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Navigating Decentralized Clinical Trials With FDA's Guidance

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On Sept. 18, the U.S. Food and Drug Administration issued final guidance titled "Conducting Clinical Trials With Decentralized Elements," for sponsors, investigators and other interested parties to support drug, biologic and medical device development.[1]

Decentralized clinical trials, or DCTs, are reshaping traditional clinical research by shifting some or all trial-related activities to remote locations, including participants' homes, local healthcare facilities or mobile units, rather than conventional clinical trial sites.

This model aims to make trials more accessible, improve participant diversity and increase operational efficiency. However, the remote nature of DCTs also presents distinct legal and regulatory complexities that sponsors must navigate carefully.

This final FDA guidance, while not legally binding, reflects the FDA's current thinking on the subject, and serves as a road map for sponsors, investigators and others involved in DCTs to ensure trial integrity and participant safety.

For sponsors, adapting to the DCT framework means building strategies that align decentralized protocols with traditional regulatory requirements, while addressing potential barriers such as cybersecurity risks, data integrity concerns and telehealth privacy laws. Additionally, DCTs often require engagement with regulatory bodies like the European Medicines Agency, or EMA, to harmonize requirements across international sites.

This article provides a detailed examination of the FDA's DCT guidance, the legal implications for sponsors, and strategic recommendations and practice tips to overcome the challenges in this evolving regulatory landscape.

Structuring Decentralized Clinical Trial Protocols

The FDA's guidance emphasizes the importance of developing well-structured protocols for DCTs. A thorough protocol helps mitigate variability and bias introduced by decentralized data collection, ensuring the reliability of trial data.

Sponsors are encouraged to specify clear instructions for trial activities conducted remotely, which could include local laboratory testing, home health visits or self-administered assessments by participants. In a

decentralized environment, protocols need additional details regarding each location's role, outlining where and how data is collected, consistency in data format, and communication across platforms, in addition to clarifying roles for local healthcare providers, trial personnel and participants.

From a legal perspective, the FDA advises sponsors to consult early with agency review divisions, especially for trials where statistical approaches might present challenges in remote settings. For instance, noninferiority trials in which drug effect sizes were established in traditional settings may yield different outcomes in a decentralized environment, affecting the calculation of noninferiority margins.

Such challenges underscore the need for early FDA consultation to align DCT protocols with regulatory expectations.

Remote Visits, Monitoring and Data Collection

Remote clinical visits and decentralized monitoring are central features of DCTs, providing participants flexibility but requiring robust data management and privacy safeguards. The FDA guidance allows sponsors to replace certain in-person visits with telehealth or local healthcare provider interactions, as long as participant safety and trial integrity are preserved.

For example, telehealth can replace physical visits for participants with conditions that do not necessitate immediate in-person assessments. However, the guidance also recommends that sponsors include provisions for adverse event management, specifying how remote adverse events will be identified, reported and addressed in a timely manner.

The reliance on remote data collection presents unique compliance challenges. Federal and state telehealth laws, as well as international data protection regulations, such as the European Union's General Data Protection Regulation, may govern the transfer and storage of participant data.[2]

Sponsors must ensure that remote data acquisition methods — including telehealth and digital health technologies, or DHTs — adhere to these laws. Protecting participant privacy and complying with applicable privacy regulations is critical, particularly as remote interactions increase the risk of data breaches.

To facilitate compliance, sponsors should develop a comprehensive data management plan that details the origin and flow of data, methods for secure data transmission, and a protocol for managing potential adverse events in remote settings. A risk-based monitoring approach can help identify and address data inconsistencies, outliers and protocol deviations.

By centralizing oversight and prioritizing data accuracy, sponsors can mitigate risks associated with remote data collection and ensure trial compliance.

Leveraging Digital Health Technologies: Benefits and Cybersecurity Challenges

DHTs, such as wearable sensors, mobile health apps and remote monitoring devices, are integral to many DCTs.[3] These technologies enable real-time data acquisition, allowing trial participants to record health metrics from any location.

The FDA guidance supports the use of DHTs, but stresses the need for secure and reliable data handling. Cybersecurity and data protection are paramount, especially in international trials where sponsors must

navigate various regulatory standards.

For sponsors, cybersecurity protocols must address potential vulnerabilities in data transmission and storage, ensuring that all trial personnel receive training on secure data management practices. In the event that participants lack access to compatible DHTs, the guidance advises sponsors to provide devices to maintain participant inclusivity.

This inclusiveness is particularly important for reaching diverse socioeconomic groups and minimizing the digital divide, which can otherwise lead to participant underrepresentation.

Sponsors should assess the regulatory requirements for DHTs not only with the FDA, but also with global regulators such as the EMA. A coordinated approach to cybersecurity standards across jurisdictions can prevent costly regulatory hurdles, minimize delays and support global trial scalability.

Ensuring that cybersecurity measures meet the standards of each regulatory body involved will also help sponsors protect participant data and maintain compliance.

Defining Roles and Responsibilities for Decentralized Trials

The FDA guidance delineates specific responsibilities for sponsors and investigators within DCTs, underscoring the need for clarity and accountability in remote settings. Sponsors are responsible for ensuring appropriate coordination, especially when contracting with networks of local healthcare providers or utilizing remote trial personnel.

This coordination should include a record of roles, tasks and qualifications for all contracted service providers, ensuring alignment with trial protocols and adherence to regulatory standards.

The legal implications of managing such a decentralized structure can be significant. Since data may originate from multiple sources, sponsors must establish a clear chain of accountability and define a monitoring framework for trial consistency.

The guidance recommends that sponsors use centralized and risk-based monitoring techniques to oversee protocol adherence, manage deviations and proactively address data irregularities. Sponsors must also ensure that DCT participants represent the intended patient population, taking steps to improve diversity and inclusivity.[4]

Expanding trial access through local healthcare providers and at-home visits can help sponsors reach underrepresented populations, ultimately contributing to more generalizable trial outcomes.

Investigators retain primary responsibility for participant safety and data integrity, even when activities are delegated to local providers. Protocols must include explicit instructions for local providers conducting trial-related activities, such as obtaining vital signs or performing basic examinations.

Though delegation is permitted, investigators must regularly review data submitted by local providers, monitoring for quality and consistency. To maintain oversight, investigators are encouraged to use telehealth for direct participant interactions, allowing for real-time assessments and intervention when necessary.

Informed Consent and IRB Oversight in Decentralized Settings

The FDA's guidance clarifies requirements for obtaining informed consent in DCTs, especially when using electronic consent tools.[5] Informed consent must still adhere to FDA regulations, whether it is obtained in person or remotely.

Sponsors and investigators are encouraged to use a centralized institutional review board, or IRB, to streamline consent processes, particularly in multicenter or international trials.[6] The process of informed consent in a decentralized trial setting must address unique privacy and data protection challenges.

Participants must be informed about who will have access to their data, especially when local providers or third-party contractors are involved. Sponsors are required to outline the specific roles of each party with access to participant data, ensuring transparency and regulatory compliance. Importantly, remote consent interactions should be documented comprehensively, including the name of the individual who obtained consent and the type of remote interaction used.

The guidance also stresses that local healthcare providers, while able to perform certain trial tasks, should not handle informed consent. This responsibility should fall to individuals with a thorough knowledge of the protocol who can answer participant questions and address concerns, preserving participant autonomy and compliance with FDA standards.

Management of Investigational Products in DCTs

One of the key challenges in DCTs is managing investigational products that may require specialized handling, administration or monitoring. While some products, particularly those with well-characterized safety profiles, may be suitable for direct shipment and home administration, others with higher risk profiles require in-person supervision at a clinical trial site.

The FDA guidance advises sponsors to evaluate the suitability of each investigational product for remote administration, considering both the complexity of the product and the participant's medical condition. For trials that involve direct shipping of investigational products, the FDA requires detailed tracking protocols to maintain accountability.

Trial personnel must be trained in handling, packaging and documenting these products, ensuring that proper storage and usage instructions accompany every shipment. Sponsors should also implement mechanisms for tracking receipt and return of unused products to mitigate risks of loss, contamination or unauthorized use.

While the FDA guidance does not address insurance coverage for remote equipment and services in DCTs, there is a growing potential for sponsors to engage with insurance providers to cover essential remote trial elements. This could include costs associated with DHTs, mobile units and telehealth equipment required by participants.

As DCTs expand, remote monitoring devices and home-based care services play critical roles in data collection and participant engagement, yet the expenses associated with these decentralized resources may place a financial burden on both sponsors and participants. Some sponsors are beginning to explore partnerships with insurance providers to offset these costs, particularly to increase trial accessibility and participant retention.[7]

This proactive approach could help streamline DCT budgets, reduce out-of-pocket expenses for participants and support equity in trial participation by ensuring that socioeconomic factors do not hinder access to remote trial infrastructure.

Harmonizing International Standards and Cross-Border Considerations

DCTs involving international sites necessitate careful coordination with regulatory authorities outside the U.S., including the EMA. Sponsors are encouraged to engage with international regulators early in the trial planning process to address jurisdictional differences and harmonize standards across trial sites.

This collaborative regulatory approach can help mitigate delays in DCT approval and reduce barriers to market entry, ultimately facilitating broader access to innovative treatments.

Working with global regulatory agencies requires sponsors to account for differing privacy, telehealth and data protection regulations. Sponsors will need to navigate data transfer laws in each jurisdiction, and ensure that cybersecurity and data protection measures align with both FDA and EMA standards.

Effective coordination can expedite trial initiation, facilitate regulatory compliance and reduce operational friction in international DCTs.

Conclusion

The FDA's guidance on decentralized clinical trials reflects the agency's commitment to modernizing clinical research, offering sponsors an opportunity to expand trial accessibility and enhance participant convenience. However, the decentralized model also requires sponsors to adapt operational processes, establish robust cybersecurity measures and build transparency into trial management.

By engaging with regulatory agencies and adopting structured data management practices, sponsors can address the unique challenges posed by DCTs and drive greater inclusivity in clinical research.

In the evolving landscape of decentralized clinical trials, sponsors who proactively develop compliance strategies and engage in cross-border regulatory discussions will be well-positioned to lead in the next generation of clinical innovation. With careful planning and adherence to regulatory guidance, sponsors can leverage DCTs to improve trial efficiency, diversity and overall data quality, advancing healthcare outcomes on a global scale.

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[1] U.S. Dep't of Health and Human Servs. et al., Conducting Clinical Trials With Decentralized Elements Guidance for Industry, Investigators, and Other Interested Parties, U.S. Food and Drug Admin. (Sept. 2024), https://www.fda.gov/media/167696/download. A draft guidance of this finalized guidance was previously issued on May 3, 2023, titled "Decentralized Clinical Trials for Drugs, Biological Products, and Devices."

[2] The European Union's General Data Protection Regulation (GDPR), effective since May 25, 2018, is a comprehensive data privacy law that establishes strict guidelines for the collection, processing, storage and transfer of personal data within the EU and European Economic Area. It aims to safeguard individuals' privacy rights by enforcing principles such as data minimization, accuracy, purpose limitation and accountability. The GDPR requires organizations to obtain explicit consent for data processing, uphold individuals' rights to access and delete their data, and implement appropriate security measures. Noncompliance can lead to significant fines, making GDPR one of the most stringent privacy regulations globally. See European Commission, Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (General Data Protection Regulation). Available at: https://eur-lex.europa.eu/eli/reg/2016/679/oj/eng.

[3] See also U.S. Dep't of Health and Human Servs. et al., Digital Health Technologies for Remote Data Acquisition in Clinical Investigations Guidance for Industry, Investigators, and Other Stakeholders, U.S. Food & Drug Admin. (Dec. 2023), https://www.fda.gov/media/155022/download and U.S. Dep't of Health and Human Servs. et al., Electronic Systems, Electronic Records, and Electronic Signatures in Clinical Investigations Questions and Answers Guidance for Industry, U.S. Food and Drug Admin. (Oct. 2024), https://www.fda.gov/media/166215/download.

[4] See also U.S. Dep't of Health and Human Servs. et al., Diversity Action Plans to Improve Enrollment of Participants from Underrepresented Populations in Clinical Studies Guidance for Industry Draft Guidance, U.S. Food and Drug Admin. (June 2024), https://www.fda.gov/media/179593/download.

[5] See U.S. Dep't of Health and Human Servs. et al., Informed Consent Guidance for IRBs, Clinical Investigators, and Sponsors, U.S. Food and Drug Admin. (Aug. 2023), https://www.fda.gov/media/88915/download. See also U.S. Dep't of Health and Human Servs. et al., Use of Electronic Informed Consent Questions and Answers Guidance for Institutional Review Boards, Investigators, and Sponsors, U.S. Food and Drug Admin. (Dec. 2016), https://www.fda.gov/media/116850/download.

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[7] See, A Complex Picture: What to Know About Clinical Trials Insurance, Applied Clinical Trials (May 15, 2023), 32(5), https://www.appliedclinicaltrialsonline.com/view/a-complex-picture-what-to-know-about-clinical-trials-insurance. See also, Insurance Coverage of Clinical Trials At a Glance, American Society of Clinical Oncology (ASCO) (July 2019), https://society.asco.org/sites/new-www.asco.org/files/content-files/research-and-progress/documents/2019-ASCORCF-InsuranceCoverage-AtaGlance.pdf.