



# Innovative Solutions to Improve Access

## Clinical Trials with Decentralized Elements Regulatory Perspective

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# Hot off the Press!

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## Conducting Clinical Trials With Decentralized Elements

Guidance for Industry,  
Investigators, and Other  
Interested Parties

# Oncology Center of Excellence Rare Cancers Program



- Orphan Drug Act defines a rare disease or condition as one which affects less than 200,000 people in the United States
- Challenges in rare cancer drug development
  - Difficulty enrolling enough patients
  - Challenges with randomized trials due to small patient numbers and/or lack of suitable comparators
  - Insufficient understanding of cancer biology
  - Limited access to timely molecular testing
  - Limited financial incentives
- Multifaceted approach needed; innovative trial designs with decentralized elements are one option

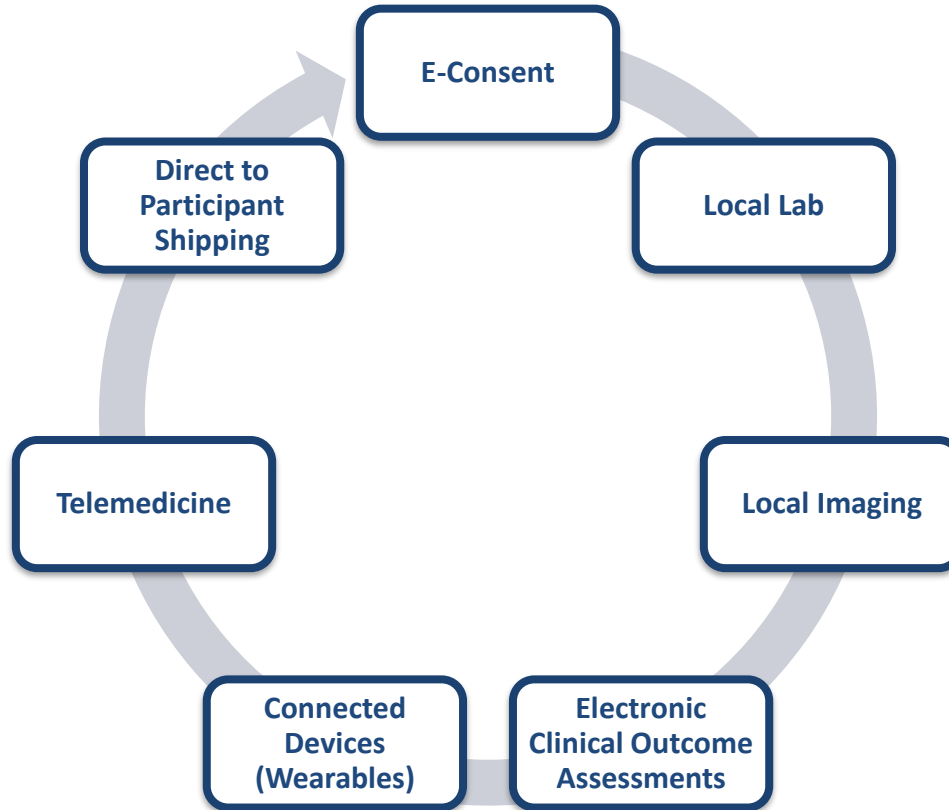
# Decentralized Clinical Trials (DCT)

In FDA DCT guidance<sup>1</sup>, a DCT refers to a clinical trial that includes **decentralized elements** where trial-related activities occur at locations other than traditional clinical trial sites



<sup>1</sup> Conducting Clinical Trials with Decentralized Elements, 2024

# DCT Elements – Strategies to Bring the Trial to the Patient





# Why are Regulators Interested?

- Patient convenience
  - Travel, time off work
  - Decreased attrition?
  
- Accessibility
  - **Rare diseases**
  - Improved accrual & retention
  
- Experience with COVID-19



# DCT Design Considerations

- FDA's regulatory requirements for investigations of medical products are the same for DCTs and traditional site-based clinical trials
- A DCT does not need to be an all or nothing endeavor; DCT elements
- Appropriate DCT elements for a particular trial will be **context dependent**
  - Complexity of administration
  - Safety profile
  - Stage of drug development



## DCT Guidance - Sponsor's Role and Responsibilities

- Sponsor responsibilities are the same for DCTs and traditional site-based clinical trials
- For a DCT with multiple data sources, the data management plan should at least include:
  - Data origin and data flow from all sources to the sponsor
  - Methods for remote data acquisition from trial participants, trial personnel & vendors
  - A list identifying vendors for data collection, handling & management
- The trial protocol should describe the operational aspects of the DCT, including:
  - Scheduled and unscheduled clinical trial visits (remote vs at trial site)
  - Transmission of reports on activities performed at different locations
  - Delivery & accountability of IP to trial participants, if applicable
  - Safety monitoring and management of adverse events
- FDA encourages a risk-based monitoring approach and use of centralized monitoring to identify and proactively follow up on missing data, inconsistent data, data outliers & potential protocol deviations





## DCT Guidance – Investigator’s Role and Responsibilities

- Responsible for the conduct of the DCT & oversight of individuals delegated to perform trial-related activities
- Investigators may delegate trial-related activities to local HCPs that require in-person interactions with trial participants (e.g., physical examinations or procedures)
- Quality control measures should be in place to help reduce variability, including regular review by investigators of participant data entered by local HCPs



## DCT Guidance – Local Healthcare Providers

- Local HCPs, such as doctors or nurses, may be used by sponsors or investigators to perform certain trial-related activities
- The trial-related services they provide should not differ from those that they are qualified to perform in routine clinical practice
- These services should not require a detailed knowledge of the protocol or the investigational product

# DCT Guidance – Informed Consent and Institutional Review Boards (IRBs)

- The regulatory requirements for obtaining informed consent and the IRB review process do not differ for DCTs
- Investigators may obtain electronic informed consent from trial participants at their remote locations
- Recommend to the use a central IRB in DCTs to facilitate efficient review of the protocol, informed consent documents, and other relevant trial-related information



# DCT Guidance – Safety Monitoring Plan (SMP)

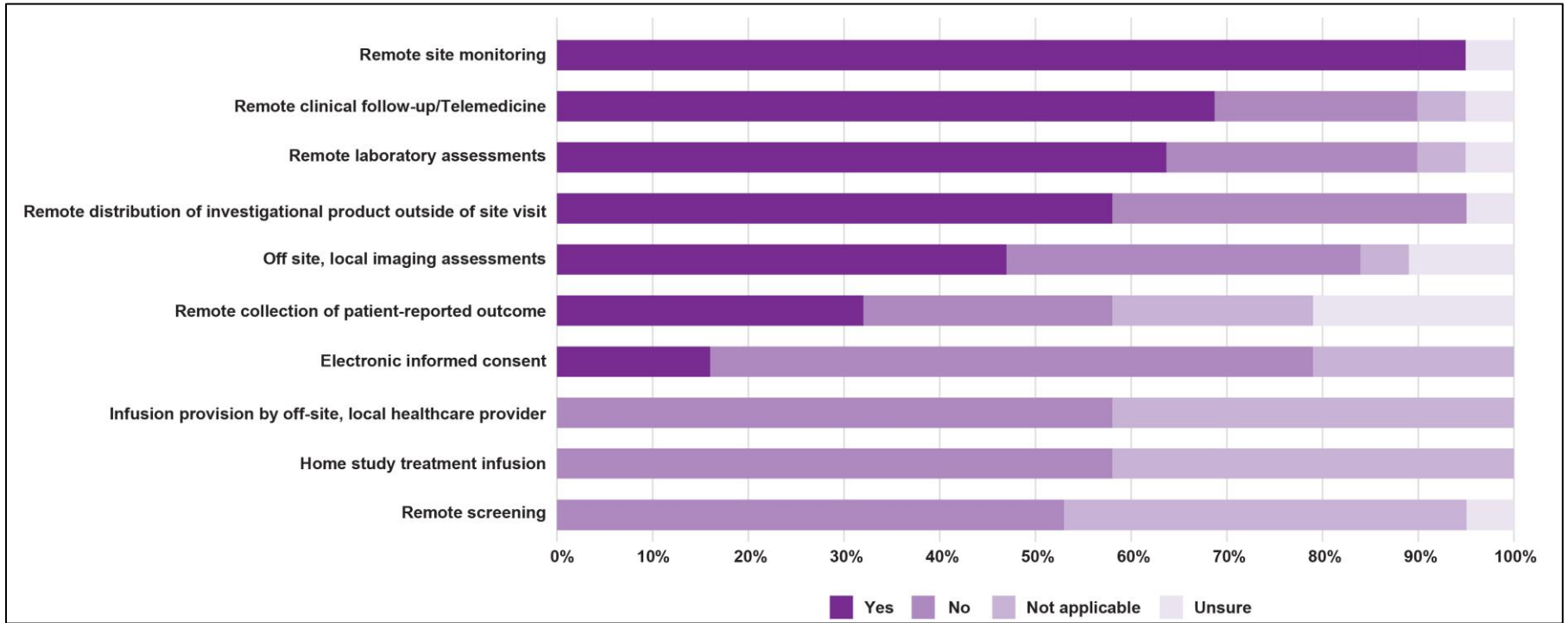
- SMP should describe how participants are expected to respond to and report adverse events, including where to seek medical assistance locally when necessary and where to receive follow-up care
- Trial participants must be able to contact trial personnel to report adverse events and have pertinent questions answered
- Trial participants should be able to arrange for an unscheduled visit using telehealth or an in-person visit, as appropriate
- If authorized in the protocol, routine safety monitoring involving laboratory testing and imaging may be performed using local clinical laboratory facilities
- If significant safety risks emerge because of remote administration or use of an IP, sponsors must discontinue remote administration or use

# DCT in Oncology – What Do We Know?

- During COVID, Sponsors did incorporate DCT elements in ongoing & new clinical trials
- Multiple oncology trials that incorporated DCT elements led to an FDA approval
- Which DCT modifications were used in trials leading to FDA approval?



# DCT Elements Utilized by Sites in Oncology Trials Leading to FDA Approval



Source: FDA & CTTI – Unpublished Data



## Potential DCT Challenges

- Coordination of trial activities with individuals and facilities in multiple locations that are not traditional clinical trial sites
- Specific issues related to the feasibility, design, implementation, or analysis of a DCT should be discussed early with the relevant FDA review divisions
- Appropriate training, oversight, and up-front risk assessment and management will be key to implementing a DCT successfully



# Modernizing Evidence Generation

1. The FDA Oncology Center of Excellence supports efforts to modernize clinical trials and evidence generation, particularly in rare cancers
2. Whether a decentralized element is appropriate depends on the type and complexity of assessments and the clinical and treatment context.
3. FDA's regulatory requirements for investigations of medical products are the same for DCTs and traditional site-based clinical trials.





# Acknowledgements

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- **Leonard Sacks, MD** – Associate Director for Clinical Methodology, Office of Medical Policy, FDA
- **Ryan Robinson, MD** – Office of Medical Policy/Clinical Methodology, FDA



# References

- **Conducting Clinical Trials With Decentralized Elements** – FDA Draft Guidance for Industry, Investigators, and Other Stakeholders
- **Digital Health Technologies for Remote Data Acquisition in Clinical Investigations** – FDA Final Guidance for Industry, Investigators and Other Stakeholders
- **Rare Diseases: Considerations for the Development of Drugs and Biological Products** – Guidance for Industry



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