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INSIDE

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Research Professionals Question Structure, Effectiveness of IRBs

An upcoming GAO report may promote communication

By Sue Coons

Finding ways to evaluate IRB ethical quality and effectiveness has been an elusive ideal. Two research professionals are advocating for directly measuring quality of board oversight, rather than relying on the structure of the IRB. An upcoming U.S. Government Accountability Office (GAO) evaluation of commercial IRBs also may promote the conversation.

For many IRBs, quality measures include licensing from the Association for the Accreditation of Human Research Protection Programs, confirmation of regulatory compliance, board member expertise and training requirements, investigator and board member satisfaction, and efficient turnaround of submitted protocols, wrote **Holly Fernandez Lynch**, JD, MBE, and **Stephen Rosenfeld**, MD, MBA, in a recent issue of the *Annals of Internal Medicine*. "Yet it is not clear that these industry-standard approaches offer meaningful assessments of ethical quality, nor is it clear what ought to be viewed as satisfactory in this regard."[1]

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"As we articulate in the paper, we really don't have a clear sense about how best to evaluate IRBs," says Fernandez Lynch, assistant professor of medical ethics in the Perelman School of Medicine at the University of Pennsylvania. "If we had a mechanism

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of directly assessing their quality and effectiveness, we wouldn't have to rely on proxy measures based on their structure. But in the absence of those measures, we have to ask if their structure might create concerns about the influence of payment, obligations to investors, or competing interests of research institutions, all of which may distract from attention to the interests of the research participants."

Commercial IRB Structure

According to a 2016 report, more than 70% of reviews are handled by commercial IRBs. Multisite protocols are challenging and, per regulation, NIH policy sites cannot review them individually.[2] "It needs to be a single IRB oversight, and there is value in the professionalism that commercial boards offer. For people who sit on IRBs at academic sites, this may be just one of their committee assignments. They are also trying to get their own research done and all of the other things that come along with their day jobs. On the for-profit boards, this is what they do. And they can get things done quickly." The professional board members can have many more board meetings; they can participate in a board meeting a week or a couple times a week. "As a matter of efficiency, you can see why these boards are attractive compared to the academic boards."

However, some people hold concerns about the structure. "If you are beholden to investors, then it is possible you will choose the pathway that is most efficient and legally permissible, but perhaps not ethically superior." Fernandez Lynch says she is not suggesting that for-profit boards are violating the regulations. "They clearly are going to be following them, but the regulations are not the be-all, end-all of ethical research." If IRBs are pressured to be responsive to investors and profit motives, are they doing the bare minimum of regulatory compliance and saying something is approvable? Or are they considering ways to make it ethically better? "How can we put an ethical gloss over all of our reviews? That's the concern about incentives set up under the commercial model." Fernandez Lynch emphasizes this is not about any nefarious intent, but rather the limits imposed by structural conflicts of interest.

The discussion is about the business model, not the actual board members of the commercial IRBs, Rosenfeld agrees. "This has gotten confused recently. When we talk about these companies as IRBs, the actual IRB [is comprised of] the scientists and laypeople who are convened to discuss protocols. They are not the business. They have to be kept separate," explains Rosenfeld, chair of the U.S. Department of Health and Human Services Secretary's Advisory Committee for Human Research Protections (SACHRP) and president at Freeport Research Systems in Freeport, ME. "The people who are in marketing and business development, and even potentially compliance, don't sit on those boards. The people who do give their time to those boards are very well-intentioned and worry about this stuff. They are doing their jobs, but they are guided by the SOPs [standard operating procedures] and standards that are established by the companies. This [discussion] is about the companies that convene the boards and what authority and scope they allow those boards to address."

Rosenfeld started working in the independent, for-profit IRB industry in 2008. He is a former board chair of Advarra and Quorum Review, and former president and CEO of Western IRB.

"When I started in that industry — and when that industry itself started, which was decades before that — there was real question about whether ethical review could be done for profit because the people paying for the reviews were obviously the sponsors and scientists, not the research participants," he explains. "A consequence was that there were a lot of structural controls put in place to separate the deliberations of the actual IRB, the board of experts and representatives, from the concerns of running a business."

Typically, the people on the board were not employees. The business convened an actual IRB panel and supported all the administrative tasks, distribution of materials, and getting things to and from the clients. "The actual deliberations of the board were kept entirely separate. It was that structure that made this whole IRB model acceptable to the community," Rosenfeld says. A community of independent IRBs existed as well. "The combination of competitive forces and the structural concern that I raised kept our focus on research participants, which of course is what the IRB is supposed to focus on."

Since then, the independent IRBs have been bought and consolidated into the large commercial firms. At the same time, changes in the regulations and general acceptance of the model seems to have decreased the concern about structural controls, Rosenfeld says. In addition, the regulations around IRB decisions are broad. "They leave a lot to the discretion of the committee. That is necessary because IRBs have to respond to changing science and changing social conditions," he says.

That also can mean limited reviews that can answer the letter of the regulations but not necessarily put the interests of research participants first can be considered compliant. "These are structural issues," Rosenfeld notes, emphasizing that he is not suggesting any bad intent in the commercial IRB industry. "But I think it is naïve to believe that these very large companies at this point will not behave in their own business interest, and that may not be completely aligned with the interests of research participants."

Rosenfeld also is concerned about new ethical questions that have arisen in the past decade, such as privacy concerns, internet-based research, group harm, social justice, and genomics. Although the regulations are broad enough for IRBs to address these issues, companies may decide not to send them to the board for consideration. "By restricting what the IRB actually looks at, you are perversely actually adding to the burden of research as people look to other avenues to address these emerging ethical issues. The incentives for IRBs don't support them embracing these things unless they have to."

An Independent, Nonprofit Alternative

Rosenfeld has been advocating for the formation of an independent, nonprofit IRB as an alternative to the current models. "His idea is a nonprofit commercial IRB, which is intended to take the benefits of the academic model, particularly not being beholden to investors, and the benefits of the for-profit model, especially having extensive professional support and expert review," Fernandez Lynch explains. "You get the best of both worlds, allowing attention to ethical considerations that might go beyond the regulatory requirements."

Nonprofit IRBs likely will have more leeway to emphasize the ethical side of review than IRBs separated from research institutions. This might prevent the associated conflicts that come with institutional affiliations, including the need for research funding, Fernandez Lynch and Rosenfeld noted in their article. "Independent, nonprofit IRBs could take advantage of economies of scale that have made for-profit boards so efficient, as well as the professional model of membership that treats protocol review as a full-time, expert position, all while reinvesting resources in structures and processes likely to promote high-quality review," they wrote. "Without the need to constantly grow market share, this type of board also might be positioned to serve as 'laboratory,' testing different approaches to research ethics oversight and sharing results to inform others."[1] If he or someone else could start this nonprofit and people responded to the idea of being more responsive to ethics, then the commercial IRBs likely would do the same as competitive businesses, Rosenfeld says.

The challenge in creating this model, Rosenfeld says, is that people are not particularly interested primarily in IRBs themselves. Instead, they are interested in scientific research and moving the needle on cures and knowledge. "This is one of the great challenges. The current structure gets IRBs out of the way of that," he says. "In some ways, it is very responsive

to the needs of the scientific community. That's what most grantors are interested in, understandably: promoting cures and advancing knowledge."

The idea would attract people who are primarily motivated by protecting the rights and welfare of research participants, he says. However, the current structure is not always viewed as a problem, and most people outside the research community do not know about IRBs or how they are structured. "If they do know IRBs exist, they just assume [IRBs] are doing their job," Rosenfeld says.

The AEREO Consortium

Concerns about the shortcomings of common-sense approaches to evaluating IRB quality and effectiveness and the difficulties of learning about IRB policy, practice, and performance motivated Fernandez Lynch to launch the Consortium to Advance Effective Research Ethics Oversight (AEREO) in 2018. AEREO is a collaboration of IRB leaders, academics with expertise in research ethics and empirical methods, and other stakeholders aiming to make progress toward defining and measuring IRB effectiveness. Fernandez Lynch says AEREO is undertaking several projects, including:

- Efforts to build a set of precedents against which IRB decisions can be compared and from which IRBs can learn;
- Develop stronger understandings about what type of expertise and perspective is needed for ethical review and how to best facilitate ethical deliberation among a diverse group of decision-makers;
- Consider whether the protections imposed by IRBs are likely to achieve their goals;
- Pay attention to the views and experiences of the research participants whom IRBs aim to protect.

"These are long-term engagements that do not lend themselves to a simple quality checklist, and go well beyond questions of regulatory compliance," she says.

Implications from the GAO

Some of the conversation may change with the GAO's investigation into the practices of commercial IRBs at the request of U.S. Sens. Elizabeth Warren, D-MA, Sherrod Brown, D-OH, and Bernie Sanders, I-VT. *(For details, see related story in this issue.)* The agency has its work cut out for it, Fernandez Lynch says. "What the senators are looking for is some assessment of quality, effectiveness, and efficiency of these review boards. This is something bioethicists have been working on for decades, and we really have not made much headway on it."

The ideal often is described as some set of metrics or a checklist, she says, with the notion that if an IRB sticks to the list, there is confidence that participants are protected. "But it's not so easy because each board is being asked to apply ethical standards that are kind of fuzzy," Fernandez Lynch says. "If they were clear, we wouldn't need IRB review."

Boards can reach conclusions that are different from one another. "There is not a clear way of saying 'This board got it right and this board got it wrong,' unless it was egregious where everyone would agree that a particular board got it wrong," she explains. "These are all research ethics debates: What kind of consent do you need for standard of care research? Is a placebo control arm appropriate? Do you need to have concrete plans for post-trial access? It's hard to say that there is one right answer, which makes these checklist-type approaches very difficult."

The system of research ethics does not lend itself to an easy checklist of items that indicate if something was performed ethically. For example, consider the metric of how many protocols a board approves on first submission. Fernandez Lynch says that does not really say much about quality. "It could be that a board is approving 100% of protocols, but they aren't rubber-stamping things. Instead, it could be that they have a robust system in place where the sponsors of the research and the researchers are engaged with the staff of the IRB before they even submit anything so that submitted protocols are in really great shape. They have worked out all the kinks. They are clearly resolving ethical concerns so that by the time they are actually getting to the board, the protocols are approvable. This is the IRB actually working exactly as we would had hoped in the most efficient manner of dealing with any problems before things get to the board."

Rosenfeld says he is not sure what will come out of the investigation. "I am quite confident that at least the two big IRBs are completely compliant with the regulations. I think that has become their role." In the GAO's last investigation of commercial IRBs, Coast IRB in Colorado Springs approved a fraudulent study. The IRB later shut down.[3] "I don't think there is anything [like the Coast IRB issue]," he says. "They were obviously not doing the right thing. I don't think there will be any smoking gun

this time." If complying with the regulations is the definition of the "right thing," then commercial IRBs will point to the regulations and say they are doing what they are supposed to do, he says.

"In my view, IRBs are about protecting the rights and welfare of research participants — not demonstrating compliance with the regulations, but the regulations are the mechanism that we enforce that protection through," he adds. Therefore, if the IRBs are compliant with the letter of the regulation, then the GAO may not find anything unexpected.

However, Rosenfeld hopes the investigation opens the door to a conversation about the purpose of IRBs. "I think one of the issues with IRBs is that the people they are meant to protect, in most cases, don't even know they exist," he says. "There is no real oversight or accountability to people who may one day be research participants, or to society in general. Maybe the GAO will give us an opportunity to have that conversation." ■

REFERENCES

1. Fernandez Lynch H, Rosenfeld S. Institutional review board quality, private equity, and promoting ethical human subjects research. *Ann Intern Med* 2020;173:558-562.
2. Kaplan S. In clinical trials, for-profit review boards are taking over for hospitals. Should they? *Stat*, July 6, 2016. https://bit.ly/32PQzuk
3. Koziatek S. IRB seals fate by approving fake protocol in federal sting. *IRB Advisor*, July 2009. https://bit.ly/32Na3jm

Government Accountability Office to Study For-Profit IRBs at Senators' Request

The investigation should begin in early 2021

By Sue Coons

The Government Accountability Office (GAO) agreed to "investigate the operations" of commercial IRBs at the request of U.S. Sens. Elizabeth Warren, D-MA, Sherrod Brown, D-OH, and Bernie Sanders, I-VT. "GAO accepts your request as work that is within the scope of its authority. Consistent with GAO Congressional Protocols, given broad congressional interest in these issues, and upon agreement with your staff, we will allow other congressional committees of jurisdiction and interested members of Congress to become co-requesters of this work," Orice Williams Brown, GAO managing director for Congressional Relations, wrote in a letter released on Aug. 10.

The senators did not say how the topic of commercial IRBs became a focus of their attention. On Nov. 19, 2019, the senators released a letter saying they had sent letters to the large private equity-owned IRBs ,WIRB-Copernicus Group (WCG) Clinical and Advarra. This letter raised questions about whether for-profit IRBs "are vulnerable to conflicts of interest that could inhibit their ability to protect research subjects, and whether the two companies are maintaining appropriate ethics standards." The lawmakers also requested information on the IRBs' approvals, processes, policies, and quality metrics.[2]

"The recent trend of private equity ownership is especially troubling, given the pressures to reduce costs and ramp up profits that often accompany private equity's entry into a field," the senators wrote. "If managers see their primary responsibility as generating returns for their investors, they may emphasize speed over thoroughness in the review process, creating risks for patients."[2]

The senators also said they were concerned about reports of "pay to participate" clinical trials, where patients must pay for the opportunity to enroll in a research study. "These studies may take advantage of vulnerable patients and their families, restrict access to treatment to those who can afford to pay, create incentives to oversell the potential benefits of the trial, and potentially compromise the design of the clinical trial," they wrote.[2] The Food and Drug Administration (FDA) and the National Institutes of Health (NIH) also have said they are asking committees to consider how these scenarios should be handled.

In a report from Aug. 19, 2019, **Michele Russell-Einhorn**, JD, chief compliance officer for Advarra, talked about the increasing number of protocols that ask for participants to pay to be in the study. She mentioned one that was $7,000 to enroll,

and another requested "upward of $250,000." There were "serious concerns about how ethical it was to charge people to participate in the research — and whether it was absolutely necessary," she said.[3]

However, comments on Twitter pointed out that Advarra had approved such a study for the Lung Institute in Dallas (ClinicalTrials.gov Identifier: NCT03040674). The informed consent form for this study indicated there is no cost to participate in the data collection and investigation of the patient's response to study treatment. However, it continues, "[a]t this time, insurance companies are not covering the cost of cellular therapy for chronic pulmonary diagnosis; therefore, the cost of study treatment is the responsibility of the participant."

Questions from Senators

In the letters to Advarra and WCG, the senators requested information regarding approvals, processes, policies, and quality metrics for each of the past five years. Former Advarra CEO **Patrick K. Donnelly** wrote extensive comments to the senators, defending the company's procedures and its commitment to excellence. "Advarra IRB conducts high-quality review of research, which is guided by a talented team well-versed in the regulatory and ethical standards governing human subjects research, as well as a robust internal compliance program, and written policies and procedures." Donnelly said Advarra had reviewed only a relatively small number of "pay to participate" protocols. Some were disapproved; others were pended for more information. For each of these studies that was approved, the IRB required the study sponsor to make "significant revisions" to the original study proposal, he said, "as well as materials provided to the prospective human subject participants before the study could be approved."[4]

In a follow-up letter to the Senators on April 8, 2020, Advarra President and Chief Research Services Officer Scott Uebele gave additional data, including more on "pay to participate" protocols. He said, to the best of his information, Advarra had reviewed only nine studies that met this criterion. Four were disapproved, three were withdrawn or tabled, and two were approved.[5]

WCG's **Donald A. Deieso**, executive chairman and CEO, responded similarly to the senators. "Our practices make certain that we scrupulously adhere to all regulatory requirements, that no panelist has any financial interest in any study that they review, and that there are no conflicts of interest in our mission to protect human subjects."[6]

GAO Request

The senators told the GAO they were not satisfied with the responses. The companies responded with generalities, they said, with assurances their review process was thorough and high-quality but provided few data to corroborate these claims. "WCG's response failed to address key concerns about conflicts of interest, 'pay for participation' trials, and quality metrics," they wrote. "Advarra provided some information about its conflict of interest policies and the number of 'pay to participate' trials it has reviewed, but did not provide specific data or examples."[7]

The senators asked the GAO to address these questions:

- What is the current market structure for IRBs? To what extent has the use of commercial IRBs increased relative to the use of academic or other nonprofit IRBs? What has driven the market consolidation of for-profit IRBs? What role does private equity play in this process? How does it affect the ability of IRBs to appropriately review research proposals and protect patients and scientific integrity?
- Have commercial IRBs established appropriate protections to address the inherent conflicts of interest posed by their profit-seeking mission? Have they created appropriate procedures to address and ensure transparency regarding conflicts of interest among panel members who may have industry ties?
- Have commercial IRBs established appropriate processes and procedures to protect patients and ensure the scientific integrity of "pay-for-participation" studies?
- Do existing standards of quality, efficiency, and effectiveness provide adequate protection for participants in IRB-approved clinical trials? How can IRBs, the FDA, and the Department of Health and Human Services address any shortcomings in the system to improve quality and patient outcomes?
- How do procedures and outcomes differ between academic and commercial IRBs?

In the GAO response, Williams Brown said the investigation would begin in about six months, which should be February or March 2021. She gave no indication of how long the investigation may take.[1] ■

REFERENCES

1. Letter from GAO to Senator Elizabeth Warren, Aug. 10, 2020. https://bit.ly/2H6kdDU
2. Letters from Senators Warren, Brown,

and Sanders to WCG Clinical and Advarra, Nov. 19, 2019. https://bit.ly/2IH5JLA
3. Robbins R. Amid rising concern, pay-to-play clinical trials are drawing federal scrutiny. *Stat*, Aug. 6, 2019. https://bit.ly/35BaPSc
4. Response to letter requesting information on Advarra IRB, Dec. 12, 2019. https://bit.ly/3nrldSH
5. Letter from Scott E. Uebele, CEO of Advarra, to Sens. Warren, Brown, and Sanders, April 8, 2020. https://bit.ly/38MBpJY
6. Letter from WCG to Senators Warren, Brown, and Sanders, Dec. 12, 2019. https://bit.ly/2Hbc5Ce
7. Senators Warren, Brown, and Sanders call for the government watchdog to investigate for-profit institutional review boards (IRBs), June 18, 2020. https://bit.ly/36BxqgM

Self-Assessing IRB Operations Can Help HRPPs Stay Compliant, on Track

By Melinda Young

If an IRB sets a goal of greater efficiency, then giving researchers self-assessment tools and using self-auditing tools on IRB operations is a method that can work.

These tools can help study coordinators and investigators turn their study protocol submissions from a hot mess into a submission that is mostly compliant and easier to pre-review. IRBs can use self-auditing tools to ensure their human research protection program (HRPP) is compliant with regulations. These can inform quality improvement projects.

"What any program has to do is make sure they themselves are in compliance," says **Lisa Denney**, MPH, CIP, deputy director in the research compliance office at Stanford University. "We try to create consistency. But, still, every research study has its own nuance, so we do a self-assessment on our own program to see if we're consistent and compliant and make sure we've gotten the required documentation."

Whether IRBs create tools for self-audits of IRB operations or for investigators to use, the goal is uniformity. *(See story on study site self-auditing tools in this issue.)*

"You will see one uniform approach for how we do those," says **Sana Khoury-Shakour**, PhD, CCRP, director of the office of research compliance review at the University of Michigan. "We make sure the look and feel of the tools is the same. It starts with an introduction on how to use the tool, and we include cross-references to available resources."

Often, when IRBs receive studies from investigators, they're not ready to be reviewed. "Sometimes, they're a hot mess; people just put down their ideas," Denney says.

That is where IRB offices can help through pre-review processes. Making self-assessment tools available for researchers also can help. "We help investigators create a concise, harmonious package," Denney says.

This requires a lot of work, details, and communication with investigators, who might say IRBs are nitpicking or annoying.

"That's why we have to perform quality reviews," Denney explains. "It takes effort. Sometimes, things are complicated, and sometimes, things get missed, so we have to get them fixed." Consent form templates might be unclear, or checklists might be missing an item.

Stanford University has eight IRBs, each staffed by two people. Combined with management, there are about 20 HRPP employees, Denney says. To keep staff consistent when they assess protocols for regulatory compliance, senior IRB staff train and mentor newer staff.

"It's a lot of work to train a new person," Denney says. "It's part of senior people's job."

Some senior IRB staff enjoy training others, and Denney will ensure they have more of that responsibility. New IRB employees will review protocols, forward the protocols to senior IRB staff to review, then send the protocol and changes to the study team. This might continue for several months.

"They perform the review and the trainer shadows them, and that's the bulk of the training," Denney explains. "We shift work to what people like. Training is continuous."

IRBs also can provide self-auditing tools to investigators. The University of Michigan offers a dozen checklist and self-assessment tools on its research ethics and compliance webpage. The tools include a checklist for ClinicalTrials.gov registration, data security, Department of Defense research, eligibility criteria, and others. *(The tools are available at this link: https://bit.ly/36Ry4IS.)*

Stanford University's HRPP maintains consistency in IRB staff reviews of protocols by asking IRB members to follow a four-page protocol checklist for medical research.

The checklist includes dozens of items, such as:

- Whether the study uses non-significant risk device and the justification;
- Appropriate child risk determination indicated and justification provided;
- Plan to review responses to questionnaires asking about suicidal ideation provided;
- Protocols if targeting participants with impaired decision-making capacity;
- Whether study is listed as both multisite study and collaboration.

Consistency and quality improvement policies and practices are important among IRB staff, but should be a part of the culture and not seen as punishment, Denney says.

"Continuous quality improvement should not be punitive; it should be affirmative," she explains. "You can say, 'That's great! We're on target, so there's good news.'"

The IRB can hold standing staff meetings to review hot-button issues and talk about interesting protocols so the staff can learn from each other, Denney says. For example, one new issue that comes up with studies is related to the COVID-19 pandemic. Some pharmaceutical studies will require participants to undergo a COVID-19 test, she explains.

With these tests, the question IRBs might ponder is whether the COVID-19 test is just for the study and should be paid by the study, or whether it is standard of care because the person might have gone to the hospital for other care anyway, she says.

"We have to unpack this, and we don't have a precedent for this situation," Denney adds. "These are the kinds of things our managers get together and talk about."

Whatever decision the IRB makes about handling new situations that arise with studies, this decision should be handled consistently. One way to maintain quality and consistency is to create a real-time staff review of protocols under continuing review. "We work on continually reviewing our process, but doing a real-time review," Denney says.

For example, rather than hearing about a study problem that occurred two years or even two months ago, the IRB will catch it and address it in real time, helping investigators fix the issue well before the continuing review date occurs.

"At the time of continuing review, we do a spot check on them," Denney says. "This is a pretty fast-paced process, depending on what the issues are."

Another way to assess the IRB's work is to perform targeted audits of protocol reviews to ensure they have been completed properly.

"A person can run a report, identify a certain number of studies, and review to see if they met the review criteria," Denney explains. "This is a more programmatic review of our program." ■

Investigators Benefit from Using Online Self-Auditing Tools

Outcomes inform QI initiatives

By Melinda Young

One method to improve regulatory compliance while maintaining IRB efficiency lies in teaching investigators how to conduct self-audits of their protocols and studies.

"We have thousands of studies, and we can't talk to every single research team. We have to be innovative in the way we do things," says **Sana Khoury-Shakour**, PhD, CCRP, director of the office of research compliance review at the University of Michigan. "We mainly do compliance reviews. Those outcomes inform our quality improvement [QI] initiatives."

The office developed a self-audit process that can be used for any study and is available online. "We established this process to keep educating those study teams," Khoury-Shakour says.

"It morphed into self-audit tools," she adds. "We found that it was very helpful to study teams. We thought about how we could expand it and create additional self-assessment, self-audit tools that can be used for any study."

The tools are available to the public. Multiple research institutions have asked if they could adapt the tools for their own

use. "We're all about sharing the practices and have shared them," Khoury-Shakour says. You don't need a login to access them online." *(The tools are available at: https://bit.ly/36Ry4IS.)*

The research compliance review office started with its existing tools, building on those and designing them to be self-administered. Making the tools available publicly online was part of the plan.

"Every year, we add one or two," Khoury-Shakour says. "These do not replace any of our compliance reviews; they just complement it."

This is how self-auditing tools were designed:

• **Develop plan, goals, timeline.** Creating the tools took a little time and required a plan, goal, and target dates.

"When we first started this, we investigated it for a few weeks before we had a target," Khoury-Shakour explains. "Each year, we develop an annual plan of what we want to achieve. This project was one of the goals for that year."

The office dedicated staff time and effort to the project with the goal of publishing six checklists. "Initially, we did invest some time into developing the tools," Khoury-Shakour says. "Once you have the templates, it's just thinking about it and not reinventing the wheel."

Since the IRB office already used checklists, monitoring tools, and templates, they knew it would not be too challenging to make those existing tools available for study teams to use, she adds.

• **Start each uniformly.** "You will see one uniform approach for how we do those," Khoury-Shakour says. "We make sure the look and feel of the tools are the same. They each start with an introduction and explanation on how to use the tool."

It includes a table in which the investigator can insert study-specific information, Khoury-Shakour says. "We try to make them in a way that each study can tailor them to suit their study. We just try to create them in a way that people can download them and need minimal tweaking when they start to use them."

• **Create tools as needed.** The University of Michigan's office of research compliance website offers a dozen tools for download, including:

- ClinicalTrials.gov registration and results quality assurance/quality improvement checklist;
- A data security form for assessing the adequacy of data protection mechanisms for a study;
- Eligibility criteria;
- Informed consent documentation that study teams can modify to reflect the specifics of their study;
- Protocol adherence for researchers to assist in the required documentation of monitoring.

• **Incorporate feedback.** "People think the tools help them improve oversight, and they believe the checklist is educational in itself, putting best practices to the forefront," Khoury-Shakour explains.

Researchers have noted the resource helps them improve the quality of their work. They find the self-auditing tools easy to tweak and tailor to their own studies. "I've heard mainly from people who like to oversee multiple studies within certain units," she says. "They've used them in that way for various units within our schools and colleges that want to provide oversight or improve internal quality improvement for their own studies."

Study teams use the tools to document their progress, and they report these tools are helpful. "The exercise of going to and using the checklist results in discussions among study teams and department leads. I think people are finding a way to improve their recordkeeping," Khoury-Shakour says. "That information is readily available to them when they're ready to submit a continuing review to the IRB."

• **Use tools for training.** Sponsor-investigator studies, where faculty hold the investigational new drug (IND) application, require additional training. The self-auditing checklists are provided to them as part of that training, she says.

"That is one way those checklists have been used," Khoury-Shakour says. "Units also are using them to improve oversight and improve the quality of the conduct of studies within their units."

The checklists also are used for nonsignificant-risk device studies and in research for which monitoring is required by the Food and Drug Administration (FDA).

The FDA requires documentation proving investigators are providing oversight and self-monitoring. "This also is something we recommend if certain teams want to provide for any outside inspection," Khoury-Shakour says. "It's a good tool to document how they are monitoring and documenting their work. We also have a monitoring unit, but it is not to replace those services."

• **Provide minimal education.** The research compliance review office needed to provide little education and outreach about the self-auditing tools.

"When we first posted them, we published the information in various internal newsletter articles to let the community know there was a new resource available to them," Khoury-Shakour says. "When we conduct a study start-up and routine audits, we remind study teams that this tool

is available to them, and we hand them the tool, saying it could be really useful to their study."

Since not every checklist is applicable to every study, compliance review staff point out the specific tools that could be useful to the study team.

"We work closely with IRBs, and all are aware of the checklists," she adds. "They also can point people to use them and download something and provide assistance." ■

IRB Websites Can Offer a Wealth of Useful Tools

Short forms in 21 languages

By Melinda Young

An important and useful function of an IRB's website is its ability to give researchers — as well as the public — access to a wide variety of forms, guidance, and tools.

When created well, an IRB's website can be easy to navigate. It also should be updated with new and revised information regularly. Like crowdsourcing websites and with permission, an IRB's website also can adopt and adapt tools that researchers and other IRBs have found useful.

One example is Northwestern University IRB's webpage, which lists a variety of forms and templates, including informed consent short forms in 21 different languages. *(The forms are available at this link: https://bit.ly/2HHN5mr.)*

Develop Short Form Consent

When a researcher encounters a non-English-speaking potential study participant, an informed consent short form, written in the person's primary language, can provide essential information. Then, an interpreter can review the full consent form or the full form can be translated once the person decides to enroll in the study, says **Lisa Linn**, CIP, biomedical IRB manager at Northwestern University.

Short form consents provide some flexibility in the informed consent process. It is desirable to offer a short form for every language spoken and read by potential research participants. But IRBs might not have the resources to translate dozens of short-form consents, so a form of crowdsourcing is helpful.

"A couple of years ago, we reached out to the University of Minnesota and obtained some translated short forms with their certificates of translation for a couple of languages we run into quite often," Linn says. "We made these available online for our research community."

The IRB's webpage library of short-form consents grew as new languages were added, including Gujarati, Lao, Hindi, Oromo, Somali, Khmer, Tagalog, and Korean.

"Through the years, as short form requests came in, researchers brought in short forms and certificates of translation for their studies, and they shared these with the research community," she adds. "The library has grown, slowly, over time."

The English short form consent is a single page. It gives potential participants an idea of what investigators will tell them as part of informed consent. For example, the form states: "Before you agree, the investigator must tell you about (i) the purposes, procedures, and duration of the research; (ii) any procedures which are experimental; (iii) any reasonably foreseeable risks, discomforts, and benefits of the research; (iv) any potentially beneficial alternative procedures or treatments; and (v) how confidentiality will be maintained."

The short form also provides names and phone numbers of people to contact if they have questions about the study.

Other IRBs can use Northwestern's short form consents, if needed, says **Nathalia Henry Whitely**, MS CIP, CHRC, executive director of the IRB office.

"If someone finds them on our website and reaches out to us for permission to use them, it would be ideal," Whitely says. "It's possible that other places have stumbled onto our website and borrowed and modified [tools], and that's OK, too."

Create a Media Relations Form

Another tool on the IRB's website involves how researchers should interact with media. Called the Media Relations Form, the four-page document includes several pages of instructions on which media relations materials must be submitted to the IRB, including these explanations:

• "When the material pertains to a study that is still open at NU (data

lock is not in place and medical records may still be accessed for research purposes); or,

• "When the activity involves a non-scripted interview of a study participant who is currently enrolled and actively participating in the research study. The participant should sign a revised consent form or an addendum to the consent. The consent document should be submitted with this form for IRB review."

The form includes these five sections:

• study information;

• media relations material;

• financial conflict of interest information;

• requirements, the press release, subject activities in study;

• materials.

"This form is for when studies are open and recruiting," says **Braden T. Van Buskirk**, MSW, CIP, social and behavioral IRB manager. "The main focus is there wouldn't be exaggerated claims or statements made either by a participant or a friend that might be misleading or overstating benefits," Van Buskirk says.

Sometimes, investigators are invited to speak on TV or radio, or are interviewed by newspaper journalists about their studies. The Media Relations Form is relevant to those situations, Whitely says.

It is important for the IRB to use a Media Relations Form to prevent blurring the line between the research recruitment process and auxiliary media events in which investigators engage. "What we often hear is this was not an intended method of recruitment; it wasn't their idea," Whitely says. "Someone approached them."

The IRB trained researchers to understand that if they use the media as part of their recruitment, they should let the IRB know. If the media event occurs after the study is closed, then the Media Relations Form and materials do not need to be submitted to the IRB.

If a current study subject is asked about participating in a media interview, the person should be told that engagement is voluntary. There could be an addendum to the informed consent about the interview, Linn notes.

"This situation comes up from time to time," Whitely says. "It gives the research community a resource about media relations because the average clinical investigator doesn't know the process of getting media approvals on campus."

"We give them information on what to do, what to expect, who to call, and it works well," she adds. "Having those materials out there has reduced random phone calls and emails to our office."

In another section of the website, the IRB provides a list of study support resources and templates. *(For more information, visit: https://bit.ly/3kOT72E.)*

"We created a document for the research community to use: The delegation of authority log," says **Piper Hawkins-Green**, MS, CIP, IRB compliance manager.

This webpage includes tools for various activities, such as:

• Assent and parental permission enrollment log;

• Biomedical research delegation of authority;

• Consent form collection alternative;

• Social-behavioral research eligibility checklist;

• Device accountability log;

• Research record components;

• Participant identifier log;

• Protocol deviation log.

"These are basic tools to allow researchers and study teams to be successful," Hawkins-Green says. "We identified a need from post-approval monitoring activities and self-assessment. We found that quite often — because we cover both biomedical and social-behavioral research — that some investigators were equipped to conduct research, but they didn't have the support documents to ensure the regulatory portion."

With the templates, investigators can plug in their own information and meet compliance expectations. "Whenever we perform a for-cause audit, we prefer investigators to use these [tools] throughout the life of a research study," Hawkins-Green says.

The IRB also offers post-approval monitoring tools to assist with self-audits and self-monitoring. "Those are tools they can use to assess every component of their study, from initial approval to closure," Hawkins-Green says. "We include questions on the regulatory piece, the IRB piece, a clinical trial checklist, and an FDA-specific inspection checklist that helps study teams prepare for FDA inspection."

Investigators are instructed to assess their own research studies. "Especially with COVID, we can't go out into the field to do post-approval monitoring," Hawkins-Green says.

Investigators are encouraged to conduct self-assessments as part of post-approval monitoring activities. They can find checklists and other tools on the IRB's website.

"They do complete [self-assessments]; we have an 85% completion rate," Hawkins-Green says. "Because of COVID, some requested postponement because study teams are not on campus, so it would be difficult to complete full assessment activities." ■

IRB ADVISOR

CME/CE INSTRUCTIONS

To earn credit for this activity, please follow these instructions:

1. Read and study the activity, using the provided references for further research.

2. Log onto **ReliasMedia.com** and click on My Account. First-time users must register on the site. Tests are taken after each issue.

3. Pass the online test with a score of 100%; you will be allowed to answer the questions as many times as needed to achieve a score of 100%.

4. After successfully completing the test, your browser will be automatically directed to the activity evaluation form, which you will submit online.

5. Once the completed evaluation is received, a credit letter will be emailed to you.

CME/CE QUESTIONS

1. **Which is a project the Consortium to Advance Effective Research Ethics Oversight is undertaking?**

   a. Investigate other IRBs for evidence of unethical practices.
   b. Pay attention to the views and experiences of the IRB participants whom IRBs aim to protect.
   c. Collaborate to create new, universal informed consent templates.
   d. Collaborate to help investigators with ethical recruitment of study subjects.

2. **Northwestern University IRB's website lists a variety of forms and templates including informed consent short forms for:**

   a. providing study-specific informed consent in a variety of languages.
   b. listing the study's chief risks, benefits, and procedures.
   c. giving potential participants an idea of what investigators will tell them as part of informed consent in the participant's primary language.
   d. a summary of the first page of the full informed consent document.

3. **Stanford University's human research protection program uses a protocol checklist to maintain consistency in IRB staff reviews of protocols. Which is an item on the checklist?**

   a. Plan to review responses to questionnaires asking about suicidal ideation provided.
   b. Vulnerable elderly patients' risk determination provided.
   c. An international checklist completed with local IRB approvals.
   d. Historic research protection education provided.

4. **Which is a question U.S. Sens. Elizabeth Warren, Sherrod Brown, and Bernie Sanders asked the Government Accountability Office to address?**

   a. Are patients pressured to enroll in pay-to-participate trials?
   b. Are commercial IRBs using proven quality metrics?
   c. Have commercial IRBs reported research results from closed trials?
   d. How do procedures and outcomes differ between academic and commercial IRBs?