According to a recent study (Study) regarding the impact that the COVID-19 pandemic has had on the conduct of oncology clinical trials, the COVID-19 pandemic has materially disrupted the conduct of clinical research and trials in much of the world. The observed disruptors include an observed decrease in patient enrollment in clinical trials and the operational challenges arising from the need to protect patient safety and comply with the social distancing, shelter-in-place and other rules and regulations that have become key elements of the public health response to the pandemic. As a result of these and other disrupters, investigators who participated in the Study reported that they are, “adopting or planning to adopt technology-based interventions aimed at reducing on-site monitoring visits and in-person patient visits to minimize potential viral exposure and spread, including telemedicine, remote electronic medical record access for monitors and virtual monitoring of data and study documentation.”

As discussed below, we maintain that the investigator comments reported in the Study are evidence that long-time discussions and debates regarding the viability and value of “decentralized or virtual” clinical trial models – commonly defined as clinical trials where one or all of the patient visits do not happen in the traditional setting, such as a clinic or hospital, but are rather performed in the home via telemedicine and, in some cases, sensors and biowearables – have taken center
stage during the current public health emergency. As such, this article will discuss (i) the increased attention being given to decentralized/virtual trials as a result of the COVID-19 pandemic, (ii) the impact that the pandemic has had on existing clinical trials, and (iii) the long-term viability of the decentralized/virtual trial model as a way to improve the efficiency and reach of clinical trials by using telehealth and other remote technologies – technologies that have been refined and improved in some part because of the COVID-19 pandemic’s impact on access to healthcare at all levels.

The Effect of COVID-19 on Clinical Trials

While the idea of moving clinical trials off-site to a virtual setting was already gaining traction prior to the COVID-19 pandemic, the pandemic has become a catalyst for the reconsideration and expansion of decentralized clinical trials. As a result of these and other challenges, COVID-19 has already resulted in clinical trial delays and recruitment pauses for pharmaceutical companies.[iii] Consequently, decentralized clinical trials, which were previously a mere alternative to the traditional in person clinical trial methodologies, are now at least in some instances a necessity to be able to continue to conduct clinical research at all during the pandemic.

While there are benefits to conducting decentralized clinical trials, there are many practical and regulatory challenges that are part-and-parcel to the decentralized model. For example, a prominent issue that has to be considered when in-person trials become virtual is the applicability of state telemedicine laws in the states where study participants are located. Interestingly, some of these challenges to decentralization have been reduced in connection with guidance and waivers issued by government agencies in response to the COVID-19 pandemic, making virtual clinical trials even easier to implement than they would have been without such guidance and waivers.

FDA Guidance for COVID-19 Encourages Remote Participation

On March 18, 2020, the U.S. Food and Drug Administration (“FDA”) issued guidance for investigators and institutional review boards (“IRBs”) conducting clinical trials during the pandemic (the “Guidance”), which will only remain in effect for the duration of the COVID-19 emergency. The Guidance provides recommendations for assuring the safety of trial participants, maintaining compliance with good clinical practice, and minimizing risks to trial integrity in clinical trials conducted during the pandemic.

The Guidance acknowledges that due to challenges such as quarantines, clinical site closures, travel limitations and interruptions to supply chains, certain protocol modifications may be required and protocol deviations may be unavoidable.[iv] Necessary public health control measures for clinical trials will vary depending on many factors, including the disease being studied, the trial design and the region where the study is being conducted. The Guidance encourages study sponsors to consider whether in-person visits are necessary and whether alternative methods for safety assessments such as phone contact, virtual visits or alternative locations for
assessment could be implemented to assure the safety of trial participants.

**Clinical Trial Protocol Submissions to the FDA**

Before beginning a clinical trial with an investigational new drug, a sponsor has to submit an Investigational New Drug Application (“IND”) to the FDA.[v] The central focus of the IND submission is the general investigational plan and the protocols for the study.[vi] A protocol amendment can be submitted to make changes in previously submitted protocols, but the protocol change must be approved by the FDA and IRB.[vii] Consequently, an adoption of new protocols to shift an already established clinical trial to a virtual setting would generally require the approval of the new protocols by both the FDA and IRB.

The Guidance, however, provides for some flexibility for implementing protocol changes to protect the safety of research subjects in connection with COVID-19 by allowing such changes to be made without obtaining the prior approval of the IRB or submitting a protocol amendment to the FDA, as long as such changes are reported afterwards.

**Investigational Medical Product Accountability**

Investigational Medical Product (“IMP”) accountability and dispensing laws and regulations vary by state and the product’s registration status with the FDA (investigational or approved) or legal status in a particular state can also affect which laws and regulations apply. Direct-to-trial participant shipping of an IMP requires a review of state law requirements for each state where the IMP is being shipped. Depending on the nature and stability of the IMP, some practical considerations of shipping the IMP may be at issue as well. Procedures for direct-to-trial participant IMP shipment should be included in the protocol.[viii]

According to the Guidance, the requirements for maintaining investigational product accountability remain despite the COVID-19 pandemic. Moreover, the Guidance provides that if the study protocol provides for pharmacy dispensing for self-administration at home and this is changed to direct-to-patient shipments, then a protocol amendment is required. However, if home delivery is limited to certain participants and not the entire population described in the protocol, documenting the change in the mechanisms of distribution of investigational product through protocol deviations may also be acceptable.

**COVID-Related Suspension of State Telemedicine and Licensing Laws**

Conducting decentralized clinical trials across state boundaries raises state licensure issues since investigators cannot deliver investigational medical products or prescribe treatment to study participants located in a state where the investigator is not licensed. This can often be managed by using a separate licensed investigator in each state where the clinical trial is being conducted.[ix]

There are also telemedicine laws that are implicated, which need to be considered on a state-by-state basis. For example, some states require the initiation of the
provider-patient relationship to be initiated in person before it can be shifted to telemedicine. Whether or not an in-person meeting is feasible will inevitably affect the states in which the clinical trial can be conducted. Protocol design needs to take into account both state licensing and telemedicine laws during their development.[x]

COVID-19-related actions to suspend certain regulatory restrictions has at least temporarily reduced the licensing and telehealth restrictions in many states, including, for example, prohibitions on out-of-state providers providing telehealth services in state.[xi] At the federal level, in response to COVID-19, the Centers for Medicare and Medicaid Services has expanded Medicare coverage of telehealth services during the COVID-19 outbreak, which further facilitates the use of telemedicine during the pandemic. In some states, governors, departments of health, and Medicaid administrative agencies are taking similar actions to suspend current telehealth limitations and/or expand Medicaid coverage of telehealth services as well.

Are Virtual Clinical Trials Here to Stay?

While federal guidance and state regulatory waivers currently create a favorable environment for trial sponsors to be conducting decentralized clinical trials, these will only be in place for the duration of the emergency. Once the COVID-19 pandemic has passed, these restrictions will be back in place, which raises the question of whether study sponsors who turned to remote options during the pandemic will continue to utilize virtual methodologies after the pandemic is over. Only time will tell if the environment created by COVID-19 will have a long term impact on how clinical trials are conducted in the post-COVID.

This article is not an unequivocal statement of the law, but instead represents our best interpretation of where things currently stand. This article does not address the potential impacts of the numerous other local, state and federal orders that have been issued in response to the COVID-19 pandemic, but which are not referenced in this article.

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FOOTNOTES


[ii] “What Are Virtual Clinical Trials? An Interview with Science 37’s Jonathan Cotliar” by Mark Terry, biospace.com (July 15, 2019).


[vi] 21 CFR § 312.22(c).
[ix] Id.
[x] Id.

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