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INSIDE

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Implementing the New Common Rule Is No Easy Task

Harmonization remains a challenge

By Melinda Young, Author

Among the bigger challenges with the new Common Rule, which went into effect on Jan. 21, are the new regulations involving exemption and informed consent.

"There are new categories of exemption that didn't exist before, and the regulatory language from the Office for Human Research Protections (OHRP) doesn't provide a lot of description of what it means to implement them," says **David Borasky**, MPH, CIP, vice president of WIRB-Copernicus Group in Cary, NC.

The new rule also forces institutions to decide whether older studies should move forward under the new Common Rule or be grandfathered under the old rule, he adds.

"There have been a lot of questions about the transition and what to do with existing studies — the old versus the new," Borasky says. "There is information out there, and we'll know within the first 12 months how well the implementation is going and where there are points of friction."

> THE FDA HAS STATED THAT ITS GOAL IS TO ALIGN ITS RULES WITH THOSE OF THE NEW COMMON RULE, AND THE 20TH CENTURY CURES ACT COMPELS THE FDA TO HARMONIZE.

Also, regulatory harmonization is not yet a reality. "We'll be operating under a few different regulations for the foreseeable future," Borasky notes. "FDA rules and regulations are not updated."

The FDA has stated that its goal is to align its rules with those of the new Common Rule, and the 20th Century Cures Act compels the FDA to harmonize. So far, the agency has taken what amounts to baby steps toward harmonization, he says.

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"The FDA decided to use its enforcement discretion to allow IRBs to use the same waiver for informed consent as allowed under the Common Rule," Borasky says. "But if you have an FDA-regulated study, you continue to follow FDA regulations, where those are more stringent than the revised Common Rule."

Also, there are some informed consent requirements in the new Common Rule that go beyond FDA regulations. But this change is easier to deal with because research sites are allowed to go beyond what the FDA requires, he notes.

"The informed consent changes are not in the FDA regulations, but they do not conflict with the FDA regulations," Borasky says.

"Keeping track of which requirements will apply to which studies is challenging," he adds. "It depends on that institution and the IRB's portfolio work."

A main informed consent change involves adding a summary statement to the document research participants must sign.

"One of the requirements is that a succinct summary contain key information that a reasonable person would want to know to determine whether to participate in the study," says **Brian Moore**, director of the IRB and the human research protection program at Wake Forest School of Medicine in Winston-Salem, NC.

"There are a lot of terms in that description that are pretty vague," Moore says. "Instead of having one person sitting at a desk, thinking, 'This is what I'd want to know,' we wanted to pull together a group of people familiar with research and patients and who knew what they need and what's important to them."

The Wake Forest IRB worked on developing a template for the informed consent summary statement. *(See story on creating informed consent summary statement, page 27.)*

While developing the template, Moore and IRB members sought to answer these questions:

- What is the key information?
- How long is "succinct"?
- Who is the reasonable person?
- What are they expected to know when they make an informed decision?

Collaboration and work groups are how IRBs can implement multiple changes related to the new Common Rule and other new rules.

For example, the University of Texas at Arlington formed a work group to review and revise policies and procedures per reliance agreements and the new Common Rule.

"We wanted to understand everybody's policies and procedures for reliance," says **Alyson Stearns**, CIP, regulatory services manager at the University of Texas at Arlington.

"Sometimes, we would contact an institution, and their policies were so different from our policies, and we weren't sure of who their contact was," she says. "We had a whole lot of opportunity with the revised Common Rule to look at how we do not reinvent the wheel."

The answer is a work group that was started in 2017 in preparation for the Common Rule.

"We reached out to every institution we could think of in the Dallas-Fort Worth area, and we have 12 institutions in the group and a mix of hospital and medical and nonmedical academic institutions, as well as a private university," says **Kirstin Morningstar**, CIP, CPIA, director of regulatory services at the University of Texas at Arlington.

About 20 people attend the work group's meetings, she adds. *(See story on how to build collaboration between regional IRBs, page 28.)*

Research institutions might struggle to become familiar with the new regulations because there is a lack of guidance from OHRP and other regulatory agencies, Borasky says.

Even in the absence of concrete guidance, there are pathways to being compliant, he says.

"Some organizations find the lack of guidance disconcerting, but others are less concerned and are moving forward with regulations, as they see fit," he says. "Until IRBs and researchers have some practice with some of these new areas of regulations, there will be a time of sorting it out and figuring out best approaches and practices."

Yet another challenge involves the logistics of revising electronic IRB submission systems.

For instance, an IRB system might automatically assign continuing review dates for every study. That no longer would be necessary for some studies. IRBs will need information technology help to make some of these logistical changes, Borasky says.

IRBs that review sociobehavioral research studies need to review the new exempt categories and develop implementation plans. "The impact will vary," Borasky says. "Some pieces are easier to implement than others."

OHRP has provided limited assistance and guidance to IRBs and institutions preparing for the new regulations.

IRBs should be caught up on updating their standard operating procedures (SOPs) and policies and procedures — but if they are not, there is no time like the present.

"A lot of work is required to get the SOPs up to date, but it's not insurmountable," Borasky says. "Resources are out there to help people with updates and revisions." ■

IRB Develops Method for Creating Informed Consent Summary

Assess local priorities

The informed consent template that now is required through the revised Common Rule can be developed thoughtfully and effectively through the use of an expert panel or working group, experts say.

Wake Forest School of Medicine in Winston-Salem, NC, asked IRB members to rate the 10 required elements of informed consent (IC). The idea was to use the top-rated items in the IC summary.

"We asked our members to rate them from one to 10, most important to least important, with the most important at number one," says **Brian Moore**, director of the IRB and the human research protection program at Wake Forest School of Medicine. "Then we averaged all of the scores, and the elements with the lowest scores [more #1s] were the ones we determined to be the most important."

"The results were interesting," he adds.

"They were pretty distinct in that there were about three groups," he explains. "There were a couple of elements that were ones everyone felt strongly were important and should be in there; and then there were three to four in the middle group that some people felt were important and others did not; and the third group had several elements that were consistently on the less important side of the scale."

The lowest ranked IC items, meaning these were ranked as most important, included the following:

- an explanation of the purposes of the research and the expected duration of participation;
- a description of any foreseeable risks or discomforts;
- a description of the procedures to be followed and identifying which procedures are experimental.[1]

With those data, the IRB developed a one-page template that could fulfill the informed consent summary requirement.

"It's succinct and represents what reasonable people want to know," Moore says. "It contains key information about a study, and we think it checks all the boxes in what the regulations require."

The summary also is written in simple, reader-friendly language. The word choice is basic, and it has a low reading level, he adds.

For example, the paragraph about voluntary participation and risks states, "Your participation in this study is voluntary. You do not have

to participate in this study if you do not want to. There may be other choices available to you. Some other choices may include..."

The next step is to survey participants in studies to find out whether the summary information is helpful. The IRB will want to know what they think of the format and whether they have any suggestions for improving it, he says.

Moore co-presented a poster about the summary template at PRIM&R's Advancing Ethical Research Conference last fall, where attendees often asked whether the IRB could share the template.

"What we communicated to those folks is, 'If you want to use our template, that's fine, and it may work for you and it may not,'" Moore says. "What I would encourage IRBs and institutions across the country to do is to not just copy and paste our template, but to repeat our methodology."

What's important to IRB members and research participants in Winston-Salem might not be the same priorities in another part of the country, Moore says.

"Our rankings and results are good for us, and while they may be good for you, too, it's probably worthwhile to develop a brief survey just to confirm this," he says.

Since the IRB began to use the summary, IRB members have found it to be very helpful, and they've asked that the summary statement be added to industry-funded studies' informed consent documents, Moore says.

"Industry-funded studies are not necessarily applicable to the Common Rule, and we can't require those studies have the informed consent summary," he explains. "But it's been a frequent request from our IRB members that the summary statement be added because it's been beneficial to participants." ■

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Collaboration Between IRBs Can Result in Better SOPs, Tools

Working group has 12 organizations

IRBs can ensure smoother, more effective collaboration between institutions and pave the way for reliance agreements through the use of an IRB working group.

For instance, about 20 people representing a dozen research institutions meet regularly with the University of Texas at Arlington, which formed the working group.

The group has grown to include hospitals, academic institutions, and a private university.

"We didn't have 12 institutions at the very beginning, but some members suggested more groups to join the working group," says **Alyson Stearns**, CIP, regulatory services manager at the University of Texas at Arlington.

The working group members are diverse from an IRB perspective. Some have many clinical trials and a large IRB office structure, and others were new — just setting up their programs.

"Some might have a large portfolio regulated by the Food and Drug Administration, and another might have solely behavioral research," Stearns says.

The working group meets quarterly or every other month. It started with monthly meetings, which helped members discuss and share information about following requirements of the new Common Rule, says **Kirstin Morningstar**, CIP, CPIA, director of regulatory services at the University of Texas at Arlington.

The meetings are flexible in scheduling and length, depending on the agenda. The first project the working group began involved creating a to-do list for the revised Common Rule. *(See to-do list, page 29.)*

The revised Common Rule necessitated changes to IRB offices' standard operating procedures (SOPs), and representatives from each institution contributed to the to-do list.

"We came up with a checklist of items to think about in preparing for the new rule and institutions' SOPs," Morningstar says. "One of the best things that came out of it was a shared resource database."

This box account — a web-based, secure location for folders and documents — made it possible for

each institution to share information and examples by uploading tools or data from their institutions.

"It's been helpful to us to have all that shared information," Morningstar notes.

"Another positive thing was some institutions opened up their educational opportunities to all working group members," she says. "That was a real benefit."

For instance, one university hired a consultant to provide training in a day-long workshop, and the institution made the workshop free and available to other organizations represented in the working group, Morningstar adds.

The University of Texas at Arlington also shared some educational sessions with others in the working group, Stearns says.

"We have a mini-conference in fall and spring semesters, and we opened some of these to other institutions — available for free," she adds.

The group discussed recruitment and training for new staff, but that was more of an issue for larger institutions that did not have the one-on-one training as did smaller organizations, Morningstar says.

"We shared resources on training and how we provide one-on-one training for new staff members, talking about our own experiences and what works for us," she adds.

At least one working group member was open to institutions assisting with cross-training, Stearns notes.

A big focus of the working group involved forming reliance agreements, Morningstar says. One of the working group members was knowledgeable about reliance agreements and presented information to the group.

"We also discussed how we each handle reliance agreements in our offices," she adds.

WORKING GROUP CREATED COMMON RULE 'TO-DO' LIST

An IRB working group in Texas created a new Common Rule to-do list through collaboration between the University of Texas at Arlington IRB and other area IRBs. The working group has shared this example of items on its action list:

• Potential burden-reducing provision: expansion of exclusion and exempt categories

- Address feasibility of broad consent and system for tracking refusals/declines for new exempt categories seven and eight. Note: If institution moves forward with broad consent option, develop informed consent document template;
- Update application forms with new exempt categories.
- Update eIRB system with new exempt categories.
- Train staff and IRB on new exempt categories. Note: Consider documentation requirements such as an eIRB system, approval letters, etc., with new categories.
- Update written procedures/SOPs with new exempt categories.
- Update any existing guidance (documents, training modules, presentations, etc.) regarding human subject research (HSR) versus non-HSR and new exempt categories. Note: example: clarify oral history, journalism, etc., and include new exempt categories.
- Update approval letter templates for new exempt category options.

• Potential burden-reducing provision: elimination of continuing review (CR) for some expedited

- Develop process for determining when CR is required, and how to document the determination.
- Address how lack of CR may affect your annual checks/processes for conflict of interest (COI) and training. Note: if IRB process is used as an action/touch point, how will it be managed now (for example, if training or COI is checked at some time of CR but CR will no longer exist for expedited)?
- Consider alternative process for studies with no CR. Note: informal/automated annual check-ins?
- Update written procedures/SOPs with new CR requirements/processes developed from items above.
- Update eIRB system. Note: allow flexibility to select CR-required or no-CR required; address requirement to document when CR is required; build in features for annual follow-ups in lieu of formal CR.
- Train staff and IRB on new CR requirements and how to document when CR is required for a study. Note: Will your IRB want certain studies to require CR (certain populations, procedures, etc.)? How to document justification or criteria for CR (review checklists, indication or comment in the eIRB system, in the approval letter, etc.)?
- Address/update approval letter templates to identify when CR is/isn't required plus expiration date only if applicable.
- Update any existing guidance (documents, training modules, presentations, etc.) regarding CRs. Note: How to explain/notify principal investigators that CR is no longer required. ■

The group's institutions began to execute agreements with each other as a result of the education on reliance agreements, Stearns says.

The group developed a shared contact list that is kept up to date with contact information of each group member.

"If a member has a question, they can send it out and get replies on the same day," Stearns says. "We requested assistance for finding a new IRB representative to do prisoner studies, and one member volunteered someone, who worked out for our IRB."

That was only one example of how well the resource worked, she notes.

"People were asking questions all the time about how does your institution do this," Stearns says.

The working group's ability to facilitate collaboration and share resources has made it so successful that the individual members plan to continue it indefinitely. In an anonymous feedback survey, 91% of respondents said they had already implemented changes to their human research protection programs as a result of the IRB working group, or they said they planned to make changes in the future.[1]

"There was one member who liked the IRB working group so much she's taken the idea and is doing a working group for other goals, including a federal compliance perspective that is not just about the IRB," Stearns notes.

All members said their participation in the working group had definitely or probably improved communication and collaboration with other local IRB offices.[1]

The survey found that working group members ranked these as their top reasons for participating in the working group:

- sharing and access to resources;
- personal education;
- networking and personal communication with colleagues;
- staying current on other local IRB policies and personnel.[1]

Stearns and Morningstar also attribute the group's success to its flexibility and engagement with its members.

"I think now there is a new kind of camaraderie between us and other IRB offices," Stearns says.

"As time went on, people were a lot more willing to volunteer their own ideas for what to put on the agenda for the working group meeting and also to just reach out to each other," she adds. When the IRB receives a call from a working group member who has a quick question about what a researcher wants to do that might involve both institutions, these discussions are much quicker because of the group, Stearns says.

"It's satisfying to have a group of people who know you," Morningstar says.

"This is your group," she adds. "We have the support of other members of the group, and we know we can rely on the other members, which is helpful." ■

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Does Federal Right to Try Law Imperil State RTT Laws?

Law professor advises abiding by both for now

By Gary Evans, Medical Writer

Adding to the considerable confusion on Right to Try (RTT) laws, by which dying patients may seek access to experimental drugs, a legal expert tells *IRB Advisor* that the 41 RTT state laws may be found unconstitutional if they conflict with the federal law passed last year.

Others say the state laws would have faced a challenge of constitutionality even before the federal law was enacted, had that been invoked. The current RTT landscape is a thicket of ethical concerns and legal questions.

"At present, patients with life-threatening conditions have 43 different pathways — expanded access [through FDA], federal Right to Try, and the 41 state laws — through which they can access an experimental medical product," **Alison Bateman-House**, PhD, MPH, MA, noted in a recent paper.[1]

An assistant professor in the Division of Medical Ethics at New York University Langone Medical Center, Bateman-House chairs the Group on Compassionate Use

and Preapproval Access (CUPA). They have argued that the FDA's established program for expanded access to experimental drugs remains the best way to deal with this issue because it requires IRB oversight. To this point, they have fought a losing battle against the expansion of state laws and the 2018 federal RTT law.

Both the state RTT law in California and the federal statute were cited in a recent decision by clinicians at the University of California, Irvine, to administer an experimental drug to a brain cancer patient. The university and ERC-USA initiated treatment with the company's investigational compound ERC1671, which is known as Gliovac in Europe. The therapy was administered to a patient with aggressive brain cancer who did not qualify for an ongoing clinical trial of ERC1671 in the U.S. According to the company, the compound is a vaccine comprised in part of freshly extracted tumor cells and lysates designed to stimulate the immune system to target cancer cells.

The use of both the California RTT and the federal law facilitated the patient receiving treatment but also raised questions about how the state laws function now that a federal statute is on the books.

"If the drug the patient received was provided outside of the FDA's expanded access program or an FDA-approved clinical trial, and if it was somehow legal, then it was because of the federal RTT law," says **Christopher Robertson**, JD, PhD, a law professor at the University of Arizona. "That would be true even if the people also complied with the state RTT law. Saying that they went through the state RTT law does not conflict with the conclusion that the access was gained via the federal RTT law."

State RTT laws, if invoked separately, could be challenged as unconstitutional, he says. "If a state RTT law was interfering with the federal RTT law, it could be pre-empted; for example, ruled null by the U.S. Constitution's Supremacy Clause."

The safest course for now is for physicians and other providers to try to comply with both state and federal RTT laws, he adds. Indeed, that is what Cal-Irvine did in the recent case, and in following the state RTT law actually invoked stronger requirements for informed consent and IRB review than federally required, says **Lisa Kearns**, MS, MA, senior research associate in the division of medical ethics and an expert on state RTT laws at CUPA.

THE SAFEST COURSE FOR NOW IS FOR PHYSICIANS AND OTHER PROVIDERS TO TRY TO COMPLY WITH BOTH STATE AND FEDERAL RTT LAWS.

"Importantly, the California law requires very strict informed consent — similar to the federal regulations in the FDA's [expanded access] program — that are not stipulated in the federal RTT law," she says. "That's a huge thing. There are extensive requirements of what the consent form must contain."

Also, California is the only state that requires IRB oversight in its RTT law. The federal law has no IRB review requirement, so the case is something of a hybrid, she says.

"This was one instance, and it didn't seem to be a big deal to anybody, but what could happen is that a state RTT law might try to do something that the federal law prohibits," Kearns says.

For example, the federal RTT law gives liability protection to the drug manufacturers providing the experimental products, she says.

"Most of the state laws [waive] liability provided that the company acted in good faith and with reasonable care," Kearns says. "You could see somebody going after a company under a state law, and accusing them of acting in bad faith. Then you would have a conflict with the federal law, which says [drug companies] are protected. I think the safe conclusion, until any of this is tested in court, is that we are not sure [of the outcome]."

Though California is the only state that expressly includes an IRB provision, individual institutions could require this oversight even though it is not their state law, she emphasizes.

Perception and Reality

We asked Bateman-House to comment further on this complex issue in the following interview with *IRB Advisor*, which has been edited for length and clarity.

IRB Advisor: You note that, in theory, the state RTT laws could have been challenged as unconstitutional even before the federal law was passed.

Bateman-House: In theory, because you would not necessarily have had that determination made unless someone brought a case forward and a judge or a court decided it was unconstitutional. On its face, talking to lawyers, it

was unconstitutional because states cannot take for themselves and govern something that has been under federal authority.

Since passage of the Food, Drug, and Cosmetic Act, the federal government has reserved for itself the ability to govern access to investigational drugs. These states were setting up laws involving powers that they did not actually have. The [state legislatures] understood this as well as anyone, but the fact of the matter is that these were technically laws that did not really have any legal "oomph." So that led to the federal law. This particular case was handled in accordance with the California law, but that state law was likely unconstitutional without the federal law that gave it backing.

IRB Advisor: Who could have challenged a state law on this basis prior to the federal RTT law?

Bateman-House: The only people who could have brought up a court case against the state RTT laws were either a patient deemed terminally ill under these laws, or the companies that were being asked to provide [investigational drugs]. The companies were being asked, but they had no reason to want to go to court and fight for something that wasn't even affecting them, and would make them look worse in the court of public opinion. These patients just can't bring things to court — they are dying, and they don't have the time or the money to do it. That is a pretty big step and nobody was going to bring a case like that.

IRB Advisor: There were concerns that FDA could be bypassed in RTT cases, but reports[2] indicate in the Cal-Irvine case that the company notified the FDA six months before the procedure.

Bateman-House: The FDA notification had nothing to do with the California law. That was the company just doing what it thought was appropriate. It still was not as safe, in my opinion, as expanded access because FDA notification is not the same thing as FDA review of a protocol. Theoretically, the FDA could have done things to this protocol to make it safer or more likely to help the patent. We will never know because the FDA did not review the protocol. They were just informed that this was going to happen.

IRB Advisor: You and CUPA colleagues argue that the FDA expanded access is still the safest, most ethical pathway and that paperwork delays and other criticisms were largely overstated. If true, how did we get so far afield from a system that wasn't broken?

Bateman-House: Because perception trumps reality sometimes. There was a perception that the system was not working well. There were some high-profile cases where patients were not getting [the investigational therapies] they wanted. When you look at those cases, you see across the board that it was the companies who were saying no.

The system that we have has no power to make a company provide something. Its products are its products, and it will decide when and where to give them to somebody. But the perception was that there was something wrong with the system. Bad actors came in to exploit that perception for their own ends, which was government deregulation. ■

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Social Media Use By Participants Can Undermine Trials

Researchers design ADEPT model to address these issues

Unfortunately, the rapid communication enabled by various devices and platforms could undermine clinical trials, allowing research subjects to share notes and possibly manipulate the study, warns **Holly Fernandez Lynch**, JD, MBE, a medical ethicist at the University of Pennsylvania in Philadelphia.

"The key is thinking about social media issues that might arise, before they actually arise," she says. "It is easier to prevent than respond."

Lynch and colleagues warn that research subjects sharing clinical trial information could affect participant recruitment and dropout rates, and alter study methodology like blinding. These problems could be worsened if the information shared is inaccurate or confusing.[1]

As a result, participants who believe they are in the placebo arm of the study may seek medication being administered to another arm of the study. By the same token, those who think they are in the treatment arm of the study may not report adverse effects that could affect their trial status.

Private Message Groups Trigger Concerns

For example, Lynch and co-authors cited a study in their institution of breast cancer patients who had recovered, but faced a risk of recurring disease. Trial participants were randomized into several arms to receive drugs approved by the FDA for other indications.

At the beginning of the trial some research participants posted information on an already established social media page for breast cancer patients. This public posting of general information was initially viewed as beneficial by researchers.

However, some of the research subjects formed a private group and did not invite the researchers to join. Investigators became concerned that the information-sharing about perceived trial arms and clinical results could undermine the study.

The situation was resolved when investigators discussed their concerns with the participants and stressed the importance of compliance to generate meaningful data that could guide care for the disease.

To address such issues, they designed a framework that could be used to approach this issue, using the acronym ADEPT to outline key components.

"This could be incorporated into templates for IRB submission," Lynch tells *IRB Advisor*. "Have investigators thought about the way social media may impact their studies? A social media plan will not be appropriate for every study, but the role of the IRB should be to help investigators know which questions to ask and think in advance about what kind of plan would be appropriate for their protocol."

"THE ROLE OF THE IRB SHOULD BE TO HELP INVESTIGATORS KNOW WHICH QUESTIONS TO ASK AND THINK IN ADVANCE ABOUT WHAT KIND OF PLAN WOULD BE APPROPRIATE FOR THEIR PROTOCOL."

The ADEPT framework encourages a structured and systematic approach, including the following steps and key features:

• Assess if social media use could pose risks for the study.

A potential red flag for impending social media issues is research on subjects with rare diseases or established patient advocacy efforts.

• Design collaboratively.

Bringing in research subjects as "partners" in a study diminishes the likelihood of social media activity that could undermine the trial.

• Educate research subjects.

In the informed consent process, emphasize the ethical duty of participants to adhere to the study parameters to maximize the benefits to themselves and future patients.

• Pre-empt problems, offer alternatives.

For example, consider proactive measures like moderated online discussions to quickly address research questions with accurate information.

• Take additional measures if needed.

Take these actions with prudence, enforcing needed measures without eroding a good faith relationship with research participants.

Gaming the System

Social media can aid in trial recruitment and can give subjects a sense of support in a shared community in an online forum, Lynch notes. However, with these benefits come the attendant risks.

"People are worried that they are going to get kicked out of the study or not be found eligible," Lynch says. "So they may find ways to contravene the eligibility criteria. If you maximize eligibility, you are going to minimize that kind of behavior."

Indeed, the design of a trial may set up temptations for participants to circumvent the rules if they see some personal advantage.

"We talked to a patient advocate in the context of writing this paper," Lynch says. "Her perspective was that when patients in clinical trials engage in behavior that could be damaging to the research, it is often because the trial wasn't designed with their concerns in mind."

As these concerns are expressed on social media between participants, there could be efforts

to game the eligibility requirements or not report adverse events.

"One of the most substantial concerns is that participants might share advice about how to avoid triggering valid and well-tailored exclusion criteria that otherwise would bar some individuals from enrolling in a desirable trial or jeopardize their continued participation," the authors concluded.

Right to Try Raises Questions

This is a particularly topical issue in light of the Right to Try (RTT) issues being raised by dying patients seeking experimental drugs.

"My advice for both the RTT context and the social media context is that it is better for everyone for the investigators to carefully select their inclusion and exclusion criteria," Lynch says. "Make sure that eligibility is as strong as practically appropriate, so you are not cherry-picking patients or being too restrictive."

Bringing patients in as partners through collaboration and education is an important aspect of the program, but it will not solve all problems, she says.

"If the patient population says we all want the experimental intervention, then the response is that would not be good science because we wouldn't have a control arm," she says.

"It is the responsibility of the investigator and the researcher to explain why that is not what patients should want. There is a fallacy that whatever is new and experimental will be beneficial. It could actually be worse." ■

REFERENCE

1. Lynch HF, Largent EA, Joffe S, et al. Protecting Clinical Trial Participants and Study Integrity in the Age of Social Media. *Cancer* 2018: https://doi.org/10.1002/cncr.31748.

Consortium Pushes for Evidence-Based Research Oversight

Participation encouraged in long-term project

Despite the considerable effort and bedrock ethical principles brought to bear in IRB oversight, the inconvenient truth is that human research oversight is not "evidence-based," says **Holly Fernandez Lynch**, JD, MBE, a medical ethicist at the University of Pennsylvania in Philadelphia.

Rather than careful forethought of action, many of the principles of human research protections are essentially reactionary, formed in the aftermath of a succession of horrific episodes of unethical experimentation. Lynch and colleagues are trying to change this status quo — in effect, to show that research oversight can be evidence-based. She invites others to join in the effort, as chair of the steering committee of the newly founded Consortium to Advance Effective Research Ethics Oversight (AEREO).

AEREO has embarked on an ambitious mission to seek input from IRB members, researchers, participants, academics, and others on the current state of human research ethics and oversight. AEREO outlines its calling as follows:

"At present, we lack valid and reliable outcome measures to assess the effectiveness of IRB and HRPP review and oversight of research with human participants," AEREO states.

"That means we can't properly evaluate IRB/HRPP effectiveness, which in turn means that we can't clearly demonstrate that the impact of the human subjects research oversight system is justified by its effectiveness or evaluate the effectiveness of new approaches. This has to change. We practice evidence-based medicine — it's time to practice evidence-based human subjects protection." *(For more information, visit: https://www.med.upenn.edu/aereo/.)*

Lynch discussed the project with *IRB Advisor* in the following interview, which has been edited for length and clarity.

IRB Advisor: Some may be surprised at AEREO's founding premise, that human research is not evidence-based.

Lynch: Human subjects research regulation is not evidence-based but neither is most regulation and law. Evidence-based medicine is the expectation, but we don't really have similar expectations yet for policymaking. The way we got the regulations we have now is through a history of scandal and the response to that. Bad things happened, lawmakers and regulators get involved, and they said, "We are going to implement some changes in response."

It is not that we have done some careful testing and controlled trials to evaluate different policy approaches and find the ones that work best. It is that something bad has happened and we have to fix it. Historically, it's been "implement now and test later." But we haven't done the testing. It becomes very challenging to do that testing because the regulations are in place.

How do you test whether the regulatory approach that we have works better than some alternative? If you took an alternative approach, you would potentially be out of regulatory compliance.

IRB Advisor: That's kind of a catch-22. How is your consortium addressing this challenge?

Lynch: What we are trying to do with AEREO is to acknowledge we want evidence about whether our practices and policies work — especially given the potential impact of IRB oversight over research. There are a lot of resources that go into it and there have been plenty of things published about complaints regarding the impact of IRBs on research.

We think it is important to gather data in both directions. Are there things that IRBs are doing that really add value to the system? Can we identify those, evaluate them, and then try to create evidence-based best practices? Can we also figure out which things that we are doing that do not add value, so we can stop doing those?

IRB Advisor: On the website, your group is inviting IRB members to participate and share their input on the process.

Lynch: That's right. The idea is that there is a collaboration between people who are at institutions who have data and academics like myself who can help design research questions and analyze that data. The more participants we have in our consortium, the better because we will be able to collect data across more sites. And to the extent we want to try out new things, we can try them out across more sites. So the bigger the [number of participants], the better the data.

IRB Advisor: How are you reaching out to research participants to get their perspective?

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Lynch: We have a proposal to try to gather data from a variety of approaches. If funded, we will basically try to talk to patients about what they want IRBs to do and how IRBs should make decisions about research. Even though we have patient engagement and patient-centeredness in healthcare and in research design and conduct, we don't yet have patient engagement around IRB oversight.

IRBs have a lay member, a community member, but that doesn't have to be a patient. If we can find out what patients want from IRBs, that can help us figure out how well IRBs are doing.

That is not the only measure of IRB effectiveness, of course. Patients are one stakeholder alongside many others, but it is an important perspective that is not well understood.

IRB Advisor: You have another project involving the Association for the Accreditation of Human Research Protection Programs (AAHRPP). What is that about?

Lynch: AAHRPP-accredited sites have to demonstrate that they evaluate their effectiveness. We are very interested in finding out how they go about doing that. I have an ongoing project right now — an interview study talking with various stakeholders in the IRB community and accredited institutions. We are trying to find out how they go about defining IRB quality and effectiveness, how do they think it ought to be measured? Then for people who are IRB directors, what do they do now to measure IRB effectiveness? That is an ongoing project. We finished our interviews and are now in the data analysis phase.

IRB Advisor: Are you concerned that some of the data collected may be too subjective, not necessarily lending itself to evidence-based standards?

Lynch: The idea is to be as objective and evidence-based as possible. It's a very long-term project. Right now, there is not clear definition about IRB effectiveness, and we have to collect data about it. This is completely uncharted territory.

We might all agree that IRBs should protect human subjects, but what does that mean? We need to actually operationally define what that means and how you define that in terms of data collection activity. We could agree that yes, protection is what we want them to do, but then more concretely they should do "X, Y or Z." Things that are easy to measure, like regulatory compliance, do not necessarily tell us that participants are being protected. It tells us that the regulations are being complied with. ■

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CME/CE QUESTIONS

1. **Which federal agency has decided to allow IRBs to use the same waiver for informed consent as allowed under the Common Rule but still requires research institutions to follow its regulations where these are more stringent?**

   a. NIH
   b. CDC
   c. FDA
   d. National Academy of Medicine

2. **The Wake Forest School of Medicine in Winston-Salem, NC, asked IRB members to rate the highest priority items on the elements of informed consent list. Which of the following was one of the items ranked most important?**

   a. A description of any foreseeable risks or discomforts
   b. A disclosure of appropriate alternative procedures
   c. A statement describing the extent that confidentiality will be protected
   d. All of the above

3. **According to Lisa Kearns, MS, MA, an expert on state Right to Try laws, which of the following states has a provision requiring IRB review?**

   a. New York
   b. Oregon
   c. Massachusetts
   d. California

4. **Holly Fernandez Lynch, JD, MBE, a medical ethicist at the University of Pennsylvania, says possible research subjects could use social media to seek advice on how to avoid triggering trial exclusion criteria.**

   a. True
   b. False