The Multi-Regional Clinical Trials Center of Brigham and Women's Hospital and Harvard Bioethics Collaborative

Thursday, February 2, 2023 | 2:00 PM – 4:30 PM EST
Virtual Meeting

Emergency Preparedness in Clinical Research
Meeting Summary

Background

Disruptive events – pandemics, wars, earthquakes, hurricanes – can impede the conduct of clinical research. These events broadly raise ethical and operational challenges for the clinical research community. The February 2023 Bioethics Collaborative addressed several such pressing questions in this domain. What are the obligations of different stakeholders, such as research sponsors and investigators, to continue conducting ongoing research in the face of disasters? Do obligations to vulnerable participants demand that clinical trial infrastructure in these situations be maintained so that the participants might potentially benefit from continued participation? Are research teams obligated to facilitate clinical trials when doing so puts them in harm's way? What actions should sponsors and CROs take, both amid disasters and proactively preparing for them?

Summary

Early in the discussion, the work during the war in Ukraine by the International Federation of Associations of Pharmaceutical Physicians (IFAPP) Ethics Working Group was summarized. Several recommendations have been advanced by the IFAPP Ethics Working Group, including the idea that abrupt study closure due to armed conflict is a severe risk for participants and that there is an obligation to make efforts to ensure the continuation of study treatments in times of conflict. In addition, different phases of trial management during different types of disasters were distinguished, including management during the initial chaotic phase of a disaster, management under continuing development of a disaster, and management during a return to normal. Each of these phases presents its own logistical and ethical challenges and demands different types of responses.

In situations where continued trial conduct at a site is not possible – such as during the initial chaotic phase of a disaster – ensuring the continuation of study treatments for participants

enrolled in potentially therapeutic trials may require transferring them to different sites and locations. Bioethics Collaborative participants discussed the ethical and logistical challenges with these situations, including efforts to transfer participants to other institutions within the home region or country and to relocate participants to geographically distant locales or international sites. There was an acknowledgment that the challenges of relocation are amplified during times of disaster, with discussants noting questions about whether or which family members should accompany relocated participants, among other concerns. Additional attention is needed to ensure that participants (and their families or caregivers) are adequately informed and do not overestimate the benefits of continued participation.

While no one objected to the idea that sponsors may materially assist participants in relocating, it was noted that the sponsor's obligations to support participants in these situations are limited and that transparent disclosure of the extent of sponsor assistance is paramount to establishing accurate expectations. There was agreement that research sponsors should not be considered humanitarian organizations, are not equipped to provide general humanitarian support, and should consider collaborating with organizations with expertise in disaster settings. It was noted that there might be possibilities for sponsors to collaborate with independent humanitarian groups to coordinate relocation and other emergency services. In addition, the receiving institutions and investigators are critical in accommodating participants evacuated from conflict zones or disaster areas. The role of receiving institutions can extend to deciding to support or host a study so that newly-evacuated individuals can continue trial participation, providing translations of consent forms and other materials, and offering general social supports to relocated individuals and families.

The importance of remaining flexible and finding creative solutions to enable continued research in times of public disaster emerged as a prominent theme. Researchers on the ground in these types of situations may find themselves needing to do such things as request increased funding to ensure the success of the study, rely on social networks to locate people and continue individual monitoring, work to intervene in local health care systems on behalf of participants (e.g., advocating to move them up a vaccine list), bring the study to the participant (e.g., in times of lockdown due to public health strictures), be flexible and dynamic with research staff and employment practices (e.g., institute pay raises, permit remote work, hire additional help), and address the specific fears and obstacles keeping individuals from returning to trial sites and study participation.

In the second half of the Bioethics Collaborative, the discussion turned to emergency and disaster preparedness and models for launching and supporting trials during public health emergencies, with the COVID-19 pandemic foremost in mind. Discussants noted the

importance of decentralized modalities and data collection mechanisms in times of disruption and, relatedly, mechanisms for making it easier for individuals to continue participation remotely, such as through telehealth and home health visits. The importance of enrolling diverse study participants and facilitating participation among under-served populations was emphasized and noted as a continuing challenge that needs to be balanced with speed and efficiency in launching research during public emergencies.

Discussants then focused on the role of sponsors and CROs in responding to emergencies and their varying obligations concerning the different stakeholders with whom they interact, namely, study participants impacted by disasters, site staff, and CRO employees. Here there was agreement that CROs and sponsors should work to assist study participants directly affected by disasters to remain on the trial if they so wish. At the same time, the needs of researchers and site staff on the ground should be given consideration. Sponsors and CROs should be aware of the stressors their staff face and make efforts to ease those stressors and workload, such as by transitioning to remote monitoring and data collection practices (when possible) and adapting study protocols to allow as much flexibility as possible. The CRO also has obligations to its own employees, which must be balanced against its commitments to participants and research staff. These include prioritizing employee safety, such as by permitting them to opt-out of study visits to impacted sites, providing personal protective equipment as needed (e.g., radiation badges for work done around Fukushima), setting limits on the risks they are asked to undertake, and forthright communication with them about both the risks and the importance of continuing their work.

Finally, the Bioethics Collaborative ended with a discussion of the importance of prompt regulatory action and clarification in times of disruption. The role of regulators consists both in ensuring that general guidelines for emergency situations are prospectively in place, insofar as possible, and in promulgating timely guidance as new or unanticipated challenges emerge. It was stressed that pragmatism is needed in times of disruption; we will need to ask which aspects of the regulations and our usual ways of doing things cannot be modified and which are flexible and can be changed. For example, a change in monitoring frequency might be acceptable when faced with a disaster or public emergency as long as it is well-documented and the rationale is sound; however, it would never be permitted to forego serious adverse event collection or reporting. It was noted that different regulatory bodies are likely to have different opinions about which aspects of which regulations might permit flexibility and which do not. Participants expressed hope that we can learn from past disasters, particularly the COVID-19 pandemic, about how different regulatory dispensations and flexibilities in times of crisis impact subject safety and data quality.