

U-MIC TRANSCRIPT: FDA Guidance on the Conduct of Clinical Trials during the COVID-19 Pandemic

In March 2020, the Food and Drug Administration (FDA) issued guidance to assist sponsors and researchers in ensuring the safety of study subjects, maintaining good clinical practice, and minimizing risks to research integrity during the coronavirus disease 2019 (or COVID-19) pandemic. Conduct of clinical trials may be disrupted by:

- quarantines
- study site closures
- travel limitations
- interruptions to the supply chain of an investigational product
- other considerations

As a result, protocol modifications may be necessary, and certain protocol deviations may be unavoidable.

The FDA guidance presents the following considerations for ongoing trials:

- Subject safety is paramount. To ensure safety, changes to study conduct may relate to subject recruitment, use of investigational products in subjects already participating, and subject monitoring. Subjects must be informed of all changes that may affect them.
- Sponsors, in consultation with researchers and IRBs, must determine whether protection of a subject's safety, welfare, and rights is best served by continuing or discontinuing administration of an investigational product, and whether to withdraw subjects from the study.
- Since the pandemic may prevent subjects from visiting study sites, sponsors should evaluate whether alternative methods for safety assessments (such as phone contact, virtual visit, or alternative locations) would be feasible and adequate to ensure subject safety.
- Subjects who no longer have access to an investigational product or means to visit the study site may require additional safety monitoring and measures, such as discontinuation of active investigational treatment.
- The need to implement or modify processes will vary by protocol and local situation. For example, it may depend on whether it would be appropriate to delay some assessments in ongoing studies, or, if the research cannot be properly conducted under the existing protocol, whether to stop recruitment or withdraw subjects.
- COVID-19 screening procedures mandated by the health care system in which a clinical trial is being conducted do not need to be reported as protocol amendments, even if performed during study visits, unless the sponsor plans to use the data collected for a new research objective.
- Sponsors and researchers should engage with IRBs as early as possible when urgent or emergent COVID-19-related changes to the protocol or informed consent materials are anticipated. Although it is permissible to implement changes to minimize or eliminate

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immediate hazards or to protect the life and well-being of subjects without IRB approval or before filing an amendment to the IND or IDE, all such changes must be reported afterwards.

- Alternative processes should be as consistent with the existing protocol as possible, and sponsors and researchers should document the reasons for implementing contingency measures.
- The FDA guidance emphasizes that study visit schedule changes, missed visits, or subject discontinuations may result in missing information. It is important to capture *specific* information in the case report form that explains the basis of the missing data, including the missing information's relationship to COVID-19.
- If scheduled visits at study sites will be significantly impacted, it may be appropriate to provide subjects with certain investigational products, such as those typically distributed for self-administration, by alternative secure delivery methods. For investigational products normally administered in a health care setting, consulting FDA review divisions on plans for alternative administration (such as home nursing or trained but non-study personnel at alternative sites).
- Consult with the appropriate FDA review division regarding protocol modifications for the collection of efficacy endpoints, such as
 - use of virtual assessments
 - delays in assessments
 - alternative collection of research-specific specimens
- If changes in the protocol will lead to amending data management and/or statistical analysis plans, the sponsor should consider consulting with the applicable FDA review division.
- If planned on-site monitoring visits are no longer possible, sponsors should consider optimizing use of central and remote monitoring programs.

In general, sponsors, researchers, and IRBs should consider establishing and implementing policies and procedures, or revising existing policies and procedures, to describe approaches to protecting subjects and managing study conduct during any study disruption as a result of COVID-19 control measures at study sites. Changes to policy and procedures might address impact on:

- the informed consent process
- study visits and procedures
- data collection
- study monitoring
- adverse event reporting
- changes in study personnel and/or monitors

Policy and procedures must be compliant with applicable policy for the management and

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control of COVID-19. Depending on the nature of policy and procedure changes, a protocol amendment may be required.

Sponsors of clinical trials impacted by the COVID-19 pandemic should describe, either in the clinical study report or in a separate study-specific document:

- contingency measures implemented to manage study conduct during disruption
- a list of subjects affected by the disruption, by unique subject number identifier and by investigational site, and a description of how each subject's participation was altered
- analyses and discussions addressing the impact of contingency measures on the safety and efficacy results reported for the study

Contact the IRB for more information about the impact of COVID-19 on the conduct of clinical trials.

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