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INSIDE

RELIAS MEDIA

New Tech Research Raises Ethical Challenges for IRBs and Investigators

Strong communication is important

By Melinda Young

When 23andMe of Sunnyvale, CA, envisioned a research program a decade ago, the company had little guidance and support for its plans.

"We were a start-up with a disruptive idea of trying to get into regulated research space," says **Katie Huber,** PhD, CIP, research ethics consultant at 23andMe. "We wanted our program to abide by federal regulations, whether or not we had federal funding. If you set high standards for yourself at the beginning, it's easy to uphold them rather than to impose them later."

Some new technology companies that are developing novel human subjects research face challenges and design issues that have never been explored, says **Leslie Wilson**, CIP, director of operations at Ethical & Independent Review Services (E&I) in Independence, MO. Companies engaging in cutting-edge technological services and solutions can raise public concerns for what they do on the business side, but there is less public awareness of privately funded research.

> SOME NEW TECHNOLOGY COMPANIES THAT ARE DEVELOPING NOVEL HUMAN SUBJECTS RESEARCH FACE CHALLENGES AND DESIGN ISSUES THAT HAVE NEVER BEEN EXPLORED.

"The Common Rule opens up the possibility for more and different kinds of research," Wilson says.

One of 23andMe's goals was to follow the Common Rule for all human subjects research and to rely

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on an external, independent IRB.[1] Another goal was to provide research participants with their results, which carries its own risks and challenges. The company wanted to do it the most ethical way, from the start.

"You only have one chance to earn participants' trust. Once that's gone, how are you ever going to get that back?" Huber asks.

Ten years ago, sharing individual genetic results was considered controversial. The American Society of Human Genetics (ASHG), at its annual meeting in 2010, held a public presentation about the implications of using direct-to-consumer and clinical genetic testing in disease risk assessment. Researchers conducted an online survey of customers of 23andMe, deCODEme, and Navigenics to learn more about why people use these services and how they felt about their results. *(More information is available at: http://bit.ly/2OOit2Y.)*

"Originally, ASHG was not in favor of research participants — or anyone — getting research results, which was a prevailing sentiment," Huber explains.

With little guidance from regulatory and industry associations, 23andMe contacted IRBs to find one that would review its protocol, eventually finding a good match with E&I. While it's beneficial for IRBs to be helpful — and even collaborate with researchers — IRBs still must maintain independence in their review.

The collaboration was helpful to both organizations, Huber notes. "E&I spent time to find out what we wanted to do and what that would entail," she says. "They asked a lot of questions, and got into the details of what a study would look like."

From E&I's perspective, the independent IRB benefited from a direct line with the sponsor, says **Erica Heath**, CIP, partner, E&I. "We talk with them about their upcoming studies, any design problems they're having, and discuss possible solutions that they might incorporate," she explains. "We work with them early on to eliminate or make clear some of the problems."

Peeling Back the Layers

The IRB brings up fresh issues, including ethical challenges and risks that genetic scientists might not imagine. *(See story on IRB and sponsor/investigator collaborations, page 28.)*

"The questions that we tend to explore a lot with E&I are new risks and benefits in the informed consent," says **Michelle Agee**, MSc, CIP, manager of regulatory science at 23andMe. "We had a lightbulb moment when we were thinking about the risks, what participants would want to know, and what they could comprehend. We worked with E&I to develop draft language and open-ended questions to get at those concerns."

These questions turned into the proverbial onion, with one question peeling away a layer that led to another question. "We worked iteratively with E&I until we felt good about the results," Agee says.

For example, the improved informed consent uses bold font to outline an explanation of what information the company would share externally. There are additional definitions to help research participants better understand what is discussed.

Performing a risk-benefit calculation is challenging when the study is about something new and unusual, Huber says. "We make decisions based on our perceptions of the risks and benefits, and those are all matters of opinion," she explains. "What I'm

concerned about might not be what you're concerned about."

When working in unknown risk territory, it is important to ask more people to look at the study and providing their input on what would worry them, Huber adds. For example, how should a technology-related study handle paradata? Coined in 1998, paradata refers to auxiliary data collected, including data from a person's online use or from a survey. *(More information is available at: http://bit.ly/38qPYQq.)* "Paradata is collected whenever you do anything online," Huber explains.

It includes this information:

- Where are you located?
- Are you on your computer or phone?
- Are you using Safari, Google Chrome, or Internet Explorer?
- How many times did you click "enter?"

"These data exist for any online interaction," Huber says. "It's all going on in the background. It sounds like very innocuous data, but it turns out you can do a lot with this information."

For instance, if someone accesses a survey online and clicks through the questions quickly, paradata might suggest the person did not take time to read the questions, which makes those answers less useful for the study.

Companies also use paradata to improve their marketing techniques. With paradata, a company can see where someone is located when they are online, and the company can send a pop-up ad for a store in that location.

23andMe does not use paradata information, Agee says. But the company is exploring ethical and informed consent questions related to use of such data, such as:

- Are paradata sometimes off limits?
- What do we do with the information?
- Can we use any of the data?
- Can we use it for research purposes?
- What else do we need to think about with paradata?

The collaboration between E&I and 23andMe has helped research program staff focus on how to explain new technology concepts, like paradata, and to make sure the research program addresses these new concepts in its policies.

"THE EARLIER THE COMMUNICATION STARTS WITH THE IRB, THE MORE LIKELY THAT THE RESEARCH IS GOING TO INCORPORATE A STRONG PARTICIPATION PROTECTION PLAN."

"A top concern was how paradata could allow a researcher to make inferences," Huber says.

If someone is filling out an online survey form by clicking boxes with a computer mouse, then someone could view paradata to note that the person was not paying attention to questions, that the person completed the survey late on a Friday night, or that it takes the person three times as long to complete the survey on the phone than on the computer, Huber explains.

"The concern is that this is something that would not be obvious to regular participants. If you want to put this information in a consent form, then make sure they understand this aspect of it," she says. "It goes back to comprehension, and whether your participants understand what you're doing."

When 23andMe started conducting human subjects research, investigators had to explain to participants what genetic results mean. Medical literacy has improved, but some terms still need explanations, Huber says.

"Paradata is not something on most people's radar; aggregate data-sharing is not something dropped at parties," she says. "People don't think about these things or necessarily understand them." The research staff's job is to help people understand complicated concepts, she adds.

IRBs can help sponsors and investigators come up with definitions and explanations that laypersons understand, but it requires a trusting and collaborative relationship between human research protection programs and the people conducting research. This means forming the collaboration early on — sometimes, as early as when the study is in design.

"The earlier the communication starts with the IRB, the more likely that the research is going to incorporate a strong participation protection plan," Wilson says. "It involves both parties: the IRB needs to be accessible, knowledgeable, receptive, and willing. It also requires the research team to have confidence and trust, and reach out to the IRB." ■

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IRBs Can Work on Ground Floor With Start-Up Technology Firms

Working relationship benefits both

New companies using cutting-edge technology can enter the research arena, but they might lack resources and a knowledge base that academic research organizations take for granted.

IRBs can help companies fill some of those knowledge and experience gaps by forming a collaborative relationship and working with them from the beginning of the study design process.

According to a recent study, IRBs can improve their relationships with researchers, leading to a more effective and balanced approach to protecting human subjects.[1] For example, a biomedical engineering company has found that working with an independent IRB is a tremendous asset when it comes to protocol development, subject safety, and adverse events.

"We communicate with the IRB on a very regular basis," says **Chelsea Frank**, manager of clinical trials for Masimo Corporation in Irvine, CA. Masimo manufactures noninvasive medical devices. Masimo research staff call their IRB weekly. "They take our calls at any time, and they provide us with any sort of advice," Frank says. "They feel like an extension of our team."

IRBs might find that it improves their customer service and value to the research community by providing start-to-submission guidance and services. "It's a way of doing business," says **Leslie Wilson**, CIP, director of operations at Ethical & Independent Review Services (E&I) in Independence, MO. "We feel it's very important to have a working relationship with our clients to ensure they have the guidance they need to keep their research programs on track. In working with investigators and sponsors, as we do, there is an experience that occurs where they recognize they can reach in and begin asking questions early."

Improve Communication

Wilson, Frank, and other experts suggest these methods of improving communication between IRBs, sponsors, and investigators, particularly with new research enterprises:

• **Take time to develop trust.** An IRB should be willing to dedicate the time necessary to develop a trusting relationship with investigators and sponsors, Wilson says.

IRBs can offer help in the early stages of study design, including information about regulatory compliance and writing informed consent forms.

Some research institutions use research advisory groups, where the IRB is part of a larger framework, says **Erica Heath**, CIP, partner at E&I. "The IRB director could say to researchers, 'We welcome early discussion of problematic issues,'" she adds.

Trust takes time for everyone involved in research. "Traditionally, IRBs were very suspicious of the motives of sponsors," Heath says. "The traditional IRB often would not talk with the people who developed the protocol." IRBs would talk with investigators when there was a protocol problem, she adds.

Start-up technology companies often work with limited staff and resources when building a research program, Heath notes. "What we try to urge is that they talk with us when building their models," she says. "They can talk with an IRB, the experts, to try to understand what is their business and what is their research."

IRBs can keep in mind that start-ups will need time to adjust as they work toward developing human research protection principles.

"It's not a quick process," says **Katie Huber,** PhD, CIP, research ethics consultant at 23andMe in Sunnyvale, CA. "You don't understand something new and different overnight. You need time to think about it and come back to it multiple times before you understand all implications of it."

When IRB staff provide above-and-beyond help, such as making calls to regulatory agencies or other experts to consult on behalf of researchers, they help build trust and confidence in the human research protection process, Frank says.

"When you start to recognize that the IRB is an advocate for you, and they're on your team, then you really start to reap the benefits of what they can provide," Frank says. "If you treat them as a vendor and someone to just move your goals forward, then you miss out on that."

Trust is a two-way street. "It's important for not only us to have trust in the IRB, but for the IRB to have trust in us, as well," she adds. "That's the relationship we've developed over the years."

• **Keep lines of communication wide open.** "An open line of communication helps to develop our relationship," Frank says.

When Masimo Corporation is developing a protocol for a clinical study and is unsure about where some aspects of the study fall within regulations, or effect informed consent, the IRB can be helpful in navigating this uncertainty, she says.

"They're really open to brainstorming with us and kind of playing devil's advocate, helping us look from all different perspectives," Frank explains. "The IRB can help us develop not only the safest protocol, but a protocol that makes the most sense."

Part of an IRB's role in communicating with researchers is sending information about regulatory changes, including the latest advisories from the FDA, she adds.

IRB staff can give researchers advice based on their previous experience, and share their wealth of knowledge about study protocols and human research protection. They also can call investigators to show they are comfortable with direct communication.

"It seems like a simple solution, but in an age where electronic communication is the norm, I think it's less frequent that conference calls occur, where people are speaking directly with the IRB," Wilson says.

"For us, what's challenging is a lot of IRBs are more focused on pharmaceutical studies," Frank adds. For device companies, it is helpful to work with IRBs that have experience with those types of studies, she adds.

"When we enter into a new, breakthrough area or new device or protocol that we haven't had any experience with, the IRB is the first one we call to try to develop those things," Frank says.

One of the best ways an IRB can improve communication between its office and the research office is remaining available for discussions before, during, and after protocol submission. Day-to-day and week-to-week interactions help build that relationship, Frank notes.

• **Ask research participants what they want.** Participant feedback can help a research organization and IRB better understand research participants' issues and concerns. The feedback can help provide a more effective review and strengthen human subject protection.[1]

There are many ways researchers can seek participant input, including holding focus groups, conducting one-on-one interviews, surveys, and providing online test/survey scenarios with a prototype of the study followed by questions about what people see, Huber says.

Questions for participants might focus on basic comprehension issues to ensure people will understand what a particular study is about, says **Michelle Agee**, MSc, CIP, manager of regulatory science at 23andMe.

"We try to describe risks and benefits," she adds. "Did we catch all of the risks, or are there other things participants are thinking about that we missed?"

Talking with potential participants is especially important in research that is not clinical in nature, Huber notes.

"With data research, the risks are much more subjective," Huber says. "There are some privacy risks that come with the use of data, but how dangerous do we think they are?"

The risk level is subjective, depending on an individual's own level of comfort and privacy, she adds. ■

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IRB Devises Efficient, Time-Saving Annual Review Process

Model is annual status report

Continuing review might have gone away for many studies, but a research protection program's responsibilities have not. This is why many IRBs have devised an alternative annual review process that combines workflow efficiency with enhanced research protection.

One model for this regular review is an annual status report (ASR), says **Sandra Meadows**, MPH, CIP, program manager, Office of Responsible Research Practices (ORRP) at The Ohio State University. Minimum risk, expedited review, and some additional studies do not need to go through the annual continuing review by the IRB, but they can be monitored through an ASR.

The ASR process requires 70% less staff time on pre-review than the continuing review process. ASR screens take an average of nine minutes, compared with an average of 30 minutes for an initial continuing review screen.[1] ORRP first devised an ASR process five years ago, anticipating changes to the Common Rule, says **Erin M. Odor**, MA, CIP, quality improvement specialist.

"When the Notice of Proposed Rulemaking [NPRM] came out in 2015, we took that opportunity to do a pilot project for research that is not subject to federal regulations to see if the [ASR] system might work," Odor explains. "We knew we could work out the kinks before the revised Common Rule went into effect."

They used the flexibility of non-federally funded research to loosen the pathway by performing a yearly administrative check instead of a formal continuing review, Meadows says. After the Common Rule's deadline in January 2019, the organization rolled out the ASR to eligible federally funded research. "This only applied to new studies," she notes.

THE ASR PROCESS REQUIRES 70% LESS STAFF TIME ON PRE-REVIEW THAN THE CONTINUING REVIEW PROCESS. ASR SCREENS TAKE AN AVERAGE OF NINE MINUTES, COMPARED WITH AN AVERAGE OF 30 MINUTES FOR AN INITIAL CONTINUING REVIEW SCREEN.

ORRP took these five steps in implementing the ASR:

- Assessed the NPRM's proposed regulations and an accreditation organization's requirements;
- Established criteria for annual status report eligibility;
- Developed an ASR option in the electronic IRB system;
- Revised policies, trained staff, and implemented the ASR application;
- Evaluated how the ASR affected staff resources and investigator burden, comparing ASR to continuing review over a three-year period.[1]

To ensure the process was consistent and expedient, they worked with information systems staff to implement the review pathway in the electronic system.

"When a new study comes in for annual review, our system will automatically put it into one of two places: the annual status report or the continuing review application," Odor says. "Our system makes the decision; our staff makes sure the decision is correct, based on investigator responses."

Odor created a decision tree that is used to determine whether a study is sent to the IRB for continuing review or ASR. The first question is whether the study is FDA regulated. If so, then it is subject to a continuing review. If not, then there are additional questions, including whether the study is federally funded, whether the study was approved prior to Jan. 21, 2019, or whether a reliance agreement stipulates continuing review by the IRB. *(The ORRP decision tree can be found at: http://bit.ly/2wdiVkN.)*

"It has a lot of complicated criteria," Odor says. "There are many ways to get to the annual status review option."

While the electronic decision tree process works well, sometimes the IRB needs to ask investigators for more information. "A tiny percentage of submissions for annual status review were not eligible,"

Meadows says. "It had a high accuracy rate — greater than 90% — for the routing."

The ASR includes these features:

• **Four research status questions.** For example, the second question asks, "What is the status of participant recruitment?" It includes checkboxes next to each of the two possible answers: "Recruitment is ongoing," and "Recruitment has been completed."

• **Research progress summary.** Investigators are instructed to summarize the progress of their research, including any interim findings.

• **Questions about approved amendments since last review.** It also features questions about changes made to research that have not been reported and approved by the IRB.

• **Questions about participant enrollment, and other comments.**

The ASR saves time on both ends of its use — with investigators completing the form, and with the IRB in reviewing it.

"Occasionally, there are inconsistent items in the status report, and we have to go back to the investigator for clarification," Odor says. "But that happens much more often with continuing review applications."

About 80% of the annual status report applications were complete when they were submitted. They were renewed automatically, without any questions for investigators, Odor says.

"For continuing review submissions, only 11% were complete when they came in. Most of those had to go back to investigators before the IRB reviewed the continuing review," she adds.

The electronic system sends investigators annual renewal reminders 90 days before expiration. It also sends reminders at 45 days, 14 days, and seven days before the study expires, Odor says.

"One of the suggestions we are considering is to reduce the annual renewal notice from 90 days to 60 days or less because it doesn't take as long to renew studies as it used to with the annual review status report," Odor adds.

Investigators are far less likely to let an ASR expire because it can be completed so quickly, Meadows notes. "Before, it would take weeks for some continuing reviews to get approved, while 63% of annual status reports are approved within five days of receipt," she says.

"We didn't see many continuing reviews expiring previously, but it was causing a lot of stress," Odor adds. "I think I can say, anecdotally, that we're not up against the clock as often now."

Use of ASRs reduced staff resources by 11 hours per week in 2019. This is expected to increase to 13 hours per week in 2020.[1] "It gives us more flexibility in how fast we can turn it around and who can look at it," Meadows says. "We have a number of these approved on the same day, and that's a huge win for everyone."

While it is true that the revised Common Rule does not require IRBs to create an ASR-like process for studies that are not required to go through continuing review, it also is true that many research institutions want to have some oversight, Meadows notes.

"We have a monthly conference call with the other Big Ten institutions, allowing us a check with peer institutions about how things are going," she explains. "The Common Rule had very little guidance associated with it, so we felt more comfortable having those conversations with each other, and gauging where they're going with this flexibility. The vast majority of the Big Ten schools elected to have some kind of annual check-in with their investigators." ■

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Consent Calendar for Continuing Reviews Can Save IRB Meeting Time

Calendar can save 30 minutes per meeting

The consent calendar is a century-old tool, but it can work well in saving time during IRB meetings. Typically, IRBs review each study up for continuing review, discussing and voting for each, separately. But that might not be the most efficient way to handle these on the board meeting agenda, says **Glenn Martin**, MD, DLFAPA, CIP, senior associate dean for human subjects research, executive director of the program for the protection of human subjects, and associate professor of psychiatry, Icahn School of Medicine at Mount Sinai in New York City.

"If you have questions to be voted on, and they are straightforward, boring material, then you can put them together on one list [for a single vote]," Martin says. "This list of items can move to the consent calendar."

Robert's Rules of Order calls this time-saving tool a consent calendar, although it also is called a consent agenda. *(More information is available at: http://bit.ly/2Hmx7u3.)* "It dawned on us at our meetings that there are a lot of continuations that are straightforward, but require the full board," Martin explains. "Maybe there were no unexpected adverse events, yet we were spending time on those items with a primary reviewer giving a brief synopsis, followed by a brief discussion." These were needlessly wasting board time, he adds.

IRB staff and an IRB member examine the continuing reviews and send any questions to the principal investigator to resolve before the board meeting. All facts about the study are included in the agenda packet for every board member to see, Martin says.

IRB members can pull up the consent calendar on their laptops or tablets. If there are no questions or issues, the continuing review can be approved in a consent calendar. Icahn School of Medicine's four IRBs made the switch more than a year ago, and they found that it has shortened meeting time and improved efficiency. A study revealed that the consent calendar saved about 30 minutes of a two-hour scheduled meeting.[1]

> A STUDY FOUND THAT THE CONSENT CALENDAR SAVED ABOUT 30 MINUTES OF A TWO-HOUR SCHEDULED MEETING.

Initially, there was some resistance to the change, Martin notes. "At first, people were skeptical," he says. "Some said, 'It doesn't feel right.'"

IRB Maintains Control

Martin pointed out that the IRB was not giving up control by switching to this faster way of approving continuing reviews. This was because any board member, at any time, could ask for a continuing review item to be taken off the consent calendar and placed back into the agenda to be discussed later in the meeting. "If you want more discussion, you're in complete control of that," Martin says.

Board members receive the list of continuing review items in advance so they can red-flag one if they have a question or concern. Since rolling out the consent calendar, fewer than 1% of items were withdrawn for further discussion and vote.[1]

"Every now and then, someone will pull an item out because of something they remember that happened with the study, and they want to talk about it," Martin says. "We put it back on the agenda."

When an item is removed from the consent calendar, the primary reviewer presents it, and the person who pulled it from the calendar can ask questions. Board members then discuss it and take a vote. All items on the consent calendar are approved with one vote.

"It's a very transparent process," Martin says. "Everyone has all the information they need before the meeting."

Switching to a consent calendar is fairly easy, although explaining to board members what it is about and how it works can take time, he notes.

"Three or four people knew what I was talking about when it was introduced," Martin says. "The rest asked to have it explained a couple of times."

Within a month of using the tool, it became clear to everyone, he adds. "People like it, and we have had zero negative comments that I'm aware of," Martin says. "The IRB staff likes

it; it makes writing this into minutes automatic, and it makes the meeting a smoother operation."

From a regulatory perspective, it is fine because items are discussed if necessary. The items on the consent calendar generally are noncontroversial and are unlikely to require further questions or discussion, so they can be approved by unanimous vote.[1]

"We rolled out the consent calendar for all of the IRBs in the same month," Martin says. "At meetings, we do the consent calendar before we start anything else." ■

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Protocol Activation Model Leads to Reduction in Time-to-IRB Approval

One tool is a consent language library

A large cancer research institution in New York City overhauled its protocol review process, devised a library of scientific terms commonly used in consent forms, and invested in more staff. Within a couple of years, the updated process resulted in a striking reduction in the median time for protocol and consent review by the IRB. Time-to-IRB approval decreased from 135 days in 2017 to 80 days in 2018. The time has continued to decrease.[1]

"Many institutions are concerned with trying to activate trials faster," says **Collette Houston**, vice president of clinical research compliance at Memorial Sloan Kettering Cancer Center (MSKCC).

MSKCC approached this goal with a complete overhaul. "It was like cleaning a blackboard and starting over," Houston says. "We started the process in 2017, and went live in January 2018."

Each fresh protocol in 2018 began with the updated centralized protocol activation core (PAC) process. "Two years in, we found out what really works, and what needs additional support and Lean processing," Houston says. "We built Lean processing into the workload so we could reach a goal of having the IRB approval and trial activation at less than 90 days. Now, we can get IRB approval accomplished in less than 75 days. We're enhancing our processes a little bit to make it leaner on that end stage of activation."

They accomplished this by building a team of experts on how the process works, she explains. "We work with investigation teams and with the committees required for protocol activation, including the budget and contracts team and the study team."

The idea behind the protocol activation core is to make the process leaner, says **Sam Briggs**, protocol activation manager at MSKCC. The team of experts includes eight protocol activation managers and two dedicated editors who have developed a library of informed consent language. *(See story on consent language improvements, page 34.)*

"The great thing about the protocol activation core is that a number of the people came from different disease management teams," Briggs says. "I came from neurology, and we have GI [gastrointestinal] specialties and blood cancer specialties. We came together to share our expertise, and with the help of the editors, we came up with some well-crafted consents."

Centralize Processes, Responsibilities

The process improvement project started with centralization of the responsibilities, Houston notes. "It was reasonably quick, and we made some drastic improvements to the IRB approval process," she adds.

The PAC team collaborates with Memorial Sloan Kettering's clinical research informatics and technology team, and the strategy and innovation team. The goal is to leverage the consent library as a primary resource for everyone involved in human research protection and informed consent.[1]

Another change was the development of a protocol review core, also under the umbrella of the human research protection program. Protocol review managers pair with a committee, such as the scientific committee, which is called the research council, Briggs says.

Protocol review managers go over submissions with the research

council, checking for essential documents and ensuring there are no preliminary questions from the committee. "It is a polished and complete submission. This has been important in reducing delays and letters from the committee, and miscellaneous holdups," Briggs explains. "We've become experts at what it takes to get any type of protocol through our review process."

For example, Briggs spends 30 to 60 minutes meeting with investigators to discuss the parts of the protocol that are most concerning.

"Those kinds of things help to cut down on time the protocol is reviewed by the research council," Briggs adds. "The great thing about the protocol activation core is that we're always meeting and brainstorming. It has a start-up feel with all of these experts." ■

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Consent Library Is Consistent With Quick Access to Better Wording

Informed consent library includes more than 400 terms

Dedicated editors help a research program manage an informed consent library of terms that can be included in consent forms as a substitute for medical/scientific language.

"With help from the editors, we have come up with some well-crafted consents," says **Sam Briggs**, protocol activation manager at Memorial Sloan Kettering Cancer Center (MSKCC) in New York City.

MSKCC created the consent library as part of its performance improvement project that resulted in the launch of a centralized protocol activation core (PAC), which includes Briggs and seven other protocol activation managers, and two dedicated editors.

"We thought that if we looked at the set of consents approved since our unit rolled out, we could basically lift the language we like from all IRB-approved consents and turn it into a library," Briggs says. "It's important to have a good system of standards."

The consent library is available electronically on a shared drive, he says. "One thing we want to do over the coming months is find a way to make it more accessible to investigators and primary study teams," Briggs adds. "We'd provide training for study teams on how to use it, and what the expectations are."

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They built the consent library, starting with risks, converting complex terms like anemia into layman's terms, he explains.

For example, the risk of anemia could be described as "low red blood cell count," which better describes the condition in layman's terms. "All lab conditions have scientific terms," Briggs says.

Words and terms describing procedures also can be put into simpler language or explained, he adds. "The most complicated part of it is drug mechanisms," he says.

Although MSKCC's studies are varied, there are overlapping features. For instance, immunotherapy might be used in different types of research, so this was an important word to describe for the consent library.

"Immunotherapy is a big category, and it was important to us to set a definition and put that into the consent library," Briggs says. "It saves activation managers' time, and saves IRBs' time."

Immunotherapy drugs are common. The PAC worked with a pharmaceutical company to create a risk section for the drug, he says. "That's one way we made this more efficient," Briggs adds. "We have that whole section to put into the consent form."

The consent library is designed as a spreadsheet. The left column lists the scientific names of informed consent terms, including adverse events.

For example, the library lists the scientific term "adrenal insufficiency" in the first (A) column to the left. The other columns are:

- **Column B.** This is the language the editor approved to describe the scientific term. For adrenal insufficiency, the editor approved text is "Decreased production of hormones by the adrenal glands, located on top of each kidney; symptoms may include dizziness, irritability, fainting, low blood pressure, skin darkening, and craving of salty foods (approved date: 02212019)."
- **Column C.** Notes/keywords: "Kidney, hormone."
- **Column D.** Description 1: "Adrenal glands (glands on top of the kidneys) may not make enough hormone, causing tiredness; weight loss; muscle weakness; feeling faint; joint, muscle, and abdominal aches; nausea; vomiting; loose or watery stools; fever; salt craving; and sometimes darkening of the skin like a suntan."
- **Column E.** Description 2: "Decreased production of adrenal hormones, which can cause weakness and/or low blood pressure."
- **Column F.** Description 3: "Decreased production of hormones by the adrenal glands, located on top of each kidney; symptoms may include dizziness, irritability, fainting, low blood pressure, skin darkening, and craving of salty foods."[1]

"We add new words to the library in batches," Briggs says. "Once a month or so, I'll go back and look at the approved consents for the past month and make sure all risk terms and procedures are in the consent library."

For instance, Briggs recently looked at a dose escalation, stage one study. "I worked closely with the editor to come up with a clear way to describe that to participants, and we put that into the library," he says. "The next time any of the nine activation managers come across [a similar study], it will save them time to just go to the library, pull it out, and tell the sponsor that this is the way we've decided to describe the term."

Sponsors rarely question these changes, Briggs notes. "The overall goal is to find ways to be as clear as we can for participants, and to keep the bar high in quality of these consent forms," he says. "These editors do an amazing job making sure these are clear, readable, and consistent."

Protection activation managers and editors share access to the library. The editors read through consent forms, looking for words that research participants might have trouble understanding.

"For a word like anemia, we want them to say exactly what anemia is: 'a low level of red blood cells,'" Briggs explains. That description can be used in future consent forms this way: "anemia, which is a low level of red blood cells."

Typically, the description would be listed once. But if the word "anemia" is used again in the informed consent form, then the description would not need to be repeated, Briggs says.

The consent library now includes 400-500 words, and is growing, he adds.

Another group at MSK is developing an e-consent platform for patients that they could access on tablets. "They'll complete the consent form and check boxes as needed," Briggs explains. "We see, in the future, having a method to type in some kind of short-word language that pulls directly from the consent library to the e-consent."

They could put a hashtag before the word, such as "#anemia," and this would be an efficient way to add the editor-approved language to consent forms, he adds. ■

CME/CE OBJECTIVES

Upon completion of this educational activity, participants should be able to:

1. Establish clinical trial programs using accepted ethical principles for human subject protection;
2. Apply the mandated regulatory safeguards for patient recruitment, follow-up and reporting of findings for human subject research;
3. Comply with the necessary educational requirements regarding informed consent and human subject research.

COMING IN FUTURE MONTHS

- Are IRBs ready for coronavirus studies?
- CLEAR Initiative improves consent language
- PIs prefer efficient revision deadlines
- Interactive informed consent template guides PIs

IRB ADVISOR

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CME/CE QUESTIONS

1. **What is paradata and its source?**

   a. Paradata refers to a short paragraph with no more than one or two sentences.
   b. Paradata refers to information collected by cameras.
   c. Paradata refers to auxiliary data collected, including data from a person's online use.
   d. Paradata refers to information collected in the cloud.

2. **IRBs might start an annual review process for studies that do not meet continuing review criteria for which reasons?**

   a. The revised Common Rule requires IRBs to hold a short-form annual check-in with all studies.
   b. The FDA requires such studies to include an annual status report.
   c. The Common Rule provides little guidance for noncontinuing review studies, but many research organizations may continue to hold annual reviews.
   d. Researchers request this annual review report to provide reassurance of their own compliance with federal regulations.

3. **At IRB meetings, the board can use a time-saving tool to bring all of the continuing review items on a list for a single vote, called:**

   a. consent calendar or consent agenda.
   b. Robert's Rules single vote.
   c. item list action.
   d. auxiliary action item.

4. **Which is an example of descriptive language that could be used to define "adrenal insufficiency" in informed consent documents?**

   a. Kidney, hormone
   b. Decreased production of hormones by the adrenal glands, located on top of each kidney; symptoms may include dizziness, irritability, fainting, low blood pressure, skin darkening, and craving of salty foods
   c. Lab test result associated with liver disease or bone disorders
   d. Rare blood disorder that occurs when the body destroys red blood cells more rapidly than it produces them