IRB ADVISOR

Your Practical Guide To Institutional Review Board Management

AHC Media LLC

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A fine mess: IRBs overloaded with unnecessary adverse event reports

Federal guidance fails to clear confusion

It's a constant refrain: IRBs are overburdened by adverse event reports (AERs) — many of which are unnecessarily reported to them and which they often lack the information to properly analyze.

This problem has been the subject of journal articles, conferences and two government guidance documents — one in 2007 by the Office of Human Research Protections (OHRP) and one released earlier this year by the Food and Drug Administration (FDA).

So why does the problem persist? Those who have studied it have a range of different answers. Some say the government entities released conflicting advice that muddies the waters and causes defensive over-reporting. The Infectious Diseases Society of America recently appealed to the FDA to ask for clarifications to its guidance.

Others blame IRBs, saying they ask for unnecessary reports, leery of trusting others to determine when AERs are a sign of a larger problem with a study. **Stephanie Zafonte**, MSN, RN, CCRP, CQA, RAC, nurse researcher for the Department of Defense's Defense Centers of Excellence, says she encountered that attitude at a conference a few years ago.

"We were sitting in a session on serious adverse events and there were between six and 10 IRB chairs in the room," Zafonte says. "And they were just militant that they needed to see not only the serious (AERs) that are possibly related to the research, but even the other ones.

"In order to respond to the pressure of liability, you have IRBs who are choosing to say 'I need to see more; I need to review it.'"

Role for data monitoring panels

But **Marjorie Speers**, PhD, executive director of the Association for the Accreditation of Human Research Protection Programs, says that in the past several years, the IRBs with whom she works have become more comfortable having adverse event reports reviewed by data moni-

toring committees and sponsors' coordinating centers.

Speers says IRBs realize that viewing every report is not only time-consuming but ultimately unproductive, because IRBs usually lack the information necessary to know whether an individual event is part of a larger trend, particularly in a multisite study.

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She says the problem is that sponsors and investigators continue to send those reports to IRBs.

"I think where the change needs to occur is with sponsors taking more responsibility for reviewing adverse events, because they can review across all of the trial sites," Speers says. "When you send all of those adverse event reports to the IRBs, essentially you're asking the IRBs to be data monitoring committees and the IRBs can't do that."

Both Zafonte and Speers say it's going to take more time and an industry-wide shift in thinking to solve the problem. Zafonte says it also requires the cooperation of various government entities, which have different reporting requirements.

"Why can't we agree on a centralized document that says this is what we're going to do with information that changes the risk-benefit ratio?" Zafonte asks. "Until you do that, I don't know how the IRBs can really do anything that's going to impact change at that level to alleviate this burden."

Guidance critiqued

Guidance released by OHRP and the FDA was supposed to help clarify matters. But some think they've confused things further.

When the Infectious Diseases Society of America released a report earlier this summer on reducing regulatory burden *(See* IRB Advisor, *September 2009, p. 103.)*, the group singled out adverse event reporting for criticism and recommendations. In September, the IDSA wrote to the FDA, asking for changes to its guidance.

The IDSA noted that both the FDA and OHRP have agreed that reporting offsite adverse events to IRBs in a multisite study is wasteful and fails to protect subjects. But it said the FDA guidance still suggests reporting certain individual offsite events — those indicating an increase in frequency of AERs, for example, or a single instance of an uncommon event that is strongly associated with drug exposure — to all the IRBs in a multisite study.

"In contrast, the OHRP guidance document suggests that local IRBs only be notified if there is a finding by the sponsor or the independent data monitoring committee regarding patient safety," the IDSA states in its letter to FDA. "IDSA supports OHRP's approach towards adverse event reporting and analysis for multicenter clinical trials and recommends that FDA

issue guidance consistent with OHRP's guidance."

William Burman, MD, an associate professor in the Division of Infectious Diseases at the University of Colorado at Denver, was the lead author on the IDSA's report. He says IRBs should have no role in the review of offsite adverse event reports and that the OHRP guidance makes this clear.

"I wish the FDA would have said something that simple," he says.

Speers says OHRP's guidance is more direct than the FDA's. "The OHRP guidance says any unanticipated event that's related to the research and involves risks to subjects or others is an unanticipated problem involving risks to subjects or others and has to be reported."

But she says the FDA guidance is helpful in that it assigns sponsors the responsibility for reviewing adverse events and determining whether they are unanticipated problems involving risks to subjects or others.

"The reason the FDA says that is that it is the sponsor or the data coordinating committee that has the information about the adverse events across all the trial sites," she says.

Zafonte notes that OHRP and the FDA use different nomenclature in describing events and have different reporting timelines.

"It absolutely is a mess," she says. "And if you bring in the Department of Defense — which is a big funder of clinical research — their regulations are again different. It really is something that should be addressed in a centralized guidance."

In the meantime, local IRBs can try to cut through the noise of so many adverse event reports by asking the sponsors of studies for summaries of adverse events that have occurred and for summaries of unanticipated adverse events that involved increased risk and are related to the study, Speers says.

"That is the practice that we encourage IRBs to use when they are conducting the continuing review of a study," she says. "That way, the local IRB can conduct a much more informative review of the trial."

Zafonte asks IRBs to consider the reporting they're requesting of investigators with an eye toward whether it is really useful information that helps protect participants.

"Step outside the box and start looking at your overall processes and programs," she says. "Take a hard look: Are they effective and efficient? Are your policies meeting the regulation or are they overkill? And are they really making a difference in the risks for your participants?"

[Editor's note: The OHRP's "Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events" is available at: http://www.hhs.gov/ohrp/policy/AdvEvntGuid.htm.]

The FDA's "Guidance for Investigators, Sponsors and IRBs: Adverse Event Reporting to IRBs — Improving Human Subject Protection" is available at: http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126572.pdf. ■

Study finds adverse reports inaccurate in cancer trials

Review of medical records shows inconsistencies

A study of serious adverse event reports (AERs) sent to an IRB from clinical trials of a breakthrough cancer drug revealed they were too often incomplete and inaccurate when compared to the original medical records from which they were taken.

The study, published earlier this year in the journal Clinical Cancer Research, suggests that incomplete reporting of serious adverse events could result in delays in identifying safety issues, which is especially problematic for cancer drugs on an accelerated approval path.[1]

But the advice from one of the study's authors for alleviating the problem may sound familiar: Stop sending a load of AERs to IRBs, and use specialized data centers for analysis. The result may be fewer, but more complete reports.

"Every IRB is basically getting inundated with a bunch of low-quality reports," says **Charles L. Bennett**, MD, PhD, MPP, co-director of the cancer control program at Northwestern University's Robert H. Lurie Comprehensive Cancer Center in Chicago." And then we try to ask each IRB to make a determination based on 40% completeness. That's just a bad way of going about it. We're not sure why the mandate is to have a huge quantity (of reports) at low quality. We should think about a system where we minimize the quantity and maximize the quality."

Comparing IRB reports to med charts

Bennett's group looked at serious adverse

drug events reported to a single IRB from 14 clinical trials of the cancer drug imatinib, which received accelerated FDA approval in 2001 for the treatment of chronic myelogenous leukemia. The study looked at Phase I, II and III trials of the drug alone or in combination with other agents. Only 73 days elapsed from initial submission to the FDA to marketing approval, underlining the importance of identifying serious adverse drug events as quickly as possible.

In looking retrospectively at the serious AERs submitted to the IRB, Bennett's team also reviewed research charts and electronic patient medical records corresponding to each event.

The team created a standardized case report form that collected information about four types of events associated with the drug: infections, fractures, congestive heart failure/pulmonary effusion and pulmonary edema. For each event submitted to the IRB, the team used two versions of this case report form — one using data submitted to the IRB and the other based on the medical records of the same event.

A total of 115 separate imatinib-related serious adverse event reports were reviewed in this way. Researchers looked at how complete the information was — did it include all the information needed by the IRB to assess the seriousness of the event? When compared, the forms drawn from IRB reports were 40% complete, vs. 95% complete for forms based on the medical records.

In looking at the accuracy of the reports, in only 19% of the events did the IRB reports match the medical records completely.

But the review of the medical records revealed something even more striking: 22 potential serious adverse events that had not been reported to the IRB.

Bennett says it's important to note that the institution in question was a National Cancer Institute-designated comprehensive cancer center, one of only three sites where FDA licensing trials for imatinib were conducted.

"We picked a site where this drug was developed," Bennett says. "So if there was anybody who was going to know about the drug and what happens with it, it's this place. It's the best of the best and when we went to the best of the best, and we got what we got, it was really surprising."

Looking for stronger signals

Bennett suggests two possible reasons for the poor reporting of serious adverse events in the trials.

He says those reporting them are specialists in the disease being studied, but not necessarily in the types of events associated with the drug.

"Secondly, the adverse event reports are often filled out by staff people, research assistants," Bennett says. "They may not understand the clinical nuances of these adverse events and by not understanding the nuances, they may not do a good job of describing them."

He says the underreporting and lack of completeness can lead to a situation where early, subtle signals of a problem aren't strong enough to be noticed.

"You won't find anything with 40% completeness and 15% underreporting unless it's something really obvious."

In coming up with a system that better analyzes adverse events, Bennett suggests that NCI-designated centers could be set up to track trials, employing specialists who are formally trained in adverse events.

"We're setting up a program now where we do adverse event reporting at centers with medical toxicologists — they're going to do the work. They're not going to do every site in the country, but we have 38 big sites."

While there may be fewer reports, Bennett says, they will be much more complete and signals of problems will be clearer.

"At the end of the day, the goal is to make sure these clinical trials are providing appropriate and good information," Bennett says. "It's not important to get a huge quantity of these reports, it's most important to get the quality of these reports."

Reference

1. Dorr DA, Burdon R, West DP et al. Quality of Reporting of Serious Adverse Drug Events to an Institutional Review Board: A Case Study with the Novel Cancer Agent Imatinib Mesylate. *Clin Cancer Res* 2009 Jun 1;15(11):3850-5. ■

Pregnant pause: Psych research and moms-to-be

Group looking for solutions to thorny ethical issues

Handling mental illness during pregnancy can be a double-edged sword. Because of the

scarcity of clinical research with pregnant women, there are no FDA-approved medications for treating such illnesses. On the other hand, untreated mental illness in pregnancy carries its own risks. For example, depression has been associated with fetal growth problems, preterm birth and longer stays in the NICU; untreated schizophrenia can lead to preterm birth, low birth weight and a greater chance of postnatal death.[1]

Doctors and patients urgently need the most complete information about the effectiveness of treatment alternatives, says **Anna Brandon**, PhD, assistant professor of psychiatry at the University of Texas Southwestern Medical School in Dallas. But because of ethical concerns, it has been difficult to conduct randomized controlled trials with pregnant participants.

Brandon says she became aware of the constraints on research while conducting a study involving non-medication therapy with pregnant women and their husbands. "Then I became acquainted with a bioethicist and a few other folks and we started putting our heads together and saying, 'This is a problem that really hasn't been addressed,'" she says.

That group plans to conduct surveys on the attitudes of IRBs, researchers, community practitioners and pregnant women regarding research. Their aim is the development of guidelines that would address the ethical issues surrounding mental health research during pregnancy.

"Psychiatric issues are different than other health issues in pregnancy, because they impair the mental and emotional functioning of the mom, which has secondary effects on the family, the fetus and the baby," Brandon says. "So we feel it has to be viewed through a different framework than, say, looking at gestational diabetes, or gestational hypertension, which are serious illnesses but don't necessarily impair the woman's functioning with her baby."

Vague guidance

Brandon says existing guidance for research with pregnant women is vague and often doesn't address the unique problems posed by mental illness. For example, the usual concerns about informed consent may not take into account a woman who is severely depressed and has difficulty with decision-making.

Brandon notes that the role of fathers, as outlined in human subjects protection regulations, isn't well fleshed out. "As it stands now, the pregnant woman is given the option to bring the father into play if he's competent, if he's involved and if she identifies him. But it's still fairly contingent on the information she presents the researcher or the obstetrician about the father."

Concerns that pit the health of the fetus against the health of the mother can actually endanger the fetus more, she says. "Because if the mother suicides, the fetus dies, too."

The absence of more clear-cut guidelines leaves IRBs understandably wary about proceeding with such studies, even when medication is not involved. Often, Brandon says, they refuse to allow a control group with minimal intervention, despite the fact that there are few proven therapies for pregnant women with mental illness.

Brandon says one colleague wanted to randomize some women to a psycho-education group and others to an exercise intervention. The IRB would not allow that randomization unless the psycho-education group also did a low-intensity exercise regimen.

"So now what (the researcher) has is one condition where women walk on a treadmill with their heart-rate being monitored and another condition where women stretch. And we're not going to know whether the active intervention is really working."

Brandon says her group is not suggesting a full-scale rush to do randomized-controlled trials with depressed pregnant women who may be assigned to no treatment. What she does suggest is a discussion to look at instances in which a no-treatment condition may be appropriate, with safeguards.

"We need to start sorting some of these things out and come up with a framework for balancing the decision," she says. "Until we have that, we have IRB administrators, perinatal investigators, funding agencies, patients, community clinicians — we have everyone operating under this cloud of 'We're afraid to do anything unless it's appropriate' and yet there's no standard for what's appropriate."

A five-year process

In an effort to achieve this goal, Brandon and her colleagues — psychiatrist **Geetha Shivakumar**, medical anthropologist and public policy expert Simon Lee, medical historian Stephen Inrig and bioethicist John Sadler — are setting out to learn about the concerns and attitudes of perinatal researchers and IRBs.

Brandon says her group, which is currently funded by the National Institute of Mental Health, hopes to get another grant that would allow it to take the conversation to other sites, and to include practitioners and participants as well, with the eventual goal of collaborative guidelines.

"I think guidelines are most effective when everyone feels like they've had a hand in crafting them," she says. "Our idea is that they would get put forth collaboratively and then adopted by (the American College of Obstetricians and Gynecologists), adopted by the IRBs, adopted by research investigators who all feel they had a part in crafting them."

The process of creating guidelines could take five years or longer, in order to ensure that all the stakeholders are included, she says. "I'm sure a set of guidelines isn't going to answer all the questions or solve the dilemma, but I think the dialogue has to be opened up."

As part of that dialogue, Brandon encourages IRB members who have ideas, questions or "provocative comments" to contact her at Anna.Brandon@UTSouthwestern.edu.

Reference

1. Brandon AR, Shivakumar G, Lee SL, et al. Ethical issues in perinatal mental health research. *Curr Opin Psychiatry* 2009 Sep 2 [Epub ahead of print] ■

New IRB requirements rankle researchers

Consent documents, increased training requirements

Requirements that IRBs see as minor or routine may have serious consequences for a practice-based research network (PBRN), says **Barbara P. Yawn**, MD, MSc, FAAFP, director of research at Olmstead Medical Center, Rochester, MN.

For example, Yawn recently detailed her experience with a PBRN study in which participating IRBs rolled out new requirements on continuing review that added time, hassle and significant expense to the project.[1]

One result from the experience: At least two of the sites in the network informed Yawn that they would never again participate in such a study. In describing the problems that emerged during this research, she hopes to encourage IRBs to consider the impact of some of their requirements of PBRN studies.

"IRBs should think about the implications of their decisions and whether it really does improve patient safety or if it just presents a bigger burden to the researchers," Yawn says.

The Translating Research Into Practice for Post Partum Depression study was a randomized controlled trial testing the effectiveness of a postnatal depression-screening tool used in community family medicine offices. The investigators signed up 31 practices in 20 states, and obtained approval from 19 IRBs, including the American Academy of Family Physicians IRB, which served as the central IRB for 13 unaffiliated practices.

Women were recruited into the study at between five and 12 weeks postpartum. Women either received standard care or were randomized to receive the screening tool; those who showed signs of depression were treated. The study conducted interviews at six and 12 months to determine levels of depression, comfort with parenting and quality of partner relationships.

The three-year study is still continuing.

At the beginning of the second year, Yawn says her team encountered problems with 13 IRBs. All had required a special site-specific approval stamp for consent forms at the beginning of the study, and on continuing review, all now required that the consent forms be replaced with a new form, unchanged in content but bearing an updated date stamp.

New participants could not be consented on the old forms, and sites had to wait for the new forms to be sent to the IRBs and returned with the updated stamp. Yawn says recruitment had to be shut down at these sites for several weeks due to a time lag in getting the new date-stamped forms back from the IRBs.

"Several times, we had people we couldn't enroll because there was no properly dated form that an IRB had approved," she says. "That's a terrible thing to do in the middle of a study — to say we're just going to stop enrollment for a month or six weeks until the IRB gets around to putting a stamped date on it."

A worrisome trend

On the second annual review, five more IRBs now required the date stamp procedure.

"I worry that it is a trend," Yawn says. "IRB personnel and representatives go to meetings and talk to each other and suddenly, 'Oh yeah,

let's do this.' Or somehow the word gets around that this is a requirement. Because several of the IRBs that we talked to said it was a federal requirement."

Yawn says her group reviewed the requirements of the Office of Human Research Protections and could find no requirement regarding dated approval stamps on consent forms.

Nor could they find a regulatory basis for another requirement that IRBs began imposing in the second year of the study: increasing the frequency of research staff training to every two years.

"Usually the training is good for three years — that's still a little bit of a pain but at least three years is pretty reasonable," she says. "And suddenly now it's two years. We asked, could you explain why, especially when nothing has changed in the human subjects rules? They just wanted them to take the same tests over again and read the same material."

Yawn says that at some practice sites, only a few people needed an up-to-date training certificate. But at others, the number could go much higher, particularly if the IRB had strict requirements about who had to take the training.

"One IRB said everybody who had anything to do with these women had to be up-to-date, and that could be 50 or 60 professionals in a practice."

In order to accommodate the rules, the research team created a slide show to review the highlights of the material in an expedited way.

The effect of both of the new rules added considerable expense to the final study, Yawn says. The group paid for overnight shipping of consent documents to get them in the hands of researchers faster, and paid some practices to compensate them for the increased staff time spent on human subjects protection training.

She estimates that the cost of all of the changes could reach $30,000.

"There's not that kind of money in practice-based research studies to allow us to cover those costs."

Just as importantly, Yawn says, adding to the burden of the small practices participating makes it less likely that the practices will attempt other studies, stymieing future practice-based research.

She says the IRB requirements that hampered her study may be appropriate for more risky research, but not for the low-risk studies PBRNs usually conduct.

Yawn would like to see IRBs sit down at national conferences with PBRN researchers to understand the impact of regulations on the research and come up with solutions.

"If you can't have dialogue it's very hard to change anything," she says.

Reference

1. Yawn BP, Graham DG, Bertram SL, et al. Practice-Based Research Network Studies and Institutional Review Boards: Two New Issues. *J Am Board Fam Med* 2009 Jul-Aug;22(4):453-60. ■

IRB cuts 35 days from protocol turnaround

Pre-review processes help a lot

When a Yale University research facilitation office first looked at improving protocol review turnaround time in late 2007, the time from intake, through development, to IRB submission and approval averaged 80 days.

Now the same process takes 45 days.

The IRB and research office have cut 35 days from that timeline through efficiencies in both the office and the IRB processes, says **Stacey N. Scirocco**, associate director at the Yale Center for Clinical Investigation and administrator for the office of research services at Yale University in New Haven, CT.

About three-and-a-half years ago, the university opened the Yale Center for Clinical Investigation, which houses the office of research services, with funding from its Clinical and Translational Science Award (CTSA). The CTSA is funded by the National Center for Research Resources of the National Institutes of Health (NIH).

One of the functions of the office of research services is to facilitate regulatory compliance and help investigators prepare protocols for submission to Yale's human investigation committee, which is what the IRB is called.

A central mission was to reduce redundancies between its internal protocol review process, inherited from the former General Clinical Research Centers (GCRC) structure, and the IRB's review, and this was done through a lean analysis process, Scirocco says.

"We also looked at the system to see if there was any wasted time in the timeline," she explains. "And we wanted to make sure there was value added in every process."

For instance, some of the existing internal protocol review processes were streamlined, so that functions are performed in tandem instead of end to end.

In all, the research services office shaved 17 days on average from the protocol review and development process, Scirocco adds.

"Part of how we did that was by providing a high level of service to investigators and maintaining a good level of communication so as to minimize delays in all parts of the process," she says.

Need for speed, accuracy

A major goal is to give investigators some of their time back by providing quality services that are fast and efficient, she adds.

Other strategies the research services office has employed include maintaining a collaborative relationship and good communication with the IRB so the IRB will know which protocols will be coming their way, she says.

"We have close ties and a trusting relationship with the IRB," Scirocco says. "We communicate almost daily and work together to coordinate the timeline for review."

"Also, once we send a protocol to the IRB, our employees in the office of research services (ORS) are on the line to see it through to approval," she adds.

In a recent example, ORS and IRB staff worked cohesively for a compassionate use protocol to provide a drug to patients when the standard treatment drug became unavailable. Through a high level of effort and communication, they were able to go through the process to IRB approval in 25 days, Scirocco says.

Another change that helped to reduce the overall submission to approval timeline involved changing which protocols would need review by the internal, science, and safety committee.

This committee conducts a review of protocols requesting to use Yale Center for Clinical Investigation research clinic space before they are sent to the IRB. To avoid duplicating IRB activities, the research office changed the SSC review requirement to only high risk and some moderate risk studies, Scirocco says.

"The science and safety committee has the additional expertise to look at these protocols in depth, and once they've requested changes to it and approved it, the protocol is in better shape and typically addresses most questions the IRB might have," she says.

Yale's IRB reduced its protocol approval time by 18 days, partly through the adoption of an electronic institutional review board module that streamlined their IRB office functions, Scirocco says.

"The electronic system enables online entry and submission of human research protocols to the Yale institutional review boards and other oversight authorities charged with the protection of Yale's research volunteers, and it gives investigators one place to go for finding their protocol's status," she adds.

This in turn reduces IRB staff and reviewer time.

Also, the IRB has administrative reviewers check out newly-submitted protocols to help get them in good shape before they go through the review process, Scirocco says.

So between the office of research services, work, and the IRB office's work, investigators receive ample help with designing their protocols, improving them, and making any IRB-requested revisions, she adds.

"We stay with the investigator along the IRB review process," Scirocco says. "Our investigators are very happy with the changes."

The research review office's assistance can be requested voluntarily, and since it was begun, the volume has increased by 100%, Scirocco says.

Early 2009 estimates show an even greater increase, she adds.

"We have many new investigators using our services, and we feel we're helping to facilitate clinical research," she says. ■

AHRQ provides free tool to help with informed consent

Sample forms, language are included

IRBs and researchers now have a new toolkit that will make it easier to ensure proper informed consent has been obtained from subjects with limited literacy and proficiency in English.

The Agency for Healthcare Research and Quality (AHRQ) toolkit is available online as an open-source document and can be downloaded and disseminated without written authorization.

While it's developed for minimal risk research, the toolkit can be adapted for any research study, says **Cindy Brach**, MPP, senior health policy

researcher in the center of delivery, organization, and markets for AHRQ in Rockville, MD.

"The development of the toolkit is an outgrowth of another research project," Brach explains. "We were looking at the impact of HIPAA on health services research."

Health services researchers said they felt there was the potential for HIPAA to have a chilling effect on research. Researchers felt that potential subjects, particularly those with limited literacy and English proficiency, would be confused when studies required both informed consent and HIPAA consent, Brach says.

"Not only individuals with limited literacy and English proficiency benefit from simplified forms," she adds. "Research shows that even well-educated individuals frequently find consent and authorization forms incomprehensible."

So Brach and co-researcher Michael Paasche-Orlow developed sample forms, including forms that combine obtaining informed consent and HIPAA authorization.

"Some IRBs may have some initial discomfort about combining informed consent and HIPAA authorization forms, and think they are not allowed to do that," Brach says.

"But you are allowed to have combination forms," she adds. "You have to meet both human subjects requirements and HIPAA requirements, but it doesn't mean you need two separate forms and two separate processes."

Brach and co-researchers entered into a lengthy discussion with both the Office of Human Rights Protection at the Department of Health and Human Services (HHS) and with the Office of Civil Rights on the HIPAA issues, to make sure they found this consistent with human subjects and HIPAA regulations, Brach says.

"The forms were tested with target populations in both English and Spanish, and changes were made to improve it," Brach says. "Of course, forms are only tools for conducting consent and authorization discussions."

The toolkit chiefly is about how to improve the process of obtaining informed consent and authorization, Brach notes.

"One of the most important features of the toolkit is a method of verifying potential subjects, understanding the so-called 'Teach-back' method," she says. **(See excerpt on teach-back method, p. 130.)**

The toolkit is 80-plus pages. The sample forms and tools and references take up all but the first 15 pages.

One of the sections that will particularly be of interest to IRBs is on improving informed consent and authorization. Strategies include the following:

Raise Awareness

- Share examples of readable informed HIPAA consent and authorization documents that have been used successfully by other IRBs;
- Educate IRB members, institutional lawyers, and researchers on regulatory requirements;
- Identify sections of documents that are not required and distract from the primary purpose of the documents;
- Host experts on health literacy, informed consent, and research ethics to educate the research and IRB communities;
- Conduct interactive workshops and online training on writing understandable documents and how to conduct the informed consent and authorization discussion;
- Create a forum to discuss ways to identify and address liability concerns outside the informed consent and authorization process;

Identify Mechanisms for Change

- Post AHRQ sample documents on your IRB Web site and encourage researchers to use them as templates;
- Establish a mechanism that researchers can easily use to test their documents and processes with potential research subjects;
- Create a community advisory board to review template language at your institution;
- Have the IRB office sponsor catered training, education, and feedback meetings that include topics related to evaluation and integration of methods to promote comprehension;
- Significantly increase the training and participation of IRB members who can represent the perspectives of research subjects, who are unaffiliated with the institution, and who are not scientists.

"IRBs have the ultimate say in what's acceptable in terms of informed consent and authorization, so we'd like them to do two things," Brach notes. "First, they should educate their researchers about both the process of obtaining consent and authorization and the forms."

The IRBs should give investigators and their institutions the clear message that the informed consent and HIPAA documents are not to manage legal liability, Brach says.

"They're to educate potential subjects about research," she says.

Second, IRB members need to accept that a

simplified informed consent form will meet all requirements, Brach says.

"Things do not have to be complex and legalistic in order to satisfy regulations," she adds. "In fact, the regulations require the use of language that is understandable to potential research subjects." **(See table on how to meet regulatory requirements, below.)**

Making these changes entails changing an institution's culture, Brach notes.

"I don't want to give the impression that the toolkit is a silver bullet," she says. "Shifting institutional culture is a huge undertaking."

AHRQ is adding to funding announcements a statement that clearly communicates the expectation to the research community that they will inform potential subjects about human subjects research and HIPAA issues in a way they can understand, she adds.

One method of affecting change is to hire staff trained in plain language to write informed consent documents, Brach says.

AHRQ toolkit provides examples of 'teach-back'

Teach-back helps ensure understanding

"The AHRQ Informed Consent and Authorization Toolkit for Minimal Risk Research," published in September, 2009, provides very concrete examples of ways investigators and IRBs can improve the informed consent process.

Here are the toolkit's examples of how to use teach-back to ensure potential participants fully understand what they've heard and read during informed consent:

Teach-Back: Part I

Start with phrases such as:

• "I want to make sure we have the same understanding about this research. Can you tell me what this project is about in your own words?"

• "It's my job to explain things clearly. To make sure I did this I would like to hear your understanding of the research project."

Teach-Back: Part 2

Make sure that the potential research subject has understood all the important elements of the study. Allow the potential research subject to consult the document when answering the questions. The purpose is to check comprehension, not memory. Listen for simple parroting; probe further if a potential research subject uses technical terms. Ask open-ended questions, such as the following:

• **Goal of the Research and Protocol**

- "Tell me in your own words about the goal of this research and what will happen to you if you agree to be in this study?"

• **Benefit and Compensation**

- "What do you expect to gain by taking part in this research?"

• **Risks**

- "What risks would you be taking if you joined this study?"

• **Voluntariness**

- "Will anything happen to you if you refuse to be in this study?

• **Discontinuing Participation**

- "What should you do if you agree to be in the study but later change your mind?"
- "What will happen to information already gathered if you change your mind?"

• **Privacy**

- "Who will be able to see the information you give us?"

• **Contact Information**

- "What should you do if you have any questions or concerns about this study?"

Teach-Back: Part 3

Correct any misinformation until potential research subjects indicate that they have understood by correctly answering all the questions. Make clear that the need to repeat is due to the complexity of the material rather than the "fault" of the potential research subject.

For example, you could say, "Let's talk about the purpose of the study again because I think I may have not explained it clearly."

• Potential research subjects should not be enrolled if they cannot comprehend the study protocol, despite repeated attempts to explain the details.

• Document completion of the teach-back process on the Researcher's Certification of Consent and Authorization.

• Ask the potential research subjects what questions they still have.

- Avoid yes or no questions, such as, "Do you have any questions?" and "Do you understand?"
- Ask instead, "What questions do you still have?" and "What would you like to hear more about?"

• If the potential research subject signs the document (unless written consent and authorization have been waived), make a copy for him or her. Alternatively, have two copies and give one to the subject.

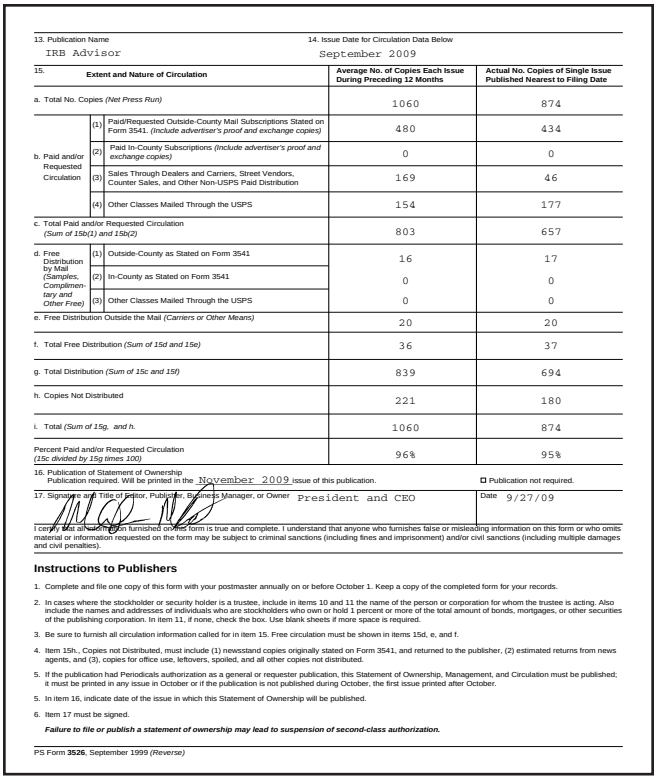
- Emphasize that subjects should keep the document since it has important phone numbers in case they have any questions or concerns later.

• Complete and sign the Researcher's Certification of Consent and Authorization.

"Some find having a centralized staff handle IRB authorization and consent forms an efficient way to encourage these changes," Brach says. "But training researchers in conducting the informed consent and authorization discussion also has to be part of the plan."

Reference

1. Agency for Healthcare Research and Quality. The AHRQ Informed Consent and Authorization Toolkit for Minimal Risk Research. Rockville, MD. September, 2009: Available at: www.ahrq.gov/fund/informedconsent/. ■



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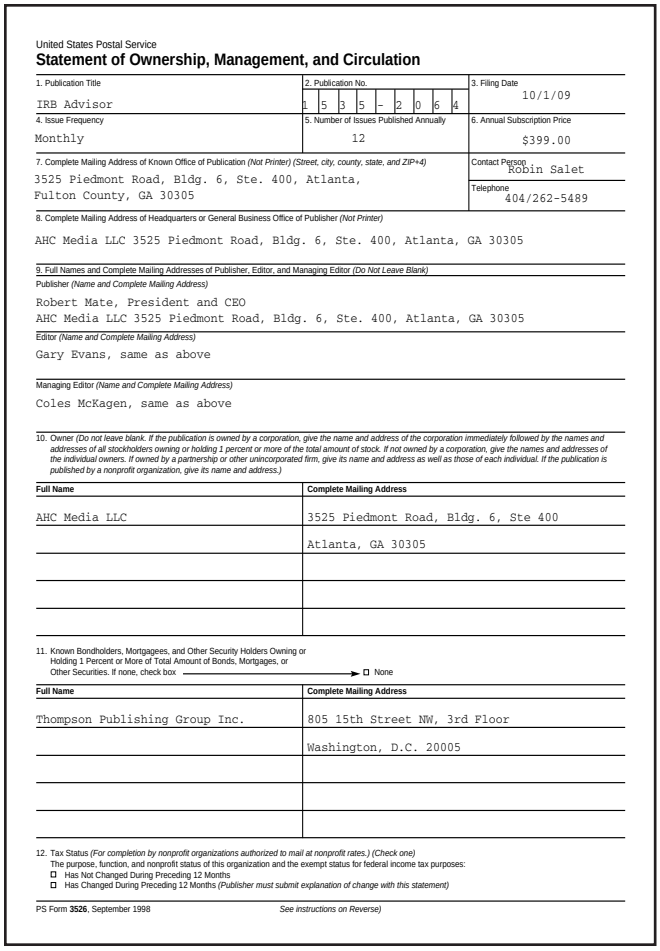

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CNE/CME Objectives

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 medical education program by reading the issue, using the provided references for further research, and studying the questions at the end of the issue.

Participants should select what they believe to be the correct answers, then refer to the list of correct answers to test their knowledge. To clarify confusion surrounding any questions answered incorrectly, please consult the source material.

After completing this activity at the end of each semester, you must complete the evaluation form provided and return it in the reply envelope provided to receive a letter of credit. When your evaluation is received, a letter of credit will be mailed to you.

COMING IN FUTURE MONTHS

■ A model consent form for phase I cancer studies

■ Novel ways to provide informed consent

■ Has the economy dampened IRB staff salaries? *IRB Advisor* survey seeks answers

■ Pediatric biobanks: What to do about consent when the donors grow up?

■ Conducting research with state-mandated blood samples from newborns

CNE/CME *questions*

17. True or False: The Infectious Disease Society of America wants the FDA to change its guidance on reporting adverse events to say that IRBs would only notified of offsite events if there is a finding by the sponsor or the independent data monitoring committee regarding patient safety.

18. A study of reporting during a clinical trial of a cancer drug revealed 22 potential serious adverse events:
    A. that prompted immediate IRB action
    B. that were not reported to the IRB
    C. related to drug dosing
    D. that the FDA investigated

19. A Yale University research services office helped cut the timeline from protocol intake through IRB submission and approval from 80 to 45 days by employing which of the following strategies?
    A. Existing internal protocol review processes were streamlined
    B. The research services office provided protocol assistance services to investigators and maintained good communication with the IRB to minimize delays
    C. The IRB changed to an electronic IRB module
    D. All of the above

20. Which of the following is not a good strategy for raising awareness of the informed consent process?
    A. Educate IRB members, institutional lawyers, and researchers on regulatory requirements
    B. Identify sections of documents that are not required and distract from the primary purpose of the documents
    C. Provide subjects with the verbatim forms sent to investigators by research sponsors
    D. Host experts on health literacy, informed consent, and research ethics to educate the research and IRB communities

Answers: 17. True; 18. B; 19. D; 20. C.