Partial Summary of COVID-19 Disruptions of International Clinical Trials: Comparing Guidances Issued by FDA, EMA, MHRA and PMDA prepared by Ropes and Gray (April 3, 2020)

Link to full guidance
https://www.ropesgray.com/en/newsroom/alerts/2020/04/National-Authority-Guidance-on-Clinical-Trials-During-the-COVID-19-Pandemic?utm_source=alert&utm_medium=email&utm_campaign=National-Authority-Guidance-on-Clinical-Trials-During-the-COVID-19-Pandemic&utm_content=coronavirus

Please note information below is limited to the United States FDA section of the guidance provided by Ropes and Gray. The guidance is directed to Sponsors however BCH has some investigators who hold their own INDs and are considered sponsors as well as investigators. It also gives all investigators considerations for all FDA regulated trials.

Clinical Trial Considerations	Summary of FDA Guidance U.S. Food and Drug Administration Prepared By Ropes and Gray
Continuing and/or Initiating a Protocol	Ensuring the safety of participants is paramount. Sponsors should consider whether COVID-19- imposed limitations pose new safety risks and the feasibility of mitigating the risks through amending study procedures. Sponsors should assess the availability of clinical investigators, trial support staff, trial supplies, vendor operations and information technology systems to provide trial oversight and properly assess and manage safety issues that may emerge during a study. If a Data Monitoring Committee (DMC) has been established, sponsors should consider the assessment of the DMC on the impact of COVID-19 modifications on participant safety. Sponsors should consider whether continuation and/or initiation of a trial could interfere with public health measures to control COVID-19
Continuing a Participant on Study	Maintaining the safety of participants is central to any decision to continue participants in the study. Sponsors should consult with investigators and IRBs to determine if a participant should continue on protocol, discontinue receipt of the investigational product, or discontinue participation in the trial. The determination depends on specific circumstances, including the nature of the investigational product, the ability to conduct appropriate safety monitoring, potential impacts on the investigational product supply chain, and the nature of the disease. Sponsors determining whether to continue administering an investigational product that appears to provide benefit to participants should consider context-dependent issues, including whether the participant appears to be benefitting from the product, the availability of reasonable alternative treatments, the seriousness of the disease, and the risks of switching treatment. If discontinuation of investigational product might present a substantial risk, the sponsor should consider, after discussions with the FDA review division, amending the protocol to limit use to participants with apparent benefit. Participants should continue to be informed of study conduct modifications that affect them.

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Implementation of Protocol	Changes to minimize or eliminate immediate hazards or to protect the life and well-being of participants may be implemented without IRB approval or before filing an IND/IDE amendment. These changes must be reported to the IRB after implementation. For studies under an IND, pausing enrollment to decrease potential exposure to COVID-19 does not require submission of a protocol amendment. Protocol amendments not required to prevent imminent safety risks can be implemented once submitted to FDA and IRB- approved. Consolidation of several protocol modifications into a single protocol amendment would be acceptable. For studies under an IDE, FDA notes its understanding of challenges to submission of 5-day Notices under 21 CFR 812.35(a)(3) due to the impact of COVID-19. Sponsors may consolidate implemented changes when submitting 5-day Notices and should update the IDE as soon as possible.
Informed Consent Changes	If a patient signing informed consent is in COVID-19 isolation, electronic methods of obtaining the participant's signature should be considered consistent with FDA's 2016 guidance on electronic informed consent. If not possible, sponsors should consider having a health care worker who may enter the room provide a consent form to the patient. The investigator may then arrange a telephone or video conference with the patient and an impartial witness. If the signed informed consent document cannot be collected, acceptable documentation includes witness and investigator attestations that the patient agreed to participate and signed the informed consent, or a photograph of the signed informed consent with an attestation of how it was obtained
Study Visits	Sponsors should consider feasible alternatives to on- site safety assessments, including telephone contacts, telemedicine contracts, or alternative locations for assessments. Since the change to telephone or video contact visits would likely result in some protocol-specific procedures not being conducted, sponsors must evaluate the potential impact on participant safety and how to mitigate the risks.
COVID-19 Screening Procedures	If health care system- mandated, COVID-19 screening procedures do not need to be reported as a protocol amendment unless the Sponsor is using the data collected for a new research objective
Monitoring Activities	If on-site monitoring visits are no longer possible, sponsors should consider centralized and remote monitoring programs and document inability to access or delayed monitoring of a site.

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Investigational Product Delivery and Accountability	Regulatory requirements for investigational product accountability remain. If sites are significantly impacted, certain investigational products may allow for alternative secure delivery methods. For investigational product dispensed through a pharmacy for self- administration at home, home delivery of the product that would not raise new safety risks may be implemented to protect patients from coming to sites. A protocol change would be required to permit home delivery for the change from pharmacy dispensing for self- administration at home to direct-to-patient shipments. If the extent of home delivery is limited to certain participants, documentation through protocol deviation may also be acceptable. If the change is then included in a protocol amendment, such change may be part of a cumulative amendment rather than an urgent protocol change. The FDA review divisions should be consulted regarding plans for alternative administration of investigational products normally administered in a health care setting. Sponsors should consider safety risks of missing an investigational product infusion due to inability to come to a site. When suitable alternative arrangements cannot be made, discontinuing investigational product treatment while continuing study participation with potentially delayed assessments may be an appropriate option
Data Capture and Study Reporting	Sponsors should consult FDA review divisions regarding COVID-19 effects on efficacy assessments and protocol changes affecting data management and/or statistical analysis plans. Sponsors should document specific protocol deviations and the reasons for such. Investigators must document as protocol deviations any modifications to protocol-specific procedures that occur prior to IRB approval and FDA submission of a protocol amendment implementing the modification.

References:

1. FDA Guidance on Conduct of Clinical Trials of Medical Products during COVID-19 Pandemic

https://www.fda.gov/media/136238/download