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RELIAS MEDIA

Big Data Are Changing How IRBs Think About Research

Privacy expectations have changed

By Melinda Young

Researchers and sponsors are adapting quickly to virtual technologies and using big data in studies, forcing IRBs and research protection programs to adapt — particularly when it comes to privacy.

When IRBs review studies that use big data, they need to be reviewed through the lens of ethical review, says **Stephen Rosenfeld**, MD, MBA, president of Freeport Research Systems in Maine. Rosenfeld is the chair of the Secretary's Advisory Committee on Human Research Protections (SACHRP).

"In the end, that's where we find the answers," Rosenfeld says. "I do believe IRBs have lost their way and have been very much about parsing regulatory language and documenting compliance as being behind the ethical principles."

The focus should be on the broader context and what it means for the future. "We should re-examine the meaning of identifiable information," Rosenfeld says. "I don't think there's anything in the pipeline to make that happen."

> "WE MAY GET TO A POINT WHERE THERE IS NO LONGER SUCH A THING AS ANONYMIZED OR DE-IDENTIFIED DATA."

With databases capable of capturing details about millions — or billions — of people, IRBs and researchers must re-examine privacy issues.

"With a little effort, you could probably identify a good number of people in a database," says **Michele Russell-Einhorn**, JD, chief compliance officer and institutional official for Advarra of Columbia, MD. "We may get to a point where there is no longer such a thing as anonymized or de-identified data. From the perspective of the IRB,

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how do you make sure the people who are participating in research understand how their data will be used by the researcher?"

IRBs might consider adding a disclosure to informed consent documents to explain the potential for de-identified data to be re-identified. This will allow participants to make an informed decision, Russell-Einhorn says.

"IRBs have to make sure that what people are told is accurate," she stresses. "Technology is moving ahead at such a fast pace that we need to make sure there is adequate education of everybody about how technology is impacting the identifiability or re-identifiability of data and how data can be used."

Investigators with project proposals using big data or biospecimens related to humans will need at least a minimal review of their studies. "Most IRBs would not accept a consent for creation of a repository that says you can do anything you want," Rosenfeld adds.

New Uses Raise Ethical Challenges

The rapid growth of information and possible research uses makes this ethically challenging. "Big data is continuing to increase at an exponential rate," says **James Riddle**, MCSE, CIP, CPIA, CRQM, vice president of institutional services with Advarra. "The amount of data we can consume or get is ever increasing. The FDA [Food and Drug Administration], in particular, has indicated they want more real-world data in the decision-making process for drugs. It's inevitable you will get more data in research and drug development."

For instance, an increasing number of studies collect data from wearable technologies like Fitbits, which are used to count steps, Riddle says.

Another example is the Oura ring, which uses sensors to measure vital signs and continuously collect and transmit the information, says **Megan Doerr**, MS, LGC, principal scientist, governance with Sage Bionetworks in Seattle. *(See story on mobile technology in this issue.)* There is ongoing research into whether the ring's sensor technology can detect changes in a person's body before symptoms of COVID-19 infection occur. *(For more information, visit: https://bit.ly/3iouZCz.)*

"Companies are even developing fabric that has sensor technology woven into them," Doerr says. "The possibilities are fast and furious."

One challenge of big data in research is how data are stored and how much it changes the usual thoughts about protecting privacy under the Health Insurance Portability and Accountability Act (HIPAA).

"Once upon a time, people would go to the World Wide Web, pull data into their personal workspace, and do whatever they wanted," says **Stephanie Malia Fullerton**, PhD, professor of bioethics and humanities at the University of Washington School of Medicine. "Big data is getting so big that this is happening less and less now. More often, people are doing things on the cloud. This is especially true in genetics and genomics."

Researchers no longer download data to individual laptops and computers because they are too big and unmanageable. "If you combine some very clear rules about what is and is not permissible about doing things that lead to identification of people, then you could get rid

of a lot of the concerns," Fullerton explains.

IRBs might ask a lot of questions about big data studies, including "Who is making up the rules?" Fullerton says. *(See story on big data and HIPAA/privacy in this issue.)*

"What's interesting is we can remember the pre-cloud years, and there are things about cloud computing that feel risky," she explains. "Who has the data? How risky is it? It's still a work in progress."

Beyond data collected through wearables and mobile technology, there are many studies with large data sets like Medicare claims data and consumer products data. Large social media companies collect data that can be combined and mined to find insights on people's consumer and economic behavior, Riddle says.

"You can combine information already used in the consumer products world and use those data to look at the real-world impact of people who take particular drugs or classes of drugs, and things of that nature," Riddle explains. "The world of massive data sets can be combined now to draw insights into particular drugs in the real world."

For example, a researcher interested in the economic and environmental effect on diabetes survivorship might purchase data from consumer product organizations. While de-identified, these data can be specific and combined with health data.

"If I am a diabetes researcher, I might be interested in combining data sets from the consumer products world and see if people based on consumer habits might have diabetes," Riddle says. "I could look at whether I could triangulate their data with a Medicare dataset and look for commonalities of what I see in the consumer products space, the medical space, and draw comparisons there." The FDA has intimated it wants to see more real-world evidence like that, he adds.

Sooner than anyone would like to acknowledge, there might be a point where there no longer is such a thing as anonymized or de-identified data. For example, with a condition like progeria, which causes premature aging, there is no information about people with the condition that could be considered de-identified because there are only about 30 people in the world with that condition, Russell-Einhorn explains.

As databases grow and become easily cross-referenced with other databases, the same might be true for anyone with any specific health conditions or lifestyle habits.

"That's the question and conversation we need to have now: Are we there, and what will it take to get there?" Russell-Einhorn asks. "If we're there, we need to have a conversation with IRBs, investigators, and everybody about what it means to have these big databases so individuals who participate in research have a clear understanding what their data set will be."

Big data sets also are an issue after people die. "It's enormously eye-opening to see how much information we give over, how little we've thought about it, and how long they persist — long after we're gone," Fullerton says. "Given that and the increasingly immortal nature of data, we cannot be blasé about privacy. We cannot." ■

Mobile Technology, Wearables Are Changing Research, Challenging IRBs

Wearable sensors broaden research limits

Mobile technology and wearable sensors are broadening the limits of research and changing how IRBs view privacy.

The voluminous data can point to health strategies previously unimaginable.

"More data mean more solutions and better solutions for pressing health questions," says **Megan Doerr**, MS, LGC, principal scientist, governance at Sage Bionetworks in Seattle. "The challenge comes in what are legal protections for those data and in what ways people consent for those data. Also, in what ways do those data implicate other people who have not consented?"

The challenge for IRBs and researchers is twofold. First, data collection can be huge and granular; secondly, there are multiple implications for privacy. "You name it, and it can be collected using a mobile device," Doerr says. "Our phones have more sensors in them than the planes used to navigate the Pacific in World War II."

Touchscreens, microphones, and other sensors are great at capturing

continuous data, and they are improving.

Privacy Is a Challenge

Privacy is more difficult to protect in the era of big data. "I think the categorization of data as health data or not health data is no longer serving us," Doerr says. "We're understanding health data includes all different categories of data, like buying patterns at the grocery store, or walking patterns on mobile devices. I don't know if HIPAA is fit for modern purpose."

Informed consent should include an explanation about how data are used and risks that might be unrelated to the study. For example, researchers might have a plan to keep data private, but third parties also could be collecting the information. These include cellphone companies and internet companies that might collect everything on the device and use the information for marketing and other purposes.

Also, when more data are collected, identifiability is easier. IRBs should push researchers to justify the data elements they require for their study. "The researcher needs to be responsible and parsimonious in their approach to the data," Doerr says.

Mobile technology makes it possible for researchers to study people's daily experiences as they live them. "These changes are a potential boon for health research. If we don't understand people's lived experience in the world, we don't truly understand their health," Doerr says. "We're seeing some recognition of that as communities start to recognize racism as a health concern. People are recognizing the multidimensionality to health."

Researchers have always wanted to capture these data. Now, everyone has a cellphone that can collect data, or already is collecting, she notes.

Unintended Consequences

Even more troubling from an IRB's perspective is determining whether a proposed study with mobile technology might inadvertently capture data without consent. When IRBs review studies involving wearable and mobile technology, there will be potential risks they had not considered. For example, Doerr was involved in research of the app-mediated mPower Parkinson's disease study, which was designed to enable participant-centered research. The app collected data from participants and asked them to perform tasks. One task involved their responding to a notification by holding the phone to their face and saying, "Ahhh," holding the sound as long as they could, Doerr explains. *(For more information, visit: https://bit.ly/3gTDJ3l.)*

What the researchers did not anticipate is that people would think of the notification as an emergency prompt. They would stop whatever they were doing, including shopping, working, or other activities, and perform the task. This meant the data collection included background sounds and voices. If someone completed the task on the bus, then it could pick up other passenger's words. Plus, people treated it as though it was urgent, which resulted it in interrupting important daily tasks, Doerr notes.

"It was through the unstructured data, where people could type in notes to us, that we learned people were saying, 'It's embarrassing when I get a notification during a work meeting and I had to step out to do this task,'" she explains. "They felt like it was urgent because it was on their phone, but they were not required to answer immediately."

IRBs can anticipate these types of problems by inviting the study's technology experts to speak about how the tool works and by asking more questions of researchers.

"IRBs can ask researchers about the kinds of instructions they are going to give them and the direction the researchers are giving," Doerr says.

For instance, with the mPower app, investigators learned they

should have told people to respond to the prompt when they had time and could complete the task in a quiet room, she says.

"It's really essential when an IRB is considering a study that has mobility technology that the IRB call on all of the experts they'll need to understand what is being collected," she says. "The technologists understand these devices. But they're a couple of steps removed from the IRB, with the researcher as the middle person."

IRBs need to ask technologists and researchers who will collect data, how information will be transferred, how it will be stored, and how it will be used.

"It's not like researchers want to do bad things and IRBs want to be unobservant or technologists want to create deviant technology," Doerr says. "But they need to work together, talk, and ask questions."

Researchers might not be experts on the technology they use. IRBs will need a technology expert there to help them conduct more homework on the details necessary for better informed consent.

"I would stress to IRBs that they can't be afraid to say they don't know something, and they can't be afraid to drill down on researchers to make sure the IRB really understands what is going on with these data and how they're being used," Doerr says.

Examples of essential questions: How are data encrypted as they are collected? Are there unintended vulnerabilities?

"You might imagine that a massive trove of data might be a bigger target," Doerr says. ■

Combining Large Data Sets Challenges IRBs, Researchers to Ensure Privacy

Re-identification easier with combined datasets

The problems with the Health Insurance Portability and Accountability Act (HIPAA) and current methods of protecting the privacy of individuals in research are being challenged in ways that were not possible in previous decades due to the ease and use of big data.

"The solution HIPAA gives us for guaranteeing privacy of health information is unsatisfactory in a lot of ways, and that's been demonstrated over and over again," says **Stephanie Malia Fullerton**, PhD, professor of bioethics and humanities at the University of Washington School of Medicine. "The question is what to do about it."

Data scientists and other savvy investigators can combine de-identified data in a way that makes cross-references and re-identification possible.

For example, the authors of a 2018 study that examined step count data from mobile technology found data that only contains the number of steps a de-identified person takes is enough information to uniquely identify individuals.[1] Another study revealed de-identified personal information could re-identify 99.98% of individuals in any data set using 15 demographic attributes.[2]

"This is where data security procedures become really important," notes **Megan Doerr**, MS, LGC, principal scientist, governance at Sage Bionetworks in Seattle. "How are the data being safeguarded? Are there ways to prevent tampering with data? These sorts of questions are important for IRBs to understand, and they can impact the integrity of research being proposed."

All an investigator has to do is purchase a commercial data set and cross-link it to health data such as information from wearables, explains **Stephen Rosenfeld**, MD, MBA, president of Freeport (ME) Research Systems. Rosenfeld is the chair of the Secretary's Committee on Human Research Protections. Anyone can purchase commercial data sets, which means that everything is readily identifiable, he adds.

"A health record for a white female in Seattle is not inherently identifiable until you combine it with other information," Fullerton says. "Combining data sets poses the privacy risk."

Cross-referencing also poses problems. However, it does give data great meaning and utility. "It gets very tricky, very quickly," Fullerton says.

Address Privacy Risk

Investigators, IRBs, and research bioethicists might be hesitant to confront this privacy issue because of the potential for useful research to be shut down, Rosenfeld says.

"We have to expect that ethics reflects the expectations of society,"

he adds. "Everyone knows about this problem, so it'd be nice if we talked about a framework for ethical expectations for research with big data and tried to understand what people found permissible and what their expectations are."

Another example is a researcher who purchases data from a large grocery store chain that includes diabetic testing kits, says **James Riddle**, MCSE, CIP, CPIA, CRQM, vice president of institutional services with Advarra in Columbia, MD. This information could overlap with a medical database, and investigators could look for clusters of people within a 25-mile geographic area to see where diabetes cases are most prevalent, he says.

Combining the information could lead to re-identification. "By themselves, the individual data sets might not even constitute human subjects research because they are de-identified," Riddle says. "But when you combine these data sets, then they could become identifiable, and there are risks that IRBs would have to evaluate and weigh."

IRBs should consider these privacy issues with studies using big data:

• **Decide on informed consent.** "The two main issues are whether they are human subjects and can you waive consent," Rosenfeld says. "Even if you don't name them, in a way you are using them as research subjects — but without names. They are virtual subjects. Whether that is deserving of protection or not is a question."

Research projects in which investigators agree to not cross-link the data with another database that would enable re-identification can be considered not human subjects research, Rosenfeld says.

"If it is human subjects research because data are identifiable, then it's the nature of big data research that you really have to have a waiver of consent," he adds.

Under the Office for Human Research Protections, the general understanding is that giving blanket consent to future research is not seen as compliant, Rosenfeld adds.

"The regulations try to address that through adoption of broad consent. It was well-meaning, but there are practical issues with its application, and I don't think anyone is using it," he says. "There needs to be limited IRB review, and you could set expectations; for example, 'I am not going to use this biospecimen in this bank for research regarding human reproduction,'" he explains. "Someone has to review individual studies to make sure they're consistent with those limitations."

Understand Data Storage

• **Protect stored data.** Data storage is somewhat different and a little more complex than it was even a decade ago. For instance, instead of worrying about laptops and computer hard drives, researchers need to consider the safety of cloud storage and wearable sensors.

If researchers have legitimate reasons to collect monitoring information using commercial wearables, Fullerton says IRBs might ask these questions:

- Where are data stored?
- Is the company that makes the device also holding data?
- Who can access the information?
- What safeguards are in place to ensure data are not used?
- What happens at the end of the study?
- Where do the data go?

"These are bread-and-butter questions," Fullerton says. IRBs should insist this information is part of the consent process, informing people the device manufacturer also is collecting data and may use it for commercial purposes, she adds.

"If you are providing an Apple watch as part of an incentive for the study, you are exposing [participants] to a risk they might not have voluntarily chosen to be exposed to," she adds. "This should be revealed as part of the informed consent process and carefully managed."

• **Maintain anonymity.** One way to retain de-identified status is through technology.

"There are technologies like differential privacy," Rosenfeld says. This is when researchers use technology to obfuscate data. They add noise and tweak values so it cannot be matched against a big data set. This could include changing ZIP codes or other information that is irrelevant to the actual research outcomes, he explains.

"You could maintain the anonymity of the data that didn't answer the big research question," Rosenfeld says. "It's possible to do that, and there's small literature on that, but the hurdle is that it has to be done on a study-by-study basis. It's expensive and adds another layer of ethical complexity." ■

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Steps for IRBs to Better Safeguard Participants

First step: Engage data scientist

Technology is moving far faster than federal human research protection laws and regulations. But there are a few things IRBs can do that will help protect study participants.

"Any investigator who comes up with a project proposal that uses that data or biospecimen will have some minimal review," says **Stephen Rosenfeld**, MD, MBA, president of Freeport (ME) Research Systems of Freeport. Rosenfeld is the chair of the Secretary's Committee on Human Research Protections (SACHRP).

"Most IRBs would not accept a consent for creation of a repository that says you can do anything you want," he says. "It does get complicated. It's a bit of a mess."

These are potential ways to improve protection of research participants:

• **Recruit a data scientist to the board.** "IRBs need to have access to information technology expertise," says **Michele Russell-Einhorn**, JD, chief compliance officer and institutional official for Advarra in Columbia, MD.

This might involve recruiting an information technology expert to the board. Or, IRBs could ask a data scientist to consult with the board. "Big data requires a certain level of expertise, and IRBs should look at their membership to make sure they have that level of expertise," she adds.

Many IRB members are limited in their knowledge and understanding of data collection, storage, and de-identification. "These are things I'm surprised that researchers don't think about more often," says **Stephanie Malia Fullerton**, PhD, professor of bioethics and humanities at the University of Washington School of Medicine.

Data scientists understand how to evaluate big data sets. If an IRB is unfamiliar with these issues, they should ask a data scientist to help them evaluate such studies and prepare for the future, says **James Riddle**, MCSE, CIP, CPIA, CRQM, vice president of institutional services with Advarra.

> "THE IRB SHOULD REVIEW THE PROTOCOL AND CONSENT, AND MAKE SURE THERE'S AT LEAST ENOUGH INFORMATION TO TELL SOMEONE HOW THEIR DATA WILL BE COLLECTED, SHARED, STORED, AND USED."

"They might also be statisticians or biostatisticians," he explains. "They understand how to combine the data and could advise the board on how likely it is a combined data set might become identifiable."

• **Make sure informed consent matches the protocol.** "One of the things that happens is you have an informed consent form that says your data will be de-identified," Russell-Einhorn says. "Then, you read the protocol and see what they're doing, and you realize that it's not really an accurate statement."

IRBs should be cautious about accepting the informed consent language as written when it describes the use of data. "You probably need context to figure out whether it's an accurate statement," Russell-Einhorn says. "The IRB should review the protocol and consent, and make sure there's at least enough information to tell someone how their data will be collected, shared, stored, and used. Also, there should be a requirement that people are told of new information and its impact on their continuing to participate in the research."

IRBs should clarify their responsibility to re-evaluate protocols and consent forms when study changes might change the accuracy of an informed consent document's wording about de-identified data, Russell-Einhorn adds.

Large data sets could include detailed information held by multiple stakeholders with different interests, similar to biobank research that has no end to the data, Fullerton says. "We need to be transparent about that. The nominal right to withdraw is a limited one."

Once a person's data are used, they cannot take it back in this environment, Fullerton adds.

• **Grant waivers cautiously.** When databases are used for purposes consistent with the original informed consent, investigators probably can proceed, Rosenfeld says.

"But we're talking in general about things that were not thought of in the original consent," he adds.

When a study is proposed that is

inconsistent with the original consent, researchers and IRBs can consider waiver of informed consent under certain conditions. For instance, the waiver cannot adversely affect the rights and welfare of subjects, Rosenfeld says.

"I think people are used to saying, 'I don't see how that will impact the rights or welfare,'" he adds. "But I don't think anyone knows what that means."

In 2008, SACHRP said the interpretation of rights and welfare should be calibrated against an individual's expectations. "Would someone object if they knew of the waiver?" Rosenfeld asks. "Would the study population in general think the waiver could cause adverse consequences for their welfare or well-being?"

Another criterion is the research could not be carried out practically without the waiver. Whenever appropriate, subjects or legally authorized representatives will provide additional pertinent information after participation.

"People say, 'We published results or let the community know,'" Rosenfeld says. "That's easy to satisfy or justify not satisfying."

• **Teach the difference between research and consumer data.** "In the consumer side of space, you would be appalled with how much the consumer products folks know about you specifically," Riddle says. "Others can go in and purchase those data."

There are several ways research participants might misunderstand how de-identification works with large databases:

• **Consider service and use agreements.** Research participants could have misconceptions about the broader implications of their data and privacy, particularly when data come from a large commercial database or the use of wearable technology.

"They often can conflict with what's said in informed consent for a research study," Rosenfeld says.

One example is if they believe their data, studied from a commercial database, is kept private through de-identification by investigators. While researchers can do their best to de-identify commercial data, it is always possible the company that holds the data does something with the same information that makes identification possible.

"What is the role of the IRB in terms of reviewing things like terms of service and using license agreements?" Rosenfeld asks. "There are a lot of circumstances where these documents are written to not be understood; they're written in ways to discourage people from paying attention to them."

For example, SACHRP studied several cases in which study populations used Apple Watches before enrolling in a research study. Investigators wanted to collect data, like steps taken, from those devices, Rosenfeld says.

If the data collected are for an app that people already were using, it means they signed a service and use agreement with that vendor. The bar the IRB has to clear is pretty low, he notes.

"They still will need to review the study and they need informed consent for research," he says.

But if the end-user license agreement already mentions the data might be used for commercial research, then adding an academic research study does not add much more risk for participants. The key point is to note all this in the informed consent.

The trickier scenario is when a study provides participants with a wearable device, and people have to sign an end-user license agreement in addition to the informed consent document, Rosenfeld says. The end-user license agreement might be much broader than the study's purpose for its use.

"The IRB has to pay a little more attention to the privacy rights they're asking people to sign away," Rosenfeld explains. "It's that kind of thing: What should IRBs do, practically, when using a device or app requires people to do certain things to use it?"

This issue is broader than informed consent. IRBs should scrutinize the risk of these situations, he adds. ■

More Research Needed Into How IRBs Operate and Make Decisions

Study examines how to increase IRB transparency

The revised Common Rule's provision that a single IRB should review protocols for multisite studies raises questions about how these IRBs handle conflicts of interest, local knowledge, and other issues.

When a group of researchers sought to answer these questions, they found a big obstacle: Some IRBs, including the largest ones, were unwilling to participate.[1]

"We thought when single IRBs were mandated, they played an increasingly important role that affects everyone's lives, and we thought it'd be important to understand best practices," says **Robert Klitzman**, MD, professor of psychiatry and director of online and in-person masters of bioethics programs at Columbia University in New York City.

Investigators wanted to understand the challenges and what helped IRBs meet those challenges.

"We conducted this study, and I was surprised — or, I should say I was struck — and disappointed that commercial for-profit IRBs were much less likely to agree to participate, and it was significant," Klitzman says. "None of the major, large, for-profit IRBs agreed to participate. This is concerning to me because IRBs are set up to be paragons of ethical behaviors and practices."

Close to 90% of drugs approved by the Food and Drug Administration (FDA) are handled by one for-profit IRB, according to 2015 data, Klitzman says.

"As an ancient author said, 'Who is guarding the guard?' If they're watching researchers to make sure they're ethical, who's watching the IRBs?" he asks.

Ethical Concerns Raised

While there is no evidence that any IRBs are doing a poor job, there also are no data on how they make decisions and handle ethical considerations. When IRBs that are overseeing the vast majority of drugs approved by the FDA do not talk with investigators about their work, there are major ethical issues and concerns raised, he adds.

Advarra, a large, independent IRB in Columbia, MD, responded to an emailed request for comment about Klitzman's study. At press time, *IRB Advisor* did not receive responses from WIRB-Copernicus Group or Pearl IRB.

"We believe protecting participants in research is paramount," says **Michele Russell-Einhorn**, JD, chief compliance officer and institutional official for Advarra. "Therefore, research on the effectiveness and underlying operations of IRB review is important for better understanding IRB review and identifying possible improvements to ensure that the system is adequately and appropriately protecting patients. Advarra is an active participant in AEREO (the Consortium to Advance Effective Research Ethics Oversight) and participated in the National Institutes of Health-funded study looking at increased use of single IRBs for multicenter clinical trials."

About 40% of IRBs agreed to participate in the study. This included close to 82% of academic IRBs and half of government single IRBs, but only 23% of commercial single IRBs. Some of the IRBs that refused full participation, which included board observations and individual interviews, cited privacy or confidentiality concerns and insufficient time and resources.[1]

How Well Are Subjects Protected?

Without data from the largest IRBs, researchers have no information on the safety of human subjects, Klitzman says.

"The scientific enterprise depends on transparency, principles of communitarianism, a sharing of best practices, and an openness that is crucial to make sure there is integrity for IRBs that are overseeing the vast majority of drugs approved by the FDA," he explains. "To say, 'We're not even going to talk to you about what we're doing,' is, to me, something that raises major ethical issues and concerns."

Although the nation's largest IRBs are accredited, this does not answer the investigators' concerns. "Accreditation agencies look at the process — not the content of reviews," Klitzman says. "They don't look at how risks are evaluated; they look at the minutes collected."

The Office for Human Research Protections (OHRP) also provides oversight, but only for federally sponsored studies. "If there's a problem, usually there would be a for-cause audit. It would be around

a particular study, as opposed to observing IRBs to see how much concern there is about risk, how much concern about autonomy, and concern about local knowledge, racial issues," Klitzman adds.

The oversight provided by research into IRB operations might be more important as research institutions increasingly rely on large, commercial IRBs. This shift was underway, partly due to understaffed institutional IRBs, before the revised Common Rule mandated an IRB of record for multisite studies. Now, the shift appears to be increasing, he says.

"What's happening is a lot of studies are saying, 'Let's have one of the large, commercial IRBs do it,'" Klitzman says. "They'll outsource to a large, single IRB."

The solution would be for accreditation organizations and OHRP to collect data on IRB issues related to risk, local knowledge, and other issues.

"I think the Department of Health and Human Services, which has jurisdiction over the Common Rule, could say single IRBs should have outside review about their functioning," Klitzman says. He suggests lawmakers could pass legislation that would require IRBs to be audited.

Large, commercial IRBs have the right to refuse to participate in research about IRB operations, but their refusal shows a lack of transparency when they often review studies funded by taxpayers at early stages of research, Klitzman says.

"American citizens and people from all over the world are affected by the benefits and risks of the drugs they are studying," he says. "I think there is a serious question of whether they have some responsibility to be open to assure people, whose lives are at risk, about the quality of their decision-making and review process." ■

REFERENCE

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IRBs, Research Organizations Adjust to New Norms in COVID-19 Era

Remote monitoring to continue in places

The research world's axis shifted in 2020 with the COVID-19 pandemic. Research organizations and IRBs should expect that shift to be the new normal. There will be no return to the way it was before.

"Many of us looked at what research would look like in 2030, and I think the pandemic has forced us to do that now," said **Christina Brennan**, MD, MBA, vice president of clinical research at Northwell Health in New York City. Brennan spoke at a WIRB-Copernicus Group (WCG) web conference on July 8.

"Many of us in the industry have had [pre-COVID-19] conversations about virtual visits and remote monitoring visits," Brennan explains. "I see this [pandemic] as a challenging opportunity in this new environment about how we conduct research."

Research organizations quickly learned how to continue studies during the pandemic. Now, they are considering how to continue these changes in the post-COVID-19 world. "How can we help our [study participants] feel safe in clinical research in a remote environment?" Brennan asked.

Focus Shifted to COVID-19

When the nation first shut down during the pandemic, research sites put many studies on pause and mandated telework policies, sending research staff home. But their focus shifted as researchers began seeking COVID-19 studies.

"We started with an expanded access program. This entry into research to get a study opened very quickly," said **Erika Siegrist**, MS, RN, ACRP-CP, director of research administration with Anne Arundel Medical Center in Annapolis, MD. Siegrist also spoke at the July 8 conference. "We took all of the staff we had in research and reassigned everybody."

First, the organization focused on access protocols and placed staff on the side of plasma donor recruitment. "It worked well for us to have our own product and blood supply," Siegrist explained. "As we went along, we did a lot of reassigning and redeploying."

Oncology studies were put on hold at first, but the organization kept much of its portfolio open. "With our staffing, we've been extremely flexible," Siegrist added.

By July, the organization resumed

elective surgeries and had staff return to clinical trials. "We worked on the logistics of doing ambulatory outpatient trials," Siegrist said.

Clinical trial sites started transitioning to the post-pandemic world by making triage decisions on studies.

"We had to decide which trials to keep open — those patients actively receiving medication, and those we had to turn into virtual visits conducted by telephone," she said. "We had to decide on the best way forward, and we had to discuss remote monitoring. We were able to conduct research while this was going on."

The research organization allowed only remote monitoring visits with active trials, providing monitors with full electronic health record access. "To this day, we have not allowed monitors to come back into our hospitals and outpatient facilities, so we are continuing remote," she said.

While research organizations and IRBs dealt with changes pertaining to their pre-COVID-19 trials, they also made decisions about new studies into SARS-CoV-2 treatment and vaccines. "The COVID clinical trial unit and we had to decide which trials we would participate in," Brennan explained.

"As it relates to COVID-19 trials, the new norm is these will go on for a long time," noted **Molly Hair**, director of site engagement and management with WCG ThreeWire of Princeton, NJ. Hair spoke at the July 8 web conference. "What has worked for us in the past three months is not necessarily what will work once all the non-COVID studies start up again. One thing many institutions and sites do is they operate with designated COVID contact teams — a select group of people who are designated to physically interact with patients diagnosed with COVID. Often times, these teams are external to the clinical research department."

Personal protective equipment may be limited, or there could be concerns about infection prevention and maintaining consistency in studies when staff might be home sick or quarantined for limited periods. "There can only be so many people interacting at a given time," Hair said. "It can also cause issues when there is a surge in hospitalizations because the number of individuals allowed to contact COVID patients are stretched thin and can lead to deviations in blood times and other procedures mandated by the protocol."

Some Studies on Hold

Non-COVID-19 studies may be placed on hold or restructured to supplement study teams. "Once a non-COVID study starts back up, and the supplemental staff returns to its prior role, study teams are left understaffed. Many sites have hiring freezes," Hair explained. "What complicates this is the second wave. Sites don't want to hire additional staff members to fill those vacancies if a second wave is going to come, and then they have to revert back to the structure that has worked for so many sites over the past three months."

This leaves research organizations with extremely difficult staffing decisions. They need more staff to prepare for returning to full pre-COVID-19 trials, plus the new COVID-19 studies. But they also have to prepare for possibly shutting everything down again. "Complicating this further are the demands of data entry and query information that comes with COVID trials," Hair noted.

With COVID-19 studies, sites cannot allow a backlog: "Sponsors are requiring data to come in 48 hours past the point of collection," Hair said. All these decisions require conversations between IRBs, sponsors, and scientists, she says.

Establish Trust with Participants

For trials where in-person visits are necessary, clinical trial sites and IRBs should consider how patients/participants feel about making these visits in the backdrop of COVID-19 outbreaks and surges.

"Patients are very anxious about returning to doctor's visits to the sites," Brennan said. "If you think about clinical research, it can become part of the norm and conversation. There are ways we can help each other bring our research visits back." IRBs and research organizations might decide in-person meetings are relics of the past, and continue with virtual meetings, she added.

Research participants need to trust and engage with clinical trial sites. Researchers should consider how participants would feel about participating in clinical research in this environment, Brennan noted.

"Also, think about safety precautions," she said. "Patients should wear masks, employees should wear masks, there should be temperature checks, social distancing, and all of these things should continue to occur in this new environment."

The key is to think about these things in a solution-oriented framework.

"We have to put these processes in place to continue in clinical research and perhaps shift the paradigm in how we conduct research," Brennan says. ■

IRB ADVISOR

CME/CE INSTRUCTIONS

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CME/CE QUESTIONS

1. **What is the IRB's chief role in big data studies and the potential of re-identified information, according to Michele Russell-Einhorn, JD?**

   a. IRBs should ask researchers to use a technological solution to prevent data from re-identification.
   b. IRBs should reject studies where re-identification is possible.
   c. IRBs should consider asking investigators to use only one database in their research.
   d. IRBs should consider including a disclosure with enough information about the potential for re-identification to allow participants to make an informed decision.

2. **For a study to have data that could be re-identified, it could include what kind of data set that is cross-linked to health data, according to Stephen Rosenfeld, MD, MBA?**

   a. Commercial data set
   b. ZIP code data set
   c. Age data set
   d. Ethnicity data set

3. **From an IRB's perspective, what is one problem with wearable technology and privacy, according to Megan Doerr, MS, LGC?**

   a. People given wearable technology might never truly understand informed consent.
   b. IRBs should include a mobile technology expert on the board to fully understand any wearable technology study.
   c. A proposed study with mobile technology might inadvertently capture data of people who did not consent.
   d. Mobile technology signals could be picked up by nearby cellphones.

4. **What percentage of commercial IRBs participated in a recent study about IRB operations?**

   a. 40%
   b. 8%
   c. 23%
   d. 61%