IRB ADVISOR

Your Practical Guide To Institutional Review Board Management

May 2012: Vol. 12, No. 5
Pages 49-60

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IRB tackles readability of informed consent forms

Use plain language as a start

IRBs continue to see informed consent (IC) forms that require high school or college reading skills when nearly half of Americans can read no higher than a 5th grade level, an IRB chair says.

"After visiting a PRIM&R conference two years ago, I became interested in readability and wanted to know what is the readability level, the understanding level of patients and potential participants in research," says **Thomas "TK" Koesterer**, PhD, ATC, associate professor at Humboldt State University in Arcata, CA. Koesterer is the chair of the university's IRB.

Koesterer used the Flesch-Kincaid Readability Statistics function of Microsoft Word to assess 61 informed consent documents reviewed by the IRB.

"Our reading level was 12th grade, when 7th grade was the average we're shooting for," he says. "There is nothing in the federal regulations that says what the readability level should be, but the regulations say the forms should be understandable by subjects."

The IRB's data on IC readability led to an initiative to improve the overall readability of informed consent forms submitted for review. The IRB encourages researchers to check their Flesch-Kincaid scores and shoot for improved readability through the use of simpler language, shorter sentences, fewer clauses, and short words. *(See plain language tips, page 51.)*

"When researchers check their Flesch-Kincaid levels they can see right away that their form is written at 15th grade level, and we can help them use simpler words with less syllables to improve it," Koesterer says.

As a follow-up to Koesterer's assessment of IC readability at the university, he would like to check readability again in a year to see if investigators have made improvements.

"Once we have that initial data, we can give it a year and assess again to see how we're doing," he says.

Also, it would be helpful to assess how well participants understand the IC forms, comparing comprehension of the revised forms with their comprehension of forms that are written without particular attention paid to lowering their Flesch-Kincaid reading levels, he adds.

"The next stage would be to provide investigators with a template for

writing consent forms, using federal plain language guidelines," Koesterer says.

For example, one tip is to use sentences that speak directly to participants, rather than to use language written in the third person, he says.

"You say, 'You will do this' or 'You will be asked to do this,'" he explains.

Here are some other guidelines for improving IC readability:

IRB Advisor (ISSN 1535-2064) is published monthly by AHC Media, a division of Thompson Media Group LLC, 3525 Piedmont Road, Building Six, Suite 400, Atlanta, GA 30305. Telephone: (404) 262-7436. Pe riodicals Postage Paid at Atlanta, GA 30304 and at additional mailing offices.

POSTMASTER: Send address changes to IRB Advisor, P.O. Box 105109, Atlanta, GA 30348.

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• **When listing items, use bullet points.** "If you use bullets and a number list, it implies an order to what is going on, and it's easier for people to look at," Koesterer says. "It's better to use bullet lists than writing the points in one long paragraph."

There is one important detail to note about using bullet points, he adds.

"If you don't put periods at the end of the bullet lines, then Flesch-Kincaid will skip over that whole section, and you won't know what the true reading level is," Koesterer says.

• **Make headings simple and interesting.** Informed consent forms need a generous number of headings to break up the copy and make it easier to follow and more readable, he says.

Readers often find headings with questions simpler to understand, Koesterer says.

"Write headings, such as 'What will you be expected to do?' or 'What are the benefits to you?'" he explains.

• **Provide writing template.** Templates can help investigators with writing informed consent documents by giving them examples of plain language to use.

"A template is a living document that keeps evolving to help with understanding," Koesterer says. "Researchers say, 'Just tell me the language to use that fulfills the federal regulations and that the subject will understand."

While there is no magical formula, IC templates can be helpful.

• **Rewrite legalese.** Research institutions often have attorneys who want specific phrases and wording placed in informed consent forms, Koesterer notes.

Unfortunately, the language they use often is complex and includes words that make the intent difficult to follow. For instance, legal phrases often include the word "shall," which is no longer commonly used in the English language, he adds.

"'Should' is past tense of 'shall,' but now people use the word 'should' to mean it's an option," Koesterer says. "I prefer to use the words 'must' and 'required.'"

This is why some simple word exchanges can improve reader comprehension.

"You can be technically correct, but people may not understand," Koesterer says.

IRBs can take this legalese and change it to simpler sentences and words. For example, rather than spend a paragraph outlining a subject's right to withdraw from a trial, the IC form can say, "You can stop whenever you want. You will not lose any benefits," Koesterer says. ■

Federal government offers these plain language tips

Checklist can work for IC

The U.S. government provides information and strategies for improving readability of documents at the plainlanguage.gov website. These same tips can help IRBs improve informed consent forms.

Here is the plain language checklist:

- Write for the average reader.
- Organize paragraphs to serve the reader's needs.
- Provide useful headlines.
- Use "you" and other pronouns to speak to the reader.
- Use an active voice.
- Use short sections and sentences.
- Use the simplest tense possible — simple present is best.
- Use base verbs, not hidden verbs.
- Omit excess words.
- Use concrete, familiar words.
- Use "must" to express requirements; avoid the ambiguous word "shall."
- Place words carefully, avoiding large gaps between the subject, the verb, and the object, and put exceptions last.
- Use lists and tables to simplify complex material.
- Use no more than two or three subordinate levels. ■

IRB develops pre-review screening process

Tabled reviews drop from 45% to 23%

IRBs have full schedules, and the little mistakes investigators make when applying for an approval can bog down the process, adding weeks and resulting in wasted time. As one IRB office has discovered, a solution that can reduce turnaround time and improve efficiency involves the use of a pre-review screening process.

"It's definitely challenging to provide a thorough review, crossing the t's and dotting the i's and turning around reviews in a timely fashion," says **Donna Hoagland**, LPN, BS, CIP, CCRC, CHRC, director of the New Brunswick/Piscataway campus IRB at the University of Medicine and Dentistry of New Jersey (UMDNJ).

The IRB's percentage of initial full board submissions that were tabled averaged 45%, and mistakes were often discovered at initial and continuing reviews, she says.

IRB staff looked at the tabled submissions to identify trends. They found that some questions on the submission forms were left unanswered, so they decided that any checklist would need to include the point that all questions should be answered, she says.

"We felt it was wasting the board's time and the investigators' time if protocol submissions were not complete," Hoagland says. "That was our challenge."

After making changes to the review process by adding an IRB staff administrative pre-review stage, the office measured the number of tabled submissions and found a significant reduction to 23% of new applications being tabled, she adds.

The IRB's solution was to start a pre-review process designed to catch the most common omissions and errors and have those fixed before the IRB reviewed the protocol.

"We had a good system, but everybody can make improvements," Hoagland says. "The trick with the pre-review process is that criteria under the regulations that only a reviewer, a fully appointed board member of the IRB can make decisions about."

So the IRB office would handle only the administrative issues, dealing with problems that did not require IRB member input.

"We came up with a pre-screen process that included pre-screen procedures, a staff administrative pre-review checklist, and an investigator submission checklist," Hoagland says.

They focused on these questions:

- Was everything from the application complete?
- Was every question answered or not applicable?
- Was every required attachment included?
- Were all sign-offs attached?
- Was the department chair's signature included when required?
- If the protocol was for a cancer study, was there an approval from the scientific review board?

"The other thing we were looking at was whether the research activities were occurring on UMDNJ-owned or -operated property. If not, did we have

either the other institution's IRB approval letter or a request for an IRB authorization agreement to be the IRB of record for that site," Hoagland says.

The pre-review process also included an Initial IRB Paper Submission Application Checklist for principal investigators. *(See sample PI application checklist below.)*

The process began with the IRB's front desk staff looking at each submission for the most basic of details, such as whether all questions were answered and whether the protocol was attached, Hoagland says.

"Did they give us a copy of the investigational brochure? Was the disclosure form attached?" she says. "If these were missing they'd send the PI an email and get the items before the protocol was put on the agenda."

Once the front desk staff check submissions, they pass the protocols to the program assistant, who has additional training and can check to make certain recruitment materials, grants and contracts, and informed consent forms or waivers of consent are included, she adds.

"If there's a disclosure on the conflict of interest form, they send the disclosure to the conflict of interest committee so those reviews could go concurrently," Hoagland says.

Here are some additional examples of the items pre-reviewed by the management assistant:

• Confirm UMDNJ paid faculty, staff or student of public health. If a student is listed as a Principal Investigator (PI) and is not from the School of Public Health, the student cannot be a PI. Return to PI.

• Confirm that all Investigators and Study Personnel have completed the CITI Training Basic Course/Refresher, as required. If not, list names.

• If funded, confirm that a Grant, Contract of Letter of Award is attached. If not, return to PI.

• If this study involves the use of Embryonic Stem Cells, confirm that an ESCRO Committee Approval

IRB's initial submission checklist works for PIs

The New Brunswick/Piscataway campus IRB at the University of Medicine and Dentistry of New Jersey (UMDNJ) has developed an initial IRB Paper Submission Checklist, designed to help principal investigators in preparing their IRB submission.

The two-page checklist includes a list of items commonly included with submissions. Each question is followed by a box to check for "yes," "no," and "N/A." Here are the IRB's checklist questions:

• Are all copies collated and stapled?

• Is the application signed by the PI and all co-investigator(s)?

• Is the application signed by the Department chair(s)?

• Does the submission contain a separate protocol with a visible footer version that details specific studies activities?

• How many CONSENT and ASSENT forms are being submitted? Enter in number of each below: Consent Forms, Assent Forms, HIPAA Auth. (if separate)

• Have you included copies of each consent/ assent form with a visible footer version on each?

• Have you included copies of CITI Human Subjects Research certificates for all investigators and study staff listed on your application? http://www.umdnj.edu/hsp/education

• Have you included a copy of the Investigator's brochure and 1572/1571? (required for all studies involving investigational drugs, devices/biologics)

• Have you enclosed package inserts for each FDA-approved drug/device?

• Have you included ALL recruitment materials (including flyers, brochures & printed advertisements, radio/TV ads, letters, telephone scripts, Internet postings, etc.)?

• Have you included ALL Questionnaires/ Surveys?

• Have you submitted ALL DATA COLLECTION sheets for this study?

• Check all that apply (AND include): If appropriate, did you include confirmation of University Committee; APPROVALS: CINJ SRB, UBHC , Radiation Safety and/or BioSafety?

• Is a FULL GRANT (including budget) or a CONTRACT for outside funding attached to this submission?

• Have you submitted the appropriate HOSPITAL/INSTITUTE SIGNOFF (e.g. KENNEDY MEMORIAL HOSPITAL, RWJUH -RUG form/ UH/UBHC, etc.)?

• A) Have you enclosed the complete signed Investigator Financial & Other Personal Interests disclosure form? B) If you have disclosed a conflict, you MUST attach copies of part 2 of the disclosure form. http://www.umdnj.edu/hsp/forms/appendices.html. ■

Letter is attached. If not, return to the PI.

IRB staff make sure reviewers and the board have a complete package with all of the information they need to complete the review, she notes.

"We developed new office procedures that go with the new pre-screen checklist," Hoagland says. "If something major is missing from the submission, like an attached protocol, then we do not accept the submission."

If the missing item is less significant, such as a human subjects protection training certificate, then the IRB office will email the PI about the missing item, copy the email and put it in the file so the IRB reviewer will see it, she adds.

"We made the investigator submission checklist available on our website along with the application so investigators could check off items as they complete the packet," Hoagland says. "We're hoping to expand pre-reviews in the future by developing a continuing review pre-screen, modification pre-screen, and a final study pre-screen checklist, as well." ■

IRB offices can educate clinical research teams

Goal is to improve overall program

One of the key attributes of a strong human research protection program is an institution's ability to optimize its resources, an expert says.

"Back in the 2000s, everybody recognized that human research protection was a shared responsibility, and there were many initiatives for those who engage in oversight of human subjects research," says **Yvonne Higgins**, CIP, director of quality management at Copernicus Group Institutional Review Board (CGIRB) in Durham, NC.

"But with the challenges of the declining economy in 2008, it became a greater challenge to maintain these customized, fairly expensive training programs," she adds.

IRBs have the Collaborative Institutional Training Initiative (CITI), which came out of discussions among research institutions about how to provide IRB training at a low cost, she notes.

"It's a web-based program and the modules can be customized to your institution," Higgins says. "That can serve as the very basic requirement for educating IRB members, researchers, and research staff, and it's a great place to start."

IRBs can expand on CITI and other training programs to create high-quality training at an affordable cost, she suggests.

For instance, interactive webinars led by professional organizations and expert consultants can be offered to IRB staff, investigators, clinical research professionals, and anyone else who is interested, Higgins says.

"We offered an interactive webinar to anyone who wanted to sign up, and we had more than 700 people registered," she says. "Then we posted the webinar to our website and allow anyone to go register online and watch it at no charge."

This is one example of how IRBs can find good educational programs available even when the research program is on a tight budget, she adds.

Higgins provides these additional ideas for educating IRB and clinical research staff:

• **Ask for ideas from peers in the IRB world.**"In my couple of decades of being on an IRB, I've found that IRB folks are among the most generous people you could meet," Higgins says.

"So if you haven't developed something yourself, then reach out to one of your peer institutions," she adds.

• **Encourage IRB staff to attend department meetings.** IRB directors can encourage their staff to attend departmental meetings, meeting one-on-one with researchers, Higgins says.

"I would encourage the IRB staff to make those connections and interactions," she says. "You don't need one trainer doing all of the training; you can help people in an office group professionally through these connections."

• **Write newsletters to reach a large group.** "Newsletters are always an easy way to reach large groups of individuals," Higgins says. "If you pick the right topic, people will open the newsletter."

For instance, CGIRB members and staff recently developed an assent form template that researchers can use when they're submitting a protocol involving research with children.

"We announced the template in our newsletter and also wrote an article about the specific challenges and ethical and regulatory requirements of having children as participants in research," she says. "We received many good responses to that newsletter offering."

Not every newsletter topic will interest research offices, but this can be a good way to provide quick, necessary information along with links to new templates and other material, she adds.

"There are a lot of researchers who are really hungry for that information," she says. "You always

want to make any offering as interactive as possible, so always include links in electronic newsletters."

• **Invite researchers to an IRB meeting.** "Another approach I took in my previous job was to invite researchers to an IRB meeting where they'd have an opportunity to come and interact with the IRB and share information about ethics and research," Higgins says.

While investigators are required to leave the meeting during the IRB's deliberation of their own protocols, they can attend to answer specific questions or provide information requested by the IRB, she adds.

• **Provide an option for one-on-one education.** "This is a resource-intensive option, so if you do that you have to balance it with all these other things," Higgins says.

"If you have a basic requirement of the completion of a web-based training program like CITI and then you augment that with some other kinds of offerings like webinars, newsletters, and small meetings, then you can allocate some time to one-on-one training sessions," she explains.

"Every institution and IRB probably has a different approach, but if you are a small institution, and you can invite your researchers to come and meet with the IRB and go through individualized training, then that is an option," she says.

This can be handled as a web-based sign-up sheet in which investigators set aside an hour or two each week for someone to meet with the IRB chair or IRB staff to discuss a research issue or broader question, she adds.

• **Rely on a robust website.** "If you go back to the original strategy of optimizing resources, you can look around and find out what works for you across other websites and get a sense for what it is you would like to develop for your audience," Higgins says. "If you are in an academic setting then you can go across campus to your web developer and ask for help."

If that is not an option, then an IRB could hire a content management service or outside contractor to help improve the website's navigation and content flexibility, she notes.

Research professionals' education and training will continue to be an important priority for human subjects research protection programs, Higgins says.

"We're in an interesting time where the discussion is reinvigorated on the part of regulators to change some of the existing regulatory framework," she explains. "This is an exciting opportunity for all of us to talk about what works and improve human research protection programs." ■

Incidental findings in genomic research

Researchers, IRBs differ on how to handle them

As the technology that enables genetic research becomes more sophisticated, it opens a kind of Pandora's box to researchers — telling us information about subjects that they weren't looking for and may not necessarily want to know.

These genomic incidental findings (GIFs) can take many forms: Evidence that a subject has a genetic predisposition for a particular condition — which may or may not be preventable or treatable. Evidence that someone is not biologically related to a parent. News that a person has a racial ancestry he or she isn't aware of.

Investigators and IRBs still are trying to catch up to the technology, figuring out when, how, or even if they should give these results to participants. So far, few guidelines exist to help make these decisions, which can be highly dependent on factors such as the validity of the test, how conclusive it is and whether the subject has expressed an interest in knowing it.

A recent survey of genomic researchers and IRB chairs underscores the lack of set policies in this area. While 42% of researchers had encountered GIFs in the previous year and 68% of IRB chairs had discussed GIFs with their boards during that time, the groups took different approaches when discussing how they should be handled, says **Janet K. Williams**, PhD, RN, FAAN, a professor of nursing at the University of Iowa in Iowa City.

The findings from this survey were published in a recent issue of the journal *Genetic Testing and Molecular Biomarkers*.[1]

Researchers generally did not express a need for general disclosure policies, except in rare circumstances. They argued that their research rarely turns up something that is useful to participants, and that the purpose of research is generalizable knowledge, rather than providing information to individuals. They noted that most of their research was not conducted in labs that meet federal CLIA standards, and so would have to be confirmed in another lab, at a cost.

IRB chairs, meanwhile, said that there should be consistent policies established and laid out in informed consent, rather than figuring out what to do with individual cases after data collection has begun.

"It did not surprise us that the IRB chairs had one

set of assumptions and that the researchers had a different set of assumptions," Williams says. "That would be very logical based on the roles that each of those groups have in the conduct of research."

Having the conversation

Williams is both a researcher who studies the psychosocial effects of genetic testing and the chairwoman of a social-behavioral IRB at her own institution. She says her experience on both sides of that divide leads her to think that there needs to be a conversation between IRBs and genetic researchers about how to handle GIFs.

Handling individual cases as they come up "takes a lot of time and resources," she says. "As investigators, we came to the realization that these kinds of questions will not be as unique as one might have formerly thought.

"Conversations between IRB programs and chairs and researchers need to happen so that the surprise and urgency of what to do when faced with this situation are laid to rest."

Some institutions skirt the question by simply stating up front that researchers will give individual results to subjects. But in the survey, researchers themselves reported finding an occasional result that they felt compelled to disclose because of its importance.

Williams says that in these days of direct-to-consumer genetic testing, it's clear that people are interested in their genetic makeup.

"Making a statement to the public who would participate in research that there is nothing for them to decide [about whether to receive incidental findings] I think is very narrow," she says. "I don't know that that is the best approach."

IRBs and researchers contemplating this issue have to consider a number of factors, Williams says:

• **Medical importance:** Is it clear what the finding means, and what it will mean for the participant? Williams says different people can interpret that in different ways.

"Probably the most conservative definition is that it's something that's life-threatening and it's treatable," she says. "It's pretty hard to argue against that."

But there are other areas that might be important to participants. Is the condition in question one that can be passed down to a person's children? Should a person be told that they're of an ethnic group they didn't know about, particularly if it has health implications?

"What is the kind of information that would make the IRB say, 'We really need to be thinking about this'?" Williams says. "Researchers will have views and IRBs will have views about what we're talking about. That's one of the biggest challenges."

Having a choice

• **Subject preference:** In some studies, subjects are asked whether they want to be contacted with incidental findings, or asked what kind of findings they'd wish to know about. Williams says IRB chairs in the study were not universally in favor of giving subjects this choice.

"Putting it into language that's appropriate and accessible for research subjects, regardless of their literacy level, that's going to be an issue for IRBs," she says. Williams says she'd like to see national guidelines that address this issue and come up with suggested language.

And how should an IRB handle things if a participant does not want to be contacted, but information comes back about a life-threatening and treatable condition?

"Do they honor that, or do they override? It's a topic they may want to consider."

• **Test validity:** If the original test that turns up a disclosable result did not come from a CLIA-approved lab, what must be done to validate the findings? And who pays for that?

• **Who discloses?** Williams says one reason researchers give for not wanting to disclose results is that it's unclear who would be best to do it. If the researcher is not the subject's physician, and is not trained in having that kind of conversation, who should do so?

"They thought that people like a genetic counselor, a medical geneticist, or sometimes they'd talk about the local provider," she says. "Those individuals need to be considered as part of this plan for disclosure. And what would be the cost to the participants?"

• **Time limit:** Biobanks can keep samples for years, complicating disclosure plans. Findings that may not be considered definitive now may take on added importance as the technology for interpreting them improves.

"These samples may have a lot of use," Williams says. "At what point are the obligations completed as far as contacting subjects?"

• **State laws:** IRBs and researchers must be aware of local laws regarding reporting of genetic findings.

• **Potential misunderstanding:** Any communications with subjects would need to be clear about what the finding shows and what it means. A genomic finding may not mean that a person

definitely will develop a condition, and Williams says this can often be difficult for subjects to understand.

There's also the potential for a type of therapeutic misunderstanding as a result of genetic testing, she says.

"If you ask people to consent to be informed if there's an incidental finding and they hear nothing, will they conclude they have a clean bill of health?" she says. "The other concern we heard is that people may want to do this as a back door way of getting genomic health information about themselves, without going through a proper clinical evaluation."

While IRB chairs and researchers had different perspectives on the idea of disclosing GIFs, Williams says both groups surveyed were very thoughtful about the issue, and really struggled with its implications.

"It goes again to our point that if there were opportunities for them to be talking with each other about them, I think that would really be a good place to start," she says.

REFERENCE

1. Williams JK, Daack-Hirsch S, Driessnack M, et al. Researcher and Institutional Review Board Chair Perspectives on Incidental Findings in Genomic Research. *Genet Test Mol Biomarkers*. 2012 Feb 21 (epub). ■

Parents find value in children's health surveys

Study shows surveys may have some benefit

IRBs frequently worry that questioning subjects who have undergone physical or emotional trauma can cause distress, but research has shown that such questions do not tend to cause additional damage to subjects.

In fact, studies with such groups as victims of child abuse or sexual assault have found that while questioning people under these circumstances can cause pain, it also has the potential to provide benefit to subjects.

A recent study, published in the *Journal of Palliative Medicine*, involved a group of parents whose children have cancer. As part of a larger study about how their children's prognoses were communicated to them by their physicians, parents were asked whether the survey itself caused them distress.

Jennifer Mack, MD, PhD, a pediatric cancer specialist at Dana-Farber Cancer Institute in Boston, says the question grew out of the researchers' experience with IRBs, as well as their own concerns.

"We definitely had experience with the IRB being concerned about these questions — in this study and in other studies that we've done," she says. "We were worried about that, too. We didn't want to be causing a lot of distress to parents, since they were nice enough to participate in the study."

Initially, the researchers intended to ask only about how distressing parents found the experience of participating in the survey, so that they could refer parents for support if necessary. But Mack says one collaborator thought the question didn't go far enough.

"Our collaborator said, 'Why don't you ask them if they found it helpful to participate and see what kind of information you get about that, as sort of a second piece of looking at this?'" she says. "And so we added that brief question as a way to understand their experience in a little more complete way."

Distress levels

The results mirrored other studies of distress among participants in research. Of 194 parents surveyed at Dana-Farber in the first year after their children's cancer diagnosis, only 1% reported being "very" distressed by their research participation. Most parents (62%) said that they were "not at all" distressed by the questionnaire, with the remaining 37% reporting that they were either "a little" or "somewhat" distressed by the questions.

Furthermore, 69% of parents also reported that the survey was useful to them personally — 39% said "a little useful," 25% "somewhat useful" and 5% "very useful."

In looking at both distress and utility, 54% of participants gauged the usefulness of the questions to be greater than the distress they caused, with 27% finding the two to be roughly equal and 18% reporting the distress to be greater than the usefulness of the questions.

Mack believes that one reason the results turned out as they did was that parents who had the potential to be greatly distressed by the questions may simply have chosen not to participate.

"I felt that the process of self-selection actually worked pretty well," she says. "We asked parents to participate, but they didn't have to and parents could choose which of the two parents wanted to participate.

"Using that technique, we only had 1% of parents who considered it very distressing and that suggested

that either it really wasn't that distressing, or the process worked pretty well, in terms of parents figuring out who was going to participate and choosing not to if they couldn't."

Experience, not prognosis

There were some factors that contributed to a less distressing experience: Parents who participated more than 100 days after their child's diagnosis and parents who had a "sense of peace of mind" about their child's illness were less likely to report being distressed. On the other hand, parents who found prognostic information distressing and those who had wanted information beyond what their physician had told them were more likely to report distress with the survey questions.

"We found it really wasn't the prognosis itself, it was how it affected them that was really a predictor of distress with the survey," Mack says. "There are lots of reasons why parents might find this kind of study distressing. But it's not always about the research itself — sometimes it's about the situation, or asking them to reflect on aspects of clinical care that they don't feel as good about."

Mack says that the reporting of benefits associated with participating help balance the total picture of how subjects were affected.

"I think that this is human life — that some experiences are hard, talking about them is hard, but it's also how we process them, it's how we come to terms with them, find meaning in them when that's possible," she says. "Parents feel like they're helping parents of the future or helping to change the way physicians take care of kids in the future. I think that can bring some real value to this experience."

She says that while she believes the regulations in place to protect subjects are appropriate and necessary, IRBs shouldn't lose sight of both sides of that balance. She says the small number of parents left very distressed by this research experience suggests that parents did a good job of deciding whether they should participate.

"These things are complicated," Mack says. "If a parent is truly informed about what this means, then it may be reasonable to let them make a decision about whether they should participate and to trust them to do that."

REFERENCE

Olcese ME, Mack JW. Research Participation Experiences of Parents of Children with Cancer Who Were Asked about their Child's Prognosis. *J Palliat Med* 2012 Mar;15(3):269-73. ■

Research slowed by military IRBs' requirements

Paperwork, slow response can delay studies

Many researchers have stories about the challenges of getting reviews from multiple IRBs for a study — the differing standards, varying risk assessments and the duplicated paperwork.

Those challenges can be compounded when one of the IRBs involved is affiliated with the U.S. military. The military sponsors a significant amount of research, through the various services themselves, military medical institutions, and the Veterans Administration.

In many cases, researchers must navigate between the competing requirements of civilian and military IRBs. It's a path that **Reg Arthur Williams** knows well. Williams, PhD, RN, BC, FAAN, is a professor in University of Michigan School of Nursing in Ann Arbor. He's also a captain in the Nursing Corps Unit of the U.S. Navy Reserves, where he has studied such topics as psychosocial care of combat casualty patients and depression interventions for Navy recruits.

Whenever Williams conducts research with military personnel, he must have his study approved by both the University of Michigan IRB and the IRB for the military facility or organization involved.

He says that over the past 16 years, he's seen changes in the way in which both civilian and military IRBs review studies.

"When we started out with the first study I had gotten funded from the Department of Defense, we had IRB approval from the Navy sooner than I had it at the University of Michigan," he says.

Now, Williams says, the situation is reversed — typically, the military IRB takes longer than the civilian board and imposes more requirements. In a recent article in the journal *Military Medicine*, he noted that recent continuing reviews of a minimal-risk study involving anonymous online surveys of military personnel took as little as three days for a university IRB to complete, while the military IRB approvals took up to seven to 12 months.

Large bureaucracies

Williams believes that as civilian IRBs have made an effort to streamline their processes, military IRBs have instead added requirements that he says don't

add protections and unnecessarily slow down the pace of research.

"I was on active duty in the Navy and working for a large research university," he says. "I am very accustomed to bureaucratic organizations, and one of the things that I know about bureaucracies is that you really can make them work if you know how to work with people in the system. It's amazing as to what you can get done in a large bureaucratic organization.

"But you also have a number of people doing reviews that are not really that knowledgeable about the research process," Williams says. "They can hang things up for months on end. And unfortunately what they do is they put a lot of civilians in positions who really don't understand what they're doing and they just create obstacle after obstacle."

Among the obstacles Williams has encountered working with military IRBs:

• A requirement that his university obtain a Department of Defense (DOD) addendum to its Federalwide Assurance (FWA) in order to do research involving military personnel. The addendum binds institutions to additional DOD human subjects protection requirements.

"I had to go through all these hoops, it took months on end, the university counsel had to get involved and the vice president for research had to sign documents," Williams says.

• CRADAs: Cooperative Research And Development Agreements (CRADAs), which must be worked out between civilian institutions or companies and military organizations when certain research is conducted. The CRADA lays out the conditions under which researchers and their military partners agree to share technology and resources, while protecting intellectual property rights to new inventions or drugs. IRBs may need to be aware of these agreements' restrictions.

Williams says CRADAs are sometimes required in situations that don't warrant them, such as in the minimal risk surveys that he conducts. He says almost nothing on the CRADA forms he had to fill out pertained to his type of research. In the end, it amounted to an agreement to give the military a free copy of any published journal article that resulted from the study. "Yet this took us nine months to get approved," he says.

• Military IRBs would conduct scientific reviews of studies, even though the study already had undergone such a review in order to obtain funding.

Williams says that in one case, a study was held up for so long that the window for data collection was shortened to only two weeks, severely limiting recruitment.

He says the civilian IRB sector seems to be more aware of the difficulties that these types of delays cause and are taking steps to address them. Williams is frustrated by the fact that military IRBs aren't keeping up.

"They [military IRBs] have the ability to address these things and could do it way ahead of civilians, if they would just do it," he says. "They could lead this in many ways."

In the meantime, he says, civilian IRBs that review studies alongside military IRBs should be aware of the potential delays. It would be helpful, Williams says, for civilian IRBs to do what they can to bring about a more efficient multiple review.

"I would have loved it if my IRB had called the IRB at the military and said, 'Let us work together to get this done in a reasonable time period,'" he says. "But what tends to happen is that every IRB acts as if they operate in a silo. They're never really sitting down and working together to facilitate the research."

REFERENCE

Williams RA, Gatien G, Hagerty BM. The Need for Reform of Human Subjects Protections in Military Health Research. *Mil Med* 2012 Feb;177(2):204-8. ■

Program uses systems approach training

Trains trial monitors on FDA warnings, audits

When **Jill Matzat** was monitoring clinical studies, she approached it the way she had approached her work in the lab and as a nurse.

"One of the things I understood is that when you're running an experiment or you're treating a patient, there's a certain approach that you take and it's instituted in your training," Matzat says. "When I started to monitor, I would create a systems approach to it so I was applying the same standard across every patient that I monitored."

This approach, she says, allowed her to catch problems that other monitors missed.

"When I was monitoring, I noticed that everybody was kind of a cowboy out there — they kind of did their own thing with Post-it notes or whatever," she says. "Or they'd inventory and say, 'Oh, the consent's present,' without thinking about the compliance component."

So Matzat, RN, BSN, CRA, now president

of Medical Research Management Inc. & CRA Solutions, Inc. in Coral Springs, FL, developed her own training program for clinical research associates (CRA) who monitor clinical studies.

That training program was selected as a 2011 winner of the Health Improvement Institute's Award for Excellence in Human Subjects Protection – Best Practice.

Using warnings, audits

Matzat says she's been fine-tuning the program since introducing a 140-hour CRA Certificate program in 1999. She says she used FDA warning letters and audit findings to help discover where monitors needed to focus their attention.

"I probably spent about three years going through a process of figuring out what worked and didn't work — looking at different issues, seeing the audit findings and then doing a gap analysis between the [findings and the] monitoring and trying to figure out why the monitors aren't picking up on these issues," she says.

She says too often, monitors simply inventory the items that are supposed to be present and go no further.

For example, in looking at consent, a monitor might check to make sure a consent document is present and signed.

But Matzat goes further, with an eight-point system, based on the regulations and guidance documents.

She would ask questions such as: Does the file contain the right version of the consent? Is it the right patient? Are the signatures from the right people? Are the dates correct? Are all the pages readable? Was the person who administered consent to the subject trained to do so? Was there someone available to answer medical questions?

"You might find that all the dates are off — why is the investigator signing this three weeks later? Or it's the incorrect version [of the consent] on 15 of 20 patients," she says.

Matzat says her program uses a similar approach to validate HIPAA compliance, protocol compliance, inclusion and exclusion procedures, and other aspects of the study.

Online and hands-on

Covering all of these points requires a rigorous training process — Matzat says students spend 70 hours doing an e-learning course and then do two weeks of hands-on training, practicing monitoring on mock studies.

Matzat says she would like to expand the course, adding more e-learning modules about such issues as dealing with electronic medical records. And because so many people are coming to the monitoring without a medical background, she says she would like to offer courses in anatomy and physiology.

But she says the hands-on component of the training is vital — too often, she says, monitors only complete an online course, but don't know how to apply the regulations to real-life studies.

"I'm not sure that just recommending e-learning

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. ■

COMING IN FUTURE MONTHS

- Follow expert advice on reimbursing subjects
- Research ethicists debate role of trials and social injustice
- Community-engage research issues reviewed
- Picking central IRB for multisite neurology trials
- What are 'equivalent protections' in international research?

is always adequate," she says. "I think that [IRBs] are best requiring some sort of way to validate their knowledge."

Matzat has trained CRAs for work in universities, private industry and at the National Institutes of Health.

She says that institutions that are concerned about ensuring quality monitoring — particularly those that have received warning letters for violations — should consider a more structured and hands-on training program.

"If these sites are having warning letters because of violations, you have to wonder how this is getting past an IRB," she says. ■

CNE/CME QUESTIONS

1. According to federal plain language guidelines, which of the following is not a good tip for use in writing informed consent forms?
   A. Provide useful headlines.
   B. Use "you" and other pronouns to speak to the reader.
   C. Use short sections and sentences.
   D. Use italics liberally.

2. When the UMDNJ IRB staff conduct a pre-review of submissions, which of the following are the main points they will want to focus on?
   A. Was everything from the application complete?
   B. Was every question answered or not applicable?
   C. Was every required attachment included?
   D. All of the above

3. What percentage of parents of children with cancer reported that survey questions were more distressing than they were useful?
   A. Nearly 20%
   B. Nearly 30%
   C. More than%

4. True or false: Genomic researchers surveyed believed it was important to establish a standardized approach to genomic incidental findings before data collection and to outline this approach in the informed consent.
   A. True
   B. False

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