VERISTAT

Strategies to Drive Clinical Development Momentum During the COVID-19 Era

Regulations and guidelines for clinical trial conduct are rapidly evolving and affecting sponsors who are running or planning clinical studies, those planning marketing applications, and those with products already on the market. At Veristat, we understand that these changes are disrupting clinical development and ultimately impacting global human health.

As you consider the impact that the COVID-19 pandemic has on your programs, there are some key strategies which could help you maintain momentum, assess your risks and minimize the delays for ongoing, new, and even COVID-19-related trials.

Stay Informed of Updated, New, and Rapidly Changing Regulations

FDA, EMA, and other health agencies around the world have rapidly issued guidance documents for immediate implementation, indicating their intent to utilize enforcement discretion with respect to approved drugs and devices being used to treat COVID-19 and for clinical trial conduct during the COVID-19 pandemic.

GUIDANCE FOR COVID-19 VACCINES AND TREATMENTS

For sponsors of investigational products that may be relevant to diagnosing, preventing, treating, or managing the symptoms of COVID-19, FDA has created a new Coronavirus Treatment Acceleration Program (CTAP) to move new treatments to patients as quickly as possible. Members of the Veristat regulatory team have already interacted with this group and can share a few preliminary takeaways:

The CTAP team at FDA is extremely responsive. Requests for feedback on clinical study designs and other development questions have received responses in as little as three days.

Sponsors seeking to access this program should be "ready to go." Sponsors seeking feedback on early development questions or encountering manufacturing challenges should expect to file a traditional pre-IND meeting request.

For products with existing INDs for other indications, FDA has been requesting submission of new INDs for COVID-19-related indications, rather than allowing an amendment to the existing IND to add the new COVID-19 indication.

GUIDANCE FOR NON-COVID-19 TRIALS

For sponsors of products in clinical trials that are not directly connected to the COVID-19 response, FDA has issued a key guidance document, FDA Guidance on Conduct of Clinical Trials of Medical Products during COVID-19 Pandemic. Veristat discussed key provisions of this guidance in a recent blog post, with recommendations including:

Remote assessment of trial participants

Handling missing patient data

Reporting COVID-19 impacts

In parallel, regulatory authorities around the world have issued guidance on conducting clinical trials during the COVID-19 pandemic, emphasizing protecting the health and safety of research participants. Links to guidance from key regions are provided in the table below.

United States: FDA	Health Canada	European Union: EMA	United Kingdom: MHRA
FDA Guidance on Conduct of Clinical Trials of Medical Products during COVID-19 Pandemic	Management of clinical trials during the COVID-19 pandemic: Notice to clinical trial sponsors	Guidance on the Management of Clinical Trials during the COVID-19 (Coronavirus) pandemic	Managing clinical trials during Coronavirus (COVID-19)

Adapting to a More Virtual Clinical Trial Ecosystem

COVID-19 can impact the operational conduct of your ongoing, new, or COVID-19-related trial in many ways. Here are some strategies to ensure the continuity of clinical trial conduct for ongoing studies and the patients involved. In addition, studies can start up during this unprecedented time by developing a virtual clinical trial ecosystem.

Utilize Remote Monitoring

Ongoing studies are faced with reduced staffing and restrictions for patient and on-site monitoring visits. Sustained review of your clinical trial data remains critical to ensuring patient safety. Create a framework to complete remote monitoring visits by developing secure, compliant electronic portals for trial sites to upload redacted source data. In addition, ask sites for access to their electronic medical records (EMR) for direct source review. Both options enable the ability to continue monitoring the study remotely to ensure patient safety and mitigate data collection timeline delays.

Transition to At-Home Patient Visits

With social distancing and limited access to sites, clinical research associates (CRAs) and patients are impacted. This has caused great concern for sponsors and patients. Transition your patient visits to at-home visits, which can include diagnostics, drug administration, drug and supply delivery, and telemedicine visits. Work with sites, institutional review boards (IRBs), and principal investigators (PIs) to ensure appropriate documentation of changes and ensure patient safety, continuity, and privacy.

Key components to develop a virtual ecosystem:

- Remote monitoring
- At-home patient visits
- Remain flexible, be agile, and rely on technology

Remain Flexible and Agile When Addressing Challenges

Each site and study has different needs. The key to success is to remain flexible and work with site staff to find the best possible solution while minimizing the additional burden placed on the site.

Remote source data verification (SDV), document exchange portals (for site start-up documentations), and offering flexible solutions have enabled Veristat to support sponsors starting or continuing their programs. COVID-19 programs pose some additional challenges:

Personal Protective Equipment (PPE)

Sites have not been allowed to use PPE from their hospitals or medical facilities for the conduct of clinical trials. In cases where we have been able to quickly randomize patients, we found that sponsors needed to provide PPE for the site staff as well.

eConsent Technologies

Many sites have restrictions on paper use in the hospital setting to mitigate transmission; therefore you must ensure that an eConsent platform is in place to process patient consent.

Protocol Amendments

During the pandemic, it may become necessary to implement immediate amendments to clinical protocols to protect patients. Be ready and creative. For example, Veristat facilitated such an amendment converting final study visits from in-person assessments to telephone follow-up assessments.

Biostatistical Considerations and Data Integrity

COVID-19 will impact each clinical trial uniquely depending on factors such as therapeutic area, study design and endpoints, study status, site location(s), and timing of COVID-19 within the relevant geographic regions, study enrollment status, and duration. Therefore, it is essential that the study's statistical analysis plan (SAP) addresses the impact of COVID-19 with a critical assessment based on the specific circumstances of the trial and the potential impact to data integrity and analysis.

Changes That Impact Analysis

A cross-functional strategy is important to keeping all relevant stakeholders informed on study changes, and should include input from members of the clinical, biometrics, and medical teams. Initially, it's important the cross-functional project team strategizes on approaches and possible changes to data collection methods, database modifications, protocol deviation documentation, and potential protocol amendments. Considerations to these changes include:

- Scientific and consistent thinking by the entire project team around the strategy to mitigate data risks is essential.
- Understanding the potential data gaps and risks to facilitate an appropriate analysis strategy within the SAP, inclusive of methods for handling missing data and sensitivity analyses.
- Careful consideration to whether the imbalance and appropriate mitigation of missing data might be different between placebo and comparator arms for any reason.

Ultimately, the planning and impact of missing, delayed, or erroneous data will lead to protocol amendments, database modifications, SAP updates, and modified as well as additional analyses. A cross-functional strategy is necessary to ultimately ensure optimization of data collection and data integrity, while minimizing the risk of any data gaps. All modifications to a clinical development program in this COVID-19 era should seek to maximize the completeness and interpretability of any and all patient data.

Statistical analysis is impacted by the following:

› Missing data

› Protocol deviations

› Protocol amendments

› Database modifications

Agility and a Scientific Mindset Are Required During These Uncertain Times

Meet Veristat

We understand that the stakes are high no matter where you are in your development program. The stress, anxiety and uncertainty about ongoing, new, or COVID-19-related clinical programs is overwhelming. We have the agility and scientific-minded experts to help you navigate these uncertain times. Get introduced to Veristat today.

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