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Report on Research Compliance Volume 17, Number 5. April 23, 2020 Restarting Studies After COVID-19 Will Require Adaptations, Scrutiny of Study Site Capacities

By Theresa Defino

Alison Lakin, associate vice chancellor for regulatory compliance at the University of Colorado, Denver, Anschutz Medical Campus, acknowledged that it might seem inconceivable at the height of a pandemic to "start thinking about ramping back up research."

But she called this "the right time to be strategically thinking about how we efficiently, collaboratively and in a coordinated manner move forward" with clinical trials and ensure the safety of participants.

Heeding the call from governments and public health officials, much research on U.S. campuses has been shut down since the COVID-19 public health emergency was declared in March.[1] Universities and other institutions have scrambled to salvage what research they could, incorporating remote visits for clinical trial participants and, in some cases, allowing only studies related to COVID-19 to go ahead.

Lakin deemed the last two months "a challenging hiatus" and said more difficult times lie ahead, when clinical research is restarted. Nevertheless, "on a positive note…we have an opportunity…to collaborate together in a different way than we've done before. There are lessons that we can learn from this experience," she said.

Already Laskin has gained insights, including that research might be changed forever in some respects—with innovations like e-consents becoming common—and she also suspects that Americans are likely to have much greater interest in supporting drug development and may themselves be more eager to participate in research.

Restarting Studies After COVID-19

Despite all the preparation, "I don't think we'd ever planned for this one," said Lakin, "and I'm not sure that our normal prioritizing of reopening is actually going to work in this environment."

Lakin shared her views as part of a webinar series last month sponsored by the WIRB-Copernicus Group on the impact of COVID-19 on research.[2] She pointed out that one reason there may not be a return to "normal" is the expectation that the nation will suffer repeated outbreaks of the virus.

"We're going to be living in this era of potential waves of disease that are going to potentially impact us nationally, regionally, and [by] state," she said. "But the [research] sites are the real local level, and there may be the need to have…continued social distancing, whether it's continuous or intermittent. We're going to have to manage the unpredictability of potential hotspots coming up, even if things do move forward, away from the isolation."

The disruption of clinical sites is also likely to continue.

"As an academic institution, we work closely with large regional hospitals, and those hospitals are very much going to…continue to be focused on clinical care, more so than some other [research] sites," said Lakin. "We have to be thinking about ramping up in a more unstable world than we have been used to."

This means that sponsors need to be "very aware of your local context" and understand that different sites will return at different times, said Lakin. This will be unlike previous disasters when there might have been a "whole-scale change" that signaled when recovery was underway.

Certain Research More Affected Than Others

Basic resources are likely to remain committed to caring for COVID-19 patients, as some hospitals are expected to become "regional COVID centers," Lakin predicted.

She noted that this will affect certain services and specialties more than others.

As a result, "if the research was connected to surgery, there may be a delay in elective surgeries restarting. Radiology procedures, pharmacy services…are going to continue to be prioritized to clinical care, which makes access to use of those services for research difficult," said Lakin.

In particular, research sites treating pulmonary disorders and infectious disease are likely to be "slower to have [research] capacity," as might anesthesiology, she said. Specialty hospitals, such as children's medical centers, in contrast, may be able to accommodate research requests more quickly than a general community hospital, Lakin added.

Research may also be hampered by a lack of staff, as many may have been reassigned to assist with clinical care, with no known date of return to their usual activities, she said. This, Lakin added, will affect "how quickly you can think about ramping back up research."

Lakin said she is often asked when new trials can open enrollment, a question that requires "work that we need to be doing now to even be able to contemplate what that would look like."

One unknown factor is how long "we're going to need to have an approach that is based [on] emergency guidance and what that looks like," Lakin said.

She added that each research site "kind of moved fairly quickly to adapt to these unusual circumstances," likely leading to inconsistencies in approaches.

Standardize Adaptations Related to COVID-19

"Now is the time to be working across the spectrum of the key parties to make sure that we all agree on how we're continuing to do the research that we're doing, what deviations have had to be put in place, and how long those deviations are going to have to continue," Lakin said.

Approaches need to be standardized so that "we don't impact data integrity, and we can actually continue to answer important research questions," said Lakin. That requires "good communication across the key parties" to assure the integrity of the trials that are currently open.

Discussions will also be necessary regarding whether protocol deviations should be continued "as we move forward out of crisis mode and into some level of consistency," she said. For example, researchers will need to know if the study will revert to the original protocol, one with deviations, or perhaps a "new hybrid."

It will also be vital to figure out "how do we operationalize that. And it may be different for different cohorts," she said. It may be best to keep new enrollment closed and continue "with these adaptations before we think about adding in new potential participants," said Lakin.

She pointed out that social distancing measures may need to be incorporated into protocols and noted that

"we're going to end up in a world where we have COVID-positive and COVID-negative participants" and asked whether this "will impact the science of the studies that are ongoing."

Officials will need to decide how to address this, paying attention, for example, to whether inclusion and exclusion categories will need to be revised. Finally, it will be important to ensure that protocols and any contracts are "matching up," Lakin said.

Another consideration will be the need to add new research sites. "We have satellite hospitals; we have clinical research units that we probably need to think about optimizing more in order to expand capacity sooner and to free up the clinical space" from the added complexity of research, she said.

This also provides a good opportunity to perhaps build in a "virtual initiation visit" instead of an on-site monitoring visit as new sites are added, according to Lakin.

The University of Colorado, she said, has been continuing to open new studies, but they have been clinical trials focused on COVID-19, with both industry and federal sponsors.

Staffing Issues Will Complicate Matters

In addition, as recommended by the Food and Drug Administration, NIH and ethicists, the university, Lakin said, has also opened new studies "considered to have a potential for high therapeutic benefit and life extensions." Other clinical trials have been put on "some level of hold or hiatus."

Reigniting the research enterprise will require "marrying those two things up and making sure we thought [through] capacity before we bring on new studies," Lakin said.

It's still too early to tell what the economic impact has been or will ultimately be on the workforce and clinical sites, Lakin said, but in addition to some reassignment of research staff to clinical areas, "we've currently got a hiring freeze, so as staff leave, we are not replacing" them.

When research is restarted, "we are going to have to think about expanding our workforce again." Lakin said she also assumes some research sites may have had layoffs, which could affect their capacity to resume research studies.

As "we're bringing on new studies," sponsors and study sites both need to "take a strategic look at how they build capacity to continue to manage in this fluctuating environment," she said.

Study design may also change.

Lakin said that new studies coming on board may have "normal protocols and research procedures," as well as an "adaptive design…so that we more thoughtfully respond to a limited crisis of a hot spot or some temporary change, and that we're doing it in a little more considered manner than we did with the initial advent of this crisis."

Capitalize on Eagerness to Participate in Research

Lakin recommended that institutions review "data and feedback" from COVID-19 studies that have been adapted, including the use of virtual visits, "to show what can be done, and what the quality of the data is," as some may be worthwhile to continue once the pandemic has passed. Virtual visits are a good example.

"I will say, as an institution, we are doing a lot more telehealth than we ever did or ever contemplated doing before this crisis," said Lakin. "And it is amazing to see how quickly people have adapted to it and how successful

it has been in this environment. I think there are lessons to be learned."

Despite acceptance, Lakin added that participants may feel a need for "social reconnection" with study personnel when this is all over, and that researchers should recognize "where they're at as things go forward."

She also noted some bright spots, including that the public is now becoming more engaged and "informed about the drug development process than they ever were before." She predicted the rise of a "more informed community that is interested in working with us to move drug and device development forward."

This provides an opportunity to "partner" in different ways to facilitate study recruitment, Lakin said, adding that new studies "may need to be different from what we were doing before."

She also expects to see "really interesting data start to come out from these [study] adaptations," which could be incorporated in study designs in the future, along with "reconnecting with the community in a different way."

Electronic Processes Take on More Importance

In addition, electronic solutions "are working a lot better than I think anybody anticipated, but I think there's still a lot of work we could do in standardizing an approach to e-consenting," for example, Lakin said.

Telehealth visits may also become more routine as participants "appreciate those options, and there's some efficiency that we're seeing in this environment that I don't think people expected," she added.

Other electronic processes may also be needed. "Moving to an electronic registry notebook, I think, is essential if we are going to contemplate [electronic] monitoring, and that includes subject binders," Lakin said. "We have to move in that direction to streamline our approach in this uncertain environment."

According to Lakin, drug accountability has proven to be an area that is "more challenging than most." Institutions need to "think about how we can adapt drug accountability to electronic solutions."

Lakin praised the "amazing" working relationships encompassing "sponsors, [clinical research organizations], the sites" and the university that have allowed adaptation and innovation, which she seemed hopeful would be maintained after the pandemic subsides.

1 Theresa Defino, "From Remote Oversight to Wind-Downs: Research Struggles in the Time of COVID-19,"*Report on Research Compliance* 17, no. 4 (April 2020), https://bit.ly/2K6bgrZ.
2 WIRB-Copernicus Group, "PART 4: Clinical Trials in the Era of COVID-19 – The Changes You Need to Make Now," webinar, April 8, 2020, https://bit.ly/2VF7N9p.