

Agency Guidance Snapshot: Decentralized Clinical Trials for Drugs, Biological Products, and Devices (Draft Guidance)

The Yale Human Research Protection Program (HRPP) has launched the “Agency Guidance Snapshot” series. The purpose of the Agency Guidance Snapshots is to highlight recent agency guidance from the Food and Drug Administration (FDA)¹, Office for Human Research Protections (OHRP), and other federal agencies that specifically impacts Yale University and affiliate stakeholders who conduct or oversee **human subjects research**.

Please Note: Yale University does not expect any immediate changes to policies due to this guidance; however, this guidance will be taken into consideration as policies and procedures are reviewed and revised in the future. Yale University may have additional requirements related to the topics covered in this guidance. For more information, please refer to the following Yale University Human Research Protection Program (HRPP) documents located on the HRPP website ([Policies, Procedures, Guidance, and Related Documents](#)) and in the Yale HRPP IRES-IRB Library ([IRES IRB LOGIN](#)): **1) Yale HRPP Policy and Standard Operating Procedure Manual**; **2) Yale HRPP Investigator Manual**; **3) Yale IRB Members and Chairs Manual**; and **4) HRPP Supplemental Guidance Manual**. Please also refer to [University Policies & Procedures](#) and policies published by the various Yale University schools and departments.

Title of Document:	Decentralized Clinical Trials for Drugs, Biological Products, and Devices (Draft Guidance)
Federal Agency:	FDA
Document Release Date:	May 2023
Stakeholders Impacted:	Investigators <input checked="" type="checkbox"/> Sponsors <input checked="" type="checkbox"/> Sponsor/Investigators <input checked="" type="checkbox"/> IRB/HRPP Staff, Chairs, & Members <input checked="" type="checkbox"/> Other <input type="checkbox"/>
Hyperlink to Document:	https://www.fda.gov/regulatory-information/search-fda-guidance-documents/decentralized-clinical-trials-drugs-biological-products-and-devices

Overview of Guidance Document:

On May 1, 2023, the United States Food and Drug Administration (FDA) released a draft guidance titled "Decentralized Clinical Trials for Drugs, Biological Products, and Devices - Guidance for Industry, Investigators, and Other Stakeholders." This draft guidance provides recommendations for sponsors, investigators, and other stakeholders regarding the implementation of **decentralized clinical trials (DCTs)** for drugs, biological products, and devices. In this 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.

¹ FDA Guidance documents represent the Agency's current thinking on a particular subject. They do not create or confer any rights for or on any person and do not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both.

In fully decentralized clinical trials, all activities take place at locations other than traditional trial sites. These trial-related activities may take place at the homes of trial participants or in local health care facilities that are convenient for trial participants. In hybrid DCTs, some trial activities involve in-person visits by trial participants to traditional clinical trial sites, and other activities are conducted at locations other than traditional clinical trial sites, such as participants' homes.

Challenges related to DCTs may include coordination of trial activities with individuals and facilities in multiple locations that are not traditional clinical trial sites.

DCTs should include specific plans to facilitate the decentralization of the trial. These plans should include, as appropriate, the use of local health care facilities, local health care providers (HCPs), and local clinical laboratory facilities; visits to trial participants' homes; and direct distribution of the investigational product (IP) to trial participants at their locations. 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.

The DCT guidance also refers to advantages throughout. Specifically, "DCTs may enhance convenience for trial participants, reduce the burden on caregivers, and facilitate research on rare diseases and diseases affecting populations with limited mobility or access to traditional trial sites. This may help improve trial participant engagement, recruitment, enrollment, and retention of a meaningfully diverse clinical population." (Page 2 of the [full guidance document](#))

The guidance also emphasizes throughout the document that the FDA's regulatory requirements for investigations of medical products and adherence to Good Clinical Practice (GCP) are the same for DCTs and traditional site-based clinical trials. In addition, compliance with other relevant laws, regulations, and local requirements is also a requirement, as these may vary across different regions such as U.S. states, territories, and countries.

Key Points for Researchers, IRB/HRPP Staff, Chairs, & Members:

Recommendations for Implementing DCTs

The sections below provide key points on specific topics for DCT implementation. For full guidance on these topics, please review the [full guidance document](#).

A. DCT Design

- 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. This location should be listed on Form FDA 1572 or for investigational device exemption (IDE) applications must be included in the IDE application.
- The variability and precision of the data obtained in a DCT may differ from the data in a traditional site-based clinical trial. This would not affect the validity of a finding of superiority in a trial using such data (although it could reduce the effect size), but it could affect the validity of a finding of non-inferiority. Remote assessments may differ from on-site assessments, particularly when trial participants are responsible for performing their own physiological tests (e.g., home spirometry). Assessments performed by local HCPs as

part of routine clinical practice (e.g., evaluation of symptoms) may also be more variable and less precise than assessments conducted by dedicated trial personnel.

B. Remote Clinical Trial Visits and Clinical Trial-Related Activities

- This section of the guidance also focuses on making trials more convenient and accessible for participants through recommendations regarding remote clinical trial visits and clinical trial-related activities.
- In general, investigators can consider telehealth visits instead of in-person visits with trial participants if no in-person interaction is needed. The protocol should specify when a telehealth visit with a trial participant is appropriate and when a participant should be seen in person.
- In-person visits and trial-related activities can be conducted by trial personnel who are sent to participants' homes or preferred locations.
- Depending on the trial protocol, in-person visits and trial-related activities may also be conducted by HCPs who are located close to trial participants' homes but are not part of the trial personnel.
- During each remote trial visit, investigators should confirm the trial participant's identity. FDA does not endorse any specific identification method.

C. Digital Health Technologies (DHTs)

- For detailed information on DHTs, please review the following FDA draft guidance document: [Digital Health Technologies for Remote Data Acquisition in Clinical Investigations](#).

D. Roles and Responsibilities

- Sponsor responsibilities are the same for DCTs and traditional site-based clinical trials.
- Investigators are responsible for the conduct of the DCT, and the oversight of individuals delegated to perform trial-related activities, including ensuring that these delegated activities and/or tasks are conducted according to the investigational plan, applicable regulations, and relevant laws. A key difference between DCTs and traditional site-based clinical trials is the extent to which the investigator uses telehealth, trial personnel working remotely, local HCPs, and/or DHTs in the conduct of the trial. Whether the trial can be conducted entirely using remote visits or a hybrid trial design is appropriate depends on the types of assessments and procedures needed to collect endpoints and monitor safety.
- The decentralized features of the trial may necessitate additional training, coordination, and standard operating procedures to ensure consistent implementation.
- Detailed information on the roles and responsibilities of the Sponsor, the Investigator, and the delegation of trial-related activities can be found starting on Page 6 of the [full guidance document](#).

E. Informed Consent and Institutional Review Board Oversight

- Obtaining informed consent remotely may be considered as part of a DCT. Institutional review board (IRB) oversight is required to ensure the process is adequate and appropriate.
- Investigators may obtain electronic informed consent from trial participants at their remote locations provided that all applicable regulatory requirements regarding informed consent are met. The process of obtaining electronic informed consent remotely may include a remote visit if needed.

F. Investigational Products (IPs) in a DCT

• Drugs and Biological Products

- The nature of the IP should be considered when determining whether administration outside of a clinical trial site in a DCT is appropriate.
- IPs that involve complex administration procedures; have a high-risk safety profile, especially in the immediate post-administration period; or are in early stages of development such that the safety profile is not well defined may need in-person supervision by the investigator at a trial site.
- For IPs for which the safety profile is well-characterized and that do not involve specialized monitoring during the immediate period following administration, it 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 designed for drugs that require supervised but infrequent (e.g., monthly) administration when administration can be done at trial sites with follow-up done remotely.

• Medical Devices

- When determining the appropriate use or administration of an investigational device in a DCT, sponsors should 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 (i.e., over-the-counter devices) that do not pose significant risks to trial participants may be appropriate for use by trial participants without the investigator's direct oversight.
- The use of medical devices that are not intended for self-use (i.e., devices used in hospital or ambulatory care settings) or that pose significant risks to trial participants should be used or administered by qualified trial personnel with investigator oversight.

G. Packaging and Shipping of Investigational Products

- Detailed information on the packaging and shipping of investigational products can be found starting on Page 12 of the [full guidance document](#).

Key Points for Sponsors:

H. Safety Monitoring Plan

- The sponsor is required to ensure proper monitoring of the investigations and to ensure that the investigations are conducted in accordance with the general investigational plan and protocols contained in the IND or IDE applications. Sponsors should implement a safety monitoring plan to ensure the safety and welfare of trial participants in a DCT.
- The safety monitoring plan should take the decentralized nature of the clinical trial into account and ensure that adverse events are appropriately captured and adequately addressed.
- Detailed information on safety monitoring plans can be found starting on Page 13 of the [full guidance document](#).

I. Software Used in Conducting DCTs

- Sponsors should consider the following regarding software used in a DCT:

- Software to support the conduct of DCTs can be run through a variety of platforms (e.g., tablets, cell phones, personal computers). Software can be used to perform multiple functions to manage DCT operations.
- Training should be provided to all parties (e.g., trial personnel, local HCPs, and trial participants) using software to support the conduct of DCTs.
- FDA considers real-time video interactions, including telehealth, as a live exchange of information between trial personnel and trial participants. These live interactions are not considered electronic records and, therefore, are not subject to 21 CFR part 11, but local laws governing telehealth may apply. Privacy and security of these real-time visits should be ensured, and the visits must be documented. If this documentation is captured in electronic form, such documentation is subject to 21 CFR part 11.
- Detailed information on software used in conducting DCTs can be found starting on Page 14 of the [full guidance document](#).

For more related information, please see the following links to additional resources:

- [FDA Website – Regulatory Information](#)
- [SACHRP Recommendations on “Decentralized Clinical Trials for Drugs, Biological Products, and Devices - Guidance for Industry, Investigators, and Other Stakeholders”](#)
- [AAMC Comments on Accelerating the Decentralization of Clinical Trials](#)
- [Clinical Trials Transformation Initiative – Planning Decentralized Trials](#)
- [The Multi-Regional Clinical Trials Center of Brigham and Women’s Hospital and Harvard - Oversight and Implementation of Decentralized Clinical Trials](#)
- [Ropes & Gray - FDA Guidance Clarifies Approach to Decentralized Clinical Trials](#)
- [Advarra - Decentralized Clinical Trials and Regulatory Changes](#)
- [WCG - Diversity & Inclusion with Technology in Decentralized Trials](#)
- [Johns Hopkins Medicine - Decentralized Clinical Trials \(DCTs\) FAQs](#)
- [Vayena, E., Blasimme, A., & Sugarman, J. \(2023\). Decentralised clinical trials: ethical opportunities and challenges. The Lancet Digital Health, 5\(6\), e390-e394.
\[https://doi.org/10.1016/S2589-7500\\(23\\)00052-3\]\(https://doi.org/10.1016/S2589-7500\(23\)00052-3\)](#)
- [Petrini C, Mannelli C, Riva L, Gainotti S and Gussoni G \(2022\) Decentralized clinical trials \(DCTs\): A few ethical considerations. Front. Public Health 10:1081150. doi:
\[10.3389/fpubh.2022.1081150\]\(https://doi.org/10.3389/fpubh.2022.1081150\)](#)