Decentralized Clinical Trials for Drugs, Biological Products, and Devices

Draft Guidance Webinar

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Decentralized Clinical Trials

In this draft guidance, a DCT refers to a clinical trial where some or all of the trial-related activities occur at locations other than traditional clinical trial sites.

Strategies to Bring the Trial to the Patient

- Video and telemedicine visits
- Digital health technologies
- Direct distribution of products
- Electronic informed consent
- Home visits
- Use of local health care providers and facilities

Why are Regulators Interested?

- Accessibility
  - Patients with rare diseases
  - Patients with mobility or cognitive challenges
  - Diversity of participants (socio-economic, cultural)
- Patient convenience
- Efficiencies
  - Travel
  - Physical facilities
  - Use of qualified community providers
- Experience with COVID-19
  - Contagious diseases

DCT Design

- Remote assessments may differ from on-site assessments
- Assessments performed by local HCPs may be more variable and less precise than assessments conducted by trial personnel
- Consideration of the statistical analysis to be performed
- For inspectional purposes, there should be a physical location where all clinical trial-related records for participants under the investigator's care are accessible and where trial personnel can be interviewed

Remote Trial Visits and Activities

- Remote visits can occur at locations such as a participants' homes or a local healthcare facility
- Telehealth visits can be considered by investigators
- Remote in-person visits and trial-related activities can be conducted by trial personnel who are sent to participants' homes or preferred locations
- Remote in-person visits and trial-related activities may also be conducted by local healthcare providers (HCPs) who are located close to trial participants' homes

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 clinical practice
- These services should not require a detailed knowledge of the protocol or the investigational product (IP)
- Trial-related activities unique to research and/or require a detailed knowledge of the protocol or the IP should be performed by qualified trial personnel who have been appropriately trained

Remotely Identified Adverse Events

- Protocol should specify how adverse events identified remotely will be evaluated and managed
- Protocol should describe how care will be provided for adverse events that require urgent or in-person attention
- Sponsor's and investigator's responsibilities to ensure that remote clinical trial visits conducted via telehealth comply with laws governing telehealth in the relevant U.S. states or territories and other countries, as applicable

Digital Health Technologies

- Incorporation of the use of DHTs into clinical trials can support decentralization
- Sponsors should ensure that DHTs are available and suitable for use by all trial participants
- Draft guidance on DHTs published in December 2021: *Digital Health Technologies for Remote Data Acquisition in Clinical Investigations*

Sponsor's Role and Responsibilities

- Sponsor responsibilities are the same for DCTs and traditional site-based clinical trials
- Should strive for diversity and inclusiveness in trial populations
- Must account for multiple sources of data collection in a DCT in the data management plan
- Should describe in the trial protocol how operational aspects of the DCT will be implemented

Sponsor: Monitoring and Compliance

- Must ensure proper monitoring of the investigation
- May use a variety of approaches to monitor DCTs, and the monitoring plan for a trial should be based on the sponsor's risk assessment
- Must comply with relevant local laws, regulations, and licensing requirements governing medical practice and IP administration when conducting a DCT

Investigator's Role and Responsibilities

- Responsible for the conduct of the DCT and the oversight of individuals delegated to perform trial-related activities
- A key difference for DCTs is the extent to which the investigator uses telehealth, trial personnel working remotely, local HCPs, and/or DHTs in the conduct of the trial
- Decentralized features may necessitate additional training, coordination, and standard operating procedures to ensure consistent implementation

Investigator Delegation of Activities

- When permitted by the trial protocol, investigators may delegate trial-related activities to local HCPs to perform trial-related procedures that require in-person interactions with trial participants
- A critical consideration when delegating trial-related activities to local HCPs is the potential for variability in the approach across different practices
- Videoconferencing and other technologies may be useful to allow investigators to oversee trial personnel performing activities described in the trial protocol at participants' locations

Documentation: Investigators, Subinvestigators, Local HCPs

- Drug trials (Form 1572)
  - When trial personnel contribute directly and significantly to the trial data, they should be included on Form FDA 1572 as subinvestigators
  - Local HCPs (as defined in the draft guidance) should not be listed on Form FDA 1572 as subinvestigators. However, local HCPs should be included in a task log.
- For device trials, local HCPs are generally not considered investigators and should not be included in the IDE list of investigators. However, these local HCPs should be included in a task log

Information Sheet Guidance for Sponsors, Clinical Investigators, and IRBs *Frequently Asked Questions – Statement of Investigator (Form FDA 1572)* (May 2010)

Task Log

- Investigators must maintain a task log of local HCPs who perform trial-related activities
- Task log should include:
  (1) The names and affiliations of the local HCPs
  (2) Description of their roles and assigned tasks
  (3) Dates these local HCPs are added to the log
  (4) Locations where these activities are conducted
- Should be dated and signed by the investigator when initially created and updated when a new local HCP is added
- Should be available to FDA during inspections

Clinical Laboratory Facilities

- Some trials will include designated clinical laboratory facilities to perform activities required by the protocol
- Others permit the use local laboratory facilities close to the trial participant to perform these activities
- If appropriate, specimens from trial participants may be collected by remote trial personnel, local HCPs, or clinical laboratory facilities and sent to designated facilities for processing
- All clinical laboratory facilities should be listed on Form FDA 1572 for drug trials or in the investigational plan for device studies under an IDE

Informed Consent and 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 the use of a central IRB in DCTs to facilitate efficient review of the protocol, informed consent documents, and other relevant trial-related information

Investigational Products: Drugs

- The nature of the drug should be considered when determining whether administration outside of a clinical trial site in a DCT is appropriate
  - Complexity of administration
  - Safety profile
  - Stage of drug development
- May be appropriate for local HCPs or trial personnel working remotely to administer the IP at local health care facilities or participants' homes
- Hybrid DCTs may be considered for drugs that require supervised but infrequent administration

Investigational Products: Devices

- Consider the type of medical device, its intended use, its instructions for use, and whether it is a significant risk or nonsignificant risk device
- Medical devices suitable for home use that do not pose significant risks to trial participants may be appropriate for use by trial participants without the investigator's direct oversight
- Use of medical devices that are not intended for self-use or that pose significant risks to trial participants should be used or administered by qualified trial personnel with investigator oversight

Distribution of IP

- DCTs may allow for the direct distribution of investigational products to trial participants at their locations
- Protocols should describe
  - how the physical integrity and stability of the IP will be maintained during shipment to trial participants
  - how investigators will track and document that trial participants receive IPs
  - procedures that investigators or participants should use to return or dispose of unused IPs and how this will be documented

Shipping of IP

- Shipping containers should include clear instructions for handling and storing the IPs and instructions for returning unused IPs
- A central distribution service can be used to ship the IP to trial participants
- Sponsors and investigators must comply with applicable Federal, State, and international laws and regulations that address shipping IPs in their respective jurisdictions

Safety Monitoring Plan

- Sponsors should implement a safety monitoring plan (SMP) to ensure the safety and welfare of trial participants
- SMP should take the decentralized nature of the clinical trial into account and ensure that adverse events are appropriately captured and adequately addressed.
- 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

Safety Monitoring Plan

- 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 significant safety risks emerge because of remote administration or use of an IP, sponsors must discontinue remote administration or use
- If authorized in the protocol, routine safety monitoring involving laboratory testing and imaging may be performed using local clinical laboratory facilities

Software in DCTs

- Software can be used to perform multiple functions to manage DCT operations
- Training should be provided to all parties using software to support the conduct of DCT
- Software programs that are used to produce and process trial records required by the FD&C Act and FDA regulations are subject to 21 CFR part 11
- Real-time video interactions, including telehealth, are not considered electronic records and are not subject to 21 CFR part 11

Docket Comments

Submit Comments by 08/01/2023

Submit Comments Online

Although you can comment on any guidance at any time (see 21 CFR 10.115(g)(5)), to ensure that the FDA considers your comment on a draft guidance before it begins work on the final version of the guidance, submit either online or written comments on the draft guidance before the close date.

If unable to submit comments online, please mail written comments to:

Dockets Management
Food and Drug Administration
5630 Fishers Lane, Rm 1061
Rockville, MD 20852

All written comments should be identified with this document's docket number:
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