FDA UPDATES RECENTLY ISSUED GUIDANCE FOR CLINICAL TRIAL RESEARCHERS AMID COVID-19 PANDEMIC

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THE U.S. FOOD AND DRUG ADMINISTRATION ("FDA") SUPPLEMENTS ITS MARCH 18TH GUIDANCE ENTITLED "CONDUCT OF CLINICAL TRIALS OF MEDICAL PRODUCTS DURING COVID-19 PUBLIC HEALTH EMERGENCY."

Less than one month after issuing guidance intended for industry, investigators, and institutional review boards (IRBs) related to addressing research-related challenges posed by the COVID-19 pandemic, FDA has added additional content to the Q&A section of that guidance addressing remote clinician-reported outcome or performance outcome assessments; remote site monitoring; electronic common technical document requirements; investigational product administration by a local health care provider who is not a sub-investigator; and information for sponsors on whom they should contact at the FDA regarding certain changes to ongoing trials. The updated guidance is posted here, and a brief summary of key provisions follows.

OPTIONS FOR INFORMED CONSENT

Where trials continue to enroll participants and those potential participants or their legally authorized representatives ("LARs") are unable to travel to the investigator location, methods other than a face-to-face consent interview may be appropriate if the method selected: 1) permits adequate exchange of information, 2) can be appropriately documented, and 3) affords the opportunity to verify the identity of the signer. Use of validated electronic informed consent capabilities is preferred, but where no such technology is available, sending the subject or the LAR a copy of the informed consent form by, for example, facsimile, e-mail, or postal mail prior to the consent interview may permit the subject or subject's LAR to read the contents of the form during a remote discussion. Researchers must consider carefully whether certain circumstances may permit a verbal consent process that does not involve the subject or LAR receiving the consent form prior to the interview. The FDA discusses various options for receiving and documenting the signed form prior to beginning study-related procedures, including verbal confirmation with subsequent return of form by facsimile, scanning the consent form and returning it through a secure e-mail account (or posting it to a secure internet address) and bringing the form to the next visit to the clinical site. Notwithstanding the flexibility expressed by the FDA, the overseeing IRB must review and approve the planned informed consent process and the person signing the consent form must receive a copy for their records.

REMOTE PERFORMANCE OUTCOME (PerfO) ASSESSMENTS OR INTERVIEW-BASED CLINICIAN-REPORTED OUTCOME (ClinRO) ASSESSMENTS

The FDA recognizes that while remote administration of interview based ClinRO assessments and PerfO assessments may be feasible, not all assessments can be completed remotely. Sponsors are required to consider whether assessments by phone or video would be safe, can be consistently conducted for all subjects and whether they would provide the type of clinical data required. In considering trial data integrity and reliability, the FDA notes that increased variability in outcome measures could compromise data quality and thus, product review.

REMOTE PERFORMANCE OF SITE MONITORING AND SOURCE DOCUMENT REVIEW

Because the regulations requiring sponsors to monitor conduct and progress of their clinical investigations[1] are not specific about the methodology to be used, a range array of approaches may be considered. In considering new methods, Sponsors must take into account technical feasibility, requirements described in the study monitoring plan (or other appropriate study-specific documents), prioritizations of activities that are essential to the safety of trial participants and/or data reliability, and whether documentation can occur at the same level of detail as on-site monitoring activities.

SHORT-TERM WAIVERS FROM ELECTRONIC COMMON TECHNICAL DOCUMENT (eCTD) REQUIREMENTS

Where a sponsor cannot meet eCTD requirements under section 745A of the Food, Drug & Cosmetic Act related to the COVID-19 public health emergency, they may qualify for a short-term waiver. Any such granted waiver would be effective only for a limited period of time. However, where technical difficulties with transmission of electronic submissions to FDA exist, sponsors are directed to first consult the FDA electronic submission staff rather than submit a waiver request.

INVESTIGATIONAL PRODUCT ADMINISTRATION BY A LOCAL HEALTH CARE PROVIDER WHO IS NOT A SUB-INVESTIGATOR

The FDA discusses where it may be appropriate to ship investigation product to be administered through infusion to a local health care provider for administration, how to document and record the activities, and when IRB review and approval of the deviation is required. Prior consultation with the appropriate FDA review division(s) is recommended.

LOCAL SOURCING OF INVESTIGATIONAL PRODUCT

Under certain limited circumstances where the investigational product is FDA-approved and the study does not require blinding, local sourcing with sponsor reimbursement may be appropriate. Under those circumstances, FDA will exercise enforcement discretion related to the absence of the 21 CFR 312.6 statement “Caution: New Drug--Limited by Federal (or United States) law to investigational use.”

CONCLUSION

The COVID-19 public health emergency continues to impact the conduct of clinical trials of medical products, including drugs, devices, and biological products in unprecedented ways. The FDA is acting quickly to consider how challenges posed by quarantines, site closures, travel limitations, interruptions to the supply chain for the investigational product, and other considerations can be addressed. Unavoidable protocol deviations due to COVID-19 must consider first and

[1] See 21 CFR 312.50, 312.53(d), 312.56(a), 812.40, 812.43(d), and 812.46.

foremost trial participant safety while also seeking to preserve maintenance of good clinical practice and trial integrity. The appendix further explains those considerations by responding to related questions the agency has received. Importantly, in its new guidance content, FDA discusses how and when sponsors should reach out to their review division regulatory project managers as their primary point of contact for communications with FDA and what sponsors can expect related to response.

If you have any questions about these pharmacy measures, please contact a member of our Life Sciences Team. For any other concerns arising from the pandemic, please contact a member of our COVID-19 Task Force.