IRB ADVISOR

YOUR PRACTICAL GUIDE TO INSTITUTIONAL REVIEW BOARD MANAGEMENT

INSIDE

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IRBs Look at How to Get Through Pandemic — and Beyond

Focus on phased-in approach

As human research protection programs (HRPPs) and IRBs enter the next leg of the COVID-19 pandemic, they can draw on experience to find the best balance between safety and efficiency.

Each institution and IRB will face its own challenges — just as they did in March 2020, when most studies were paused because of the pandemic. But one of the more common challenges as the United States copes with more than eight months of the crisis is pandemic fatigue and burnout.

"We've seen a lot of burnout among healthcare workers," said **Allecia A. Harley**, MPH, CRA, chief executive officer and chief strategy officer with Lake Shore Strategy in Chicago. Harley spoke about IRBs and the pandemic at a PRIM&R virtual conference, titled, "Research Ethics and COVID-19: Lessons Learned and Future Considerations," held Aug. 18.

"We have to be creative, especially with IRBs that are a mix of clinicians and administrators," Harley explained. "We have to make sure we're being kind to ourselves and setting appropriate boundaries."

> "MANY OF US ARE LETTING WORK HOURS BLEED INTO OUR PERSONAL LIVES IN A WAY THAT IS CHALLENGING FOR EVERYBODY."

As IRB staff continue to work partially or fully remotely, they need to differentiate between work hours and non-work hours. "Many of us are letting work hours bleed into our personal lives in a way that is challenging for everybody," Harley explains. "We should put parameters or boundaries around work time, which is critical for an individual."

IRB directors should emphasize the importance of being kind to colleagues. Everyone is experiencing stress and issues.

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"We should try to communicate that we should always keep in mind that everybody is going through something right now," Harley said. "There's not a single one of us who doesn't have a challenge or extra stress that we're dealing with."

Give Colleagues Space

As IRB staff and members communicate and hop on a call, there might be background noise of dogs barking, or their children could be climbing on their laps, or family members who need attention.

"Sometimes, we just need to give staff space to vent a little bit, so put in extra time at the beginning of a call or meeting to acknowledge them and the struggle they're going through," Harley suggested. "When people are curt or abrupt with us, it's not necessarily personal; everyone is going through something, so just give them a little space to be where they are in that moment."

Adjust Reopening Plans

As the pandemic's first year draws to a close, IRBs should consider how to adjust plans for reopening and starting studies while keeping everyone safe. They also must prepare for a second surge of COVID-19 and pausing more studies.

"What we've done at Yale is there are a number of groups that are evaluating the safety, not just from a human subjects protection perspective, but also looking at the safety of staff, researchers, and everyone on our campus," said **Linda Coleman**, JD, CIP, CHC, director of the HRPP at Yale University. Coleman also spoke at the Aug. 18 PRIM&R virtual conference.

Groups focused on the pandemic response began meeting in March. The institution established a hotline and evaluation of which types of studies needed to be paused and which could continue. "As we moved along, over time, we evaluated a phased-reopening plan with the understanding that if there is a surge in our area, then we might also have to ramp down again," Coleman explained. "At that point, we had a phase 0, where the only type of studies that could remain open were those that were essentially therapeutic with potential for direct benefit, and even those were limited."

Next was phase 1, which reopened a few more studies. The institution moved to a phase 2 and then phase 3, where more — but not all — studies are underway. "The key to phase 3 is you want to minimize contact among staff and research participants," Coleman said. "We're telling researchers that we're in a phase 3, and they can use social distancing."

The goal is for investigators to find different ways of conducting their studies by using telehealth visits and changing how they consent participants. They also can develop safer ways to conduct laboratory tests. "The key is always to minimize contact," Coleman said.

The decision to change a phase is based partly on what the pandemic looks like in the area and the availability of personal protective equipment, she added. Phasing also is related to what the university campus is doing regarding in-person work and classes.

"Certain undergraduate students are allowed to come on campus, and some semester-long visitors are allowed on campus," Coleman says. "Even though some expansion of on-campus activities is permitted in

phase 3, other safety measures are in effect."

Stay Connected

One of the more challenging changes during the pandemic is for IRB staff to stay connected. "It's really important that IRB staff and IRB members check in on each other to make sure they're OK," Harley said. "IRBs are encouraging people to use emails and other tools to check in with each other and make sure people are communicating."

As the pandemic continues, and especially if it resurges in an area, forcing institutions to put studies on pause again, IRBs should be aware of pandemic fatigue.

Every IRB member and employee will have a personal story about the pandemic's emotional impact on them. For those in need of the emotional support of coming into the office and chatting with colleagues, the pandemic has been particularly difficult, Coleman notes.

Also, some employees are caring for small children or older family members at home during the pandemic. Balancing their home family life with work-at-home life is challenging. "The university has done a good job of addressing all those situations and giving employees flexibility," Coleman explained. "If they have a sick parent at home and want to adjust their hours in the day, then as long as people know what's going on, we can all be flexible."

Remote workers tend to work longer hours. "Before, we would go across the street for a cup of coffee and would have to walk across the campus for a meeting," Coleman said. "Now, we have to remind people to take a break before a meeting."

Once IRB offices reopen with full, in-person staff, leaders should keep in mind there could be celebrations and excitement — but there also could be some shocking surprises, Harley says.

"Be prepared for how much people may have changed since they were last in-person," Harley says. "Some might have gained a significant amount of weight; some might have lost weight; some might have aged."

IRB co-workers also might have lost family members to the pandemic and are less cheerful and energetic than they were before offices closed. "We'll have to be sensitive to any range of emotions that may come up when people start getting together again," Harley said. "We need to allow people to come back without any shock, surprise, or judgment. Everyone is going through something, so they may look different and speak differently, and their perspective may be different."

The IRB office and research organization also might look different. Some places will have new plexiglass barriers and other infectious disease safety features, Harley said.

The organization can prepare workers by showing them videos before they return to work and sharing information about new rules regarding bringing in lunch and how conference room meetings might work, she added. ■

Tips for Reopening or Closing Research Studies

The 2020 landscape for clinical trials looks different than it did five or 10 years ago. Even before the worldwide disruption in research from the COVID-19 pandemic, there were systemic shifts that have squeezed trials in ways that add pressure to investigators and IRBs.

For instance, there has been a 70% increase in procedures required in Phase III trials, and an 86% increase in endpoints in Phase II trials, said **Nicholas Slack**, MBE, executive vice president and chief commercial officer at WIRB-Copernicus Group (WCG), speaking of internal data. Slack spoke at a Sept. 9 WCG webinar.

"Over the past 10 years, trials have become more complex and burdensome on sites," Slack said. "More people and more technology are required to conduct clinical trials than was needed in the previous 10-year period."

Along with the COVID-19 pandemic is the healthcare financial recession that was not present during the last major recession, he noted. "In 2008 and 2009, healthcare workers largely were not laid off," Slack said. "That's not the case in 2020 when 1.4 million healthcare workers have been furloughed or laid off. We're facing a very different situation than we previously experienced." *(More information is available at this link: https://bit.ly/2T0Iiyn.)*

As the pandemic continues and research organizations are preparing to reopen trials, there is a looming crunch because more trial volume is on the horizon.

"Do we have a perfect storm of mounting financial pressures, staff shortages, and physicians exiting trials while sponsor trial volume is increasing?" Slack asked. "Trial delays have been increasing over time, and they could get worse."

One risk is IRBs and research organizations will be inundated with

study protocols when everything is reopened. They will need to prepare for reopening all operations and all studies. There are many steps they should take before making this decision.

Discuss Successes and Challenges

The first step is to meet with IRB and human research protection program (HRPP) leaders to discuss what went well during the pandemic and the closing of in-person operations, as well as what needs improvement, said **Linda Coleman**, JD, CIP, CHC, director of the HRPP at Yale University. Coleman spoke about IRBs and the pandemic at a PRIM&R virtual conference, titled, "Research Ethics and COVID-19: Lessons Learned and Future Considerations," held Aug. 18.

Working toward a next phase of the pandemic plan is part of disaster and continuity planning. "I would encourage sites to think about what is going to work for them," said **Allecia A. Harley**, MPH, CRA, chief executive officer and chief strategy officer of Lake Shore Strategy in Chicago. Harley also spoke at the Aug. 18 PRIM&R virtual conference. "It's important to think through what works for us and how we can use the things that are working and expand them. A lot of challenges are not specific to the IRB space; it's a general issue that everybody is dealing with."

Coleman said decisions to reopen a particular study also involve these factors:

- Is the study in a hospital or standalone clinic?
- Is the study on campus or off campus?
- Is the study international?
- How is COVID-19 testing performed?
- Is the study therapeutic or non-therapeutic?
- What is the safety plan?
- Are temperature checks performed before entering the study site?

"It's very complex and complicated because one size does not fit all," Coleman explained. "We are saying, 'If you are a researcher doing research with human subjects, you have to ask for permission to reopen your research if your study was put on pause.'" Sites must ensure the safety plan is appropriate before investigators can reopen the study.

"THERE ARE LOW-COST THINGS YOU CAN DO TO STILL REMAIN RELEVANT, GET YOUR WORK DONE, AND CONTRIBUTE IN A MEANINGFUL WAY."

As the organization prepares for a second surge, the groups that evaluate the pandemic and safety will decide whether the phase needs to be reduced and more studies put on pause.

"The [COVID-19] numbers are fine right now, but that could change at any time — next week, or a month from now," Coleman said. "Researchers are aware they may have to ramp down again."

The Yale HRPP is reviewing new studies as people continue to submit research, but they will need both IRB approval and institutional approval to begin work. "We've had a lot of studies that the university has reviewed related to COVID-19. Some studies were changed to include COVID-19 in part of it," Coleman said.

The IRB did a good job of ramping down in March, and is ready to act again, if needed. "We're providing more flexibility in terms of making a modification to the study," Coleman explained. "Studies have used telemedicine and virtual communication with research participants."

The IRB gives investigators guidance from the Food and Drug Administration about how to use a remote lab and arrange for a third party to make home visits to participants. There also is information on how to safely ship investigational products during the pandemic, and how to talk with sponsors about what needs to be done.

"Regulators provided enough guidance, and we were able to do the ramp down process quickly. We could do the same thing again," Coleman said. "It might even go more smoothly."

Pivoting back and forth between in-person IRB work is easier for research organizations since they already went through the abrupt change to online work at the beginning of the pandemic.

"You don't have to spend a lot of money to make that pivot and to be prepared for remote work, or know how to manage your IRB during this time," Harley said. "There are low-cost things you can do to still remain relevant, get your work done, and contribute in a meaningful way."

Be Creative

IRBs have become creative in keeping staff safe while continuing daily operations and activities. For

example, some IRBs have met in socially distanced outdoor settings.

"I've seen people be creative and take their IRB meetings outside or on a rooftop deck," Harley said. "Sometimes, campus centers have an indoors garden, a solarium that is under glass and enclosed, but really is a park under glass. They can meet safely there."

For some staff meetings, IRBs have occasionally given staff a break and used a fun app like House Party that allows people to put on a virtual detective mask or clown hat. "They're being creative with where they meet and how they meet," Harley added.

When research studies need participants who are recruited remotely to sign informed consent and regulatory documents, some IRBs in smaller cities have approved delivering the documents to participants' homes via a staff member. Then, the staff member picks up the signed documents and scans them at the office, Harley said.

"For some organizations, DocuSign is outside of their budget, so they'll print out the documents and drop them off in people's mailboxes," she explained.

That is impossible to do in a city the size of Chicago, but might be plausible in a town the size of Peoria, IL, she added.

IRBs also have adjusted by ensuring their information technology support provides email options that are encrypted, making it safer to share private information and large files. They have offered training to IRB members to help them connect to Zoom meetings and make other electronic changes. ■

Tips to Improve IRB-Researcher Productivity and Relationship

Build trust, clarify expectations

Expectations and communication issues are the two biggest challenges between principal investigators and the IRB community.

"There's often not a recognition that expectations and communication define the nature of their relationship," says **Julie Slayton**, JD, PhD, director of the office for the protection of research subjects and professor of clinical education at the Rossier School of Education at the University of Southern California.

IRBs set expectations through their websites and response letters, but they might not have articulated those expectations to themselves and investigators. "No one says, 'What are our clear expectations? What do we expect them to do?'" Slayton explains. "If you haven't articulated clear expectations, then it's difficult to impart it in a clear way to the research community."

From the principal investigator (PI) perspective, researchers might not fully appreciate that IRBs can be advocates and not merely a clearing house or impediment to putting research in the field, she adds.

"When I did my PhD, I wasn't clear about what IRBs did until I worked for the IRB," Slayton explains. "Having those two hats on at the same time gave me a clear perspective of what each part of the conversation sounded like and what each member is asking for."

Communicate Expectations

Without clear and understandable expectations, communication problems and distrust can grow. To prevent these issues, IRBs should name their expectations, first internally, and then through intentional messaging. "Find ways to communicate your expectations in clear ways," she explains. "Both sides have pressure, so having empathy for both sides makes it easier."

IRBs also can improve communication with PIs by giving them context and helping them understand IRB requests and decisions. "Think about the context of conversation, what needs to be said, and why it needs to be said," Slayton says. "Those things are important — inside the IRB as well."

IRB staff and members should work toward building more productive, transparent relationships with the research community. The IRB's goal should be to advocate for researchers, and the research community to advocate for the IRB, she says.

"When we have things like COVID-19 and a shutdown, and it goes from five weeks to 11 weeks for an application to be approved, we want people to say, 'I have an understanding and appreciation for the work asked of IRBs,'" Slayton says. "When there is better clarity of expectations, it's more likely members of the research community will help us get the work done."

As the pandemic continues, IRBs have an opportunity to set new expectations about how disruptions and changes will be handled. "One thing we did was construct a FAQ response to the COVID ramp-down and ramp-up," Slayton says. "We set up a web page to be responsive to ramping up studies, telling investigators exactly what to expect and where to get resources to complete the actions they needed, including giving them better information and transparency."

IRBs should direct researchers to their websites, encouraging them to see the website as a resource. "When you look at our website, there is COVID-19 information," Slayton says. "The website explains what we want to focus on and who does what."

The website also tells researchers what they need to do before submitting to the IRB. "All those things are explicit on the page," she adds. "Here's what we need for you to be successful in our partnership."

Focus on Intentional Messaging

Another important step is intentional messaging. IRBs can improve their intentional messaging by following these examples:

• **Read from the PI's perspective.** "Go back to your website and ask yourself, 'If I am a researcher and read this, what is it I understand?'" Slayton says. "Who are we messaging? What is the content to it?"

Many websites are difficult to navigate and find the necessary links and information. IRBs should revisit these and make improvements, she adds.

• **Prepare for discussions.** "Today, we have two discussion with different faculty members, and we have a pre-meeting where the team and I will discuss what we want to communicate at those meetings," Slayton says. "We talk about what's extraneous, what will interfere, and who will lead. We talk through all of those things so we're not just getting into a room and starting a conversation [cold]."

If a difficult meeting is not going well and emotions are frayed, Slayton will handle it discreetly. "Last week, as I listened to someone in a meeting, the person's emotion was getting the best of him. I sent him a private text, saying, 'Take a deep breath,' and that worked," she explains.

• **Let it go and adapt.** "Be willing to let go of things," Slayton says. "We've done newsletters that are terrible, just flooding people's inboxes and not doing anything [useful]."

It is better to stop sending weekly or monthly newsletters and instead send researchers bulletins when there is something new and important to communicate.

When something affects the study submission workflow, the IRB can send an email bulletin. "We reserve that for an email that someone will recognize as very important," Slayton says.

When there is something important to tell an investigator, the IRB can hold a video or teleconference.

"I have two meetings with different investigators today to talk about challenges with their applications. We do that over Zoom, face to face," Slayton says. "The phone is OK, but it doesn't allow for visual cues."

• **Use social media.** "We have a Twitter account that went from no users to 100 users to people retweeting to their universe," Slayton says. "When something goes live on our website or in a bulletin, it gets retweeted."

• **Respond comprehensively.** It is important that an IRB's communication with investigators is consistent and comprehensive. "The way analysts write to researchers should have a tone that is thoughtful, rather than just, 'We need to tell you something,'" Slayton explains. "It's a combination of finding ways to communicate that are meeting our stakeholders where our stakeholders are. We're reassessing the quality and type of communication."

For example, an IRB analyst could write, "Your application is being returned because you didn't do A, B, C," she says. "This is stark and in your face, and might come across as confrontational."

Instead, the analyst could write, "We appreciation your application, and we would like to give you the context for why we're returning this to you," she adds. This reframes the rejection, using language that is less likely to trigger a negative emotional response.

Another way to reframe this kind of response is to recognize trigger words like "but": "Your application was good at B and C, but did not do F and G," can be improved this way: "Here are the things we need you to do to complete the review of your application, for example," Slayton says. "I'm a professor and think a lot about the writing. Things are usually vetted with me."

Slayton has worked with IRB staff to improve their empathic writing skills. "We developed a number of templates, usually particular to a specific challenge or situation," she says. "If we have something we'll be writing about a lot, then we'll correct it, and I will be one of the people who reads it."

If there is an especially contentious letter that the IRB needs to send an investigator, Slayton and the associate director will review it for tone and grammar, she adds. ■

COVID-19 Pandemic Changed Informed Consent for Biobanking

New Common Rule exception used

Researchers have used the 2018 public health surveillance exception to the Common Rule for the first time during the COVID-19 pandemic.

"The exception basically said when you're collecting specimens or data for public health surveillance purposes that it will be exempt this from the Common Rule requirement, and it would not be considered research," says **Mary Catherine Beach**, MD, MPH, co-chair of IRB3 and professor of medicine at Johns Hopkins University. Beach also is core faculty in the Berman Institute of Bioethics. "Therefore, all the protections that we would have in place for research projects may not be in place for samples collected under a public health surveillance protocol."

In the early weeks of the pandemic, researchers might have overused this exception. Federal agencies approved some protocols involving lines of genetic materials with explicit research purposes, even if these were secondary to the public health surveillance purpose, Beach notes.

"It was something you would never allow a study to do without an informed consent, in normal circumstances, and these were not the reason the public health surveillance exception was written," she says.

For example, investigators for one study collected nasal swabs, blood, and feces from children and their caregivers, and the families mailed these in. A secondary plan to use genetic information and make that publicly available was sponsored by the National Institutes of Health, Beach says.

"Another study, sponsored by the Centers for Disease Control and Prevention, involved collecting nasal swabs from healthcare providers to create some cell lines," she adds.

These data could be identifiable later, and the plans to use them for research were established in the beginning.

"If you're collecting that much material from somebody, it's not that hard to collect a consent form," Beach says.

Obtain Consent When Possible

Johns Hopkins University has a policy that all public health surveillance efforts must be reviewed by the IRB to determine whether they also might involve research and require informed consent. In some cases, the IRB decided COVID-19 public health surveillance projects were human subject research studies and could not continue without informed consent, Beach says.

"A signed consent form didn't seem prohibitive," she adds.

Several institutions allowed these types of projects to continue without informed consent. There might have been cases in which these surveillance projects were approved administratively by an IRB office without coming before a convened board, Beach says.

An IRB's goal should be for researchers obtain informed consent when it is possible and is desirable from a human research protection perspective.

"I guess it's possible for researchers, who decide to use public health surveillance specimens for a later research study, to go back to the IRB for review and ask for a consent waiver to use with the specimens that were collected without informed consent," Beach explains.

For example, if an IRB sees a protocol that uses previously collected biological COVID-19 samples, then the IRB could consider waiving consent according to appropriate criteria. The IRB might say this study qualifies for a waiver of informed consent as it will not violate anyone's rights and the research is important, she adds.

If a public health surveillance project is not intended to be used in a research study, then it would meet the exception criteria, even if specimens were to be stored in a biobank and later used in research, Beach says. But in many cases, the scientists collecting the samples know in advance they also will be used for research.

"In that case, the research project should undergo IRB review and be considered as a research project," Beach says. "There is confusion about whether the samples collected for surveillance can be used for research purposes. It's our view that any research study involving biobank samples should undergo regulatory and ethics review through the IRB, even if it's not possible for them to obtain consent." In those cases, a waiver of consent is possible.

Mainly, the IRB is concerned with a situation in which samples are collected prospectively with some intention of being used in a research study, and the investigators could fairly easily obtain informed consent but choose not to do so. "You should get consent for that kind of research even if we're in a public health emergency," she explains. "The only things allowed under the public health exclusion are those immediately necessary to solve public health problems. If we allow people to do projects on samples collected under public health surveillance, then researchers can bypass all research protections."

IRBs should tell researchers if they are conducting public health surveillance and believe they might use the samples for research, then they should obtain informed consent up front. "You may be able to collect a sample for public health surveillance purposes, but know that people may not want you to store it for future research," Beach says. "Some examples are creating cell lines with genetic material from participants, without consent, or making genetic analyses publicly available."

These uses can pose a risk to participants through the potential violation of privacy and their rights when that was not the purpose for donating their sample. "Part of the reason there has been a pushback on IRB review is because people feel the process is unduly burdensome, administratively," she notes. "In a pandemic, IRBs have a responsibility to mobilize quickly and do quick turnaround on protocols."

This way, investigators know the IRB will not hold up emergency research and create more burdens. "We met daily during the beginning of the pandemic to address these issues, and there shouldn't be any delay in any protocol as a result of our actions," Beach says. ■

FDA Answers Audit Questions from Researchers, Industry

Inspections resume in United States

The Food and Drug Administration (FDA) issued new guidance on inspections during the COVID-19 pandemic, as the agency began to resume domestic inspections in July.

According to the 12-page guidance for industry, titled, "Manufacturing, Supply Chain, and Drug and Biological Product Inspections During COVID-19 Public Health Emergency Questions and Answers," inspections were temporarily postponed in March but are resuming for prioritized activities in the United States. *(The guidance is available at this link: https://bit.ly/2Zbm5ky.)*

The FDA is using a COVID-19 Advisory Rating system to determine what categories of regulatory activity can take place in any particular region. Using this determination on a case-by-case basis, the FDA will conduct mission-critical inspections or resume prioritized domestic inspections, including preapproval and surveillance inspections, according to the guidance.

"Resumption of these domestic inspections is being done consistently with the National Guidelines for Opening Up America Again," the FDA wrote. These inspections are preannounced to sites to ensure the safety of investigators and others.

When IRBs and research sites are contacted by the FDA about an inspection, they possibly can postpone it, depending on their circumstances, says **Chris Weir**, CIP, IRB operations manager at Fred Hutchinson Cancer Research Center in Seattle.

"I was aware of another IRB contacted by the FDA. They said, 'We're in the middle of a pandemic here, and [the inspection] won't work right now,' and the FDA said, 'No problem; we'll call you back in a few months,'" Weir recalls. "They were willing to delay a routine audit."

In-person inspections can be problematic for research organizations that still do not have their full staff working onsite, he notes. For instance, at Fred Hutchinson Cancer Research Center, all the administration has been off-site, even though the IRB is still in a paper-based system. "We were going to start transitioning to a new electronic system and had already moved to an electronic system to other areas of the institution, but the IRB was on the later end of that scale," he explains.

The FDA's focus appears to be more on COVID-19-related claims and bigger issues than conducting onsite visits. "They're probably being pulled into other directions than IRB operating stuff," he says. "Even accreditation bodies are recognizing that having someone onsite is not an option right now."

Foreign preapproval and for-cause inspection assignments will continue to be postponed so long as they are not considered mission-critical, according to the FDA guidance.

Criteria for Inspections

The FDA assesses whether an inspection is mission-critical based on these factors:

- Have the products received breakthrough therapy designation or regenerative medicine advanced therapy designation?
- Are the products used to diagnose, treat, or prevent a serious disease or medical condition for which there is no other appropriate substitute?

"Both for-cause and preapproval inspections can be deemed mission-critical," the FDA wrote. "The FDA takes into account concerns about the safety of its investigators, employees at a site or facility, and, where applicable, clinical trial participants and other patients at investigator sites."

The FDA's Center for Drug Evaluation and Research and Center for Biologics Evaluation and Research will continue to evaluate applications, using a holistic approach to determine whether an inspection is warranted or no longer needed.

"The agency encourages applicants to be in communication with all their facilities and sites to ensure timely responses to any inquiries to support application assessment," the guidance stated. ■

Neurotechnology Takes Human Research Ethics to New Frontiers

It is possible that any IRB might someday review a study that involves making healthy people smarter, cognitively faster, and more resilient mentally.

Neurotechnology, including research funded by the government, also is designed to help people with Parkinson's disease, locked-in syndrome, mental illness, and other issues. But it could take things a step further for people with no chronic conditions. This potential raises ethical questions.[1]

"Novel neurotechnologies pose a particular problem because they are affecting people's brains," says **Darcy McCusker**, MA, MSEd, graduate student in the philosophy department at the University of Washington. "There are always ethical issues that come up, like drug treatments and how people in positions of power have access to experimental treatment."

Neurotechnology can give people possibilities that previously were unimaginable. For instance, one area of research involves brain-computer interfaces, using implants with which people with locked-in syndrome can communicate.

"In the old version, they could control a computer with the motion of their eyes," McCusker says. "But the brain interface takes it a step further, and people learn how to get their brain and computer to interact by the person thinking about an individual letter."

By focusing on one letter of the alphabet at a time, the person can train the computer to recognize the signal their brain makes when they think about a particular letter. The goal would be for the person to communicate in written words simply by thinking of the letters of each word, and the computer would recognize their thoughts, she explains.

"The ultimate goal is for someone with severe disability to use the computer without anyone else's help and to get their needs met," McCusker says.

With deep brain stimulators, people with depression, obsessive-compulsive disorder, and other mental illnesses could find some relief. Also, in brain stimulating-technologies

under investigation for Parkinson's disease patients, there is the possibility of side effects that make people think they are acting more impulsively, McCusker notes.

"Putting this device in someone's brain will hopefully help them with their symptoms," she explains. "But it can have an impact on people and other parts of their brain, making them question, 'Is that me doing it? Or is it the device doing it?'"

McCusker researches brain-computer interface and deep brain stimulation and how these therapies pose numerous moral risks. The results suggest ethical reflexivity practices can help build public trust in research of new technologies.[1]

"The idea of ethical reflexivity is an idea that researchers have an obligation to think about the values they're bringing to the lab," McCusker explains. "One of the most poignant examples of this is the neuroethics group I work with, and the end-user roundtables we've done."

Researchers can meet with people who can benefit from a new neurotechnology. Rather than develop technological solutions to fix a problem the researcher envisions, they can find out exactly which problems the end users want to solve. For instance, researchers might think the top priority for people in a wheelchair is to walk again. But in talking with people in wheelchairs, investigators might learn they are more concerned about bowel function and sexual function, McCusker explains.

Maybe learning to walk again is not high on their priority list, but controlling when they go to the bathroom is something that affects their quality of life, McCusker adds.

"We want researchers, even without having the experience of interacting directly with someone who will use their device, to ask them questions," she says. "How do they think about the end-user perspective or the perspective of people in the disability rights movement? Are they concerned about how their research could affect the choices they make?"

An example of ethical reflexivity in practice is the Scientific Perspectives and Ethics Commitments Survey (SPECS), which was developed by the Neuroethics Thrust with the Center for Neurotechnology at the University of Washington. SPECS researchers gather for a meeting to engage in pressing ethical issues related to their novel neurotechnology research.[1]

These are several sample prompts from SPECS:

- Ethical considerations ought to play a major role in directing neural engineering research.
- Neural engineering research focused on affective or cognitive conditions should aim to enhance affective or cognitive capabilities beyond normal functioning.
- Social inequality is a legitimate moral concern that should shape the direction of neural engineering research.

The trickiest ethical issues involve neurotechnology for the purpose of enhancement. "People think their goal is to take average people and make them better," McCusker says. "Some researchers want to help people get to their baseline before they had symptoms, to return to their previous levels of functioning, but we don't want to go beyond that; we don't want to enhance people. We don't expect them to change their minds, but we want them to recognize that they think enhancement is a good goal in neurotechnology and a goal to recognize in themselves."

This recognition helps researchers frame their own goals, inform IRBs, and help the people with whom they work.

IRBs might consider potential harms of neurotechnology for enhancement purposes. For example, a major funder could be the Defense Advanced Research Projects Agency (DARPA), an arm of the Department of Defense. The funders might be interested in neurotechnologies for military engagements, McCusker says.

A few technological evolutions from now, and IRBs might review studies of devices that could make a person run faster or that keep fighter pilots alert for longer periods. "Maybe the technology could help someone focus better," McCusker

says. "But there may be some reasons that we don't want to try and build the bionic man."

From a risk perspective, some of these neurotechnologies involve brain procedures. There is a physical risk to performing brain surgery on healthy people, she adds.

For research participants who might benefit from these technologies, IRBs should keep in mind the devices pose a psychological risk. For example, a device might help someone control their tremor, but it also could increase their impulsive behaviors, McCusker says.

"If I gamble away money, am I responsible for it, or does the device share some responsibility for it?" she asks. "It also undermines your trust in yourself in an example like that."

Research participants might worry about how they feel and what they do when the tremors stop, she adds.

Some neurotechnology devices can sense directly from a person's brain when a tremor is about to happen, and the device can automatically turn on and prevent it. Others might need to be turned on and off by a technician, McCusker says.

"You want research that's important and has a high impact, but you also want to make sure you are really engaged in what the people need, and what they want," she explains. "You should take the time to think about all of this, or at least about some of the important issues that come up with this research." ■

REFERENCE

1. Tubig P, McCusker D. Fostering the trustworthiness of researchers: SPECS and the role of ethical reflexivity in novel neurotechnology research. Res Ethics 2020; doi: 10.1177/1747016120952500. [Online ahead of print].

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CME/CE QUESTIONS

1. **Which is a good question to ask when deciding whether to reopen studies, according to Linda Coleman, JD, CIP, CHC?**

   a. Do sponsors promise to indemnify subjects in the event of a COVID-19 outbreak?
   b. How is COVID-19 testing performed?
   c. Has the IRB reviewed the study?
   d. Does the study involve the HIV/AIDS population?

2. **One way to improve communication between IRBs and investigators is to:**

   a. send investigators handwritten letters that are more likely to get their attention.
   b. ask investigators to text their questions to IRB staff.
   c. hold in-person coffee gatherings between IRB staff and investigators.
   d. use social media, such as tweeting new regulations and IRB rules, and including links to the IRB website.

3. **The Food and Drug Administration will assess whether to inspect a site based on a couple of factors, including:**

   a. if the products are in post-approval marketing.
   b. if the study related to COVID-19.
   c. if the products used to diagnose, treat, or prevent a serious disease or medical condition for which there is no other appropriate substitute.
   d. if the site had been inspected previously and there are findings that remain unresolved.

4. **What does ethical reflexivity mean in the context of human research trials, according to Darcy McCusker, MA, MSE?**

   a. The idea that researchers are obligated to think about the values they are bringing to the lab.
   b.Bioethicists should consider all angles of a potential ethical conflict.
   c. The idea that IRBs should perform a separate mini-review of a new technology study's ethical challenges before approving the protocol.
   d. IRBs should remain flexible, viewing ethics of a study based on current technology and norms instead of old standards.

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