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From Remote Oversight to Wind-Downs: Research Struggles in the Time of COVID-19

By Theresa Defino

“In an effort to minimize the risk of contracting or spreading COVID-19 in human participant research interactions and to preserve personal protective equipment for clinical care, the university is placing temporary restrictions on human subjects research effective Saturday, March 14, and continuing through Friday, May 1.”^[1]

So began the note from the University of Michigan (U-M) Office of the Vice President for Research, posted over the second weekend in March, a message that reflected the rapidly changing environment surrounding the coronavirus outbreak and the need to consider the sometimes competing needs of patients and research subjects—not to mention the desire to keep staff healthy. The announcement included that the May 1 date would be reevaluated.

Indeed, U-M later updated that note with one that sounded more urgent: “The university encourages you to develop a research Continuity of Operations Plan by the end of this week (Friday, March 20). Consider how the work of your groups could be slowed for the coming weeks to be prepared for a reduction in operations, and what steps you would follow if the work had to be placed on hold with short notice. The planning you do now will support the long-term success of our laboratories and research groups.”^[2]

In a subsequent post on March 21, U-M noted that regardless of all the other changes, “our research support units (Research and Sponsored Projects, Technology Transfer, Research Ethics & Compliance, Consulting for Statistics, Computing & Analytics Research, etc.) remain operational.”^[3]

As the outbreak that first took hold in China and Europe began to spread in the last month to the United States, U-M and other universities took immediate and, in most cases, unprecedented steps, often in concert with their institutional review boards (IRBs). As U-M demonstrated, research compliance officials kept working, usually at home, their days a blur of conference calls, emails, video meetings and regular checks of agency websites to get the latest guidance.

Some actions were inevitable based on requirements from local governments and state officials, but often preceded those mandates.

For example, on March 2, New York University (NYU) Langone Health banned “all domestic and international work-related travel and attendance at outside business and academic meetings, conferences, etc. for at least the next 60 days.” This decision was two weeks or more ahead of widespread travel bans.

Near the end of the month, many organizations were forced to consider shuttering research labs because government agencies began telling the public they had to stay home unless they worked in “essential” positions or businesses. At a minimum, ongoing studies were transitioning, whenever possible, to remote monitoring or oversight of trials.

‘Mt. Sinai Is Standing Down’

On March 20, Dennis Charney, dean for academic and scientific affairs, and Rosalind Wright, dean for translational biomedical sciences, at Icahn School of Medicine at Mount Sinai, issued a notice to faculty, staff and students.^[4] It was one that had become both familiar and inevitable.

“We felt it would be helpful to summarize where we are and to offer further specific guidance as this dynamic situation continues to evolve,” they wrote.

- “We are suspending in-person screening and enrollment visits in our clinical research studies, with the exception of studies evaluating interventions for COVID-19 or for other life-saving interventions. Please contact your IRB to ensure that your study falls in this category as previously advised.
- “We are suspending in-person follow-up visits for all subjects unless discontinuing or deferring the protocol presents a clear and present harm to the study patient (see previous guidance).
- “For patients already enrolled or randomized, please continue to collect protocol-specified data remotely via telephone or telehealth if possible. Data elements that can be collected remotely include medication adherence, quality of life and functional status instruments, hospitalizations, adverse events and complications.” Charney and Wright provided the name of an individual to contact “for consultation on methods for remote follow-up.”
- “Extension of protocol-defined data collection windows, where possible, will provide flexibility and will minimize data loss. Obviously, late data is better than no data.”
- “Remote data collection and extension of data collection windows are strategies that can be implemented as modifications for previously approved research, as stated in [45 C.F.R. § 46.108 and 21 C.F.R. § 56.108] (to eliminate immediate hazards to human research subjects).”

Agencies Offer Extensions

Institutions could also look to information from NIH, the National Science Foundation and other funding agencies as they grappled with how to maintain or suspend operations, and what the impact might be on award-funded research.

NIH issued guidance on March 12 and again on March 16 “outlining the flexibilities available to recipients conducting NIH-funded clinical trials and human subject studies.” NIH noted that award recipients already may “extend the final budget period of the approved project on active grants one time for up to 12 months without requesting prior approval from NIH.”

Beyond this, to “support participant health and safety, and continuity of research during this public health emergency, NIH will allow for additional extensions, including mid-project period extensions, for awards supporting NIH-funded clinical trials and human subjects research. Recipients should contact the awarding Institute or Center to provide details on the effects of COVID-19, and the need for an extension,” the agency said. “NIH is committed to working with its recipients during this public health emergency.”

NIH added that, generally, “project periods for NIH awards supporting clinical trials and other human subjects research are limited to seven years. NIH will allow project periods to extend beyond the 7-year timeframe for extensions related to COVID-19.”

Two days later, the Food and Drug Administration (FDA) put out guidance for sponsors and investigators related

to COVID-19, but it stopped short of identifying any types of trials that should or should not proceed. Essentially, FDA wove a theme of “safety first” throughout the guidance, stating that this consideration might require trial modifications. (For links to specific agency updates, see story, this issue.)^[5]

Regarding amendments to IRB-approved protocols, the HHS Secretary’s Advisory Committee on Human Research Protections recently developed recommendations for what is often referred to as “re-consent” (see story, this issue).^[6] The recommendations may prove especially helpful during the pandemic as a plethora of changes to protocols are expected.

Borrowing From Research for Clinical

Some institutions also looked to organizations, including commercial IRBs, for recommendations. WIRB-Copernicus Group (WCG) held several webinars and announced it planned to hold a weekly series related to the impact of COVID-19. During the first, held on March 13, Paul Biddinger, chief of the Division of Emergency Preparedness and director of the Center for Disaster Medicine for Massachusetts General Hospital, described what the institution was going through at that time.^[7]

All of the activity connected with the outbreak has “definitely [had] an impact on our clinical research capabilities,” he said. “At the same time, there’s an incredible need for knowledge. With an outbreak like this we certainly have to understand what is going on; we have to continue to acquire knowledge.”

Expressing the feeling of many, “We don’t want to also, frankly, just put the entire scientific enterprise on hold for a year and stop the advancement of medical knowledge,” Biddinger said.

But like others, Mass General and Harvard had to engage in “hard discussions about how to continue elective research studies and when we need to stop other research studies,” he said, adding, “it’s a balance of safety and resource utilization and the importance of the project.”

Biddinger noted that there had been “very unfortunate challenges” on the clinical research side, noting it was “hard for us to be able to continue to support clinical encounters with patients where either the research assistant or the researcher might come into contact with COVID, and just from a risk management standpoint and a resource utilization standpoint.”

‘Greater Good’ Takes Precedence

Mass General “cannot use a single piece of personal protective equipment that could be used otherwise to protect the health care worker or a patient in the course of clinical care,” he added. “We have made massive changes to how we’re using students, to how many people enter a room for every COVID patient. We actually have rolled out iPads on poles in a COVID patient’s room so that the nursing and physician team have to enter that room fewer times, therefore consuming fewer gowns, gloves, masks, et cetera.”

In a subsequent webinar also sponsored by WCG, Art Caplan, professor of bioethics and founding director of the Division of Medical Ethics at NYU Langone Medical Center, discussed the “moral framework for trying to do research in a pandemic.”^[8]

Caplan said medicine is usually guided by the principle of putting the patient first, and ensuring that subjects are protected.

“However, in this pandemic, minimizing harm to large numbers of other people has to override the traditional respect for patient autonomy. Meaning even if somebody says, ‘I want to continue in research,’ or ‘I have certain

requests about how to do it,' we might try to accommodate that under normal circumstances," he said. "But in a pandemic, we really have the duty to protect the community, and that is the community of health care providers, the general public, our colleagues and peers in the workforce. So that makes the moral equation shift a little bit—less autonomy, more, if you will, protection and minimization of harm."

In practical terms, "that means we want to try and keep people out of the hospital. That's why elective surgeries have been canceled, because we don't want to expose people to a risky environment. We want to minimize exposure and transmission of the virus by not having people come together when they don't have to; they're better to socially isolate right now," said Caplan, who also echoed the need to save resources for clinical uses.

Secondarily, he said institutions also have a moral obligation to not "abandon those who are reasonably benefiting in research," when choosing which research should continue.

Weigh Individual Requests

"If someone was in a late Phase 3 trial and we knew that they were benefiting from treatment of their cancer or some other ailment, I would try to do a calculation assessing the risk and benefit of getting to the hospital and the exposures and hassle factor that that involves versus they're not getting care," said Caplan. "I can imagine someone in a study who is reasonably benefiting, saying 'Look, to cut me off here and end this study midstream is going to harm me. I am getting benefit. It has to continue.' That has to be weighed in trying to decide whether or not a particular research project should continue."

But, added Caplan, "we don't want to be pursuing the admirable goal of getting new knowledge about things unless it has direct potential for benefit. Obviously that could be in managing the pandemic or some direct potential benefit for related studies like preventive vaccination, that sort of thing."

In his view, the kinds of studies that have to be scaled back are "observational studies, pragmatic trials, Phase I studies, and animal studies," because "they're not going to directly benefit in any imminent way the battle against the virus. And so that's the kind of thing where I think we're probably morally obligated to stop."

Pandemic Research Triggers Special Concerns

Regarding whether to initiate a trial during this period "involves sensitivity to the windows that patients may face," such as having "a disease that's really taking them down rapidly. Somebody may say, 'I've got something that could help them. I was about to initiate that.' There could be an argument to trying to do that. I can think of a gene therapy situation that might justify doing that for a particular child that was slipping away fast. But I think those situations will be very rare."

He added that, in addition to assessing the risk profile of subjects, the "integrity of the supply chain" must be considered, along with whether researchers are "going to be able to access agents that you want to administer."

Caplan also warned to be on guard against therapeutic misconception when COVID-19 research begins recruiting subjects, and the need to ensure they understand that "oftentimes there's more risk involved than there would be benefit" in early phase studies.

¹ Rebecca Cunningham, "New Restrictions for Human Subjects Research," University of Michigan-Flint, March 13, 2020, <https://bit.ly/2WDgymA>.

² Rebecca Cunningham and Susan Collins, "COVID-19: Faculty, Staff and Students in the Research Workplace," last updated March 16, 2020, <https://bit.ly/3afAaAS>.

³ Office of Research, the University of Michigan, "COVID-19: Research Operations at U-M,"

<https://bit.ly/2wAqDpt>.

4 “COVID-19 Research Guidance for MSHS,” Icahn School of Medicine at Mount Sinai, March 20, 2020, <https://bit.ly/3ac36tB>.

5 Theresa Defino, “Agencies Make Allowances for Impact of COVID-19 on Spending, Deadlines,” *Report on Research Compliance* 17, no. 4 (April 2020).

6 Theresa Defino, “SACHRP: Sharing of New Info Doesn’t Necessitate Full ‘Re-Consent’ Process,” *Report on Research Compliance* 17, no. 4 (April 2020).

7 WCG, “COVID-19 Preparedness: Information from the Experts,” webinar, March 13, 2020, <https://bit.ly/3a9rhsG>.

8 WCG, “PART 1: Clinical Trials in the Era of COVID-19—The Changes You Need to Make now,” webinar, March 18, 2020, <https://bit.ly/3aeHBsm>.

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