How Technology Makes Virtual Clinical Pharmacology Phase 1 Studies Possible

With the current COVID-19 pandemic, drug developers and researchers are searching for drug development strategies that limit human contact. For certain drugs and certain types of Phase 1 studies, a "virtual" Phase 1 trial might be possible.

A recent guidance issued by the FDA to address current pandemic concerns states:

> "Since trial participants may not be able to come to the investigational site for protocol specified visits, sponsors should evaluate whether alternative methods for safety assessments (e.g., phone contact, virtual visit, alternative location for assessment, including local labs or imaging centers) could be implemented when necessary and feasible, and would be sufficient to assure the safety of trial participants."

Here we examine current solutions that could allow Phase 1 clinical pharmacology trials to be conducted as either partially virtual or completely virtual trials.

Phase 1 Studies That Could be Conducted Virtually

Certain Phase 1 studies are more amenable to virtualization. Studies that require frequent in-person interactions between subjects and investigational study staff (e.g., to collect blood for pharmacokinetic analysis) present distinct challenges. The clinical pharmacology studies best suited for virtualization are those that involve drugs that have already been tested in humans and that enroll healthy volunteers under a simple study design with minimal evaluations and low safety risk. These studies include:

- Food Effect
- Bioequivalence/Bioavailability (BE/BA)
- Simple Drug-Drug Interaction (DDI)
- Simple Single Ascending Dose (SAD)
- Multiple Ascending Dose (MAD)

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Studies That Would be Difficult to Conduct Virtually

Some clinical pharmacology studies could be difficult to conduct completely virtually because they involve one or more of the following – potential safety risks that require careful observation, a difficult to recruit and/or fragile subject population, complex dosing regimens, or complicated study designs with multiple assessments requiring direct interaction.

Clinical trials involving unstable drugs that require special storage and handling procedures or trials with samples that require immediate processing following collection (e.g., blood and urine) would also be challenging to conduct virtually. Studies that may prove difficult to conduct virtually include:

- First-Time-in-Human (FTIH)
- Thorough QT (TQT)
- Hepatic Impairment
- Renal Impairment
- Site of GI Absorption
- Radio-Labeled Mass Balance (ADME)
- Complex DDI and SAD/MAD

Despite the challenges that these studies present, the implementation of new technology and creative study design strategies may allow for portions of these studies to be conducted virtually.

Technologies & Strategies for Virtual Phase 1 Studies

There are many recent innovations that could enable a Phase 1 trial to be conducted either partially or completely virtually. These include:

1) MOBILE STAFFING

A key aspect of Phase 1 clinical trials is collecting blood and urine samples. In order to make this happen without an onsite trial, reliable collection and processing services and appropriate sample storage must be utilized. Study staff or a third-party vendor can visit a study subject's home to draw blood for clinical laboratory and PK analysis. Samples may be processed by the remote technician and shipped overnight to a bioanalytical lab for analysis or stored by the sample collection company for batch shipping later. This type of sample collection has seen a steady increase in demand, especially among older populations that cannot travel easily.

2) WEARABLE TECHNOLOGY

Wearable sensors are now readily available to measure heart rate, blood pressure, skin temperature, oxygen levels, breathing rate, electrodermal activity, actigraphy, and more. Aside from the convenience these devices offer the user, there are other benefits. For example, wearable devices can mitigate the effects of "white coat syndrome," thus reducing the occurrence of anxiety-induced blood pressure elevations in study subjects and reducing the potential for misleading blood pressure data. Wearable devices also provide continuous subject monitoring, offering a more comprehensive view of a subject's health versus the "snapshot" that is achieved during a single site visit.

3) TELEMEDICINE PLATFORMS

Telemedicine, or telehealth, involves the utilization of telecommunication and electronic information sharing as a mechanism for providing health care outside the context of a doctor's office, hospital, or clinic. There has been an incredible surge in telehealth for routine health care visits since the start of the COVID-19 pandemic. This practice may also be applied in Phase 1 studies. In a typical Phase 1 trial, subjects are confined to a Phase 1 clinical research unit and monitored continuously for adverse events, concomitant medications, food and beverage limitations, and so forth. In a virtual trial, monitoring can be done via video conferencing software and can even be set up to monitor the subject 24/7. In addition, informed consent may be obtained over telemedicine platforms. Because of the benefits that these platforms provide, sponsors should consider conducting at least some screening and follow-up assessments using these technologies.

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4) DRUG COMPLIANCE TECHNOLOGY

In a typical Phase 1 study, in-person dosing is conducted to ensure adherence to the study protocol. In an at-home or contactless setting, this presents some unique challenges to ensure that subjects are taking the study drug as intended.

One existing technology that encourages adherence to the medication regimen is a "smart pill bottle" that can track when it is opened and closed and the weight of its contents. While this can be useful, it does not guarantee that the subject has consumed the pill. Bioingestibles are another promising compliance technology than may help solve this issue. These devices send a signal using radio-frequency identification (RFID) technology to track adherence.

The ID-Cap system (etectRx™) is an example of a currently available drug compliance system with an ingestible component. This FDA-cleared event marker is comprised of a gelatin capsule containing a sensor. When ingested, the sensor transmits signals to a wearable reader that relays to a smartphone-based app and secure cloud-based server. ID-Cap was recently selected for use in a once-daily HIV drug study conducted at the University of Colorado Anschutz Medical Campus in partnership with the National Institutes of Health. The principal investigator, Dr. Jose Castillo-Mancilla, MD, said, "we believe this is a very innovative way to perform pharmacokinetic studies in which adherence is critical to understanding drug concentrations and drug response."

5) MOBILE APPS

There are few existing apps that combine all the necessary technologies and capabilities for performing virtual trials into what could be considered a comprehensive virtual trial solution. The ideal clinical trial app should be pairable with wearable devices and seamlessly integrate monitoring, compliance, and patient engagement into a single, portable, easy-to use, and secure hub.

One example of an app that is currently used in clinical trials is the TrialMax® App from Signant Health. As part of the broader TrialMax eCOA platform, this customizable smartphone app allows for the collection of patient data (including surveys), integration of sensors and wearables, patient engagement (including electronic informed consent), and helps ensure compliance through automated patient reminders.

For any virtual clinical trial app, sponsors should remember that validation may be required and that patient access to the devices, as well as their ability to use them properly, should be considered early in the study planning process.

Mixing Virtual & In-Person Options

The overall goal for virtual clinical pharmacology studies is to minimize interactions between site staff and subjects while protecting subject safety and the integrity of the study. Some mixture of the options proposed above and traditional clinical trial approaches could be implemented in a given study to achieve this goal. For example, subjects could visit the clinical site only for blood draws and be discharged as soon as sampling is complete. Afterwards, subjects could be monitored remotely via wearable apps and 24/7 telemedicine for adverse events and concomitant medications.
In the next blog Nuventra will outline the steps to implement a virtual Phase 1 study by using these technologies and strategies.

Conclusions

With the proper planning and technology, a fully or partially virtual Phase 1 trial is an option to keep your program in motion, even in the midst of the COVID-19 pandemic. The pros and cons of using virtual tools should be considered for their potential impact on subject safety and study objectives. If you choose to pursue a virtual or partially virtual clinical trial, it is imperative to understand the capabilities and limitations of the technologies and related solutions being implemented and to maintain constant communication with participants to ensure the scientific integrity of the study data and the safety of study subjects.

Nuventra has the resources and experience to help you consider options for executing a Phase 1 trial, whether it be with a traditional Phase 1 unit or in a remote setting. Contact us today to discuss your options.

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