On Remote Control: FDA Issues Draft Guidance to Facilitate Use of Digital Health Technologies for Remote Data Acquisition in Clinical Trials

 During the COVID-19 pandemic, decentralized clinical trials and remote patient monitoring and data acquisition became a necessity, accelerating the use of digital health technologies in clinical trials. Acknowledging that technological advances "have revolutionized the ability to remotely obtain and analyze clinically relevant information from individuals" and that "DHTs [ ] are playing a growing role in health care and offer important opportunities in clinical research," the FDA issued during the last week of December 2021 a draft guidance, *Digital Health Technologies for Remote Data Acquisition in Clinical Investigations*, which provides recommendations for sponsors, investigators and other stakeholders to facilitate the use of DHTs for remote data acquisition in clinical trials, including clinical trials that will be submitted to the FDA in a marketing application for a medical product.

The draft guidance defines a digital health technology (DHT) as a system that uses computing platforms (such as a mobile phone, tablet, or smart watch), connectivity, software, and/or sensors for healthcare and related uses. Some DHTs may meet the definition of "device" under the Federal Food, Drug and Cosmetic Act, but the draft guidance specifically does not address the circumstances under which a DHT would meet the statutory definition of a device and notes that DHTs used in clinical investigations generally are exempt from premarket clearance or approval requirements, as long as the clinical investigation is compliant with 21 CFR Part 812.

The draft guidance explains that sponsors must foremost ensure that a DHT is "**fit-for-purpose**" for its proposed use in a specific clinical investigation. In essence, the level of verification and validation associated with the DHT must be sufficient to support its use and interpretability in the clinical investigation. This may require sponsors to work with the developer or manufacturer of the DHT, patients, caregivers, and other technical and clinical experts to assure that the DHT is suitable for its intended purpose in the clinical investigation. The draft guidance advises sponsors to select a DHT that corresponds to the clinical outcome to be assessed, and that considers the clinical trial population and the design/operating characteristics of the DHT that may affect trial participants' use of the DHT.

Sponsors should also be prepared to describe how they will analyze data collected from DHTs in their statistical analysis plan, including prespecifying "**intercurrent events**" (defined as events that occur after treatment initiation that result in missing or erroneous data associated with the clinical outcome of interest) that may be related to the DHT and/or the general purpose computing platform, and how these events will be accounted for in the analysis. To maintain data integrity, FDA

recommends that the output of the DHT and associated metadata be transmitted to a **durable electronic data repository** that is protected from alterations and maintained until the end of the record retention period. FDA generally will consider data in such a repository to constitute the source data and should be made available for inspection and to reconstruct and evaluate the clinical investigation.

FDA further notes that "unique privacy risks" may arise when DHTs are used in a clinical trial. Sponsors are advised to evaluate the risk of potential disclosures of personally identifiable information through breaches of the DHT, the general computing platform on which the DHT runs, and/or the durable electronic repository, assure appropriate security safeguards are in place, and consider including such information in the informed consent documents for the clinical trial.

The draft guidance recommends that sponsors:

- train trial participants and trial personnel on the use of DHTs and develop a plan to provide technical assistance to trial participants and study personnel;
- develop a risk management plan to address potential problems with the DHT (e.g., interference between mobile applications, or loss, damage and replacement);
- develop a safety monitoring plan that addresses how abnormal measurements related to participants' safety measured by DHTs will be reviewed and managed; and
- develop a contingency plan for any changes to the DHT (e.g., discontinuation of a specific model, operating system updates)

The draft guidance includes appendices with specific examples of how different types of DHTs could be incorporated into a clinical investigation. Given the particular circumstances of each DHT and clinical investigation, the draft guidance encourages sponsors to engage early with the appropriate FDA Center responsible for the medical product under development to discuss the proposed use of DHT(s) in a clinical investigation and, for DHTs or DHT-collected endpoints that require qualification, engage with an appropriate FDA qualification program, such as the Medical Device Development Tool Qualification Program.

Comments on the draft guidance are due March 23, 2022.