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Clinical Trials During the COVID-19 Pandemic

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In light of the COVID-19 pandemic, the Food and Drug Administration ("FDA") issued recent non-binding guidance ("Guidance") on the conduct of ongoing clinical trials of medical products. The FDA acknowledges that the public health emergency may result in unavoidable protocol modifications and/or deviations.

Quarantines, site closures, travel limitations, interruptions in the supply chain for the investigational product, and infection of site personnel and trial subjects can all disrupt protocol-specified procedures, such as mandatory visits, administration of the investigational product, or laboratory testing. The Guidance provides FDA's thinking on how sponsors, clinical investigators, and Institutional Review Boards/Independent Ethics Committees ("IRBs") should, notwithstanding the current challenges, approach trial participant safety, compliance with good clinical practices (GCP) and risks to trial integrity.

Highlights from the Guidelines include:

Trial Participant Safety

It is clear that for each changed circumstance necessitated by the COVID-19 emergency, trial sponsors (together with investigators and IRBs) should first consider the impact on participant safety. Decisions regarding continued participant recruitment, continued use of an investigational product, changing patient monitoring practices, discontinuing the trial, or other modifications should be considered with trial participant safety as the paramount factor.

FDA considers it critical that trial participants be informed of all changes that could impact them.

Participants may not be able to travel to investigational sites for protocol-mandated visits. Sponsors should evaluate whether alternative methods for safety assessments, such as delayed patient visits, phone calls, or virtual visits, are sufficient to assure trial participant

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safety. If any trial participants are unable to access the investigational product or the investigational site, they may need additional safety monitoring.

Sponsors may also consider whether there are alternative means to administer the investigational product when scheduled site visits are impracticable. However, FDA states that regulatory requirements regarding investigational product accountability remain in effect and should be addressed and documented.

COVID-19 Screening; Changes to Study Protocol

The FDA states that COVID-19 screening procedures mandated by the investigational site do not need to be reported as an amendment to the protocol (even if performed during clinical study visits), unless the sponsor is incorporating the data collected as part of a new research objective.

In addition, although sponsors are encouraged to engage with IRBs as soon as possible about urgent or emergent protocol changes, such changes to study protocols or informed consent as a result of COVID-19 that are intended to minimize or eliminate immediate hazards or to protect the life and well-being of trial participants may be implemented without IRB approval or amendment, or before filing an IND or IDE with FDA, but must be reported after such implementation.

Documenting and Analyzing Study Changes and Impact

In addition to trial participant safety, the other key takeaway from the Guidance is that FDA expects sponsors to document and explain all efforts to minimize the impact of any protocol modifications or deviations on the safety of trial participants and study data integrity. This documentation should include: (1) what contingency measures were implemented to manage study conduct (including their duration and how they were necessitated by COVID-19); (2) a listing of all affected participants by unique study identifier, and a description of how the individual's participation was affected; and (3) analysis and discussions addressing the impact of such contingency measures on the safety and efficacy results reported for the study.

Importantly, if there are missed visits, changes in visit schedules, or other facts that result in missing information, then each affected case report form should include specific information that explains the missing data and its relationship to COVID-19. This information should also be summarized in the clinical study report.

If changes in the study protocol lead to changes to efficacy assessment methods, amendments in data management or statistical analysis plans, the FDA requests that the

sponsor consult with the applicable FDA review division.

The FDA states that sponsors, investigators, and IRBs should all consider adopting policies and procedures (or revisions to existing policies) to address potential disruption as a result of COVID-19. The FDA provided examples of potential changes: impact on the informed consent process, study visits and procedures, data collection, study monitoring, adverse event reporting, changes to investigations, site staff, and monitoring resulting from regional or nationally imposed travel restrictions or quarantine measures or illness. Depending on the nature of revisions to the policies and procedures, applicable regulations may require a protocol amendment.

Undoubtedly, the current public health emergency will impact ongoing clinical trials. The extent and nature of that impact will vary depending on the trial, the investigational product, the disease being studied in the trial, the ability to conduct safety monitoring, and other factors. The FDA recognizes these facts, and the Guidance stresses two fundamental points. First, all trial activity, and each modification or deviation to a trial protocol, should be assessed with trial participant safety as the principal consideration. Second, all changes necessitated by COVID-19 should be carefully documented and analyzed in the clinical trial report to explain their connection to COVID-19 and their impact on participant safety and trial data integrity.

A copy of the full guidance issued by the FDA can be found at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/fda-guidance-conduct-clinical-trials-medical-products-during-covid-19-pandemic

If you have further questions, please contact the authors or any member of Dorsey & Whitney's health care transactions and regulations practice group.