Cooley

COVID-19 Pandemic: FDA Recommendations for Companies Involved in the Conduct of Clinical Trials

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The COVID-19 global pandemic has quickly evolved into a historic public health crisis. This crisis presents challenges and risks to companies involved in the clinical development process, including those related to quarantines and shelter-in-place orders, travel limitations, site closures and restrictions, supply chain interruption, as well as SARS-CoV-2 infection risk to trial participants, investigators or site personnel. These challenges may lead to difficulties in meeting protocol-specified procedures and result in protocol deviations, including administering or using the applicable product candidate or adhering to protocol-mandated visits and laboratory/diagnostic testing.

In an acknowledgement that protocol modifications may be required, and that there may be unavoidable protocol deviations due to COVID-19 illness and/or COVID-19 control measures, the US Food and Drug Administration released a **guidance document** taking immediate effect. The guidance document includes several considerations to assist sponsors in assuring the safety of trial participants, maintenance of Good Clinical Practice compliance and minimization of risks to trial integrity given the major challenges to the healthcare system and to clinical trial subjects posed by the COVID-19 pandemic. The FDA recommends that sponsor (or contract research organization) GCP policies and procedures should be reviewed and revised as applicable to ensure protection of patients and management of study conduct related to COVID-19 control measures being used at sites, which are subject to change as site resources and the nature of the pandemic shifts.

In an **agency statement** accompanying the guidance document, the FDA underscored its focus on patient safety: “The FDA released this guidance to emphasize that at all times, patients’ safety should continue to be at the forefront of considerations. We want to support the continuance of these clinical trials in compliance with good clinical practice and minimizing risks to trial integrity, while also safeguarding the health and well-being of study participants.”

The FDA’s recommendations in the guidance document include the following:

- There will be no one-size-fits-all solution – each trial, each site and each subject’s participation may need to be evaluated to determine whether and which protocol deviations or amendments are needed to ensure patient safety
- COVID-19 screening that may be mandated by the clinical trial site does not need to be reported as an amendment to the protocol, unless the sponsor is including the collected data as part of a new research objective
- Changes to a protocol to limit exposure to COVID-19 may be implemented without approval by the Institutional Review Board but must be reported in the existing investigational new drug or investigational device exemption application afterward
- Robust efforts should be made to minimize the impact on trial integrity, including documentation of the reasons for protocol deviations
- Missing case report form data as a result of COVID-19 should be summarized in the clinical study report
- Sponsors should contact the responsible FDA review division if alternative efficacy assessment methods may be needed
- Sponsor monitoring of investigative sites should be maintained with central or remote monitoring, if on-site visits are not

available

What should your clinical operations and regulatory functions do now?

- First and foremost, let the safety of patients and site staff guide your decision-making
- For each trial and site, in conjunction with your contract research organization, site management organization or other applicable vendors, specifically determine what local COVID-19 related impediments may hinder ongoing enrollment and completion of protocols
- Determine and document the COVID-19 screening and prevention steps being taken by sites to prevent spread of the virus
- For subjects or sites that will not be able to operate on a regular basis, consider transfer to alternative sites or means of providing assessments, and if efficacy related, contact the FDA review division to determine if a protocol amendment is necessary to change assessments on a protocol-wide basis
- Keep track of notifications required to IRBs, ethics committees, FDA and foreign regulatory authorities
- Document, document, document – as always, remember that if you didn't write it down, you didn't do it. Specifically, the guidance document provides that sponsors should describe in appropriate sections of the clinical study report (or in a separate study-specific document) the contingency measures implemented to manage study conduct during disruption of the study as a result of COVID-19 control measures; a listing of all participants affected by the COVID-19 related study disruption, and a description of how the individual's participation was altered; and the impact of contingency measures on the safety and efficacy results reported for the study

The FDA also designated an email address for the receipt of further questions on clinical trial conduct during the COVID-19 pandemic: Clinicaltrialconduct-COVID19@fda.hhs.gov.

The guidance document is undoubtedly only the opening salvo in the FDA's efforts to assist the life sciences industry and investigators in navigating the COVID-19 pandemic and to help assess how to move forward with critical clinical trials. We will continue to monitor the FDA's COVID-19 related guidance and actions as they unfold throughout the crisis.