutic misconception”) is obscured.</td>
</tr>
<tr>
<td>• Integrate clinical research with the clinical care setting by allowing access to EMR</td>
<td>• The Physicians and clinicians applying investigational therapies are not researchers and are not delegated as such.</td>
</tr>
<tr>
<td>• Providing research support as an ancillary service.</td>
<td>• Research staff are overseen remotely by PI and often do not report to local clinicians.</td>
</tr>
<tr>
<td>Clinicians are not impressed into service as PIs or Sub-Is but are supported by remote PI and local research team members.</td>
<td>• Point of research is often characterized as “location” rather than “research site”.</td>
</tr>
<tr>
<td><strong>The Goal:</strong></td>
<td>• Integration of EMR with research data creates challenges in the return of research results and incidental findings.</td>
</tr>
<tr>
<td>• Integrating clinical research into the clinical care setting allows:</td>
<td>• Data sharing allows integration of research and clinical data. Researchers are provided broad and deep access to enrich research.</td>
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<td>• No more “one-and-done” investigators</td>
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<td>• Higher rates of participation</td>
</tr>
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<td>• Greater patient centricity and ease of participation</td>
</tr>
<tr>
<td>• Greater patient centricity and ease of participation</td>
<td>• Integration of EMR with research data creates challenges in the return of research results and incidental findings.</td>
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</table>
PI Oversight: IRB Response

Protocol should provide a clear picture of how the PI will provide oversight that ensures protocol compliance and subject safety.

Oversight and monitoring plan should include clear description how training will be provided and how/when communication with non-study HCPs will occur.

IRB should consider complexity of the protocol and risk profile in weighing whether oversight plans are adequate.
IRB/DCT Tools and Resources

› Pamela Tenaerts, MD

› Leanne Madre, JD
IRB/EC Considerations for DCT review

Quality
Privacy
Security

Participants & Technology
DTP Shipping
eConsent
Recruitment
Study close out
Real-time data monitoring
Devices

Notifications & Reminders
Helpdesk
Rewards
Connected sensors
Remote visits

People
Remote data collection
Data Oversight

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People

- Recruitment
- eConsent
- Direct to Participant Shipping
- Participants and Technology
- Notifications & Reminders
- Helpdesk
- Rewards
Recruitment

Potential participants may be recruited through social media (SoMe)

- Interaction by research staff members with specific individuals with the aim of enrolling them in research.

- Distributing recruitment materials (ads, posters, flyers) with the aim of attracting potential participants to contact the research team for more information and for consideration of enrollment.
Recruitment: Considerations

- Proposed social media recruitment techniques
  - List of all channels/websites to be deployed in recruitment
  - Script of the information, images and format to be displayed
- A description of recruitment methods - active, passive
- Compliance (or lack of non-compliance) with the policies and terms of use of relevant websites
- Recruitment strategy respects all relevant ethical norms
  - Respect for the privacy and other interests of social media users
  - Investigator transparency (no skulking, snooping, or lying)
- When SoMe is used to recruit, it may be more likely that trial participants regularly engage on SoMe. Therefore, a formal communication plan is needed to manage SoMe activities among enrolled participants.
- Compliance with applicable country, federal and state laws
eConsent: Considerations

- Description of trial risk – determines nature of review, e.g., assistance may not be required for minimal risk studies

- Method by which participant (or Legally Authorized Representative) identity will be verified

- Attention to eConsent content
  - Language should be reviewed in similar manner as paper consent
  - Particular attention to visual images, videos and other associated information
  - Review of the consent language may be done as the platform is designed and developed; once the platform is developed, an expedited review of the platform can be completed

- Assistance that will be offered to potential participants
- Measures implemented to assure platform security
- Storage of eConsent records, e.g., will any vendors or 3rd parties have access to the records?
- Implementation of eSignature - process should comply with local laws and regulations
Direct to Participant Shipping: Considerations

Some DCTs involve shipping a research product directly to the trial participant. Who ships the research product will impact the ethics review, given that participants’ personal information will be collected.

What is the item being shipped (e.g., IMP, device, sensor)?
- Product specifications, storage, accountability
- Concordance with national, state, and local laws
- Participant instructions, training and resources

• How will items be labeled and shipped?
  - Plan appropriate for item being shipped
  - Labeling should balance ease of identification by participant with privacy concerns

• What is the plan to verify arrival?
  - Contingency plans for shipping error

• What is the burden of responsibility on participant?
  - Sharing of personal information
  - Instructions and training
  - Barriers related to population or location
Participants & Technology: Considerations

For a DCT, participants will likely interact with one or more technologies that will facilitate consent, communication, and/or data collection.

- Equitable access to the study
  - How will technology be accessed? BYOD vs. provisioned?
  - Location issues
  - Cost
- Device considerations - see devices, help desk, and direct to participant shipping sections
- Participant education, resources and training
  - What type of information will participants have access to via the technology?
  - Instructions regarding devices and technology
  - Support from research team / help desk
  - Nature and appropriateness of materials
- Privacy and confidentiality
- Special populations - children, prisoners
Notifications & Reminders

In these trials, the site investigator or study team can create and send both automatic and on-demand notifications and reminders to the participant to help increase the completion of study procedures in a timely fashion.

Patient Preferences

As much as possible, digital engagement platforms should be implemented and/or communications (e.g., through a personal mobile phone) should be configured to facilitate participant choice.

Risk Mitigation

Confidentiality
- Device or display may not be private
- Confidential information
- Malicious stealing or hacking
- Platform security

Communication Not Received
- Communications ignored, turned off or blocked
- Participant annoyance
- Undelivered notifications and reminders
Notifications & Reminders: Considerations

- Is the implementation of notifications or reminders likely to create an undue burden or introduce risks to privacy or confidentiality?
- Does the communication contain potentially sensitive or identifiable information? Can the inclusion of that information be further minimized?
- Are there data security concerns introduced by these communications? If so, can they be eliminated?
- What control does the participant have over the form, frequency, & content of the communication?
- What is the plan if the participant fails to respond to a safety-related notification?
- What are the consequences, risks, and potential harms of communication failures?
- Is there a monitoring plan for the system of notifications and reminders?
- Does the study include participant feedback, and is it elective?
Helpdesk

- Typically provided by vendor or sponsor
- Technical help only
- Trained not to provide medical advice
- Access to personal private and health information
- Confidentiality provisions important
- Data retention and storage considerations

- Typical provided by investigator and team
- Medical advice must conform to state licensure requirements
- Confidentiality provisions important
- Data retention and storage considerations
- Helpdesk documentation tracker
Helpdesk: Considerations

- Helpdesk personnel should have appropriate qualifications, training, and delegation for their role in the study.
- Calls by participants to the Helpdesk should be logged, but no record linking the identity of the caller to the study, condition, or sensitive data should be maintained unless necessary, and if necessary, appropriate procedures to maintain confidentiality and privacy should be in place.
- Call logs, tracking, and reports should be audited for retention of personal health or identical information.
- Additional considerations regarding the participant experience.
- Will trial participants have 24/7 access to Helpdesk support?
- How will the participant and their questions be triaged?
- Does the Helpdesk have scripted questions that are routinely asked?
- Will the Helpdesk accommodate underserved and underrepresented populations?
Rewards

The nature of rewards in DCTs can extend beyond financial payments.

Examples of gamification and devices that have value outside of clinical trial.

MyHeartMate Rewards
Not advertisement or endorsement

Apple watch fitness gamification/challenges

New devices
Rewards: Considerations

- Will providing rewards in the planned fashion change the willingness of the participant to share their personal data in ways that create undue risk of harm?
- Are there any rewards or features of a reward program that are of particular concern?
- Have any conditions of the reward been considered? For instance, if the gift is earned only at the completion of the trial, will that inappropriately influence the participant’s decision to withdraw?
- Can the promise of the gift of the device and/or software be considered “undue influence,” impacting the voluntariness of participation in the study?
- Will depreciation affect the value of the device and/or software over the course of the research?
- Is the value of the gift of the device or software proportionate to the time and burden of the research and appropriate for the protocol?
- Is there any functionality, information, or other feature that should be removed, disabled, or modified prior to transfer to the participant as a reward?
- As in other aspects of DCTs, particular attention to access, transfer, use, disclosure, and safe storage of personal information is necessary.
Remote Data Collection

- Devices
- Remote Visits
- Connected Sensors
Remote Data Collection

Bringing trials to the Patient

Connected Sensors
- Vitals
- Organ
- Activity

Remote Visits
- TeleVisit
- In-Home
- Local Provider

Devices
- Smartphones
- Tablets
Connected Sensors

- Devices that support the measurement of vital signs
  - Example: fingertip pulse oximeter

- Devices related to measurement of organ function
  - Example: spirometer, CGM

- Devices that measure activity level, number of steps, etc
  - Example: pedometer
Connected Sensors: Considerations

- Purpose of the sensor (critical vitals/at risk group)
- Regulatory status of sensors
- Frequency of monitoring of the sensor data
- Where sensor data is stored
- Burden of sensor to participants
- Clarity of where to get help for sensor issues
- Disposition of sensor
Remote Visits

- TeleVisit
- In-Home
- Local Provider

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# Remote Visits: Considerations

<table>
<thead>
<tr>
<th>Consider whether access to internet, cellular data, devices, software, and technical support will be equitable across participants</th>
<th>Televisit</th>
<th>In-home</th>
<th>Local provider</th>
</tr>
</thead>
<tbody>
<tr>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ensure multiplicity of language availability of software and software programs</td>
<td>✓</td>
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<td></td>
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<tr>
<td>✓</td>
<td></td>
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<tr>
<td>Verify Modifications and accommodations for inclusion of people with disabilities exist</td>
<td>✓</td>
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<tr>
<td>✓</td>
<td></td>
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<tr>
<td>Verify Methods of data validation and remote monitoring</td>
<td>✓</td>
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<tr>
<td>✓</td>
<td></td>
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</tr>
<tr>
<td>Shipment, receipt, administration and disposal of IMP and other research products</td>
<td>✓</td>
<td></td>
<td></td>
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<tr>
<td>✓</td>
<td></td>
<td></td>
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<tr>
<td>Ensure Participant preferences for method of interaction with research study team</td>
<td>✓</td>
<td>✓</td>
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<tr>
<td>✓</td>
<td>✓</td>
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<tr>
<td>Evaluate and Mitigate Risks to privacy and confidentiality of participant</td>
<td>✓</td>
<td>✓</td>
<td></td>
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<tr>
<td>✓</td>
<td>✓</td>
<td></td>
<td></td>
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<tr>
<td>Ensure Data privacy and security in collection, transfer and storage</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Ability of PI to provide adequate oversight of HCPs recruited for study activities</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Verify status of healthcare provider: competencies, licensure, protocol familiarity, Form 1572</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>✓</td>
<td>✓</td>
<td></td>
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<tr>
<td>Verify Task log for providers and third-party vendors, consider if they are engaged in research</td>
<td>✓</td>
<td>✓</td>
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<tr>
<td>✓</td>
<td>✓</td>
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<tr>
<td>Ensure availability of emergency and other care if needed</td>
<td>✓</td>
<td></td>
<td></td>
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<tr>
<td>✓</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>The need for a face-to-face participant visit, laboratory tests, or imaging study</td>
<td></td>
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</tbody>
</table>
Devices

Provisioned

- Provided by sponsor or investigator
- Technical training and help often necessary
- Internet access and cellular data plans provided
- Terms of Use to be reviewed
- Data access and confidentiality provisions important
- Consequences/process for loss or failure to return (if applicable)
- Regional considerations (e.g., inducement in some countries)

BYOD

- Typically provided by participant
- Device assessment for study
- Confirmation of security & confidentiality of data transfer
- Incremental cellular data plan may be necessary
# Devices: Considerations

- **Equity: Consider**
  - Equity issues when minimum device requirements are not met
  - What the options are for participation if data plan is insufficient?
  - Security and confidentiality in data transfers

## Ensure Consent includes:
- Costs and use of device and whether replacements devices are available (at what cost)
- Ensure Instructions and process are available if device lost, damaged, stolen

## Consider disposition at end of study (keep or return)

## Ensure appropriate instructions and training

## Ensure access to helpdesk troubleshooting
Data Oversight

- Real Time Data Monitoring
- Study Closeout
Real Time Data Monitoring: Considerations

Elements that can be monitored:

- Participants’ completion of tasks and scheduled activities
- Participant requests to the Helpdesk and the study team
- Notification schedules and responses to those notifications if enabled and required
- Sensor data, e-Patient Reported Outcomes, and other outcome measures
- Safety signals
- Endpoints and outcome measures
- Investigator and sponsor reports
- Overall compliance

Impact on Participant:

- Dynamic, real-time data or results return
- ICF includes data monitoring details
- Participant burden and quality of AE reporting
- Mitigation to assure compliance with completion
- Study staff availability and response time
- Parsimonious data collection
- Back up system
Study Close Out: Considerations

Data
- Retain only required PHI
- Remove/deactivate participant access from device or sensors
- Secure data storage, retrieval and backup

Investigational Product
- Local and @home IMP retrieved and accounted

Documentation
- eConsents & admin data retained
- Reconciliation of provisioned devices and connected sensors

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Cross Cutting Themes

**Quality**
- Ensure participant safety, inclusiveness, and transparency
- Data accuracy and completeness
- Confidence in remote approach

**Privacy**
- Review additional contract terms, processes, and potential vulnerabilities of participants' private information, as well as participants' knowledge of who will have access, how their private information may be used, and what choices they can make.

**Security**
- Consider how the security of data collected remotely be assured, where the information will be stored, who will have the ability to retrieve the data, and what parameters are in place to securely transfer the data to the PI and the clinical trial record.
Website and next steps

Barbara E. Bierer, MD

https://mrctcenter.org/project/oversight-and-implementation-of-decentralized-clinical-trials/
Our Work

Clinical Trials & Research
Oversight and Implementation of Decentralized Clinical Trials
Ensuring appropriate oversight and conduct of decentralized clinical trials...

Clinical Trials & Research
Diversity, Inclusion, and Equity in Clinical Research
Developed a systematic guidance document and supplementary toolkit to enhance diversity in multi-regional clinical trials...

Clinical Trials & Research
Health Literacy in Clinical Research
A collaborative project to support the development of tools and resources that more fully incorporate health literacy concepts into clinical research materials...

https://mrctcenter.org/project/oversight-and-implementation-of-decentralized-clinical-trials/
Oversight and Implementation of Decentralized Clinical Trials

The MRCT Center is collaborating with Medable and other organizations to address the oversight and conduct of decentralized and hybrid clinical trials (collectively, DCTs), with a focus on planning and monitoring the trial appropriately.

While almost every trial utilizes some elements of technology, DCTs are highly variable in terms of the elements of 'decentralization' deployed throughout the trial, from remote recruitment utilizing social media, electronic consent, remote visits through either virtual visits or local providers, and use of devices and software for data collection, among others. There is also significant variability in IRB understanding of DCTs and, therefore, often prolonged delay in approval.

Working with a multi-stakeholder task force, the first initiative of this project addresses the ethical review of DCTs, focusing on how DCTs differ from traditional clinical trials. Next, specific recommendations for the roles and responsibilities of PIs (including IRB oversight) and sponsors will be addressed.
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- **OBJECTIVES**

- **KEY MILESTONES**

- **PROJECT LEADERSHIP & STAFF**

Project Resources
OBJECTIVES

- Provide guidance and tools for IRBs, sponsors, investigators and their study teams regarding ethical review and approval of DCTs
- Consider the specific responsibilities of principal investigators, sub-investigators, study staff, sponsors, and vendors in DCTs
- Develop resources for use by stakeholders involved in DCTs

KEY MILESTONES

PROJECT LEADERSHIP & STAFF

Project Resources

PRESENTATION

June 15, 2023
IRB/EC Considerations for DCT Review
OBJECTIVES

KEY MILESTONES

PROJECT LEADERSHIP & STAFF

Project Resources

June 15, 2023
IRB/EC Considerations for DCT Review
Recommendations

Cross-Cutting Themes

- Quality, privacy, and security
- Participant considerations
- Remote Data Collection
- Data oversight

IRB/EC Considerations for DCT Review

Executive Summary

With decentralized clinical trials (DCTs), some or all aspects of the clinical trial are conducted in locations that are not centralized at a specific clinical or research site. DCTs are trials executed either in whole or in part remotely, through telemedicine, mobile technologies, local sites, and mobile healthcare providers. This may greatly increase the efficiency and/or reach of a trial, but there are specific differences between a DCT and a traditional trial that an Institutional Review Board (IRB) or Ethics Committee (EC) should consider. This guide is intended to summarize these considerations to help investigators, sponsors, and IRBs/ECs understand these differences in order to implement the appropriate level of oversight of DCTs. The recommendations contained herein are based on discussions of a multi-stakeholder task force of experts representing academia, IRBs, patients, regulators, trial sponsors, and sites. The Multi-Regional Clinical Trials (MRCT) Center of Harvard and Medable, as the initiative co-hosts, used the discussions to create resources to support IRB/EC review of clinical trials with decentralized elements.

As shown in Figure 1, the primary concerns are to ensure the rights and welfare of the participants (people), the integrity and security of remote data collection (data collection), and the adequacy of trial and data oversight (remote data oversight). Each of the 12 potential DCT elements falls within one of these domains. In addition, several cross-cutting themes—quality, privacy, and security—are part of the review of any DCT.

Figure 1: IRB/EC Considerations for DCTs
Devices (smartphones and tablets) in DCTs

Introduction

Smartphones and tablets (here, collectively termed “devices”) can be configured either as Bring Your Own Device (BYOD) or provisioned devices. They are often used in DCTs to help participants, investigators, sites, and sponsors collect data. Devices can be vehicles for participant data collection through electronic patient-reported outcomes (ePROs), observer-reported outcomes (ObsRO), and other eCOAs (electronic clinical outcome assessment). These assessments are usually deployed using applications downloaded onto the device.

Note that some studies involve investigation of the application or software itself, which raises questions of risk and benefit for the IRB/EC. For instance, a study may involve an app for the assessment of cognition. While this app may be part of a DCT and loaded onto a device, the IRB/EC will wish to review additional potential safety and other issues than those described here.

This document covers only non-investigational devices (smartphones and tablets) devices as objects in common use, deployed for the purpose of conducting the DCT; for information about wearables, connected devices, and applications, see the Connected Sensors section.

IRBs should understand which types of devices (provisioned or BYOD) are being used.

Differences between categories of Mobile Devices

- **Provisioned**: Provided by sponsor or investigator, technical training and help often necessary, internet access and cellular data plans provided, terms of use to be reviewed, data access and confidentiality provisions important, consequences/process for loss or failure to return if applicable, regional considerations (e.g., inducement in some countries)
- **BYOD**: Typically provided by participant, device assessment for study, confirmation of security & confidentiality of data transfer, incremental cellular data plan may be necessary

Device logistics and cost

- Sponsors rarely handle the logistics of their own devices, and either buy the device outright or lease it from a technology partner.
- When the device is a required tool for trial participation, participants should be provided with appropriately administered and documented instructions to use the device properly.
- Trial participants should have access to a Helpdesk (see helpdesk tool) device troubleshooting.
- Cost considerations:
  - IRBs/ECs may wish to consider the cost of the device in their deliberations, particularly if possession of the device may subject the participant to risk of harm (e.g., in some settings, possession of the device will expose the person to privacy risks or risk of theft).
  - IRBs/ECs may wish to consider situations where the participants are allowed to retain the device after the trial, and whether the possibility of retention is an appropriate incentive to participate in the trial. In that context, the depreciated value of the device at the end of the trial should be considered.

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PDFs available

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Quality, privacy, and security

Quality, participant privacy, and security are areas that may require particular attention throughout a DCT regardless of which decentralized approaches are used.

Quality.
“Quality” in clinical trials is defined as the absence of errors that matter to decision-making—that is, errors that have a meaningful impact on the safety of trial participants or the credibility of the results (and thereby the care of future patients). In the context of an ethical review of a decentralized element, the IRB/EC focuses on both data and safety aspects. Safety considerations are broad and include everything from remote reporting of (and acting upon) adverse events to assuring the ICF appropriately discloses all information potential participants need to know relative to aspects of a trial that will be decentralized. In addition, because DCTs are often used to reach more participants through technology and local/mobile providers, issues related to equity, inclusiveness, and diversity are often more pronounced and require the examination of specific ethical questions. Similarly, data collected through remote approaches (including sensors, tech apps, and local providers) raise data accuracy and completeness questions, as well as questions about the validation of the technology used. A protocol developed through a quality-by-design approach, and which comprehensively describes the decentralized elements of a trial, facilitates a more efficient and effective ethical review of a DCT by an IRB/EC.

Privacy.
Thank You!

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Next steps

- Communications
  - Presentation at DIA: June 27 12:30-1:00 PM
    - #241: Medable Innovation Theater: Driving the New Era of Clinical Development
  - Peer-reviewed publication (in progress)
  - Videos (forthcoming)
- Encourage use and welcome feedback [add]
- Engage in SoMe
  - @MRCT @Medable @barbarabierer @pamelatenaerts @leannemadre
Discussion,
Questions,
Thank you