Strategies to Keep Drug Development Moving During COVID-19

During the current COVID-19 pandemic, it is important to find strategies to keep your drug development program moving forward. With many studies now paused, canceled completely, or in the early stages of restarting, this time offers a rare opportunity to re-evaluate your program and to pivot in the direction your data are suggesting. Here we will highlight strategies to help minimize delays and keep your program moving.

Early Termination of Paused Clinical Studies

If you have a study that is currently paused, your first question is likely to be, "When can I restart my study?" While the desire for a swift return to normalcy is understandable, perhaps a better question to ask is, "Do I even need to restart my study?"

To answer this, you first need to evaluate whether you have enough high-quality data to terminate the study without significantly sacrificing any study objectives; this can be accomplished through an interim analysis. If the data support terminating the study, this saves you from all of the challenges that go with a restart, including recruitment, screening, and potential stability issues for both samples and your investigational product.

Conducting an interim analysis works best for studies that are not pivotal to your submission, although they may be critical for informed decision making. While early study termination will not be a realistic solution for every program, it is worth considering under the right circumstances given its potential to save time and other resources.

Re-initiation of Paused Clinical Studies

If your interim data suggest you should move forward with your study, there are some things to keep in mind before restarting. First, **begin planning now**. This can be especially challenging given all the uncertainties in the world today but being proactive and anticipating potential issues before they arise can make all the difference.

Operate under the assumption that the world is not going to return to "normal" anytime soon, particularly as future surges in COVID-19 cases appear to be likely. Strict, government-imposed mitigation efforts, like shutdowns, are worth planning for in the event of another COVID-19 spike.

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Along with being mindful of future pauses in drug development efforts, you should also start aligning your study protocols and standard operating procedures (SOPs) with any new social distancing and safety guidances from relevant regulatory agencies. Measures that may warrant consideration include smaller cohorts, staggered dosing, direct-to-subject drug shipments, virtual safety assessments, and at-home visits.

Frequent communication between sponsors and study sites is also important during this time, as these sites may be shifting their own procedures, and regulatory requirements can vary depending upon where the site is located. You should also ensure that Institutional Review Boards (IRBs) and Independent Ethics Committees (IECs) are in agreement with the updated terms of your study so that you are able to restart the study as soon as possible. IRBs may also serve as a valuable resource as you continue to assess new strategies for navigating the pandemic.

Continue to stay abreast of current guidances from regulatory authorities that may impact study design decisions. The FDA has issued a guidance to address conducting clinical trials during the COVID-19 pandemic. This is a living document that the Agency plans to update regularly with the latest information and industry regulations and should be consulted throughout the planning and study implementation phases.

To increase efficiency, consider activities that you can complete now like generating reports (or even report shells), ICFs, eCRFs, and other critical documents in advance of restarting your study. Finally, remember that any pandemic-related changes to the study must be documented in the final Clinical Study Report (CSR), including potential impacts on the interpretation of results and study outcomes.

Initiating New Clinical Studies

With COVID-19 pausing most clinical activities for non-COVID-19 indications, the backlog of studies that still need to start or re-start continues to grow. As a result, this momentary shutdown is likely to affect stakeholders for months and years to come.

Even if you are not planning to conduct your study until next year, you should get a head start on planning **now**. You can be proactive by writing or amending your protocols and engaging with the study sites and IRBs early to understand any special requirements.

When deciding on study site locations for a new study, keep in mind the regional impact of the pandemic. Having a backup clinical site in place for your study is a good idea. Keep in mind, however, that regulations vary regionally and should be considered for each potential site. This is especially important if you are considering moving a study outside of the US, where regulations may be different.

Conducting a Gap Analysis

With the expected backlog of studies, the programs that are the most prepared will presumably be given priority. Regardless of where you are in development, this is a good opportunity to assess your program. Performing a gap analysis can help you take advantage of any "down" time while normal activities are paused.

A proper gap analysis will provide you with a critical assessment of your program, identify risks to clinical progression and the marketing application, and offer a list of recommendations to ensure that your program stays on track. In your gap analysis, you should pay special attention to how any planned studies may be impacted by the pandemic.

When considering your ongoing development plan, think about critical activities, such as a drug-drug interaction (DDI) study, that could be completed earlier than originally planned. Doing so may add efficiency to your program and help avoid potential obstacles down the road.

Simplifying Your Protocol

With COVID-19 adding an element of chaos to an already complicated drug development process, now is a good time to consider simplifying your program wherever you can. For example, your study's pre-pandemic protocol may have called for the analysis of

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multiple complicated endpoints. While those endpoints may provide "good-to-know" information, you and your team might now ask, "What do we really **need** out of this study?"

For this, you should determine the key endpoints that will maximize your success and best utilize your resources. Spend some time reevaluating the necessity of your secondary and exploratory endpoints. However, do not forget to document any changes made to your study protocol. Moreover, do not feel the need to scrap these ideas altogether, as they may be worth exploring in the future.

Virtual At-Home Options

In-person study site visits are likely to face major challenges as the COVID-19 pandemic persists. Creativity and adaptability will prove important as sponsors prioritize remote means of achieving study goals that once required frequent in-person site visits.

Telehealth and virtual appointments (with appropriate IT training for study subjects) may allow for remote collection of informed consents, certain patient assessments, and questionnaires. However, at-home study visits by qualified health professionals may be a valuable tool for collecting study data for more intensive clinical activities. These home health services can provide support for drug accountability, drug administration (e.g., home infusion), PK sampling (e.g., blood draws), and vital signs assessments. Although, even this method is not entirely risk-free, as it will require study staff to travel to the study subject's home.

Another option to further minimize study site visits could be directly delivering drug supplies to subjects. Safety should be the top priority in deciding whether study materials can be shipped, especially if the materials are temperature sensitive; shipping on ice may be necessary, and this comes with added cost.

For more information on virtual and at-home options for drug development, please see our blog post on Strategies for Virtual Clinical Pharmacology Phase 1 Studies, where we examine current solutions that could allow certain studies to be conducted as either partially or completely virtual trials.

Off-Site Patient Visits

While remote options should be considered when possible, clinical site visits may not be altogether avoidable. Thus, you may need to get a little creative with your off-site patient visits. If you are running a Phase 2 or 3 study, consider collaborating with Phase 1 clinical units. Some Phase 1 sites will not be impacted as much in terms of having to treat COVID-19 patients and may be able serve as an alternative to Phase 2 or 3 sites that have suspended non-essential activities. Phase 1 units are fully equipped for study-related activities and offer less exposure to acutely ill patients.

Supply Chain and Transportation Issues

With massive disruption to flights and other forms of transportation, you should anticipate delays in shipping timelines and plan for the worst-case scenario for delivery of study materials. Furthermore, manufacturing has also been affected by the pandemic, resulting in shortages of some materials.

These delays and shortages are especially relevant to the safety of study site staff and subjects, as demand for personal protective equipment to combat COVID-19 continues to outpace global supply. Shipping delays can also affect laboratory and clinic supplies, PK samples, lab samples, and, importantly, the drug supply. Work with your team to streamline supply chain and shipping efforts as much as possible and allow yourself some buffer time to avoid having to dispose of unused, expired study drug.

Conclusions

The COVID-19 pandemic has dramatically impacted the pace of drug development around the world. Following a months-long pause, studies will be gradually restarting, albeit in a decidedly different environment. Being proactive, realistic, and mindful of the ever-changing world in which we now live, and understanding the impacts that those changes can have on how drugs are developed, will give you an advantage when you are ready to start up again. Contact us to learn how Nuventra can help you navigate these uncertain times and keep your program on track.

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