# FDA Draft Guidance Summary

## Decentralized Clinical Trials for Drugs, Biological Products, and Devices

The US Food and Drug Administration (FDA) has released a draft guidance document on decentralized clinical trials (DCTs) for drugs, biological products, and medical devices. This guidance outlines the FDA's recommendations for designing, executing, and evaluating these trials and provides guidance on ensuring patient safety and the accuracy of the data generated. Additionally, it includes information on how sponsors of these types of trials can use emerging technologies and remote monitoring methods to conduct the trials while still ensuring the safety of patients and the accuracy of the results.

Decentralized clinical trials (DCTs) are a modern approach to conducting clinical trials that allow some or all trial-related processes to be carried out at non-conventional locations. This can be more convenient for trial participants, as they may be able to complete trial-related activities in places like their homes or local healthcare facilities. A hybrid DCT combines traditional clinical trial settings with alternative locations for different activities. These new approaches offer exciting possibilities for clinical trial research and can improve patient participation.

FDA Nonbinding Recommendations for Decentralized Clinical Trials: M*ay 2023, Not for Implementation*[1]

## DESIGN OF DECENTRALIZED CLINICAL TRIALS

Decentralized clinical trials (DCTs) are becoming increasingly common, allowing trial-related activities in non-traditional locations like local healthcare facilities or the patient's home. Although the investigator oversees all activities like imaging and lab services, a physical location for clinical trial-related records and personnel interviews are required. This location must be disclosed on Form FDA 1572 or included in the investigational device exemption (IDE) application.[2]

## REMOTE CLINICAL TRIAL-RELATED ACTIVITIES

- When planning strategies for remote clinical trials, it is essential to keep in mind the convenience and accessibility these trials offer to participants. Consider the following points when creating your non-traditional clinical trial plans:

- Consider telehealth visits when in-person interaction is not required.[3] Case report forms and required documentation should be completed for all telehealth visits.

- In-person visits and trial-related activities can be conducted by trial personnel at participants' homes or other suitable locations.

- Activities related to the trial may also be done by health care professionals (HCPs) close to the trial participants' homes but not a part of the trial staff. These services should not require deep protocol knowledge or the investigational product (IP).

- Investigators must verify the identity of the trial participant during each remote trial visit.

- The protocol for the trial should outline how any adverse events identified remotely will be assessed and handled.

## DIGITAL HEALTH TECHNOLOGIES (DHTS) FOR REMOTE DATA ACQUISITION

Decentralized clinical trials are being powered by Digital Health Technologies (DHTs), which enable remote healthcare services. DHTs are versatile and can be used for various health purposes, including general wellness and medical device applications. Popular examples of DHTs include wearables, sensors, mobile health apps, and telemedicine platforms.

Through the use of DHTs, sponsors, clinical investigators, and participants can remotely measure critical clinical events and characteristics of interest. These technologies allow data transmission from anywhere, making trials more affordable, efficient, and safe. With DHTs, study participants can transmit data from anywhere, eliminating the need for constant in-person monitoring.

## ROLES & RESPONSIBILITIES OF SPONSORS AND INVESTIGATORS

The **responsibilities of sponsors** are the same for both DCTs and traditional trials conducted at a site.[4] It is important for sponsors to ensure that the trial population is diverse and inclusive.[5] To account for multiple data collection sources in a DCT, the sponsor should create a data management plan (DMP). This plan should include information about the origin and flow of data from all sources to the sponsor, such as a diagram showing how the data is created and stored. Additionally, the plan should detail the methods used for remote data acquisition from trial participants, trial personnel, and contracted service providers (e.g., local clinical labs and healthcare practitioners performing trial-related activities).[6,7] Lastly, the plan should contain a list of vendors involved in data collection, handling, and management.

**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 tasks are conducted according to the investigational plan, applicable regulations, and relevant laws.[8,9] When allowed by the trial protocol, a trial investigator may delegate trial-related activities to local HCPs to perform medical procedures requiring in-person interactions with trial participants (e.g., physical examinations).[10] These procedures may occur at the participant's location or another local healthcare facility as outlined by the trial protocol.

## INFORMED CONSENT AND IRB OVERSIGHT

Investigators can get electronic consent from trial participants at their remote locations as long as all necessary regulations regarding informed consent are met. Institutional review board (IRB) oversight is required to ensure the process is carried out correctly.[11] Obtaining electronic consent remotely may include a remote visit if necessary. The informed consent should detail who will have access to the personal health information gathered during the trial.[12]

## INVESTIGATIONAL PRODUCTS IN A DECENTRALIZED CLINICAL TRIAL

### Drugs And Biological Products

The investigator responsible for the trial must administer investigational products (IPs) only to participants under their direct supervision or the supervision of a sub-investigator.[13] The IP's complexity should be considered when deciding whether administration in a DCT is appropriate. IPs with a high-risk safety profile, especially in the immediate post-administration period or those still in the early stages of development such that their safety profile is not yet known, may require the investigator to be present at the trial site. However, if the safety profile of the IP is well-established and does not require specialized monitoring immediately following administration, it may be feasible for HCPs or trial personnel to administer the IP at local healthcare facilities or participants' homes.

Hybrid DCTs may be suitable for drugs that require supervised but infrequent (e.g., monthly) administration, as the administration can be done at trial sites with follow-up done remotely.

### Medical Devices

When deciding the proper use or application of an investigative device in a clinical trial, sponsors should consider the type of medical device, its purpose, how it should be used, and whether it poses a significant risk.[14] Medical devices that are safe to use at home (such as over-the-counter devices) and do not present substantial risks to the trial participants may be used in a DCT without the investigator's direct supervision. On the other hand, medical devices not meant for self-use (such as those used in hospitals or ambulatory care settings) or that pose a significant risk should be operated or administered by qualified trial personnel, and the investigator should be present to oversee it.

## PACKAGING AND SHIPPING REQUIREMENTS FOR INVESTIGATIONAL PRODUCTS

DCTs may allow investigational products to be directly distributed to trial participants at their locations.[15] The protocol should detail how the physical integrity and stability of the IP will be maintained during shipment, including the packaging materials and methods that should be used (e.g., temperature control). A central distribution service may be employed to ship the IP to trial participants. It is the responsibility of the investigator or delegated trial personnel to control the release of the IP from the distributor, monitor receipt and use by trial participants (or their legal representatives) according to the protocol, and monitor the return or disposal of any unused product as directed by the sponsor.[16] It is important to adhere to applicable Federal, State, and international laws and regulations that address the shipping of IPs in the respective jurisdictions.

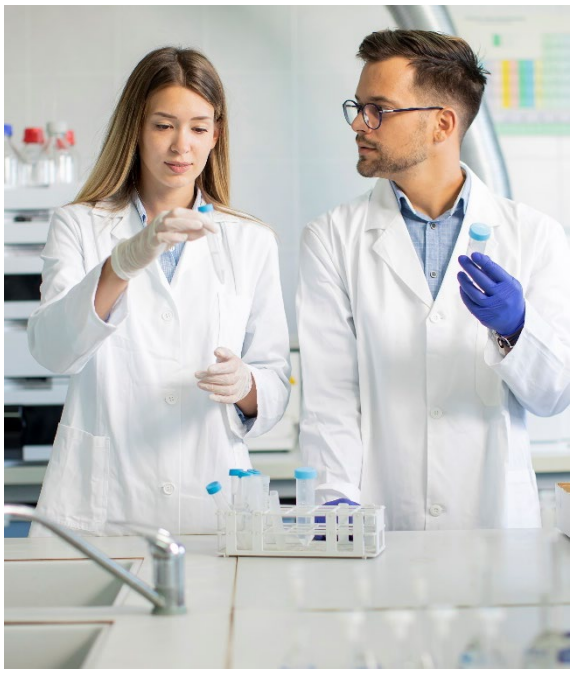
## SAFETY MONITORING PLAN

The sponsor must ensure the investigation is monitored correctly and carried out according to the general investigational plan and protocols in the IND or IDE applications.[17] A safety monitoring plan should also be implemented to guarantee the safety of participants in a DCT, including information on how to report and respond to any adverse reactions, as well as where to find local medical help and follow-up care.[18] If any significant safety concerns arise from the remote administration or use of an IP, the sponsor must immediately stop the remote administration or use, inform the FDA, IRB, and all the investigators involved, and decide if the trial should go on.[19]

# SOFTWARE USED FOR MANAGING DCTS

Software can be used to help manage clinical trials (DCTs) on various platforms, such as tablets, cell phones, and personal computers. This software can be used to perform many tasks, including managing electronic informed consent forms, capturing and storing reports from remote trial personnel and HCPs, managing electronic case report forms (eCRFs), scheduling trial visits and activities, tracking the shipment of IPs to trial participants, syncing data recorded by DHTs, and serving as a communication tool between trial personnel and participants. Local HCPs can submit trial-related data to be included in records in several ways, such as entering it directly into the eCRF or uploading forms and documents through secure data transfer methods.[20] Investigators or other trial personnel are then responsible for entering this data into the eCRF, and any remote trial personnel or local HCPs submitting data directly should be on the sponsor's list of authorized data originators.[21,22]

Software programs used to generate and manage trial data required by the FD&C Act and FDA regulations are subject to 21 CFR Part 11. These programs must ensure the data's accuracy, security, privacy, and confidentiality.[23,24] Real-time video interactions, such as telehealth, as a live exchange of information between trial personnel and participants, are not considered electronic records and are not subject to 21 CFR Part 11. However, local laws related to telehealth may still be applicable. It is important to ensure the privacy and security of these real-time visits and to document them.[25] If this documentation is stored electronically, it is subject to 21 CFR Part 11.



# SUMMARY

Digital technology is opening up a wide range of possibilities for clinical trials. Remote activities involving participants no longer need to occur exclusively at traditional clinical trial sites using software solutions and services capable of running fully remote, virtually managed decentralized clinical trials (DCTs). However, implementing DCTs comes with its challenges and complexities. For example, remote assessments may differ from on-site assessments, especially when trial participants are responsible for performing their own physiological tests (e.g., home spirometry).

Assessments done by local healthcare professionals (HCPs) as part of their regular clinical practice, such as evaluating patient symptoms, may also be more variable and less precise than assessments done by dedicated trial personnel. Combining in-house and HCP expertise with the latest technologies can help minimize patient testing variance, while enterprise risk assessments and secure data management systems can help ensure data collection and privacy remain protected.

The potential benefits of DCTs are vast. They expand access to more diverse patient populations, increase trial efficiency, and provide greater convenience for participants and caregivers. Telehealth, digital health technologies (DHTs), and remote data collection enable trial participation from different locations. This can help improve participant engagement, recruitment, enrollment, and retention of a more meaningfully diverse clinical population.

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# REFERENCES


[1] This guidance has been prepared by the Center for Drug Evaluation and Research (CDER) in cooperation with the Center for Biologics Evaluation and Research (CBER), the Center for Devices and Radiological Health (CDRH), and the Oncology Center of Excellence (OCE) at the Food and Drug Administration.

[2] See 21 CFR 812.20(b).

[3,4] See 21 CFR parts 312 and 812.

[5] FDA, Diversity Plans to Improve Enrollment of Participants from Underrepresented Racial and Ethnic Populations in Clinical Trials – Draft Guidance, April 2022, https://www.fda.gov/media/157635/download, accessed May 23, 2023.

[6,23] FDA, Electronic Systems, Electronic Records, and Electronic Signatures in Clinical Investigations: Questions and Answers – Draft Guidance, March 2023, https://www.fda.gov/media/166215/download, accessed May 23, 2023.

[7] FDA, Digital Health Technologies for Remote Data Acquisition in Clinical Investigations —Draft Guidance, December 2021, https://www.fda.gov/media/155022/download, accessed May 23, 2023.

[8] See 21 CFR 312.60, 312.61, and 812.100.

[9] FDA, Guidance for Industry Investigator Responsibilities — Protecting the Rights, Safety, and Welfare of Study Subjects, October 2009, https://www.fda.gov/media/77765/download, accessed May 24, 2023.

[10] See 21 CFR 312.3 and 812.3.

[11] See 21 CFR 56.103, 56.104, and 56.105.

[12] See 21 CFR part 50, 21 CFR 50.25, 21 CFR 50.27, and FDA, Use of Electronic Informed Consent: Questions and Answers – Guidance for Institutional Review Boards, Investigators, and Sponsors, December 2016, https://www.fda.gov/media/116850/download, accessed May 24, 2023.

[13] See 21 CFR 312.61.

[14] FDA, Information Sheet Guidance for IRBs, Clinical Investigators, and Sponsors — Significant Risk and Nonsignificant Risk Medical Device Studies, January 2006, https://www.fda.gov/media/75459/download, accessed May 24, 2023.

[15] See 21 CFR 312.61. 39 and FDA, Guidance for Industry CGMP for Phase 1 Investigational Drugs, July 2008, https://www.fda.gov/media/70975/download, accessed May 24, 2023.

[16] See 21 CFR 312.61, 312.62(a), and 812.110.

[17] [21] CFR 312.50, 21 CFR 812.40 and FDA, Oversight of Clinical Investigations — A Risk-Based Approach to Monitoring — Guidance for Industry, August 2013, https://www.fda.gov/media/116754/download, accessed May 24, 2023.

[18] FDA, E6(R2) Good Clinical Practice: Integrated Addendum to ICH E6(R1) — Guidance for Industry, March 2018, https://www.fda.gov/media/93884/download, accessed May 24, 2023.

[19] See 21 CFR 312.56(d) and 812.46.

[20,22,24] FDA, Guidance for Industry Electronic Source Data in Clinical Investigations, September 2013, https://www.fda.gov/media/85183/download, accessed May 24, 2023.

[21] See 21 CFR 312.62 and 812.140.

[25] See 21 CFR 312.62(b) and 812.140(a)(3).

All CFR regulations cited above can be accessed through this portal: National Archives, Code of Federal Regulations Title 21, March 28, 2023, https://www.ecfr.gov/.