COVINGTON

FDA Releases Guidance on Clinical Trial Conduct During COVID-19 Pandemic

March 19, 2020

Food, Drugs, and Devices

The U.S. Food and Drug Administration (FDA) released a direct-to-final guidance on March 18, 2020 entitled "FDA Guidance on Conduct of Clinical Trials of Medical Products during COVID-19 Pandemic" (Guidance).[1] The Guidance comes at a critical time, as clinical trial sponsors, investigators, and Institutional Review Boards (IRBs) grapple with the measures needed to ensure the safety of clinical trial participants while maintaining good clinical practice (GCP) and preserving clinical trial integrity during this unprecedented public health emergency. FDA is implementing the recommendations in the Guidance immediately, but comments may still be submitted to the Agency for consideration.

At the outset of the Guidance, FDA acknowledges that COVID-19 and the public health measures that have been implemented in response to the pandemic can result in challenges for ongoing clinical trials. Quarantines, site closures, travel limitations, and supply chain interruptions, for example, may require protocol modifications and protocol deviations. Although protocol changes typically are not implemented before review and approval by the IRB (or ethics committee), FDA explains that "**changes to minimize or eliminate immediate hazards or to protect the life and well-being of research participants (e.g., to limit exposure to COVID-19) may be implemented without IRB approval or before filing an amendment to the IND or IDE**" but must be reported afterwards.[2] Still, FDA encourages sponsors and clinical investigators to engage with IRBs and ethics committees as early as possible when protocol and informed consent changes are anticipated because of COVID-19.

The protocol changes that may be necessary will vary from trial to trial, but FDA outlines several considerations to assist sponsors in protecting participant safety, maintaining GCP compliance, and minimizing risks to trial integrity. FDA's recommendations include the following:

- Participant safety is "paramount," and sponsors should focus on the potential impact on the safety of trial participants and modify study conduct accordingly (e.g., changes to trial recruitment and patient monitoring). **In all cases, trial participants should be kept informed of the changes**.[3]
- Sponsors should evaluate whether alternative methods for safety assessments (e.g., phone contact, virtual visit, alternative location for assessment, including local labs or

[1] The Guidance is available at https://www.fda.gov/media/136238/download.

[2] Guidance, at 6-7 (emphasis added) (citing 21 C.F.R. 56.108(a)(4), 21 CFR 56.104(c), 21 CFR 312.30(b)(2)(ii), and 21 CFR 812.35(a)(2)).

[3] *Id.* at 5.

imaging centers) could be implemented when necessary (e.g., the participant cannot come to the investigational site) and feasible, as well as sufficient to assure trial participant safety. In making the decision to continue use or administration of the investigational product, the sponsor should consider whether the safety of trial participants can be assured with the implementation of the altered monitoring approach.[4]

- Depending on the study protocol and local situation, some sponsors may need to consider whether it is appropriate to delay some assessments, or, if the study cannot be properly conducted under the existing protocol, whether to stop recruitment or withdraw trial participants (which may require additional safety monitoring).[5]
- To the extent possible, implementation of alternative processes should be consistent with the protocol. **Sponsors and clinical investigators should document the reason for any contingency measures implemented—e.g., how COVID-19 restrictions led to the study changes and the duration of those changes, and which trial participants were impacted and how they were impacted**.[6]
- When changes in study visit schedules, missed visits, or patient discontinuations lead to missing protocol-specified information, **case reports should capture specific information that explains why the data are missing, including the relationship to COVID-19**, and this should be summarized in the clinical study report.[7]
- **Certain investigational products (e.g., self-administered products) "may be amenable to alternative secure delivery methods." Sponsors should consult the appropriate FDA review division for alternative administration approaches (e.g., home nursing or alternative sites by trained by non-study personnel) for investigative products usually administered in a health care setting.** Regulatory requirements for maintaining investigational product accountability still apply and should be addressed and documented.[8]
- **Sponsors should consult with the appropriate FDA review division for protocol modifications for the collection of efficacy endpoints** (e.g., virtual assessments, delayed assessments, alternative specimen collection). **The reason(s) for failing to obtain the efficacy assessment—including the specific limitation imposed by COVID-19 that led to the inability to perform the assessment—should be documented for the individual instances of non-collection**.[9]
- Sponsors should consider consulting with the appropriate FDA review division if protocol changes will lead to amending data management or statistical analysis plans. Sponsors should address how COVID-19 related protocol deviations will be handled for the prespecified analyses before locking the database.[10]

---

[4] *Id.* at 6.

[5] *Id.*

[6] *Id.* at 7.

[7] *Id.*

[8] *Id.*

[9] *Id.*

[10] *Id.* at 8.

- Sponsors should consider using central and remote monitoring programs to maintain oversight of clinical sites if planned on-site monitoring visits are not possible.[11]

FDA further recommends that sponsors, clinical investigators, and IRBs establish and implement policies and procedures (or revise, as applicable) to describe their approach to protecting trial participants and managing clinical study conduct during possible COVID-19 related disruptions. FDA advises that these policies and procedures should comply with applicable regional or national policy for the management and control of COVID-19. Policy and procedure changes may require a protocol amendment under FDA's regulations.[12]

Finally, FDA explains that sponsors should describe in appropriate sections of the clinical study report (or a separate study-specific document) COVID-19's impact on the trial. This includes contingency measures undertaken due to COVID-19 related study disruptions, a list of all participants affected by the COVID-19 related study disruption (listing unique identifier, trial site, and how participation was altered), and analyses and discussion addressing the impact of the contingency measures on the safety and efficacy results reported for the study. FDA expects "robust efforts" by sponsors, investigators, IRBs and ethics committees to maintain the safety of trial participants and the integrity of study data, and documentation of such efforts is key.

For further questions on clinical trial conduct during the COVID-19 pandemic, FDA has provided the following email address: Clinicaltrialconduct-COVID19@fda.hhs.gov.

If you have any questions concerning the material discussed in this client alert, please contact the following members of our Food, Drugs, and Devices practice:

Denise Esposito	+1 202 662 5562	desposito@cov.com
Michael Labson	+1 202 662 5220	mlabson@cov.com
Matt Hegreness	+1 202 662 5418	mhegreness@cov.com
Kaetochi Okemgbo	+1 202 662 5419	kokemgbo@cov.com
Julia Post	+1 202 662 5249	jpost@cov.com

***

To best advise our clients on the rapidly evolving public health situation in the U.S., our COVID-19 task force is staying abreast of daily developments and tracking the latest federal, state and local policies related to COVID-19.

[11] *Id.*

[12] *Id.*