U.S. FOOD & DRUG ADMINISTRATION

PUBLIC MEETING:

Mitigating Clinical Study Disruptions During Disasters and Public Health Emergencies

October 18 and 19, 2023
MEETING REPORT

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Executive Summary

The Coronavirus Disease 2019 (COVID-19) pandemic has presented unprecedented challenges to the conduct of clinical trials globally. The U.S. Food and Drug Administration (FDA or Agency) has been at the forefront of the nation's response to the pandemic. While the COVID-19 public health emergency (PHE) declared by the Secretary of the Department of Health and Human Services under section 319 of the Public Health Service Act (COVID-19 PHE Declaration) has ended, COVID-19 remains a risk to the public, and activities to protect and promote public health in this area remain FDA priorities. An important aspect of FDA's response is using the knowledge gained from the global experience and response to COVID-19 to inform preparedness and future response efforts. In addition to the lessons learned, FDA acknowledges the collective resiliency of the clinical trial ecosystem and a willingness to promote best practices and embrace changes that will advance the conduct of clinical studies during future disruptions, such as a PHE.

One of the key roles of the Agency during the COVID-19 PHE was to provide recommendations to the clinical trial community on how to adapt trials to help ensure patient safety and continue trial conduct or maintain operations, as appropriate. In March 2020, within 2 months of the COVID-19 PHE Declaration, the Agency published the guidance for industry, investigators, and institutional review boards (IRBs) titled *Conduct of Clinical Trials of Medical Products During the COVID-19 Public Health Emergency* (COVID-19 Clinical Trials Conduct guidance). The guidance included recommendations to address complex clinical, scientific, and ethical issues raised due to major disruptions of clinical trials during the COVID-19 PHE. As the pandemic evolved, FDA updated the guidance multiple times to address questions the Agency received from sponsors, investigators, and other interested parties.

Section 3605 of the Food and Drug Omnibus Reform Act of 2022 (FDORA)[1] requires FDA to convene a public meeting, no later than 180 days after the date on which the COVID-19 PHE period ends, to discuss the recommendations provided by FDA during the COVID-19 PHE to mitigate disruptions of clinical studies, including recommendations provided in the COVID-19 Clinical Trials Conduct guidance. The COVID-19 PHE Declaration expired on May 11, 2023. Pursuant to the mandate and under a cooperative agreement with the Clinical Trials Transformation Initiative, the Agency organized a 2-day virtual public meeting titled "Mitigating Clinical Study Disruptions During Disasters and Public Health Emergencies" on October 18 and 19, 2023.

Section 3605(b) of FDORA also requires FDA to publish a report within 90 days of the meeting on topics discussed at the meeting. To satisfy this FDORA requirement, this report summarizes the discussions at the public meeting with an emphasis on the following topics: (1) the actions sponsors took to utilize such recommendations and the frequency at which such recommendations were employed; (2) the characteristics of the sponsors, studies, and patient populations impacted by such recommendations; (3) a consideration of how recommendations

1 Enacted as part of the Consolidated Appropriations Act, 2023, Public Law 117-328.

intended to mitigate disruption of clinical studies during the COVID-19 emergency period, including any recommendations to consider decentralized clinical studies when appropriate, may have affected access to clinical studies for certain patient populations, especially unrepresented or underrepresented racial and ethnic minorities; and (4) recommendations for incorporating certain clinical study disruption mitigation recommendations into current or additional guidance to improve clinical study access and enrollment of diverse patient populations. The report is intended only as a summary of the meeting and does not provide guidance or reflect FDA's current thinking on this subject.

Introduction

FDA organized the 2-day virtual public meeting in collaboration with the Clinical Trials Transformation Initiative to fulfill a requirement under section 3605 of FDORA. The attendees represented pharmaceutical and medical device industries, U.S. and non-U.S. government organizations, patients and patient advocacy groups, and other entities involved in clinical trials (e.g., IRBs). The meeting provided an opportunity for speakers and panelists to share their experiences on how they implemented FDA's recommendations in the COVID-19 Clinical Trials. Conduct guidance and other experiences with mitigating disruptions of clinical trials.[2] Synthesizing these collective experiences into opportunities and strategies is invaluable for mitigating clinical study disruptions and planning for future disasters and PHEs. This report summarizes the presentations and discussions by crosscutting industry experts.

Utilization of Recommendations in FDA's COVID-19 Clinical Trials Conduct Guidance

FDA issued the COVID-19 Clinical Trials Conduct guidance at the outset of the pandemic to provide general considerations to assist sponsors in helping to ensure the safety of trial participants, maintaining compliance with good clinical practice, and minimizing risks to trial integrity for the duration of the COVID-19 PHE. The appendix to the guidance further explains those general considerations by providing answers to questions that the Agency received about conducting clinical trials during the COVID-19 PHE. Some of the major topics covered in the guidance and appendix include continuation and initiation of clinical trials, informed consent, remote outcome assessments and implications for data management and statistical analysis plans, continuation of investigational product administration, protocol amendments and deviations, and communication with FDA.

The discussions at the meeting highlighted how the timely guidance issued by FDA addressed unprecedented issues that emerged during the pandemic and helped clinical trial operations proceed by implementing many of FDA's recommendations. The following are some of the FDA-recommended approaches utilized to help ensure continuity of a clinical trial while helping to ensure the safety of trial participants: electronic informed consent forms, flexibility in conduct of the informed consent process, remote monitoring, increased use of telehealth, partnering with local health care providers to continue care, remote data capture (e.g., digital health technologies, patient-reported outcomes, electronic medical records, mobile nursing for lab draws and study assessments), alternative approaches to delivery of investigational products to participants, appropriate and prespecified definitions of protocol deviations, and documentation. Ongoing conversations between FDA, sponsors, IRBs, and other health authorities helped to clarify interpretations and facilitate efficient use of the

2 In this document, trial and study are used interchangeably.

COVID-19 Clinical Trials Conduct guidance in the initiation and continuation of certain clinical trials. Meeting participants acknowledged that clear, constant, and current guidance from FDA were crucial not only for initiating new trials to address the COVID-19 PHE or continuing clinical trials paused during that time but also for returning to pre-pandemic levels of clinical research conduct and operations.

Additional discussion at the meeting included (1) using risk-based monitoring and data-based tools to assess the impact of the pandemic and prioritize participant safety and study visits to mitigate disruptions to studies and (2) streamlining statistical analysis plans to capture essential data and increase the use of remote outcome assessments to facilitate study continuation while maintaining data integrity. The discussion noted a significant increase of centralized and off-site remote monitoring during the COVID-19 PHE. A panelist presented a landscape analysis on over 3,000 ongoing studies from 2019 to 2023 describing comparative trends in monitoring before, during, and after the COVID-19 PHE. The data showed an increase of over 100% in centralized and off-site/remote monitoring between 2019 and subsequent years.

Speakers representing industry sponsors reported meeting with FDA to share data on the impact of disruptions on their clinical trials at the site level, helping FDA to understand the challenges in real time as well as promoting further understanding of the successes and challenges associated with the implementation of FDA's recommendations. Open dialogue between FDA and global health authorities was also especially important in utilizing FDA recommendations (e.g., when exploring possibilities for safely delivering investigational products to patients).

The meeting included a live poll of day 1 participants to solicit information about how frequently attendees utilized FDA recommendations provided in the COVID-19 Clinical Trials Conduct guidance. A total of 216 attendees responded to the live poll. The recommendations identified as most utilized pertained to remote study visits (78%), clinical trial monitoring (67%), documentation of protocol deviations (59%), informed consent (58%), data collection (43%), study drug access (38%), communications with FDA (28%), laboratory examinations (19%), and inclusion of underrepresented populations (11%).

Some key barriers in implementing FDA's recommendations included challenges with interpreting and navigating differences in policies and guidance regarding clinical trial operations at the institutional, State, Federal, and international levels; investigator and site personnel experience with implementing new approaches; increased burden on sites to learn and operationalize new processes; lack of site familiarity with telehealth and remote monitoring systems; and challenges with coordinating data across multiple sources.

Impact of the COVID-19 PHE on Studies, Study Sites, Study Populations, and Patient Experience

Studies

Unlike more localized emergency situations that can disrupt clinical trials in specific regions, the COVID-19 PHE had global impact on trial enrollment. Data shared during the meeting highlighted that global enrollment in clinical trials decreased by 65% from March 2019 to March 2020. The countries with the largest decreases in trial enrollment were India (–83.9%), the United Kingdom (–80.1%), France (–68.2%), Spain (–68.1%), China (–67.5%), and the United States (–66.7%). Countries with enrollment rates that were less impacted were South Korea (–61.1%), Italy (–52.3%), Japan (–43.5%), and Germany (–32.5%). Data from study protocols with at least one substantial amendment indicated that unplanned disruptions were a common occurrence with clinical studies even before the pandemic. From 2013 to 2015, the percentage of protocols with at least one substantial amendment in phase 2 or phase 3 was 77% and 66%, respectively. From 2018 to 2021, these percentages increased to 89% in phase 2 and 82% in phase 3 trials. A comparative study quantifying the impact of COVID-19-related disruptions on pre-PHE and PHE studies identified a significant increase (33% versus 85%) in the proportion of patients with at least one protocol deviation. Overall, FDA flexibility and guidance in the areas of decentralized trials, remote site monitoring, and remote patient visits were critical in enabling recovery in U.S. research compared to the rest of the world. Data presented by a panelist on enrollment and number of engaged sites from medical device trials conducted before, during, or after the COVID-19 PHE period also indicated more effective mitigation strategies and recovery in the US compared to the rest of the world during and post-COVID-19 PHE.

To address disruptions, sponsors prioritized studies related to treatment of COVID-19 and studies of life-saving therapies; non-urgent procedures or trial activities were suspended or delayed. As sponsors were considering whether to pause enrollment of ongoing studies, the safety of participants and study personnel were paramount. Other major considerations for prioritizing the initiation or continuation of studies included mitigating the risk of harm to participants from study treatment disruptions (e.g., by minimizing pauses in studies for oncology and other serious and progressive diseases), maintaining study integrity, and upholding data quality. Changes in the types and levels of risk to participants and study locations as well as policies, such as those related to government lockdowns, also impacted decisions on continuing study enrollment. Closure of health care sites also posed extensive challenges for device studies requiring post-operative follow-up. Some sponsors noted the approach of broadening the number of acceptable qualifying sites during disruptions by including additional qualified sites and physicians to perform follow-up or routine care.

Study Sites

During the COVID-19 PHE, academic medical centers and hospitals increased their market share of industry-funded clinical trials, while many smaller or community-based sites decreased their share or exited the research enterprise. Data shared at the meeting comparing data from 2011 to data from 2022 indicates that academic medical centers/hospitals conducting clinical trials increased from 40% to 43%; dedicated clinical trial sites increased from 8% to 12%, and the percentage of community-based sites conducting clinical trials decreased from 52% to 45%. The same panelist presented landscape data about clinical trial sites. Comparing data from 2011 to 2022, clinical sites conducting one trial per year decreased from 68% to 43%, while sites conducting 2-5 clinical trials increased from 23% to 37% and sites conducting 6 or more clinical trials increased from 9% to 20%. By 2022, 3,000 smaller sites had exited the clinical research enterprise. Sites with limited experience or infrastructure were more vulnerable to closure during the COVID-19 PHE, specifically the sites for rare disease trials. In some cases, sponsors provided additional funding to help some sites remain open.

Study Populations

Panelists reported that clinical trial disruptions were more severe in certain therapeutic areas. Data shared during the meeting comparing new subject study enrollment between March 2019 and March 2020 indicated that endocrine studies were most impacted by COVID-19 (–80.5%). Study enrollment in other therapeutic areas during this same time period also decreased as follows (in descending order): cardiovascular (–69.7%), central nervous system (–68.5%), dermatology (–64.0%), oncology (–48.4%), infectious diseases (–46.8%), and respiratory (–33.7%). Regarding differential impact of the pandemic on studies in various therapeutic areas, one panelist mentioned that study sites in shopping centers, such as in eye care centers conducting ophthalmology studies, were closed to participants and study personnel, making it impossible to continue enrollment and obtain study data. In contrast, during the COVID-19 PHE, COVID-19 vaccine development, including clinical trials, were not delayed by COVID-19 disruptions. COVID-19 vaccine development timelines were compressed by 70% (24 months versus 83.1 months for typical vaccine development) as the result of trusted collaborations, public-private partnerships, shared data and development risk, community and clinical care engagement, rapid deployment of virtual and remote technologies, proactive and accommodating oversight, and parallel clinical phase activity.

Patient Experience

For patients in the rare disease community, fear of exposure to COVID-19 led to reduced participation in clinical trials and routine medical care, contributing to severe health problems and possibly untimely deaths. Data from another survey conducted in the summer of 2020 by a rare disease patient advocacy organization indicated that 80% of respondents reported cancellation of medical appointments. Similarly, potential exposure to COVID-19 was a barrier to trial participation for immunocompromised patients. For many patients, caregivers or medical advocates are integral to care and facilitate their attendance at trial visits. Therefore, visitor restrictions imposed additional barriers to patients' participation in clinical studies during the COVID-19 PHE. Frequent and up-to-date communication with the trial sponsor was a key factor for the patient community to navigate the uncertainties of study participation during the COVID-19 PHE. Participants indicated that having trial staff that were readily accessible by phone and email, sponsors that shared information and results in layperson-friendly webinars that were attended by members of the research team who were available to answer questions, and frequent updates from the research team helped to build trust and made participants feel respected and viewed as equal partners in the design and conduct of clinical research. Patient-led information sharing about specific clinical trials through social media allowed patients to connect with each other and help educate their community about particular studies, thereby improving enrollment in those studies.

Patient panelists emphasized that during the COVID-19 PHE they realized the importance of sponsors sharing information and building relationships with patients during all aspects of medical product development to understand their needs and challenges with participation. The inclusion of patients and caregivers in the design of research can help make clinical trials more efficient, accessible, inclusive, and meaningful for the patient community. For example, it can be difficult for participants to learn new technology and use multiple systems or devices to participate in a clinical trial, and some technology is not accessible to some people with disabilities or in certain geographic locations. Including patients as partners in protocol design can help research teams understand the patient population's experience with provided tools and technologies and how that might impact the proposed study activities. Including patients and patient advocates who represent a broad range of demographics, abilities, and disease areas are key to empowering patients as valued partners in research.

Decentralized Trials During the COVID-19 PHE

Meeting participants discussed the widespread implementation of decentralized trial practices. Some panelists expressed that the broad implementation of decentralized trial practices during the COVID-19 PHE may have improved enrollment and retention of study participants overall and within the rare disease community. The examples shared by the panelists included the use of decentralized processes for recruitment, screening and enrollment, and delivery of investigational medical products directly to participants or local sites. However, the different methods available to obtain electronic informed consent (e.g., PDF form, tablet with a web-based application) created variability across clinical trial sites, which proved to be a challenge in standardizing consent practices. Many patients reported having positive experiences with decentralized trials, including, remote consent and remote patient visits, which facilitated participation and enabled access to a more diverse trial population.

A panelist participating in a clinical trial evaluating the safety and effectiveness of a COVID-19 vaccine in immunosuppressed patients reported appreciating the decentralized features of the trial. For example, a sponsor built flexibility into the protocol by allowing participants to draw their own blood at home with an easy-to-use blood withdrawal device. Trial personnel subsequently collected these samples from their home. The panelist considered the option to draw their own blood at home to be an effective strategy to address their concern about potential exposure to COVID-19 at a clinical trial site.

The Trial Innovation Network (TIN), a collaborative national network within the Clinical and Translational Science Awards (CTSA) of the National Center for Advancing Translational Sciences, combined radio, television, internet media, and mailing approaches to improve recruitment for TIN COVID-19 Plasma Trials. This approach led to the enrollment of Black (14%), Hispanic (14%), Native American (1%), and pregnant women (<1%) participants.

While there were many benefits of incorporating decentralized trial practices, there were also challenges. One panelist attributed the limited use of wearables and other digital tools to remotely capture study data during the COVID-19 PHE to the lack of available data necessary to validate the tools. Recommendations from health regulators on obtaining and documenting informed consent, including use of electronic informed consent, was critical to the ability to continue enrollment. However, the different methods available to obtain electronic informed consent (e.g., PDF form, tablet with a web-based application) created variability across clinical trial sites, which proved to be a challenge in standardizing consent practices. The use of home health care providers for lab draws, investigational product administration, and safety monitoring enabled the continuation of clinical studies that required in-person follow-up. However, shortages of qualified home health care providers and available health care vendors proved challenging.

Additional Topics Discussed

Innovative Trial Designs

Using innovative trial designs was another strategy for addressing challenges in clinical trial operations during the COVID-19 PHE. For example, one panelist indicated that, to increase efficiency, the National Institute of Allergy and Infectious Diseases designed its Adaptive COVID-19 Treatment Trial (ACTT) as a platform trial, a type of master protocol designed to evaluate multiple medical products for one or more diseases or conditions. The master protocol was conducted under one investigational new drug application, and the same IRB reviewed each new intervention sub-study. The platform protocol design eliminated the need for new site contracts for different interventions within the trial. The ACTT platform protocol was streamlined to gather data most necessary to evaluate the safety and effectiveness of the candidate products from clinical records.

Collaboration Across the Clinical Research Enterprise

Unprecedented levels of information sharing and collaboration across the clinical research enterprise were critical in assessing risks associated with trial conduct disruptions and developing appropriate mitigation approaches during the COVID-19 PHE. For example, in the early months of the pandemic, 50 to 100 clinical operations leaders from a pharmaceutical trade organization met biweekly to share real-time best practices to mitigate disruptions with the common goal of continuing to serve patients and trial participants around the world. The clinical trial community is also leveraging collaborative efforts to modernize clinical trial operations utilizing lessons learned during the COVID-19 PHE. The Modernizing Clinical Trial Conduct Initiative is one such example.

Leveraging Existing Networks and Centralized Research Support

Leveraging existing networks and centralizing research support were invaluable to implementing timely responses during the COVID-19 PHE. Meeting panelists expressed the importance of early planning and proactive inclusion of strategies to mitigate disruptions such as those caused by the COVID-19 PHE. Federal partners on the panel shared the following examples of lessons learned about leveraging existing networks for continuity of clinical trial operations during the COVID-19 PHE:

- To expedite the process of standing up sites for a vaccine trial, the National Institute of Allergy and Infectious Diseases recounted how using existing sites in the Infectious Diseases Clinical Research Consortium allowed for rapid implementation of clinical trials during the COVID-19 PHE. Through this approach, the first trial participants were able to receive the investigational vaccine on March 16, 2020, just 66 days after the genomic sequence of the virus was posted.

- The National Cancer Institute (NCI) utilized centralized functions that were in place before the pandemic to mitigate disruptions during the pandemic. The organization has a network of 2,200 sites across North America. NCI-sponsored trials require all U.S. sites to use a central IRB that operates completely electronically. Additionally, NCI has a 24/7 Cancer Trials Support Unit for regulatory and administrative functions, a Radiotherapy and Imaging Core Center, and an electronic common data management system with central hosting for data collection. The established network and centralized functions allowed the organization to immediately track and evaluate the pandemic's effect on clinical trial accrual in real time. Surveys of network sites also helped NCI to understand where sites had to pause or stop trial activities and which mitigation strategies were most helpful (e.g., virtual visits, working with local health care providers, shipment of investigational product to patients, eConsent, remote monitoring).
- TIN is a collaborative national network within the CTSA Program of the National Center for Advancing Translational Sciences. TIN is composed of three organizational partners: Trial Innovation Centers, Recruitment Innovation Centers, and CTSA Program institutions. TIN focuses on operational innovation, operational excellence, and collaboration while leveraging the expertise, diversity, and broad reach of the CTSA Program. Features of the CTSA Program that help expedite the clinical trial process include use of a single centralized IRB, use of master service agreements, quality-by-design approaches, and a focus on evidence-based strategies for trial participant recruitment and engagement.

  The network has a large research professional team with around 750 research nurses employed by CTSA Centers and over 1,000 research coordinators. The network is diverse with over 60 hubs comprising 93 million patients (13% African American, 13% Hispanic, 6% Asian American, and 2% American Indian). One percent (1%) of the patient pool resides in a rural area. TIN successfully utilized the network to conduct clinical trials efficiently during COVID-19 PHE. For example, TIN locally prioritized studies and identified research teams to participate in COVID-19 treatment trials. TIN's accelerated start-up and trial management processes (e.g., standard agreements) were instrumental in significantly reducing study start-up timelines during the COVID-19 PHE from 103 days to 16 days for the Passive Immunity Trial for Our Nation (PassITON) study.

Global Clinical Trial Challenges

When implementing mitigation strategies during the COVID-19 PHE, sponsors of trials conducted in multiple countries found it challenging to navigate the differences in health authorities' policies and guidance. Although telehealth and remote monitoring were important components of many clinical studies during the COVID-19 PHE, privacy laws restrict their use in some countries. Some panelists noted the importance of communications between regulatory authorities to facilitate the mitigation of study disruptions and to encourage cross-border and global harmonization where possible.

Other difficulties in continuing global clinical trials during the COVID-19 PHE included disruptions in supply chains due to flight cancellations, illness, and participant migration. For example, at times, sponsors had to liaise with government officials to ensure that participants who moved across borders could receive investigational products.

Future Improvements in Clinical Trial Operations

There was unanimous agreement that the use of decentralized approaches can provide flexibility for trial participants and facilitate the inclusion of diverse patient populations in general and especially during disruptions. However, decentralization of clinical studies does not ensure health equity. New technologies, such as wearable digital health technologies, used in decentralized trials, should be equitably available to avoid excluding groups who do not have access to these technologies. Panelists advised that assumptions about the study population's familiarity with and access to technology should be evaluated before considering use of the proposed technology as a mitigation strategy to ensure it does not lead to inadvertent exclusion. Panelists also suggested that sponsors verify whether new technologies or strategies are reaching the intended populations. To utilize technology tools, sponsors may consider investing support and resources in sites closest to communities that may have fewer resources.

Training for existing and new sites on how to safely continue studies that cannot utilize decentralized methods would also be beneficial. Although decentralized methods were critical in helping studies to continue, these methods are not appropriate for every clinical study or participant; thus, panelists advised that sponsors make decentralized methods available as one of the options but not require them to be the only option in emergency situations.

Potential opportunities to improve the conduct of clinical trials during disruptive events such as disasters or public health emergencies include:

- Collaborating across the clinical trial enterprise to explore and develop harmonized guidelines to address disruptions
- Appointing a clinical trial coach at the outset of the trial to help coordinate the clinical trial experience for participants
- Integrating flexibilities in trial design prospectively and proactively to minimize protocol deviations (i.e., study flexibility that is fit-for-purpose and permits options including flexible study visit windows)
- Advancing modalities and innovative technologies (e.g., digital health technologies, artificial intelligence) to reduce burden and enhance the inclusion of diverse patients as partners in clinical trials, focusing on patient perspectives about what worked and what did not throughout the trial
- Incorporating patient input to augment best practices in clinical trial conduct
- Using lessons learned during the COVID-19 PHE to determine which approaches can be continued or poised to be ready for use when appropriate and embracing changes that prove to be effective during disruptions.

Advanced Planning and Emergency Preparedness

Although disasters and PHEs may have different challenges, general lessons learned from the COVID-19 PHE can help mitigate future disruptions to clinical trials. These learnings span the entire spectrum of the clinical trial enterprise, including study planning, regulatory requirements, patient recruitment and consent, study conduct, and participant follow-up. Some mitigation strategies implemented during the COVID-19 PHE, such as the use of decentralized elements, including eConsent and remote visits, were successful and are now incorporated routinely to improve the conduct of clinical trials. Other strategies that were necessary during the COVID-19 PHE may not necessarily be appropriate to implement in the day-to-day conduct of clinical research but should be considered for future emergencies or disruptive situations. Moving forward, it is important to identify areas where individual and collective responses were inadequate during the COVID-19 PHE to consider how the clinical study ecosystem can be more resilient during disruptions in the future.

Building Emergency Preparedness into Clinical Studies

To effectively prioritize clinical studies and patient safety in the event of a disaster or emergency, organizations should proactively plan for such circumstances when designing clinical trials. In modernizing the design and conduct of clinical studies, making trials more resilient, agile, and flexible should be the norm to help manage disruptions of any type. Emergency preparedness plans should consider the investigational product, study population, outcome measures, and impact on local and global environments. Emergency preparedness plans are fundamental for studies evaluating treatments for severe or life-threatening diseases. In terms of developing disruption plans within protocols, panelists recognized the importance of determining which mitigation strategies and decentralized methods cannot be implemented globally. Emergency preparedness plans should consider the potential need for additional training for sites and participants. For example, when study protocols include decentralized elements that allow flexibility, such as variable approaches to study visits and/or assessments, it is important to train study personnel on what constitutes a protocol deviation in this context. Patient safety is a top priority during disruptions and should be the primary consideration while developing emergency preparedness plans.

Remote site monitoring is another activity that sponsors widely used during the COVID-19 PHE; however, moving forward, panelists suggested that sponsors strive to refine remote site monitoring strategies and virtual site visits as part of emergency preparedness. Efficient use of remote site monitoring as part of an emergency preparedness plan should include efforts to reduce duplication of on-site monitoring. Identifying where data are collected and stored and the ability to access such data is also critical to effective remote site monitoring. Data stored in multiple systems creates challenges to effectively review data and site operations remotely. Sponsor and site panelists supported integrating data

sharing technologies to decrease the number of systems for which monitors need access. Providing additional training to clinical study sites on the use of new remote site monitoring technologies would also be beneficial and may reduce costs over time.

Panelists also encouraged the routine use of risk management approaches to identify critical trial procedures and data and to design study management systems that are fit for purpose, consistent with FDA recommendations. Such approaches are particularly important to mitigate future disruptions by focusing on the procedures and data most critical to the study. Identifying standard key indicators for tracking to enable quick and real-time assessments of what is happening across studies and across sites in different locations will also be beneficial.

Additional suggestions for emergency preparedness pertained to proactive plans for initiating or continuing new trials during disruptions, decreasing variability in trial operations, and conducting site surveys. Panelists suggested that sponsors should implement emergency preparedness systems that facilitate prospective tracking of those sites that can initiate new trials or can continue to operate during a disaster or emergency depending on the type of disruption. One suggested approach to mitigate future disruptions was to generalize learnings across multiple development programs to decrease variability in how clinical trial sites approach study conduct during disruptions. Site surveys conducted throughout the development program may be helpful tools to better understand site and participant perspectives. Such surveys may also provide patients with an opportunity to be directly involved in the study and to suggest improvements that could be made during disruptions.

Regulatory Considerations

In preparing for future disruptions, panelists discussed the importance of communication between health authorities during the COVID-19 PHE to facilitate global harmonization of regulatory recommendations. The rapid publication of FDA guidance documents and frequent communication between FDA and sponsors enabled some studies to continue throughout the COVID-19 PHE. Panelists agreed that this strategy should continue as an effective approach to mitigating clinical study disruptions during disasters and PHEs. However, challenges remain including the need for health authorities worldwide to pursue efforts to further harmonize regulatory expectations and approaches.

Conclusion

The public meeting panelists agreed that the COVID-19 PHE served as a catalyst to accelerate innovation and modernization of clinical study conduct and operations. Maintaining momentum to embrace modernization and continue innovations in clinical research is crucial because disruptions can occur at any time during the conduct of clinical studies and can happen for many different reasons. Several panelists highlighted FDA's recently issued guidance titled *Considerations for the Conduct of Clinical Trials of Medical Products During Major Disruptions Due to Disasters and Public Health Emergencies* (September 2023) as a step forward in leveraging lessons learned from the COVID-19 PHE. The guidance recommends approaches that sponsors of clinical trials of medical products can consider when there is a major disruption to clinical trial conduct and operations due to disasters or PHEs, including but not limited to hurricanes, earthquakes, military conflicts, infectious disease outbreaks, or bioterrorist attacks. FDA looks forward to continuing engagements and mutual learnings across the clinical research ecosystem to facilitate adoption and implementation of best practices that will ensure timely access to safe and effective medical products and advance public health through resilient and agile clinical studies. It will be the collective responsibility of the clinical trial community to apply the lessons learned from the COVID-19 PHE to modernize future clinical studies.

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Link to the Public Meeting Recording, Materials, and Resources

Virtual public meeting recordings and slide decks are available at FDORA 3605 Public Meeting – Mitigating Clinical Study Disruptions During Disasters and Public Health Emergencies.

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