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Your Practical Guide To Institutional Review Board Management

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All IRBs should prepare for possible disaster interruptions

Flooding, storms on the rise

IRB directors who think their areas are safe from natural disasters should think again. Some U.S. IRBs learned the hard way that even in non-coastal cities and areas they can find their IRB offices underwater. Or they could experience earthquakes, tornadoes, hurricanes, and fires. And any research institution and IRB is at risk of an epidemic that leaves them short-staffed.

As demonstrated by the recent East Coast earthquake, which could be felt from New York to South Carolina, by the hurricane that caused major flooding in Pennsylvania and other Northeastern states, and by mile-wide tornadoes that destroyed whole towns in Missouri and Alabama, natural disasters are on the rise.

In a series published in February, 2011, *Scientific American* catalogued 960 natural disasters worldwide with record-breaking financial costs. Extreme floods have tripled globally in the past three decades, according to reinsurer Munich Re.

One reason for flooding damage is heavier rainstorms, which are more likely to lead to flooding. Climate change has resulted in more moisture being captured and stored in the warmer atmosphere. This leads to increased droughts and heavier rainfall once it's released, scientists say.

The result is a world in which IRBs and research institutions need to prepare for the unpredictable.

"We felt safe before tropical storm Allison hit in 2001," says **Paula Knudson**, special advisor at the University of Texas Health Science Center (UTHSC) in Houston (TX). Knudson had been the IRB director when the storm struck.

"We thought the worst would be a hurricane that blew out a window upstairs," Knudson says. "Instead, we had a flood coming up from the basement."

The storm and flooding resulted in the ground floor IRB office filling with nearly a foot of water, reaching the second drawers of filing cabinets. The office lost its electricity and telephone service, and about one-third of the IRB files were destroyed. Also, the IRB office was uninhabitable for more than a

month, she recalls.

To recover the damaged IRB files, the institution had to send them to NASA for document recovery. But even collecting them was a slow, tedious process that created potential health risks for staff. They were able to enter the office after a couple of days, but because there was no air filtering or air conditioning each person could only tolerate 30 minutes in the building, Knudson says.

"You could be overcome by the heat or smell," she notes.

The smell was unbearable because it included the odor of dead animals since the building's basement had housed research animals, which all had been killed in the flood, she explains.

"The IRB chair and I went in together, holding flashlights under our chins," Knudson recalls. "We went in every day for several days, trying to salvage what we could and stacking things in boxes."

Louisiana State University Health Sciences Center (LSUHSC) in New Orleans, LA, felt the full impact of Hurricane Katrina's devastating flooding in August and September, 2005. One of the main problems after the disaster involved communication between IRB staff, investigators, and research participants, says **Kenneth E. Kratz**, PhD, director of the office of research services at LSUHSC. Kratz also is the IRB chair.

"Some coordinators left for Mississippi and Boston," he says. "Initially finding those people was difficult because of problems with the phone service, and then that put the process of oversight on hold for a couple of weeks."

Retrieving paper files was less of a problem for the IRB office because of a fortunate decision the office had made months earlier: "Six months prior to the storm we started using a new, commercially-available database and management software system for the IRB review process," Kratz says. "Those are housed in a server in New York, and we had access to that over the Internet."

There was some delay in retrieving the information and continuing the IRB's work because of the fact that some IRB staff did not have access to computers and the Internet right after the hurricane, he notes.

"One person was living in a camping trailer in a state park," Kratz says.

Also, the IRB office had to move to temporary facilities in Baton Rouge, where it stayed for more than half a year, he adds.

"We were able to re-establish our office at a sister campus in Baton Rouge, and begin paperwork and oversight," Kratz says. "We slowly re-established contact with our investigators and began holding a meeting of the IRB at the end of October, beginning of November."

Kratz and Knudson share these lessons learned for future disaster planning efforts:

• **Establish a back-up communication plan:** When a major natural disaster strikes, a research institution likely will lose electricity and telephone service for

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an indefinite period of time. Even cell phone service might be blocked or limited. So IRB offices need to plan ways to reach staff, IRB members, and investigators when this occurs.

After Hurricane Katrina, LSUHSC staff had no landlines or cell phones that worked, Kratz recalls.

"So communications were difficult to say the least," he says.

The university put important emergency contact information and directions on its website, but not everyone thought of checking there. So now staff is trained to go to the website's emergency information page both prior to an anticipated disaster and after it happens, he adds.

"Everyone is made aware of what is going on through the institution's emergency preparedness system," Kratz says. "First thing you do is go to the website and look at the emergency notification section."

Also, the IRB now keeps a complete list of contact information for all IRB staff, member, investigators, and research coordinators, he adds.

"We have an emergency contact tree developed with information about each of our employees, and I keep this on my own computer," Kratz says.

UTHSC also found IRB communication limited to a single phone number in the university president's office after the 2001 floods. But should a similar disaster happen again, the IRB office is better prepared, Knudson says.

The IRB keeps a continually updated list of all possible contact numbers for IRB staff and others, she adds.

• **Establish safe back-up storage for data:** Knudson learned the hard way that even when the IRB system relies on hard copies, these should be stored electronically in a safe place.

After the Houston flooding, the UTHSC IRB office discovered that all of its back-up disks were floating in water, she says.

IRB offices should make sure that all files are backed up on a safe server or on disks that are stored in a secure off-site location.

The IRB office at LSUHSC had just made the transition to a new software management system prior to Hurricane Katrina. It stored data in a server in New York, so it wasn't impacted by the disaster, Kratz notes.

But all folders specific to individual protocols were still stored as hard copies in the IRB office, and these were difficult to access after the disaster, he says.

"I could go back in the office on an intermittent basis to get things and pull them out to take to Baton Rouge, but that was pretty difficult," Kratz explains. "Fortunately, all of the basic information about the trials was in the new management system, and having access to that information was the only way we could get started as quickly as we did."

Now, the IRB has expanded its use of electronic software management, putting as many documents as possible into the system, Kratz says.

Initial IRB submissions still come as hard copies, but they're now making a transition to a fully electronic system, he adds.

"The other thing we have done is give each coordinator a laptop and wireless internet cards so they have access with their laptops to the Internet and can get to this management system wherever they are," he says. "That's a significant change because [when Katrina struck] six years ago many coordinators did not have access to computers." ■

Research institution's QI checklist aids process

IRB provides hard stop

When IRBs and research organizations' quality improvement offices work together, the net effect is a more thorough and efficient human subjects research process, experts say.

The Emory Healthcare office of quality in Atlanta, GA, created a clinical trial readiness checklist that is completed by researchers at the beginning of a study, says **Sarah Putney**, JD, IRB director at Emory University in Atlanta.

The project was created after various clinical research stakeholders met to analyze and discuss ways to improve efficiency and safety, she adds.

While the IRB assesses the overall safety of a clinical trial, it's less attuned to the study preparation process, notes **William A. Bornstein**, MD, PhD, chief quality and medical officer at Emory Healthcare.

"This checklist is an attempt to create a linkage between the planned efforts and the reality and to see if the staff really knows about this trial," he says. "Do they know what kind of impact it will have on the laboratory and radiology and investigational drug services?"

The checklist is a collaborative effort between the QI office, the IRB, and the office of clinical research, Putney says.

"As with any good QI program it has to include hard stops," she says. "So the way it works is the IRB

helps to educate study staff when they submit a new study for us to review."

IRB staff directs them to the checklist, which is listed on the website.

"The IRB tells the study team they need to complete this, and then we continue on with our regular protocol review," Putney explains. "The IRB can go ahead and approve a clinical study, but we won't release the validated consent forms and HIPAA forms until the office of quality says the checklist is complete."

If investigators have any questions about the checklist, they are sent to the office of quality.

"There are two ways to think of the checklist," Bornstein says. "It's useful to make sure researchers have done what they need to do, and it's also useful as a way to provide organizational controls around the way they get things done."

The checklist itself is a simple, one-page form in table format. It lists these items:

- Study title
- IRB #
- Principal investigator
- Clinical research coordinator
- Protocol orders:

— Clinical facility approval of study site feasibility; signatures by EHC executive

— Approved/PI signed protocol orders written and reconciled with study and care delivery team and delivered to applicable care areas; signatures by PI, pharmacist, clinical nurse manager, and CRC

— Clinical in-service to entire clinical unit for protocol; occurs after all orders are signed off on; CNS educated if applicable; signatures by clinical nurse managers

— Stakeholder ancillary services in-service (depending on study requirements); occurs after all orders are signed off on; signatures by PI, lab, radiology

- Education

— Protocol education and training provided to research team, including MD investigators, nurses, and CRCs; signatures by PI and CRC

- IDS

— The study has fulfilled IDS requirements? Signature by IDS pharmacist

- Billing/compliance

— The study has been received by OCR? Signature by OCR representative.

Each item on the checklist represents an accountability sign-off step in the process.

"The intent is to give investigators something they have to look at and say, 'I haven't done this yet,'" Bornstein says. "Behind each sign-off there's another checklist to make sure things get done."

For example, before the investigational drug service sign-off can occur, the investigator will have to complete the IDS checklist of tasks to be performed.

"The pharmacist's signature represents they've checked and made sure they're responsible for saying the study team is ready to go from their point of view," Putney explains.

The clinical trial readiness checklist and the hard-stop involving the IRB releasing the informed consent document and HIPAA form are a way to enforce responsibility and accountability along each step leading up to the initiation of a clinical trial.

The quality improvement office doesn't monitor all of the steps required before officials sign the checklist, but it is assumed that if someone signs the form then the investigator has meet all of their requirements, Bornstein says. ■

BEST PRACTICES SPOTLIGHT

Give IRB staff & members Rules of Review refresher

Discuss nuances of each rule

IRB offices might improve their staff and IRB members' training and education if they provide an occasional refresher course on the National Institutes of Health (NIH) Guidelines for the Conduct of Research Involving Human Subjects, also known as the Rules of Review.

These guidelines provide the basis for IRB review consideration and discussion, but they provide room for flexibility and common sense, an expert says.

For instance, the first rule asks IRBs to minimize risk, but this is not a mandate to prevent all imagined possible risks.

"I think IRBs need to realize they can't think of every potential bad thing that could go wrong," says **Susan Kornetsky**, MPH, director of clinical research compliance at the Children's Hospital of Boston (MA).

IRBs should not reject a research protocol based on a very small chance that something of minor risk might occur, she notes.

The seven rules are published online at the website: http://ohsr.od.nih.gov/guidelines/GrayBooklet82404.pdf

Kornetsky offers these suggestions for how to discuss and train staff and IRB members on the NIH Rules of Review:

1. The proposed research design is scientifically sound & will not unnecessarily expose subjects to risk.

"You should think about physical, psychological, economic, and social risks," Kornetsky suggests. "And make certain the study's scientific design meets the aims of the protocol and that there is an important scientific question that the protocol will address."

For example, IRBs should ask themselves if the protocol outlines preliminary data, qualified staff and resources, and discusses minimizing risks to research participants.

If the study involves socio-behavioral or socioeconomic research, these issues are more problematic, she notes.

"Social and economic types of risks do not necessarily happen immediately, and they're not always clear," Kornetsky says. "So I think IRBs spend a lot of time with what-if scenarios while with medical risk protocols you can look for concrete things."

IRBs sometimes spend too much deliberation time on rare minimal risks, she adds.

"You can build things into the protocol so those risks are minimized if done by the appropriate people or staff," she says.

For instance, if a study involves an in-person questionnaire, then the IRB can check to make sure the investigator employs qualified people to conduct the interview, Kornetsky explains.

"Give study participants resources or hotline information," she adds. "Someone might not exhibit distress during the interview, but later they could go home and think about it."

2. Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of knowledge that may reasonably be expected to result.

This rule pertains to risk-benefit assessments.

"At least in medical research if you can combine research procedures with other clinical oriented procedures you could reduce risk," Kornetsky says.

With socio-behavioral research, IRBs could get caught up in trying to improve risks that already are minimal, she notes.

"Recognize that for behavioral and social research, if something starts with minimal risk then you don't have to tweak it so much," she adds. "If it's minimal risk, then you can move on."

3. Subject selection is equitable.

The IRB's review of inclusion/exclusion criteria focuses on safety issues, considering pre-existing conditions, Kornetsky says.

"The IRB looks at inclusion/exclusion criteria to make sure it meets the need of the research design, and they look at whether potential populations are vulnerable to coercion or undue influence," Kornetsky says.

IRBs should review the study site's screening procedures to determine whether they are justified, she adds.

Sometimes the criteria are so narrow that study sites have difficulty enrolling participants.

"IRBs respond to what investigators and sponsors propose, so many times they make the criteria so narrow that we'll see after a month or two that a study is open that they'll expand the criteria," she explains. "We see this all the time."

Investigators sometimes will approach the IRB to see if the IRB will grant them an exception for enrolling a subject who does not meet the criteria, but is otherwise eligible, Kornetsky notes.

"We say, 'You might want to consider expanding the criteria,'" she adds.

4. Additional safeguards required for subjects likely to be vulnerable to coercion or undue influence.

IRBs need to review study recruitment procedures to make certain they're acceptable, Kornetsky says.

"IRBs will spend a lot of time looking at recruitment, including the setting, timing, and making sure recruitment activities are well defined," she adds.

When investigators fail to include this information in their protocols, it takes the IRB longer to complete the review, she notes.

IRBs do not necessarily have to review an exact script the study site's recruiters will use, but any details about how, when, and where the recruitment encounters will occur are helpful, she says.

"This information gives the IRB a good chance to understand the nature of what the discussion is," Kornetsky says. "They should have a general idea of what is said during recruitment."

5. Informed consent is obtained from research subjects or their legally authorized representative(s).

IRBs typically spend a considerable amount of time reviewing informed consent documents and learning more about how the study site will conduct its informed consent process.

But they also should consider all initial encounters between potential study subjects and their legal guardians and the study team, Kornetsky says.

The recruitment encounters between potential study participants and investigators or study staff are important and the beginning of the informed consent process, she says.

6. Risks to subjects are minimized.

"When we consider risks we make sure they are adequately described in the protocol and informed consent form," Kornetsky says. "Here's where you want to put the risks into some type of context."

IRBs also might ask investigators to discuss their plans for sharing some study findings with subjects, she suggests.

For example, if the study includes a physical assessment that turns up some potentially important clinical information for a subject, then the study site should have a process in place for handling that information.

In addition to minimizing risks, IRBs could suggest ways that sites could maximize benefits, and sharing pertinent information is one way of doing so, Kornetsky says.

"If you are doing cognitive testing or other types of assessments, then share these with the family so they can use it as a potential benefit," she suggests. "Not everything has potential benefit, but sometimes we overlook the small things we can do to maximize personal benefit."

However, if the informed consent document states there are no personal benefits, then the IRB shouldn't try to find one, she adds.

7. Subject privacy & confidentiality are maximized.

"Privacy and confidentiality are two different concepts," Kornetsky notes. "Investigators spend a lot of time on confidentiality, but privacy also is what participants expect."

Privacy is one's concept of one's self, she explains.

The goal is to keep study data confidential, and this can be handled through electronic and physical data protection protocols and procedures.

Kornetsky adds an eighth rule, pertaining to monitoring data and managing risks involved with this process.

"If a study really has minimal or no risk, then you don't want to spend a lot of time monitoring data for safety," she says.

For studies that involve significant risk, then the IRB will want to see a plan on how data and safety are monitored, she adds.

These are some questions to ask of investigators:

— How frequently are data monitored?

— What type of data analyses are conducted during a trial?

— Are there rules for stopping the trial?

— What is the plan to detect unexpected harms or increases in the severity or frequency of harms?

— Is there an adequate plan to stop the protocol if benefits outweigh harms or if harms outweigh benefits?

"Some trials want data safety monitoring boards (DSMBs), and others rely on independent people and investigators," Kornetsky says. "It's important that every trial involving risk to subjects has a plan, and the IRB doesn't need to see every single event, but they need to know there is a plan embedded in the protocol, and someone is looking at it." ■

Common Rule extension could end 'unchecking'

IRBs say extending regulations to non-federally funded research could add to burden

In the past several years, many IRBs across the country have been seeking to carve out areas of flexibility in the federal regulations by "unchecking the boxes" on their federalwide assurance (FWA).

That action releases them from having to apply every aspect of the regulations to every study at their institutions. IRB officials at these institutions argue that it allows them to find more appropriate ways to review low-risk research that isn't federally funded and that doesn't fit well within the regulatory framework.

Now, with the proposed revision of the Common Rule, that option may no longer be available. The advance notice of proposed rulemaking (ANPRM) released this summer by the U.S. Department of Health and Human Services would, if approved, extend Common Rule protections to all research conducted at an institution that receives any funding from a Common Rule agency.

"It appears that it will take away much of the flexibility that organizations have now," says **Marjorie Speers**, PhD, president and chief executive officer of the Washington, D.C.-based Association for the Accreditation of Human Research Protection Programs (AAHRPP).

Forty-six percent of AAHRPP-accredited agencies reported in 2010 that they unchecked the boxes applying federal regulations to all research regardless of funding. Another 9 percent checked the box applying only Subpart A to all research.

Speers says there have always been institutions

that declined to check the boxes, but that number has grown in recent years. One institution that made the decision to uncheck the boxes is the University of Southern California in Los Angeles, which has formed a Flexibility Coalition to explore ways in which low-risk, non-federally funded studies can be handled more effectively.

At USC, that's meant adding exempt categories not included in the federal regulations, says **Susan Rose**, PhD, executive director of the Office for the Protection of Research Subjects.

"So a simple student project that uses a game, or tasks, or some other word that is not found in the six exempt categories, could be called exempt, rather than expedited," Rose says.

USC also has extended continuing review periods to two years on these low-risk, non-federally funded studies.

Greater burden

While the ANPRM would make similar changes to low-risk studies — introducing new exempt or "excused" categories, lessening continuing review requirements — Speers says other parts of the revised regulation would create greater regulatory burdens on institutions if the Common Rule is extended to all research.

"The ANPRM describes the major risk with behavioral and social science research as an information risk, and proposed to apply data security rules, which means HIPAA," she says. "That doesn't make sense. Researchers have voiced very strongly over the last eight years the challenges they have in applying the HIPAA regulations to research. To extend it beyond that isn't going to provide any better subject protection and it's going to be tremendously burdensome."

She notes other problems raised by the extension of the Common Rule to non-federally funded research:

• The federal regulations make it difficult to do social and behavioral research with pregnant women because of Subpart B's requirement that research has to either directly benefit the woman or fetus or contribute to the development of "important biomedical knowledge."

"That's going to be difficult for an institution that conducts behavioral or social science research to meet, because the regulations don't allow that to occur, because the regulations say biomedical knowledge," Speers says.

An institution that unchecks the box relating to Subpart B may be able to allow non-federally funded behavioral research with pregnant women, but extending the Common Rule would eliminate that option, she says.

• Speers says unchecking the boxes can allow institutions to write more appropriate consent forms, by eliminating unnecessary language that doesn't apply to non-clinical studies.

"So in behavioral and social science research, where it might not make sense, for example, to talk about loss of benefits because there are no benefits to lose, you wouldn't have to include that statement."

• For surveys of children, the regulations make it difficult to waive parental permission. Speers uses the hypothetical example of a non-federally funded survey of gay teenagers. "Especially if we're talking about 16- and 17-year-olds, it's not necessarily in the children's best interest — and could put them at risk — to get parental permission."

Reporting requirements

Unchecking the boxes also gives institutions more leeway in their reporting requirements to federal agencies, says **Moira Keane**, MA, CIP, director of the University of Minnesota's Research Subjects Protection Program in Minneapolis. As an example, she points to a student researcher who might have an incident or compliance problem with a study.

"If it were federally funded, we would have a reporting obligation to the federal agency," Keane says. "When we have unchecked our box, we have reporting obligations internally, based on our own policies, but we would not have to report to the federal agency.

"And we see that as a significant advantage on our part, to work collaboratively with our researchers, keep them in compliance, but not jeopardize their future opportunities by creating a spotlight on their minor infractions."

Speers says the flexibility that institutions have been employing doesn't lead to two tiers of protection for subjects in federally funded and non-federally funded studies.

"Unfortunately when we talk about unchecking the boxes, it's described in terms of not having to meet certain reporting requirements and not having to apply the regulations," she says. "But that doesn't mean a lessening or lowering of the protections for human subjects. It can mean just the opposite."

Rose says she would like to see HHS consider some of the innovations created by flexibility

initiatives such as USC's incorporated in the final revision.

"A middle ground would be really wonderful to take advantage of the creativity of these various institutions, but to expand what they're capable of doing," she says. "That would be a wonderful contribution, to do it through a regulation." ■

IRB, researchers team up on card study review

Method allows practice-based researchers to conduct quick surveys during appointments

Practice-based researchers have long complained that IRBs don't understand their work, which is based in physicians' practices and often consists of low-risk activities such as chart reviews and surveys.

But the experience of a practice-based research network in Cleveland shows that IRBs and researchers can work collaboratively and creatively to find more appropriate ways to review research methodologies that don't fit the usual mold.

The subject of the collaboration was a type of survey called a "card study," in which physicians use pocket-sized survey cards to collect information from patients during regular appointments.

While the approach has been used for more than 20 years, IRBs tend to be unfamiliar with it, says **Michelle Hamilton**, BA, who served as a clinical research facilitator with PBRN Shared Resource at Case Western Reserve University in Cleveland.

That unfamiliarity can lead to questions and restrictions that discourage physicians from participating, Hamilton says.

"In general, most of the people in practice-based research networks are practicing clinicians," she says. "They're not really used to going through the IRB process in the first place. So when the IRB starts raising all of these issues, they immediately say, 'I don't know what to do with this.' And just the thought of going through that can be a really big barrier."

Recognizing the problem, lead investigators at the network reached out to **Philip Cola**, MA, vice president for research and technology with University Hospitals in Cleveland and head of its IRB administrative office.

"They approached me and said, 'Phil, we're worried that as we try to bring research into the community and into these practices, practice-based researchers are going to get scared away by the perception of the regulatory burden that they're not used to,'" Cola says.

'Parent protocol'

One of the researchers' major concerns, Cola says, was that as studies evolved and new questions were added to cards, researchers and physicians would have to go back to the IRB and start the approval process all over again — re-educating the board about how card studies worked each time.

So Cola came up with a solution: Create one "parent protocol," detailing a list of standard procedures for a generic low-risk card study, which included collection of de-identified data. Each time a new card study was created, it would be added to the parent protocol as an amendment. This amendment would still require IRB approval, but wouldn't be treated as a fresh protocol.

"You're starting from close to the end point, versus starting from back at the beginning each time you do this," Cola says.

Cola himself helped introduce the idea to the two IRB committees that would be handling the studies. He says they initially had a lot of questions about the approach. Would the model work if the studies were about two different conditions, such as diabetes and hypertension?

"They wanted to know if the generic framework would hold in both those instances," he says. "And I said, 'You guys tell me — is there something we have to do differently at a fundamental level if we're asking questions about diabetes or hypertension?' And the answer really was no."

He says that the parent protocol has been open now for more than a year and a half, with numerous amendments to it. The IRB actually likes the approach, because it helps members focus on what is important about the individual study, Cola says.

"They've seen the basic protocol over and over again," he says. "Where they need to focus now is on what's different within that framework. From the perspective of a reviewer, if you can tell me coming in to the review where to focus and what's new and different, that makes my life easier."

Setting boundaries

One key to the success of this project is that it places strict boundaries on what can be accepted as an amendment to the parent protocol, Cola says. For example, he says a card study applies to visits in which a physician and a patient interact face-to-face.

"This is designed for a busy private practice physician to pull a card out of his pocket and say, 'Now that we've done our visit, here are a couple of extra questions I'm going to use as part of a research study, and here is a consent form for you to sign," Cola says.

He said it wouldn't apply, for example, to a physician who wanted to call patients at home and ask these questions. "You've changed the method and now that would have to be reviewed separately as a new protocol for the IRB."

Cola sees the potential for this protocol to continue to be open indefinitely, with periodic reviews to ensure that it continues to satisfy regulations.

"The regulatory environment changes over time, at least the interpretations of those regulations change," he says. "The question is will we view this the same way in 2015 that we did when we first reviewed this protocol in 2010?"

In addition to yearly continuing review, the IRB office looks at protocols that have been open for at least five years to specifically question whether they still are in accord with current regulatory thinking.

While this parent protocol approach may not have wide application to other types of research methodologies, Cola says the lesson from this experience is the value of bringing people from the research and IRB sides together to work out solutions before a protocol is submitted.

"Investigators should be going to their IRBs as they're planning a study, and saying, 'Hey, can you help me think about this differently and meet me in the middle somewhere?'" Cola says. "This idea lends itself to any type of IRB, any discipline, but it brings the IRB into the development of research design much earlier than most people do."

REFERENCE

Hamilton MD, Cola PA, Terchek JJ, et al. A Novel Protocol for Streamlined IRB Review of Practice-based Research Network Card Studies. *J Am Board Fam Med* 2011 Sep-Oct;24(5):605-9. ■

Measuring misconception in clinical trials

Tool could help show whether participant understands difference between research and treatment

Therapeutic misconception in clinical trials continues to be a significant concern for researchers and IRBs. Studies have shown that misunderstandings persist about the therapeutic value of research interventions among participants and even among research staff.

Now, a new screening tool has been developed to measure therapeutic misconception. The hope is that the tool can be used not just to screen potential research participants, but to aid further research on the phenomenon itself: What factors lead people to hold inaccurate or overly optimistic ideas about research? In what types of studies does it occur most frequently?

"We would like to see it used across disease conditions and phases of clinical trial research, to tease apart where this phenomenon is more likely to appear than others," says **Norm O'Rourke**, PhD, RPsych, an associate professor and clinical psychologist at Simon Fraser University in Vancouver, British Columbia. O'Rourke's student, Pak Hei Benedito Chou, developed the tool as part of his master's thesis.

O'Rourke says there have been previous screening tools for therapeutic misconception, but they tend to be too long for use in clinical trials. In addition, he says, Chou's tool takes into account more recent work that defines therapeutic misunderstanding in a more nuanced way.

Three facets

That work, by Sam Horng and Christine Grady at the National Institutes of Health, identified three facets of therapeutic misunderstanding, all of which may contribute to research subjects' incorrect beliefs about participation in clinical trials:

—Therapeutic misconception, the tendency to conflate research and clinical treatment because the subject doesn't understand research methodology;

—Therapeutic misestimation, a subject's unrealistic estimation of risks and benefits, for example if a participant doesn't understand the odds of being assigned to a placebo in a study;

—Therapeutic optimism, in which a subject understands these other factors but continues to

be overly optimistic about the potential for benefit from a trial.

"A person may well understand that there's a 50-50 chance that they'll be taking a placebo, but they choose to believe that they're taking active medication," he says. "Or there's a 5 percent chance that this will have any therapeutic benefit, but they assume, even with an understanding of that information, that they'll be part of that 5 percent."

Therapeutic optimism is not necessarily a problem for a research participant, O'Rourke says.

"Optimism in fact can be quite health inducing, both mentally and physically," he says. "Positive illusions seem to be positively associated with physical as well as mental health outcomes."

He says that Chou's inclusion of a measurement of therapeutic optimism in his screening tool can help differentiate between people who fundamentally don't understand that they're participating in research and people who do, but who choose to be hopeful about their prospects.

"One reason why I think the scale may be good as far as moving the field forward is that it captures this concept," O'Rourke says. "Misestimation and misconception are measured as well as positive optimism."

The screening tool asks the participant to imagine being asked to participate in a clinical trial. A short paragraph describes concepts such as research vs. treatment and randomization. Participants are then asked whether they agree with 20 statements such as these:

— "The main reason that people will be recruited for this study is so that they can benefit from the special treatment in this research project."

—"Taking part in this research study would cure my illness."

— "I look forward to participating in this study with hope and enthusiasm."

Testing tool

O'Rourke says the tool was tested on 464 people, all older than 50, who were recruited online. Once the survey was developed further, it was administered to 37 people who had previously participated in a clinical trial.

He says both groups demonstrated similar degrees of misconception, despite the information given to them in the introductory paragraph.

"Ironically, all the information was there, to answer these questions 'correctly,'" O'Rourke says. "But it really didn't seem to make much difference."

And he noted that in a real clinical trial, this information is typically buried in a much longer, more complex informed consent document.

O'Rourke says he would like to see this screening tool widely used among researchers trying to learn more about therapeutic misconception. He says they purposely included the tool within the study, which was published recently online in the journal *Aging and Mental Health*, so that it could be easily accessed and disseminated more widely.

"Ideally, this will help us do better research around that (topic)," he says. "And yes, it could also be used as a secondary screening tool to ascertain to what degree people fully understand what they're enrolling in," particularly in pharmaceutical trials where there is risk of significant adverse effects.

REFERENCE

Chou PH, O'Rourke N. Development and initial validation of the Therapeutic Misunderstanding Scale for use with clinical trials research participants. *Aging Ment Health* 2011 Sep 9 Epub. ■

ASK 2-4U

Expert tips on preventing persistent IC problems

Use checklists in meaningful way

[Editor's note: Wendy Lloyd, LPN, CCRP, CIP, regulatory affairs and compliance specialist, at Vanderbilt University Medical Center in Nashville, TN, has compiled a list of frequent audit findings of the informed consent document process. She answers questions for IRB Advisor about these findings in this question and answer session.]

IRB Advisor: What is one of the chief problems you see with informed consent documentation?

Lloyd: A huge problem with documentation is they don't realize you have to document re-consent and assessing cognitive status. It's very important to assess cognitive status, willingness to continue the study, and re-consent. So often what happens is people write a good document

and don't document what they've done with informed consent throughout the study. So it's a myth that they're conducting the process as it's supposed to be conducted, which should be interaction throughout the study. A person volunteering for a study has free will to withdraw from the study, and you should be documenting whether the subject wishes to continue the study.

IRB Advisor: How can research sites make sure they're following all of the regulations and rules for informed consent?

Lloyd: Checklists are good to use. However, I would caution against completing just the blanks on the checklist because you may not be focusing on the patient and other issues. If you're just marking checkboxes, you're not assessing the whole person. Some people like to use checklists, and I think they're a good idea, depending on how they're used. For example, a checklist for the elements of the consent document is good. But when people use a checklist for the process, it concerns me. Each study and each person is different, and it's important to be in tune with the subject and not just completing a checklist. A checklist might be good for documentation, but you have to go beyond the checklist for informed consent. ■

CNE/CME OBJECTIVES & INSTRUCTIONS

The CNE/CME objectives for IRB Advisor are to help physicians and nurses be able to:

- establish clinical trial programs using accepted ethical principles for human subject protection;
- apply the mandated regulatory safeguards for patient recruitment, follow-up and reporting of findings for human subject research;
- comply with the necessary educational requirements regarding informed consent and human subject research.

Physicians and nurses participate in this continuing education program and earn credit for this activity by following these instructions.

1. Read and study the activity, using the provided references for further research.
2. Log on to www.cmecity.com to take a post-test; tests can be taken after each issue or collectively at the end of the semester. First-time users will have to register on the site using the 8-digit subscriber number printed on their mailing label, invoice or renewal notice.
3. Pass the online tests 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 last test of the semester, 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 e-mailed to you instantly. ■

CNE/CME QUESTIONS

1. Which of the following might be included in a clinical trial readiness checklist?
   A. Clinical facility approval of study site feasibility
   B. Approved/PI signed protocol orders written and reconciled with study and care delivery team and delivered to applicable care areas
   C. Clinical in-service to entire clinical unit for protocol
   D. All of the above

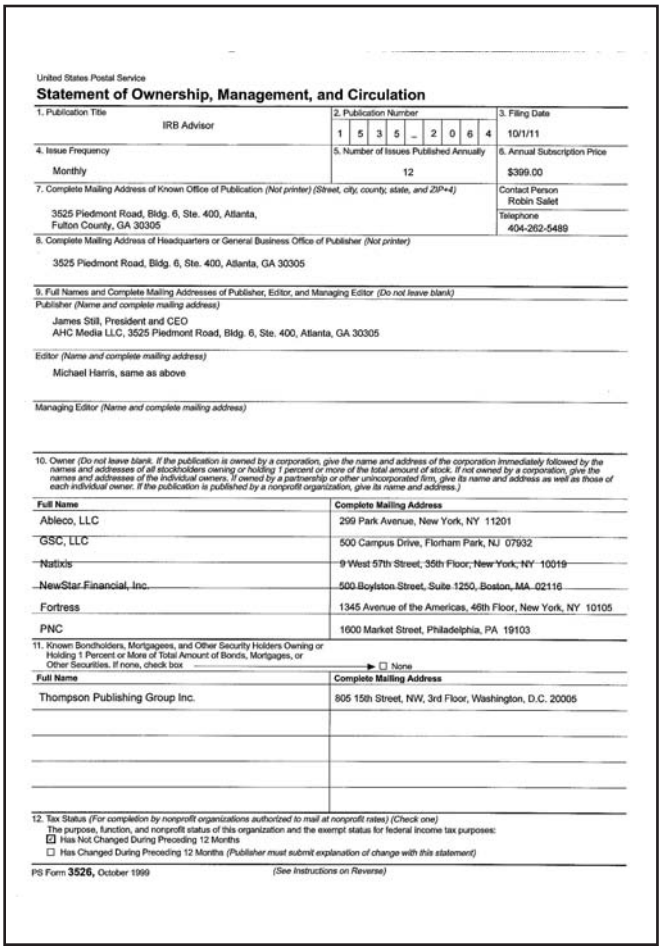
2. Which of the following is not a part of the NIH Rules of Review?
   A. Additional safeguards required for subjects likely to be vulnerable to coercion or undue influence
   B. Informed consent is obtained from research subjects or their legally authorized representatives
   C. Investigators provide the IRB with evidence supporting risk-benefit analysis
   D. Risks to subjects are minimized

3. True or False: The proposed revision to the Common Rule (contained in the ANPRM) would make it possible to conduct social and behavioral research with pregnant women even if it doesn't aid in the development of "important biomedical knowledge."

4. Which of the following three facets of therapeutic misunderstanding is not necessarily considered problematic for a research participant?
   Therapeutic misconception
   Therapeutic misestimation
   Therapeutic optimism

COMING IN FUTURE MONTHS

- ■ Informed consent readability: Are we improving?
- ■ Address subject population's health literacy
- ■ IRB's compliance efforts make "A" grade
- ■ The ANPRM and central IRBs
- ■ Create a clinical trial risk tool



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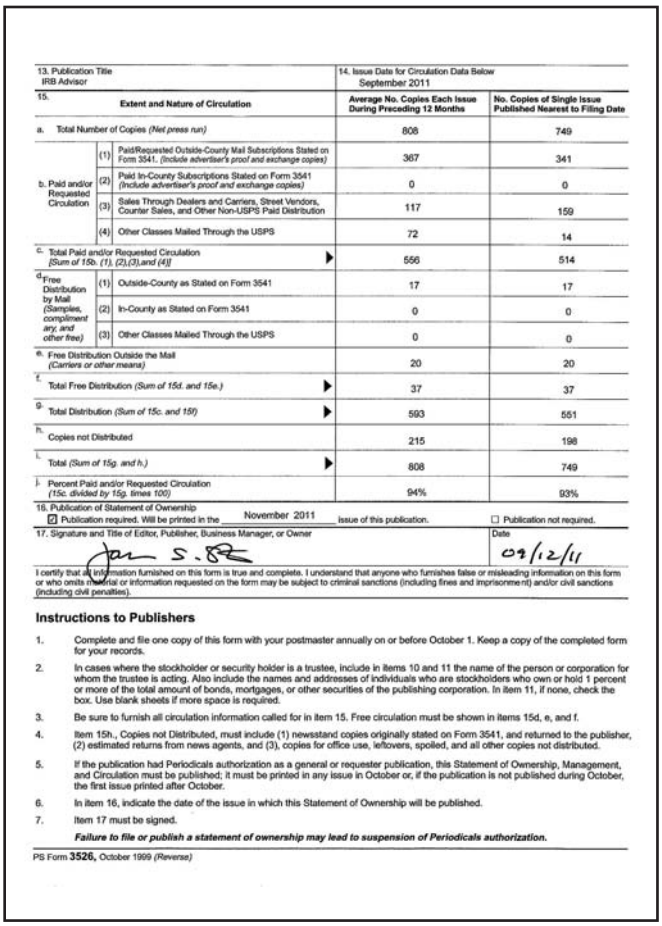

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