FDA Guidance Offers Additional Clarity for Decentralized Clinical Trials

May 30, 2023

On May 2, 2023, the Food and Drug Administration ("FDA") released new draft guidance (the "Draft DCT Guidance") detailing key recommendations for entities conducting decentralized clinical trials ("DCTs") for drugs, biological products and devices.[1] DCTs are studies where subjects are not required to be assessed at a designated study site but instead may be geographically dispersed. Decentralization has emerged as a key strategy for modernizing clinical trials, and the new Draft DCT Guidance reflects FDA's commitment to expand DCT use as an important tool to address public health needs.[2] FDA is accepting comments and suggestions regarding the Draft DCT Guidance through August 1, 2023, but the agency has indicated that it will accept comments submitted after that date as well.

The Draft DCT Guidance highlights the long-term benefits that DCTs may provide: improved patient engagement, recruitment, enrollment and retention of diverse clinical populations; reduced financial and caregiver burdens; and more efficient trial timelines. DCTs offer particular benefits to companies engaged in rare disease research, where it is often challenging to identify a sufficient number of potential subjects in close proximity to traditional study sites. The shift toward virtual studies can also improve health equity by offering state-of-the-art research opportunities to low-income and rural patients who might not otherwise have the time or resources to take part in clinical trials.

The global DCT market is growing at a rapid rate, reflecting the recent surge in deal volume in this space which coincided with the COVID-19 pandemic and the pandemic-related focus on telehealth and remote patient monitoring. Similarly, venture capital investment in this sector increased significantly, most notably exemplified by Blackstone Growth's $304 million Series D investment in Medable, Inc., one of the

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1 *See Decentralized Clinical Trials for Drugs, Biological Products, and Devices: Guidance for Industry, Investigators, and Other Stakeholders*, available here.

2 U.S. Food & Drug Admin., Statement by FDA Commissioner Scott Gottlieb, M.D., on New Strategies to Modernize Clinical Trials to Advance Precision Medicine, Patient Protections and More Efficient Product Development (2019), https://www.fda.gov/news-events/press-announcements/statement-fda-commissioner-scott-gottlieb-md-new-strategies-modernize-clinical-trials-advance.

fastest growing DCT platform providers, in 2021. The Draft DCT Guidance will supply additional impetus to this growth in DCTs by providing greater clarity on how sponsors, investigators, and other industry stakeholders may satisfy regulatory obligations.

Background: Decentralized Clinical Trials

DCTs are studies with assessments or visits that are conducted at locations other than the investigator site. Investigators conduct assessments or visits through (i) telehealth; (ii) mobile or local healthcare providers (including local labs and imaging centers); and/or (iii) home delivery of investigational products. Some DCTs may use a hybrid approach where some visits are conducted onsite and others are performed remotely. While DCTs may involve a complicated network of locations for trial participants, investigators, trial-related services, and local healthcare providers, the Draft DCT Guidance recommends, for inspectional purposes, maintaining at least one physical location where all clinical trial-related records for participants are accessible and where trial personnel can be interviewed by FDA.[3]

The healthcare industry's embrace of DCTs reflects rapidly evolving regulatory oversight of the clinical trial sector. FDA, which has been actively involved in developing policies related to DCTs, issued draft guidance in March of 2020 to facilitate DCTs in response to the COVID-19 pandemic.[4] FDA then issued draft guidance in December 2021 on the use of digital health technologies to collect data from clinical trial participants remotely.[5]

While the Draft DCT Guidance, of course, does not impose binding requirements on affected parties, when finalized, the Draft DCT Guidance will represent FDA's current thinking on DCTs.[6]

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[3] The DCT Guidance further clarifies that this physical location should be listed on Form FDA 1572, or for investigational device exemption ("IDE") applications, the physical location should be included in the IDE application.

[4] The 2020 guidance is available here.

[5] U.S. Food & Drug Admin., Digital Health Technologies for Remote Data Acquisition in Clinical Investigations: Draft Guidance for Industry, Investigators, and Other Stakeholders (2021).

[6] *See Decentralized Clinical Trials for Drugs, Biological Products, and Devices: Guidance for Industry, Investigators, and Other Stakeholders*; *see also* 21 C.F.R. §§ 10.115(d)(1)-(2). FDA addresses DCTs in its recent discussion paper on artificial intelligence ("AI") and machine learning ("ML") in the drug and biological product development process (highlighting how AI and ML can supplement the design and efficiency of DCTs). *See Using Artificial Intelligence & Machine Learning in the Development of Drug & Biological Products*, available here. For more information on FDA's discussion paper, see Debevoise In Depth: Artificial

Key Takeaways from the DCT Draft Guidance

Key provisions from the Draft DCT Guidance include:

- **No New Regulatory Requirements**. DCTs are subject to the same regulatory requirements that apply to traditional site-based trials. The recommendations contained in the Draft DCT Guidance clarify how sponsors and investigators may fulfill their regulatory obligations.

- **Promoting Diversity**. FDA highlights the importance and benefit of recruiting and retaining a diverse patient population (e.g., by race, ethnicity, age, sex, and geographic location).

- **Fully Remote vs. Hybrid DCTs**. The Draft DCT Guidance provides factors to help sponsors determine whether it is appropriate to conduct a DCT on a fully remote basis or with a hybrid approach. For example, simple investigational products that are relatively easy to administer or that have a low-risk safety profile may be appropriate for fully remote DCTs, while those with complex administration procedures or high-risk safety profiles should utilize a hybrid approach.

- **Sponsor Oversight**. Because study sponsors are ultimately responsible for the proper monitoring of an investigation, the Draft DCT Guidance recommends: (i) maintaining a data management plan to coordinate multiple sources of data; (ii) specifying certain operational aspects of the DCT in the trial protocol (e.g., scheduled and unscheduled clinical trial visits, transmission of reports of activities performed at different locations, delivery of investigational products to trial participants); (iii) implementing a robust safety monitoring plan; and (iv) maintaining a monitoring plan that will address, among other things, protocol compliance, data quality and integrity.

- **Consulting FDA**. While DCTs greatly expand the geographic reach and population of clinical trials, they may present issues related to study feasibility, design, implementation and analysis. FDA recommends, particularly for non-inferiority DCTs, consulting the relevant FDA review division early in the trial process. [7]

Intelligence and the Life Sciences Industry: FDA and FTC Regulatory Update (May 16, 2023), available here.

[7] FDA suggests consulting FDA review divisions for non-inferiority trials as the variability and precision of data obtained from a DCT may differ from that obtained in site-based trials, which could affect the validity of non-inferiority findings and margins.

- **Proper Training**. FDA suggests that all parties to a DCT receive proper training depending on their role. Trial personnel should receive training on the specific decentralized features of a DCT; conducting trial-related activities including the administration of investigational products, and the handling, packaging, and shipping of investigational products to trial participants' locations; and follow-up procedures related to medical devices. All parties should be trained on how to conduct or participate in a telehealth visit[8] and how to use software to support the conduct of DCTs.

Additional Investor Considerations

The proliferation of DCTs is indicative of the healthcare industry's acceptance of telemedicine and the corresponding industry-wide shift toward remote care. The ability to untether research studies from traditional, in-person trial sites advances health equity by expanding the pool of potential participants to marginalized communities that traditionally have been excluded from clinical trials due to a lack of time, resources and access and, ultimately, will help to expedite the process of bringing new therapies to market—particularly for companies developing therapies for rare diseases.

Further, the projected growth of the DCT industry presages a significant opportunity for investors in the life sciences industry in both companies developing drugs and devices that can benefit from sponsoring DCTs, and companies that provide DCT support.

In addition to the significant benefits associated with DCTs, investors should also consider potential regulatory complexities:

- **Fraud and abuse assessment**. While DCTs promise substantial benefits, they may bring uncertainty and risk with regard to fraud and abuse laws (e.g., the federal Anti-Kickback Statute). This is of particular concern given that the DCT Draft Guidance recommends that sponsors ensure that sponsor-provided digital health technologies used in DCTs are available for all participants, while simultaneously recommending that sponsors seek greater diversity of patient populations that may have diminished access to the very digital health technologies in use. Stakeholders should conduct

[8] The Draft DCT Guidance also clarifies that, while real-time telehealth interactions are not themselves considered electronic records subject to 21 C.F.R. Part 11, such visits must nonetheless be documented; documentation of telehealth visits, and software programs used to produce and process trial records, are both subject to 21 C.F.R. Part 11 (setting forth requirements for electronic records), and other applicable local laws.

both FDA and fraud and abuse risk assessments regarding DCTs and investors should inquire into target companies' compliance with such laws during diligence.

- **Data privacy and security issues**. DCTs may implicate a myriad of international, federal, state and local laws. In particular, various potentially conflicting data privacy and security laws and regulations may apply to DCT-related tools (e.g., telemedicine, real-time video conferencing, electronic health records, wearable devices) and practices. It is important to examine the risks associated with applicable laws, including whether: (i) appropriate safeguards are in place to protect sensitive participant data, and (ii) blockchain technology is utilized for clinical trial data management.

- **Data licensing and ownership rights**. The DCT Draft Guidance leaves open the possibility that DCT participants may, in certain circumstances, use their own mobile and other devices. General-purpose devices with end-user licensing agreements or terms of service (e.g., mobile phones) may, however, have provisions that allow for data sharing with manufacturers and other parties.[9] In light of such agreements, investors should assess whether trial sponsors are ensuring that their informed consent protocols contain sufficient disclosures with regard to who may have access to participants' trial data (e.g., sponsors, contract research organizations, technology vendors and other partners).

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We will continue to monitor the status of the DCT Draft Guidance and other similar federal and state legislative developments regarding decentralized clinical trials.

[9] This was highlighted in FDA's prior draft guidance on DHTs: DIGITAL HEALTH TECHNOLOGIES FOR REMOTE DATA ACQUISITION IN CLINICAL INVESTIGATIONS: DRAFT GUIDANCE FOR INDUSTRY, INVESTIGATORS, AND OTHER STAKEHOLDERS, *supra* note 15, at 16.

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