Decentralized Clinical Trials

Regulatory Perspective

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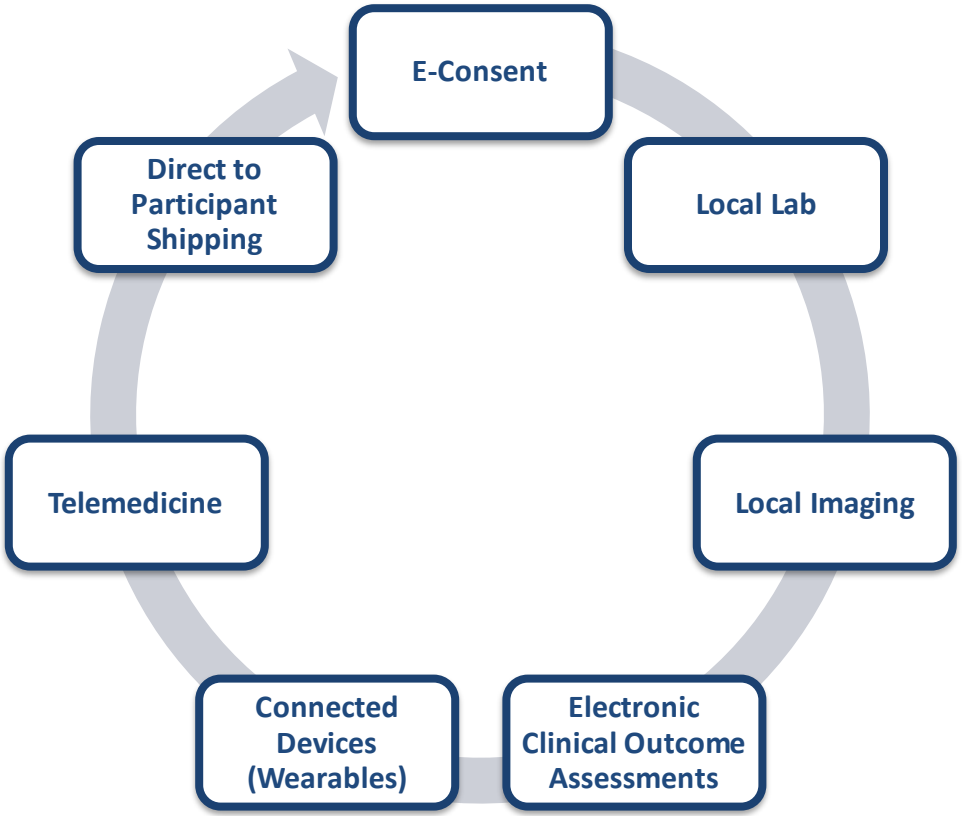
Decentralized Clinical Trials (DCT)

In FDA draft guidance[1], a DCT refers to a clinical trial where some or all trial-related activities occur at locations other than traditional clinical trial sites

[1]Decentralized Clinical Trials for Drugs, Biological Products, and Devices – FDA Draft Guidance for Industry, Investigators, and Other Stakeholders, 2023

DCT Elements – Strategies to Bring the Trial to the Patient



Why are Regulators Interested?

- Patient convenience
  - Travel, time off work
  - Decreased attrition?

- Accessibility
  - Diversity of participants
  - Improved accrual

- 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

Draft 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

Draft 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)

- Quality control measures should be in place to help reduce variability, including regular review by investigators of participant data entered by local HCPs

Draft 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

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

- The regulatory requirements for obtaining informed consent and the IRB review process due 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

Draft 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?

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.

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.

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References

- **Decentralized Clinical Trials for Drugs, Biological Products, and Devices** – 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


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