Compliance Tips For Running Clinical Trials During COVID-19

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Navigating the path forward to conduct clinical research in the midst of the COVID-19 pandemic has introduced unique challenges for sponsors and research institutions alike.

Industry sponsors and institutions are facing unprecedented issues resulting from the COVID-19 outbreak, such as clinical trial site closures, travel restrictions, limitations on the availability of investigational product and threats to the health and well-being of research personnel and study participants.

Sponsors and institutions are struggling to address the impact of COVID-19 on study data, reporting obligations and various human subject protection requirements. The clinical trial landscape has changed dramatically, and the entire research community has been forced to adapt.

In an effort to assist entities facing such challenges, the U.S. Food and Drug Administration and the Office for Human Research Protections have each recently issued guidance documents outlining issues that sponsors and researchers should consider. Taking that guidance into account, this article will provide practical insight for sponsors and institutions regarding the conduct and oversight of clinical trials during COVID-19.

Assess whether changes to an existing protocol are required in order to protect the safety, welfare and rights of study participants.

Sponsors and institutions, in consultation with institutional review boards, or IRBs, must determine whether the safety, welfare and rights of study participants are best protected by continuing the study according to the existing protocol, revising the protocol or by discontinuing subject participation in the trial altogether.

This is a fact-specific determination and will depend on factors such as the nature of the investigational product, the ability to conduct appropriate safety monitoring, the potential impact on the investigational product supply chain and the nature of the disease under study in the trial.

The inability of study participants to make protocol required in-person visits at investigational sites (e.g., because of shelter in place orders, lack of transportation, or because the study participant is at high risk with respect to COVID-19) must be specifically considered, especially in the context of safety assessments. Alternative communication methods, such as phone calls or virtual visits, must be carefully assessed to determine whether they will suffice to ensure the safety of participants.

Proposed changes to previously approved protocols due to COVID-19 may be submitted to the reviewing IRB at any time. To the extent the changes are necessary to eliminate apparent immediate hazards to study participants, the required changes may be

implemented prior to obtaining IRB review and approval, provided such changes are reported to the IRB as soon as possible. For instance, an investigator is entitled, in his or her discretion, to cancel or postpone nonessential study visits or to conduct remote visits instead of in-person visits without prior IRB approval, provided the IRB receives notification as soon as possible.

Note that decisions made by institutions or investigators (as opposed to the IRB) regarding the suspension or termination of approved research are not required to be reported to the OHRP. Only suspensions or terminations of approved research that are mandated by an IRB must be reported to OHRP.

Modify clinical trial protocols, informed consents and methods of data collection and analysis as appropriate to account for COVID-19-related deviations.

Modifications to clinical trial protocols, informed consent documents and data collection and analysis methods in light of COVID-19-related deviations will necessitate IRB involvement and compliance with institutional policies.

With respect to protocol modification, deviations that may be particularly relevant due to COVID-19 include changes in subject screening, efficacy and safety assessments and site monitoring, such as the use of virtual technology to interact with study participants. Sponsors should also consider whether it will be necessary to implement alternative methods for delivering and administering investigational drugs to study participants, particularly in situations where participants do not have access to the health care setting in which the investigational drug is traditionally administered.

Study participants must be informed of changes to the study and monitoring plans that may have an impact on them, and these changes may require amendments to informed consent forms. All amendments to informed consent forms must be submitted to the IRB.

Modification to the collection of efficacy endpoint data may also be required, as well as changes to statistical analysis or data management plans to account for modifications made to the protocol.

Keep careful documentation of all COVID-19 modifications.

Sponsors, institutions and investigators should carefully ensure proper documentation of all modifications due to COVID-19 on case report forms and other study related documentation. This includes documenting the duration of any modifications, the study participants affected and the nature of the impact on such participants.

Sponsors, in particular, should account for missing information in case report forms resulting from changes in study visit schedules, missed visits or patient discontinuations and should be prepared to explain the basis of any missing data to the FDA, including whether and the extent to which COVID-19 is a factor.

Appropriately distinguish between research activities and clinical/public health activities.

It is important to appropriately distinguish between research activities required under a trial protocol and clinical activities and/or activities related to public health, as different IRB reporting obligations and regulatory requirements apply to each.

Actions taken for public health or clinical purposes, rather than research purposes, are not research procedures and therefore do not require IRB approval before implementation. By way of example, mandatory clinical screening procedures related to COVID-19 for all individuals arriving at an institution, including study participants, would not require IRB review and approval before implementation.

Similarly, because these COVID-19 screening procedures would not constitute research, an institution would arguably not need IRB approval in order to share screening results with public health authorities or the study participants (although other authorizations may be required under state law or institutional policy). Clinical activities and/or public health activities are not required to be submitted to the IRB as an amendment to a protocol (even if they will be performed during a study visit) unless the sponsor intends to incorporate the COVID-19 data as part of its research objectives.

Additionally, because many institutions and researchers are being asked to participate in various public health surveillance activities to assist public health officials in monitoring and managing the COVID-19 outbreak, it is important to understand the different regulatory requirements (and exceptions) that apply to public health activities versus research activities.

For example, if required by law, institutions and investigators may make disclosures of certain information (including individually identifiable information about a study participant) that are inconsistent with the study participant's informed consent and that are otherwise prohibited under Federal privacy laws, provided such disclosures are required by law and relate to an individual's COVID-19 status. The investigator should inform the study participant of any such disclosures.

Similarly, certain public health surveillance activities, including collection and testing of information or biospecimens, conducted, supported, requested, ordered, required or authorized by a public health authority are entirely excluded from the requirements of the Revised Common Rule. However, FDA regulations may continue to apply if the activity involves the use of an investigational drug or in vitro diagnostic device.

Consider whether modifications to existing institutional policies and procedures are required in light of COVID-19 and moving forward.

Sponsors and institutions should consider revising existing human subject research policies and procedures to the extent they do not already address emergency situations, such as the COVID-19 pandemic. Changes to policies and procedures may be needed to address the impact on the informed consent process, study visits and procedures, data collection, study monitoring, adverse event reporting and changes in investigator(s) and study staff. Sponsors should also consider training study monitors to assist investigators in addressing the risks presented by COVID-19, as well as any necessary deviations in or adjustments to study protocols or practices.

Conclusion

Ultimately, sponsors and institutions should consider all critical circumstances with a specific focus on the impact on study participants. When considering necessary changes in light of COVID-19, sponsors and institutions should think broadly about the immediate and long-term impact of the pandemic on clinical trial recruitment, investigational product administration and efficacy and safety monitoring. Sponsors and institutions are encouraged

to engage with their IRBs as early as possible when protocol or informed consent changes may be necessary.

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