Public Health Crises and the Human Subjects of Biomedical Research: A Focus on COVID-19

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The widespread social and economic disruption caused by the novel coronavirus disease 2019 (COVID-19) is clearly apparent and has affected all walks of life. The biomedical research enterprise is no exception. According to the 2015-2016 Global Participation in Clinical Trials Report published by the US Food and Drug Administration (FDA), there were 40,385 clinical trial participants in the United States during that time period. Given exponential advances in biotechnology, it is expected that this number has grown considerably over the past 5 years. As such, there are many thousands if not hundreds of thousands patients actively participating in a clinical study in the United States. Like us and all sectors of the health care economy, their lives are severely affected by the restrictions, risks, and angst over the COVID-19 global pandemic as declared by the World Health Organization. We believe that it is critical to review the obvious and potential challenges faced by the various stakeholders involved in biomedical research as public and private institutions and organizations grapple with the situation.

HUMAN SUBJECTS OF RESEARCH

The most obviously affected happen to be the most vulnerable of all—patients volunteering for clinical research. The imminent challenges faced by research participants in intervention clinical studies beyond the fear of unknown include concerns for adequate access to and availability of experimental therapeutic agents that are not available outside regulated clinical trials, travel arrangements to be made if the clinical trial site is distant, existence of adequate expertise closer to patients to deal with adverse effects, or challenges that may arise in the context of clinical trials and effect this may have on caregivers. These and other challenges are expected to cause significant anxiety and distress in clinical trial participants and their loved ones, especially those with life-threatening illnesses such as cancer.

BIOPHARMACEUTICAL AND MEDICAL DEVICE INDUSTRY

The sponsors of clinical trials are affected no less significantly. Their most active challenge is the commitment to the patients and participants of ongoing clinical trials to ensure that adequate medication supply is available, to ensure that the most up-to-date information about the experimental agent is readily available to the study sites, to meet the regulatory requirements and maintain the highest standards of manufacturing and quality control, and to maintain records. A unique challenge faced by the industry is the effect on a pipeline of compounds and clinical studies that have not started yet but are in advanced stages of development.

US FOOD AND DRUG ADMINISTRATION

As noted in its mission statement, the FDA, among other duties, is trusted with the responsibility of protecting the public health by ensuring the safety, efficacy, and security of human drugs, biologic products, and medical devices. Uncertainties and challenges posed by the COVID-19 pandemic are a significant test for the FDA as it is actively addressing the ongoing concerns of shortages of commercially available pharmaceutical compounds.
PHYSICIAN-INVESTIGATORS AND STUDY TEAMS

Clinicians involved in clinical trials and their teams are uniquely affected by these crises, perhaps more so than any other stakeholder, as they are the critical link between the patient and biomedical research. The challenges faced by the study teams include concerns for active patients on clinical studies at various stages as noted above, regulatory issues and record keeping, and risk of nonadherence to study procedures because of unanticipated disruptions, communications with the sponsors and the FDA, and uncertainty of the situation as it rapidly evolves and unfolds—all this besides keeping up with regular clinical responsibilities.

Although no precedence exists in the recent past of the scale of disruption seen in the past few weeks, the uncertainties and distress are natural and anticipated. We believe that the most important principles of biomedical research remain beneficence, justice, and respect of persons. Good faith actions that enhance the safety and well-being of study participants honor these principles and are outlined in FDA regulations (21 CFR 56.108(a)(4)) as “exceptions where necessary to eliminate apparent immediate hazards to the human subjects.”

The most important and critical step in preparing for any eventuality is for the study teams to work closely with their study sponsors to determine a course of action that supports the rights, safety, and welfare of participants without compromising the integrity of research. Some of the options available for investigators and study teams are to consider minimizing face-to-face visits, when possible, and develop plans with the sponsors for alternatives such as telephone visit and telemedicine visit using the technological expertise available at various sites. The teams should proactively contact research patients and discuss their concerns and contingency plans. The sponsors should consider conducting pre-site visits, site initiation visits, and routine monitoring visits remotely by using current advancements in remote video- and telecommunications as several HIPAA-compliant options are in existence. Documentation of these communications and plans of actions should be robustly maintained. Given these extraneous circumstances, the institutional review boards and/or independent ethics committees should not make determination of serious nonadherence for actions that are done in good faith to protect and promote the safety and welfare of the human subjects of research as long as such actions are supported by proper documentation. Finally, we believe that this national emergency identifies a unique opportunity for regulatory bodies such as the FDA to develop a formal plan of preparedness. Incorporating emergency and disaster preparedness into the Collaborative Institutional Training Initiative course and into Good Clinical Practice training courses will go a long way to ensure future preparedness. In summary, as various stakeholders involved in biomedical research gear up the plans to deal with any eventuality, it is imperative to remember the core principles that underlie the trust of society in biomedical research enterprise: beneficence, justice, and respect of persons.4

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