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*September 14, 2018*

# **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

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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



<i>Areas of Strategic Focus:</i>	SYSTEMATIC EVIDENCE GENERATION	PATIENTS AS EQUAL PARTNERS	EFFICIENT & QUALITY TRIALS	PUBLIC HEALTH CONCERN	SAFE & ETHICAL TRIALS
<i>Active Projects:</i>	<p>MCT Decentralized Clinical Trials</p> <p>MCT Stakeholder Perceptions</p> <p>Real World Evidence</p> <p>State of Clinical Trials</p>	Patient Groups & Clinical Trials	Investigator Qualification	ABDD HABP/VABP Studies	
<i>Complete Projects (now driving adoption):</i>	<p>Large Simple Trials</p> <p>MCT Mobile Technologies</p> <p>MCT Novel Endpoints</p> <p>Registry Trials</p>		<p>GCP Training</p> <p>Investigator Community</p> <p>Monitoring</p> <p>Quality by Design</p> <p>Recruitment</p> <p>Site Metrics</p>	<p>ABDD Peds Trials</p> <p>ABDD Streamlining</p> <p>HABP/VABP Trials</p> <p>ABDD Unmet Need</p> <p>Long-Term Opioid Data</p>	<p>Single IRB, Single IRB Adv</p> <p>DMCs</p> <p>Informed Consent</p> <p>Pregnancy Testing</p> <p>IND Safety, IND Safety Adv</p> <p>SAE Reporting</p>

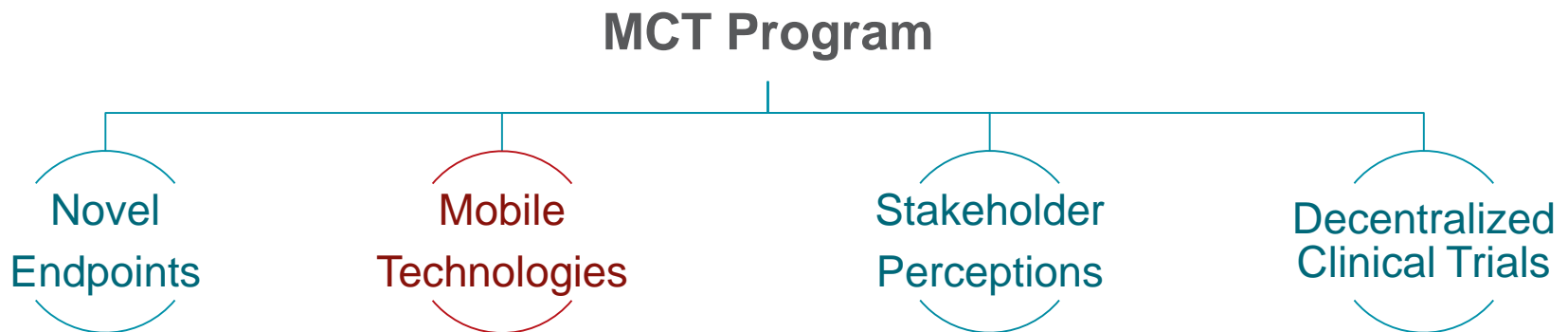
# Mobile Clinical Trials (MCT) Program

## ▶ 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

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

# 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

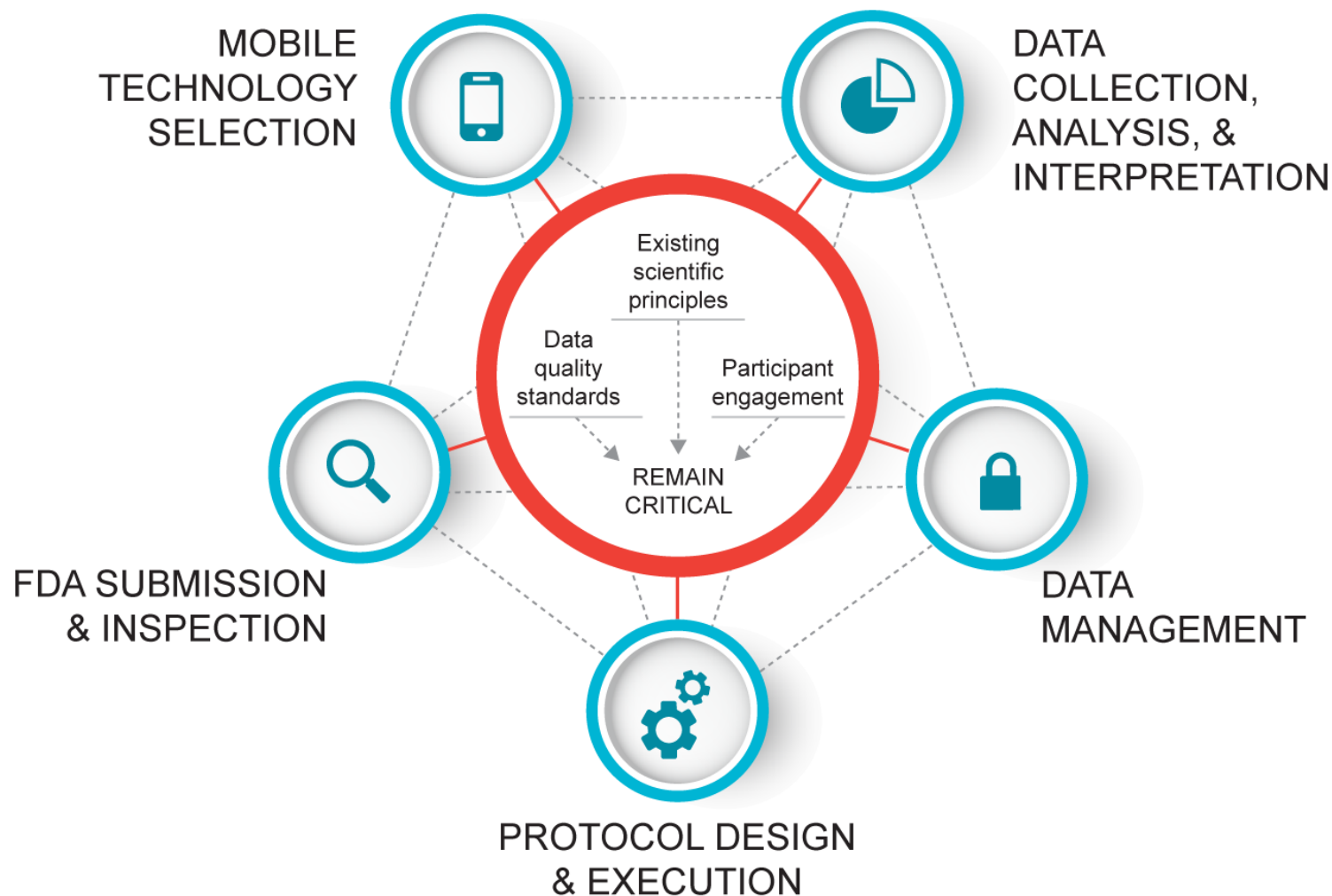


## EFFICIENCY

- 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

# CTTI MCT Mobile Technologies Project



# 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

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# 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

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# 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

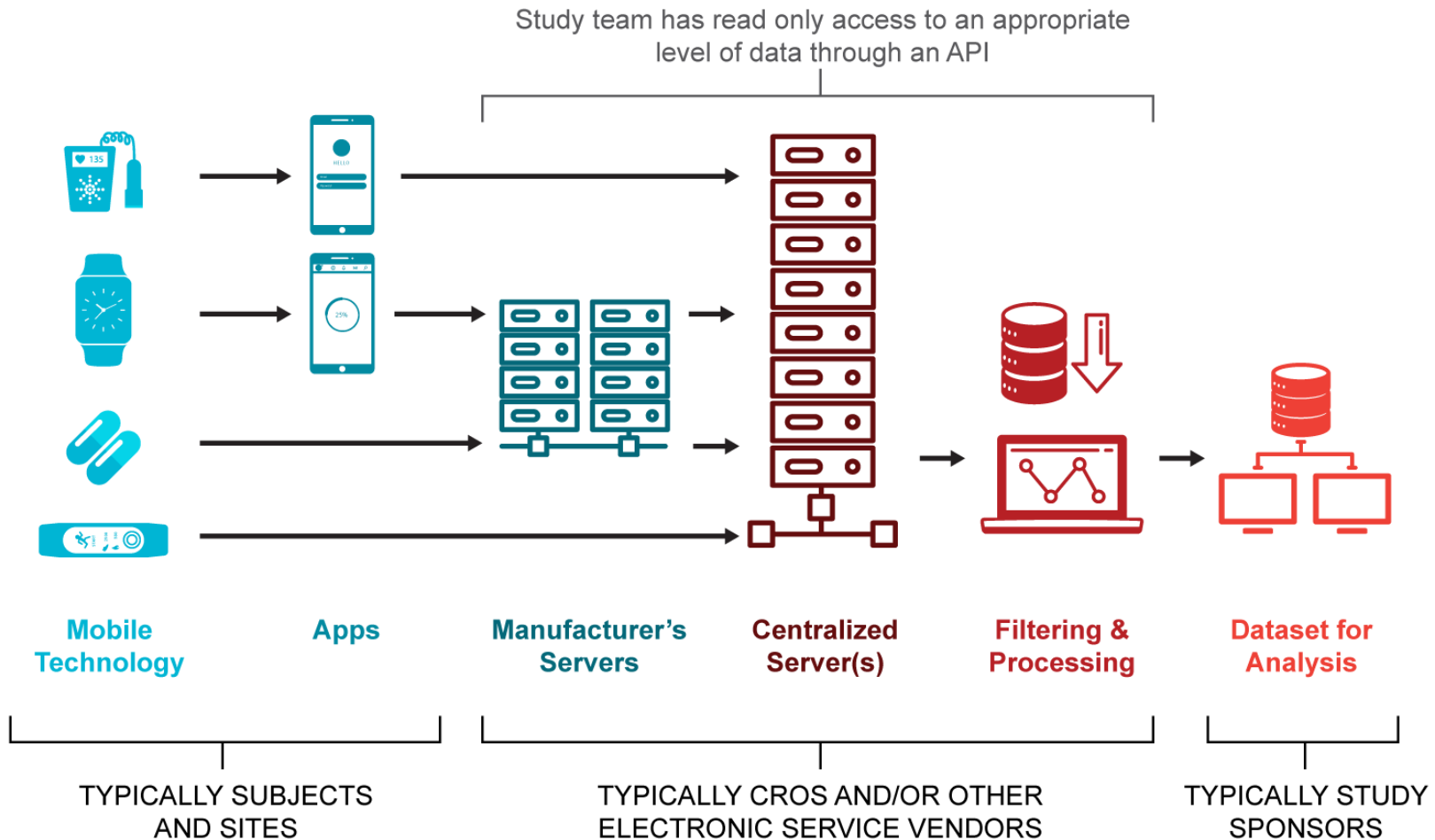
# CTTI Recommendations on Data Management

- 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

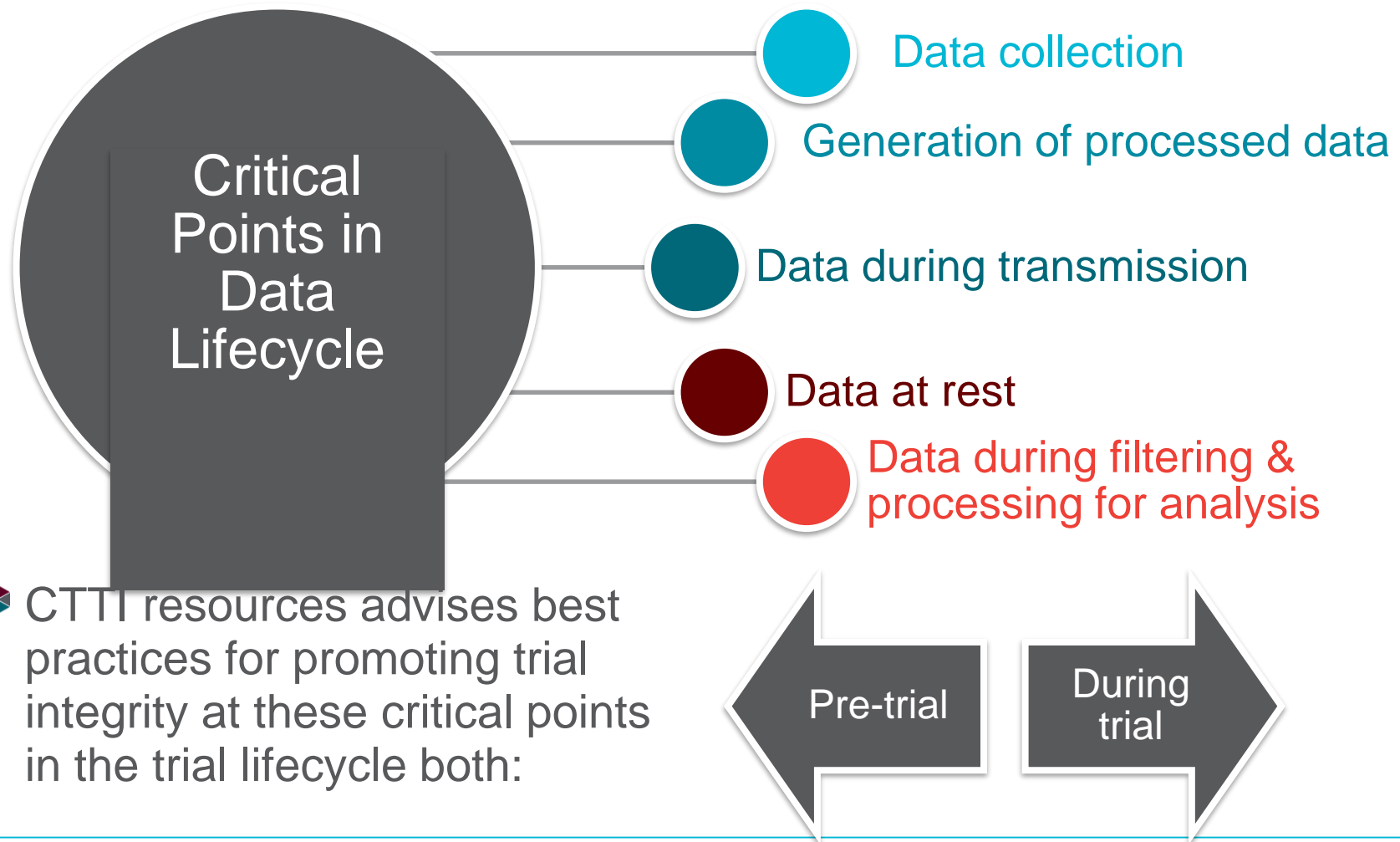
- Ensure the authenticity, integrity, and confidentiality of data over its entire lifecycle.
- Optimize data accessibility while preventing data access from unauthorized users.
- Ensure that access to data meets your needs prior to contracting an electronic service vendor.
- Apply an end-to-end, risk-based 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



Adapted from: Quisel, Tom, et al. "Collecting and Analyzing Millions of mHealth Data Streams." *Proceedings of the 23rd ACM SIGKDD International Conference on Knowledge Discovery and Data Mining*. ACM, 2017.

# Strategies for Promoting & Protecting Data Integrity



# 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.

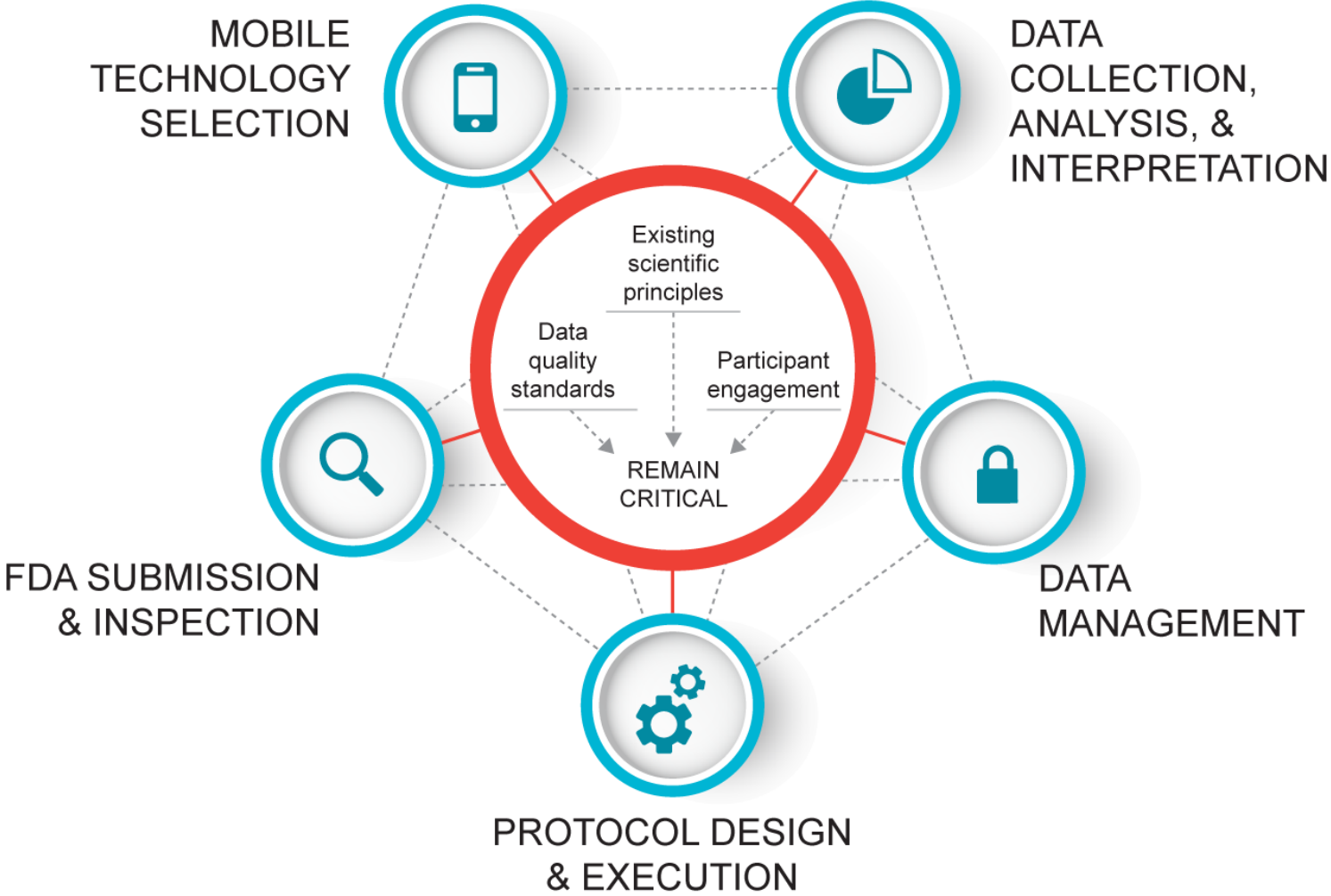


# Applying the Recommendations

John Hubbard, PhD, FCP

Genstar Capital

# CTTI MCT Mobile Technologies Project





# Take Action

- **Access recommendations and resources**
  - MCT Mobile Technologies <https://www.ctti-clinicaltrials.org/projects/mobile-technologies>

- **Contact us with questions!**

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- 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.



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# Illustrative Examples from CTTI Recs

## Verification and Validation

	VERIFICATION		VALIDATION
	Raw Data	Processed Data	Outcome Assessment
<b>Description</b>	<i>Output from physical sensor</i>	→ <i>Output from mobile technology firmware</i>	→ <i>Output from analysis algorithm</i>
<b>Example: Accelerometry</b>	Acceleration (m/s <sup>2</sup> )	→ Activity counts (n)	→ Time spent active (min) → Total sleep time (min)
<b>Example: ECG</b>	Electrical potential (mv)	→ Heart rate (beats/min)	→ Heart rate variability (e.g. pNN50)

<sup>[1]</sup> The [pNN50 statistic](#) is a time domain measure of heart rate variability (HRV).