IRB ADVISOR

*Your Practical Guide To Institutional Review Board Management*

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## IN THIS ISSUE



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# Put 'painful details' into IRB documentation, experts say

*Meeting minutes can be weak spot*

IRBs often do a good, or at least adequate, job of maintaining required documentation for studies they review, but there are several key documentation areas in which many IRBs need to improve, according to experts.

Two of these involve communication with clinical investigators and clinical research staff and preparing minutes of IRB meetings, says **Jean Toth-Allen**, PhD, biophysicist in the Office of Good Clinical Practice, Office of the Commissioner, Food and Drug Administration (FDA) in Silver Springs, MD.

"The minutes are a window into how an IRB functions," Toth-Allen says.

IRBs also need to maintain thoroughly documented policies and procedures, suggests Glen D. Drew, MS, JD, health policy analyst with the Office for Human Research Protections (OHRP) in Rockville, MD.

"The policies and procedures are the guidebook, map, and owners' operating manual for the IRB," Drew says.

"'Painful detail' is the phrase we use," Drew says. "Having things spelled out reduces the uncertainty of what to do in any given situation. It promotes fairness, reduces uncertainty, and allows transparency so investigators can see the policies and procedures and know what the rules are."

Toth-Allen and Drew offer these suggestions for how IRBs can improve their documentation from prior to when an IRB meets to review a protocol to after the decision is made:

- **Make communication with research staff more precise and clear:** IRBs are required to notify investigators in writing about their decision to approve or disapprove a research protocol, and they should outline the modifications necessary for approval. Or, when the study is declined, the IRB must include a rationale and give the investigator an opportunity to respond.

The most essential detail in communications with research staff is the date of the IRB's approval of a protocol. This is the date from which the protocol's continuing review is set, Toth-Allen says.

For studies with high risk, IRBs might choose to hold a continuing review at a shorter interval than one year. If this is the case, communication with research staff should make it clear when the continuing review will be held, she adds.

"Also, tell investigators what the principal investigator's responsibilities are," she says. "The more the IRB can put in writing what is expected from the investigator, the better."

Here are examples of other items that need to be included in investigator communications:

– Describe what the investigator should send to the IRB between continuing reviews,

– Identify the date and precise copy of the approved informed consent document,

– List continuing review conditions,

– Explain what it is the IRB wants the investigator to do next,

– Reiterate the regulations that apply to this particular study.

• **Write policies and procedures (P&Ps) that provide transparency for regulatory auditors,** IRB staff, and researchers: Investigators should be able to look at the policies and procedures and understand what the rules are and how communications between the IRB and research staff will be handled.

"The policies and procedures are living documents," Drew says. "If you encounter a situation that's not described in your P&Ps, then the IRB can create a new P&P that will ensure the situation is handled the same way in the future."

Or if the research institution made a mistake, the P&Ps will outline how future actions will prevent this error.

Here are some examples of items to include in the P&Ps:

– How the IRB appoints members,

– Information the IRB needs from researchers,

– Development of submission forms,

– Policies on how submissions are handled and who receives these,

– How to log in protocol submissions,

– Roles of IRB staff and their authority with regard to sending submissions back to investigators,

– How reviews are assigned – whether they are rotated or whether there's a primary reviewer system,

– Defining the meeting schedule for the committee,

– Describing what is done if there's a need for an ad hoc or emergency meeting about a study,

– Outlining how the institution handles and conducts IRB meetings,

– Show what type of vote is required, how the

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quorum might be comprised, and whether it's a simple majority needed to approve a protocol or some other proportion,

– Explain when it is permissible for IRB members to abstain from voting,

– Address whether the IRB chair votes or breaks tie votes or has no votes,

– When consultants are used and how they're hired and paid,

– Set policy on whether investigators are invited or allowed in meetings,

– How IRB handles continuing reviews and notifying investigators of such reviews,

– How it is handled if studies fail to apply for a continuing review,

– Giving a description of the types of conflicts of interest that would result in an IRB member recusing himself/herself from voting.

"What does an IRB consider a conflict of interest?" Drew says. "It's good to have the policies and procedures define what would constitute a conflict of interest."

The P&Ps should include details about financial conflicts of interest, professional COIs, and fraternal COIs.

"If you're a drinking buddy of the investigator, do you have a conflict?" Drew asks. "There are some issues that can be hard to define because if you define conflicts of interest too expansively, you won't have any members on your committee."

• **Put explanations and detailed discussions in IRB meeting minutes:** Unfortunately, FDA auditors sometimes find that IRB meeting minutes lack some essential details, Toth-Allen says.

For example, IRB meeting minutes from the review of a study involving a vulnerable population might not even mention that the study has a vulnerable population, she adds.

"If a study involves children, they have to record in their minutes how they looked at various required aspects during the review," Toth-Allen explains. "They should not just say, 'We reviewed it and approved it.'"

"If a sponsor thinks their device study presents a nonsignificant risk to subjects, then the sponsor is not required to send an application for the IDE to the FDA, but the sponsor still needs IRB approval," Toth-Allen says.

"It is therefore essential that meeting minutes include a summary of the IRB's discussion regarding the risk of any device study submitted to it by the sponsor as a non-significant risk study," she explains. "If the IRB agrees it presents a non-significant risk and approves the study, it is considered to have an IDE [investigational device exemption]."

When the IRB agrees with the sponsor that the study poses nonsignificant risk, the sponsor can proceed with the IDE based on the IRB's approval of the study.

"It's very important the IRB makes the correct decision and then say why they made it," Toth-Allen says. "We've found that many IRBs don't know how to make a decision about the device study's risk, and we've tried to educate them about it."

Other details that should be spelled out in the meeting minutes are as follows:

– Attendance,

– IRB actions,

– Votes, including the number of people who voted for, against, and who abstained,

– Listing IRB members who did not participate because of conflicts of interest,

– Details about why changes were required or research was not approved,

– A summary of the meeting's discussion of any controverted issues and how these were resolved,

– Waiver of informed consent and other IC issues,

– Discussion of a study's population, specifying any vulnerable population issues.

IRBs also should take certain actions to ensure all of their documentation are protected and adequately stored.

"Make sure your system is protected and your documentation is accessible," Toth-Allen says. "Documents need to be in place, and IRBs could very well be inspected by the FDA or OHRP." ■

# Best practices to engender a more balanced IRB input

*Using mentors, education, trial periods help*

IRBs should work to create balanced IRB discussions and ensure cooperation between members of diverse backgrounds.

Regulations require IRBs to include an unaffiliated and non-scientific member on the board. But it's up to the IRB and its leadership to make certain these members are encouraged to speak and fulfill their role as a voice for research participants.

"There are a number of different ways IRBs can engage the nonscientist, unaffiliated member," says **Robert V. Bienvenu, II**, PhD, CIP, public health analyst for the Office for Human Research Protections (OHRP) of Rockville, MD.

For people who don't have a science background and might never have served on an IRB before, being plopped into that environment can be challenging and intimidating," Bienvenu says.

Sometimes IRBs are imbalanced in their review discussions, notes **Tanya Carrillo**, CIP, CIM, clinical research leader, Primary Care Ultrasound Vscan, of GE Healthcare of Wauwatosa, WI. Carrillo and Bienvenu spoke about the dynamics of an IRB meeting at the Public Responsibility in Medicine & Research (PRIM&R) Advancing Ethical Research Conference, held Dec. 6-8, 2010, in San Diego, CA.

Physician scientists might dominate the IRB discussion and non-scientist members may tend to hold back because of a lack of knowledge about some aspects of the research under review.

"Being plopped in that environment can be challenging and intimidating," Bienvenu says.

Bienvenu and Carrillo offer these suggestions for how an IRB might facilitate a more cooperative environment in which every voice is heard:

• **Educate all IRB members when they are brought on board:** "Some non-scientific members don't speak up because they don't understand what their role is," Carrillo says. "Helping them understand their role is very important."

Having IRB members train in human subjects research protection history and regulations will help community members gain a perspective about how important the non-scientist voice is.

Training could include the institution's internal policies and procedures, as well.

Also, IRBs might provide ongoing member education with articles on ethical and regulatory issues or special populations, Carrillo suggests.

"When IRB members are sent out for training in different events, it should include unaffiliated members," Bienvenu says.

• **Pair scientists and non-scientists in reviews:** Another strategy is to use a primary reviewer system where scientist members and non-scientist members are paired to work together on a protocol, Carrillo suggests.

"They can present their comments before the IRB engages in deliberations on the protocol, and that obligates them to speak," she says.

Some IRBs that use this strategy have the scientist member serve as the primary reviewer with the non-scientist member serving as a secondary reviewer, Bienvenu says.

"There are issues a non-scientist member might recognize and weigh more heavily," he adds. "So they're a good combination."

• **Assign a mentor to new members:** For new unaffiliated and non-scientist members, it might be especially important to have mentors available to answer their questions and help them , Bienvenu suggests.

"This gives them someone to talk with and orients them to what's going on, guiding them, and helping them assimilate their acculturation to the IRB," he adds.

• **Have IRB chairs empower quieter members:** IRB chairs are responsible for noting when one member is disrupting or dominating the review conversation and subtly changing the focus.

"The chair has a leading responsibility to ensure that all voices are allowed to be heard in the IRB's deliberation," Bienvenu says.

"But there's also an obligation on the part of members to speak up," he adds. "If they've analyzed the protocol and seen issues that need to be raised, they certainly should bring those to the table, and the chair can facilitate that process."

The chair could keep the conversation moving, bringing in new voices to a discussion.

"The chair might call on someone who looks like he or she has something to say," Carrillo says. "I've seen that work effectively."

Chairs can help end a monologue by validating the speaker's perspective and moving the conversation to the next stage, Bienvenu says.

"A good chair should be able to recognize the appropriate thing to do," he adds.

• **Have support staff sit in different places around the table:** In Carrillo's experience, IRB support staff can help facilitate conversation by strategically placing different members around the table. This way they will notice when someone whispers a comment to a neighbor, and the staff member can prompt the person to speak up to the entire group.

"Having an IRB support staff person near them often gave them more inclination to speak up," she adds. "I'd sit next to newer IRB members for the first few months so if they had questions during the review I could answer those questions for them."

• **Give non-scientist, unaffiliated members the task of reviewing informed consent:** Some IRBs choose to divide duties this way and it has the advantage giving an important role to these members.

"So when the IRB comes to the point in the protocol review where they focus on the informed consent document, that person would report on it in the role of a reviewer of informed consent docu-

ment," Bienvenu says.

The disadvantage is it might pigeon-hole community members when their role should be the same as other members – to look at the entire study protocol, Carrillo says.

• **Put new members through a trial period:** "The first three months could be a trial run," Carrillo says. "New members might not be given protocols to review, but they could review items."

Experienced IRB members could help them learn how to analyze their IRB packet, answer their questions, point out the way they would handle a review of a particular protocol item, and provide them with a checklist, she adds.

After three months, if the new IRB member still is uncomfortable with reviewing studies, the IRB could give him or her some extra time.

"The key point is for an IRB meeting to include all parties in the discussion," Bienvenu says.

"IRBs have the full spectrum of people who are very outspoken and engage with no hesitancy whatsoever to people who are quieter and may need some encouragement," he adds. "A good chair would ensure there's a full discussion, and that all perspectives are engaged." ■

# Use researcher feedback to improve IRB turnaround

*NIH project helped identify best practices*

IRBs can learn a great deal from each other. One research institution's hard-earned lesson and resolution can be another organization's best practices.

This is one of the philosophies underlying the Roadmap for Medical Research, which was launched eight years ago by the National Institutes of Health (NIH) of Bethesda, MD. The Clinical Translational and Science Awards (CTSA) programs emerged from this. CTSA brings together research leaders at major academic research institutions. Together they tackle clinical research (CR) issues facing the industry, including the problem of IRBs having slow turnaround times on protocol reviews.

Under CTSA, there was an IRB task force that brought together major research institutions, including the University of Michigan and Yale University.

"Under the task force, we spoke with several colleagues about the things they do in their institutions to collect metrics and turn around the time from when investigators first dream of the idea of a study or receive a protocol proposal from a sponsor to when the first patient is enrolled," says **Kathleen T. Uscinski**, MBA, CIP, director of the office of human research protection in the office of research administration at Yale University in New Haven, CT. Uscinski was a co-chair of the task force.

The NIH recognizes that the cost of conducting research is high and benefits gained from research can take way too long to reach the bedside.

"So we wanted to know if there was a way to do things more efficiently from the point of administrative tasks, writing proposals, negotiating contracts, processing grants, reviewing a proposal by an IRB," Uscinski says.

The task force collected data from 37 research institutions and reviewed protocols that were reviewed by a fully-convened IRB.

"We looked at data from institutions that had inordinately long times and from those that did it very fast," Uscinski says. "A good group of them hovered around the middle group, and a few did it exceptionally well."

After considerable analysis, the task force identified time points that everyone had in common. They found that while IRBs shared these time points, the length of time it took them to process information varied greatly, from six turnaround days to 90 turnaround days.

With a second NIH award, Yale worked with the Mayo Clinic of Rochester, MN, to further explore best practices. Together the two institutions came up with six key initiatives for improving efficiency in the review process.

"The one I'm most active on is IRB processing," Uscinski says. "We compared similar categories of research and identified the ones that were more efficient."

Uscinski spent several hours speaking with Mayo Clinic's IRB staff, discussing their quality improvement initiatives that helped reduce turnaround time.

"Mayo has a series of projects where the staff and IRB evaluate work flow and business handling," she says.

They identified ways to make processes more efficient, focusing first on the low-hanging fruit. The goal was to find projects that could produce quick results at Yale.

"I asked them: 'Of all the process improvements you did, what gave you the most significant decrease in turnaround time?'" Uscinski recalls. "They said they were focused on their application

form."

The application form can cause delays if investigators misunderstand its questions or leave items blank. This will result in the IRB sending the application back to investigators, requesting revisions, clarifications, and more information.

"So one of the most time-consuming obstacles to getting the protocol approved was the back-and-forth with the investigator," Uscinski explains. "What we found out from further analysis is it's not necessarily the processes and unnecessary steps, but the quality of the applications that is causing the IRB to ask investigators for further clarification."

The problem is in how the information is written and provided to the IRB.

One potential solution to this is to engage focus groups to look at the application form and make suggestions for changes. Then it can be rewritten in a way that makes it more understandable to the research community.

A less resource-intensive quality improvement project would be to identify the sections on the application that cause the most problems for investigators and the IRB and show those questions to researchers, asking them for input on how these could be improved, Uscinski suggests.

This process can result in helping the IRB look at the application form in a different light.

"This is where the IRB staff says, 'Oh wow! I didn't know that question was so far off,'" she says.

For example, the IRB might ask investigators for information about who is approaching potential research subjects and whether there is a primary health care provider involved, Uscinski says.

"Those details and responses are critical to the IRB as it considers the protection of human subjects," she says.

For instance, if a researcher approaches someone who is a sibling of a person with a medical condition and it's because of this connection that the person is asked to participate, the sibling might feel violated, as though there was a breach of privacy, she says.

"These are the types of things an IRB evaluates," Uscinski says.

And perhaps the investigator has the most ethical approach for contacting potential study participants, but this approach is not fully communicated in the IRB application. It takes back-and-forth communication to pull that information.

"So what we wanted to do is write the application so the principal investigator fully understands what is expected, minimizing the amount of rewrites and communication between the investigator and IRB," Uscinski says. "What we're trying to do is make sure the PI writes a good solid protocol the first time it's submitted to the IRB so the IRB has the necessary information and can approve the research more quickly." ■

# Multiple IRBs, HIPAA concerns hamper project

*Researcher wants IRBs to talk to one another, seek expertise on health services research*

When a group of researchers set out to study effective ways to screen HMO members for substance abuse problems and to refer them for treatment, they expected that sensitive topic would require strict confidentiality measures.

They didn't expect nearly seven years of starts and stops due to concerns raised by three different IRBs that eventually handled the protocol. After securing approvals from two of them, they restarted the study in 2006, only to discontinue it in 2009, convinced that the IRB-mandated restrictions made the final project unworkable.

"By the time all of this was resolved and we restarted it and started looking at the data that was coming in, we realized that we had a protocol we were testing that could never be used in practice," says **Lisaann Gittner**, PhD, a research associate at Case Western University's School of Nursing in Cleveland, OH.

Her group's experience is detailed in a recent article in the Journal of Medical Ethics.

Gittner says she believes the problems that her team encountered point to gaps in federal regulations and IRB expertise in two areas – multisite IRB review and the field of health services research.

"The federal regulations are written for biomedical research," she says. "Many IRBs are biomedically focused. Some large academic institutions also have social/behavioral IRBs, but health services research isn't in either one of those categories."

She'd like to see the federal regulations changed to address those issues, and barring that, have IRBs make such changes on their own, to prevent problems like the ones she encountered.

## Choosing screening candidates

Gittner's group began in 1999 with an idea to test a process that would screen people for alcohol problems or other substance abuse. Typically, a person is not asked detailed questions about substance abuse by his or her own regular physician, but only encounters them in the emergency department after an accident.

"These screens really should be done by a PCP (primary care physician) during a routine physical or regular visit," she says. "But PCPs are reticent to do it. They're managing three to four other problems and then to add this kind of sensitive discussion on top of it in a 20-minute visit? It's probably not going to happen."

Gittner's group proposed looking at utilization patterns within an HMO's membership, and picking out people who might benefit from alcohol screening. These people, along with a control group picked at random, would be invited by mail to participate in a phone survey that queried them about their use of alcohol and drugs.

It was an opt-out study, meaning that people would receive phone calls to initiate the survey unless they returned a form saying they didn't want to participate. During the phone call, a screener explained the survey to the participant, gained verbal consent and then transferred the participant to an automated system that delivered standard screening questions ("How many alcoholic beverages do you consume in a week?" "Has anyone ever told you that you have an alcohol problem?" etc.).

A participant could withdraw from the survey at any time by hanging up. At the end, those identified as requiring further help were offered three choices: Direct feedback from the automated system, screening results sent to a nurse manager for follow-up or results sent directly to the person's PCP.

## A tale of three IRBs

Gittner says she knew the subject was a sensitive one and the study would require safeguards of participants' confidentiality. But she was unprepared for the problems she encountered at the first HMO the group approached in 1999. Its IRB tabled the protocol and sent it to the organization's legal department. Because of legal concerns, changes were requested, but after two revisions, the HMO withdrew its agreement to partner with the group.

The group approached two other IRBs over the next year, and encountered similar problems – issues raised by legal departments about confidentiality concerns, and requests for revisions.

The two IRBs' requirements were often contradictory, she says.

"They were asking for different things and then absolutely refusing to budge," Gittner says. "Whereas one IRB would say, 'You have to do B,' the other IRB would say, 'If you do B, we will not approve this.' And we couldn't get them to sit down to talk together."

Eventually, the researchers obtained approval from both IRBs, but just as data collection was about to begin, HIPAA Privacy Rule took effect in 2003, causing one IRB to raise fresh concerns.

"Nobody had understood what would happen with HIPAA, and so when it did happen, everybody erred on the side of caution," Gittner says.

In order to proceed with the study, she says researchers had to add a number of burdensome requirements. One was a Certificate of Confidentiality from the National Institutes of Health; the study was suspended for eight months until it could be obtained.

In addition to sending a consent form through the mail to participants, the initial phone screener had to read the form to the participant when calling him or her. The screener also had to read a HIPAA privacy notice.

This led to a problem retaining participants during the phone survey.

"By the time we finished re-reading the entire consent form to them – reading them all this stuff that we had already sent them in the mail – and then you hooked them up to the five-minute computer screening, many of them hung up," Gittner says. "At that point, it was already 20 minutes into the phone call."

A 2005 continuing review by one IRB noted the low response rates and the IRB agreed to a shortened informed consent. Getting final approval for the new consent and other minor changes took another six months. This took the group to January 2006 for the restart of the study.

## Talking together, seeking experts

Gittner says that many of the group's problems could have been solved if the IRBs involved had been willing to work things out together, in person or by letter, without requiring the researcher to shuttle back and forth between them.

She also believes that IRBs don't understand health services studies, in which the emphasis is not on how an intervention affects an individual patient, but how a change to a health services system affects the use of the system.

"In systems-level research, we're going to do something to the process that you interact with. And what happens to you is not as important as to where does the process go," Gittner says. "How many of these (substance abuse) screens are getting done? How many people are going into treatment? Are we effective in screening the right kinds of people?"

She recommends that when an IRB is presented with a proposal for this type of research, it should bring in a health services researcher as an outside expert.

Ultimately, Gittner would like to see federal regulations requiring such expert opinions, along with regulations that would designate one IRB to take the lead in a multisite study.

In the meantime, she says, experiences such as hers are causing health services researchers to rethink proceeding with studies based on concerns about IRB review.

"A lot of people are now not doing certain streams of research because they think this is going to happen to them or because something like this did start to happen to them and they pulled back," Gittner says.

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# Study: subjects want chemical test results

*When and how to release biomarker results is complicated issue for researchers, IRBs*

Whether to return research results to participants is a thorny question, particularly in the field of environmental health research, which tests subjects' blood for substances such as metals or chemicals.

In the case of some environmental toxins such as lead and mercury, there is substantial evidence of their effects on the human body. So when reporting on lead levels, for example, a researcher can explain the impact of that level and recommend strategies for reducing exposure.

But the effects of many other chemicals on human health are currently unclear. Is it ethical to reveal a high level of a contaminant when scientists don't know the effect of it or how to minimize or treat exposure? Would it cause unnecessary anxiety to the participant to have this information?

The National Bioethics Advisory Commission has recommended disclosing individual test results to participants only when the findings are scientifically valid, the results have significant implications for a person's health and there's a readily available way to mitigate a person's exposure or treat any ill effects.

But when asked, participants say they want to know more, even in situations where the information is incomplete, says **Stephen E. Wilson**, MD, MSc, FACP, a volunteer assistant professor of internal medicine and pediatrics at the University of Cincinnati, OH.

## 'People want to know'

Wilson was an investigator in the Health Outcomes and Measures of the Environment (HOME) Study, a federally funded study that monitored environmental toxicants such as lead, mercury, pesticides, PCBs and tobacco smoke in pregnant women and children.

As part of that study, Wilson asked mothers hypothetically what their preferences would be for receiving information about pesticide residues, explaining to them that the health effects of low levels of exposure to these residues are currently unknown. Of the 343 mothers surveyed, 340 said that they would want to know their own levels and 342 would want to know those of their children.

"Based on our data it's clear – people want to know," Wilson says. "Even when you tell them you're not clear what these results mean, people clearly want to know and have a right to know."

The study also asked mothers about how they preferred that the information be relayed to them. Wilson says the survey provides some useful guidelines for researchers and IRBs contemplating disclosure of research results.

Overall, 69 percent of women said they would prefer to receive the results in a letter, with a phone number included that they could call if they had questions. However, women who had had no college education were more likely than others to ask for a face-to-face con-

sultation instead with the investigator or with a woman's own doctor. The more college experience a woman had, the more likely she was to prefer a letter.

"I was surprised that so many people didn't want to receive the results in person," Wilson says.

While the survey didn't ask women the reasons for their preference, he noted that the group overall was somewhat more affluent and educated than average, and may be concerned about finding the time for an office visit. Wilson and his colleagues also suggest that more educated women may feel more confident in their ability to decipher the numbers themselves.

The women also were asked their preference regarding the format in which the information about the exposure should be given to them. The simplest format would be to provide an actual blood level statistic, with no comparisons to anyone in the study or national ranges for that chemical. The most complex would provide the same number, but would compare it to those in the study or national numbers. Sixty-nine percent wanted to receive the more complex information. But again, less educated mothers were more likely to ask for less complex formats.

### Providing experts

Wilson says given the different preferences of different groups, researchers should be prepared to disclose results to participants in different ways.

"They should be specifically asking study participants how they want those results presented," he says.

And even if information is disclosed in letters, there should be experts ready to discuss the results with participants who have questions. For example, Wilson says, when his group disclosed results of tests that measured exposure to second-hand cigarette smoke, he got calls from some mothers concerned about their children's findings.

He explained to them that because the group being studied was less likely to live with smokers, a child in a mid-percentile in the study would still be in a fairly low percentile for the population as a whole.

And he says mothers trying to look up information about the results themselves on the Internet may find inaccurate and even frightening information. Wilson notes that a national network of Pediatric Environmental Health Specialty Units (PEHSUs) has developed scientifically validated fact sheets about various environmental exposures to help explain results to patients.

Wilson says it's important to keep studying what patients want to know about research results and how they want researchers to communicate with them.

"As we continue to see a growth in the use of biomarkers, it doesn't seem as if the ethics have caught up with the technology at this point," he says. "We need to study this more rigorously."

REFERENCE

Wilson SE, Baker ER, Leonard AC, et al. Understanding preferences for disclosure of individual biomarker results among participants in a longitudinal birth cohort. *J Med Ethics* 2010 Dec;36(12):736-40. ■

# Depression can affect patient's understanding of informed consent

*Frequent repetition of consent information can help bolster patients' ability to give consent*

Patients hospitalized with depression may need extra help understanding the informed consent process for research, due to cognitive impairments that affect their ability to understand information being given to them about a study.

That's one finding from a study of 31 inpatients with depression recruited from a hospital psychiatric unit. The group took a battery of tests that measured various indicators related to decision-making.

The tests revealed that 15 of the participants (48 percent) had at least mildly impaired neurocognitive function. Results were published in a recent issue of the journal *Psychiatry Research*.

The study also had subjects listen to information about a fictional informed consent disclosure for a drug trial and tested them on their understanding of the information. Those indentified as impaired had correspondingly lower scores than the unimpaired inpatients and a control group.

"(The study) shows that inpatients are more vulnerable, not only to cognitive impairments, but corresponding with those impairments, they are

also more vulnerable to decision-making problems," says **Michael Basso**, PhD, ABPP-CN, a neuropsychologist, director of clinical training and associate professor of psychology at the University of Tulsa, OK.

Basso says literature over the past 15 years has shown this cognitive impairment occurs in a significant subset of depressive patients. But he says the issue hasn't received wide attention in research circles.

"I think as people come to realize that some people with depression have considerable cognitive impairment associated with the illness, they will recognize that this is a potentially vulnerable population," he says. "I don't think there's a lot of attention given to it right now."

## Cueing, repetition help

In addition to identifying deficits in some of the inpatients studied, Basso's group also looked at different ways of bolstering their ability to understand and remember informed consent disclosures. They tested three different methods of relaying information to the patients:

– Reading the informed consent aloud to the participant, without interruptions, while the participant follows along with his or her own copy;

– Reading the consent aloud in small successive steps, with pauses to ask questions of the participant. If they fail to demonstrate understanding, they're asked more specific questions;

– Providing the information in small steps, with frequent cueing and repetition of the details.

With each group – the control group, unimpaired inpatients and impaired inpatients – the uninterrupted disclosure produced the lowest scores of understanding, while repetition and cueing produced the highest scores. Basso suggests that providing repetition and cueing in the informed consent disclosure might be a way to compensate for the cognitive problems experienced by some inpatient depressives while still allowing them to participate in research.

"You could try to mitigate the weaknesses by using repetition and cueing and then re-evaluate the person, to see if they're continuing to display significant compromise," Basso says. "If they are, then it may be worthwhile to look at obtaining a proxy to provide consent – a family member or close friend, who's got some sort of official representation authority such as a health care power of attorney."

Basso stresses the people identified as having this cognitive weakness had more severe forms of depression. He says studies of outpatients with depression have shown that only a very small minority have any kind of reasoning or decision-making problems.

And he says that even impaired patients still may be capable of making a decision to participate in research.

"Just because somebody has an illness or syndrome that is associated with compromised mental status, it doesn't mean there's decisional incapacity," Basso says. "Even among schizophrenics or people with Alzheimer's disease, (research has) shown that a significant number of those people are capable of giving informed consent."

## IRB mindfulness

He suggests that IRBs should be mindful of this potential vulnerability when presented with a study that looks at inpatient depressives.

"Without wanting to put an undue burden on the researchers, I think it would be prudent to implement some means of determining whether the patient has neuropsychological impairment," Basso says. "If so, such a patient would be worthy of more careful scrutiny as far as their capacity to consent."

Basso says he himself has had little difficulty getting his research approved by IRBs – in part because he only does minimal risk research. But he also believes that IRBs may fail to recognize the potential decision-making difficulties that severely depressed patients may have.

He says there's a need for more research into other aspects of decision-making that may be compromised by depression – the willingness of patients to take risks, for example, their ability to express a choice or their potential for therapeutic misconception.

Basso also is looking at other groups that might benefit from the repetition and cueing approach to informed consent, including patients with multiple sclerosis who have cognitive impairment. He published another study last year that showed similar improvements in understanding using the repetition and cueing approach.

## REFERENCE

Ghormley C, Basso M, Candlis P, et al. Neuropsychological impairment corresponds with poor understanding of informed consent disclosures in persons diagnosed with major depression. *Psychiatry Res* 2010 Nov 30 (Epub). ■

# IRB News

## OHRP posts final guidance on IRB continuing review

The Office for Human Research Protections (OHRP) has posted its updated and finalized guidance on the IRB continuing review process.

Titled, "Guidance on IRB Continuing Review of Research," the guidance document supersedes OHRP's January 15, 2007 guidance entitled "Guidance on Continuing Review." The guidance document finalizes the draft guidance that was made available for public comment through a notice in the Federal Register on November 6, 2009 (74 FR 57487). OHRP officials say the public comments submitted on the draft document were very helpful as the office finalized the document.

To see the final guidance document, visit the OHRP website at http://www.hhs.gov/ohrp/policy/continuingreview2010.html or http://www.hhs.gov/ohrp/policy/continuingreview2010.pdf. The Federal Register notice announcing the availability of this new guidance document can be found at http://edocket.access.gpo.gov/2010/2010-30198.htm or http://edocket.access.gpo.gov/2010/pdf/2010-30198.pdf.

## Guidance on IRB approval of research with conditions is finalized

The Office for Human Research Protections (OHRP) has posted on its website a finalized guidance document entitled, "Guidance on IRB Approval of Research with Conditions." The guidance document provides OHRP's first formal guidance on this topic.

The guidance document finalizes the draft guidance that was made available for public comment through a notice in the Federal Register on November 6, 2009 (74 FR 57486).

The finalized guidance document is available on the OHRP website at http://www.hhs.gov/ohrp/policy/conditionalapproval2010.html or URLs http://www.hhs.gov/ohrp/policy/conditionalapproval2010.pdf. The Federal Register notice announcing the availability of this new guidance document can be found at http://edocket.access.gpo.gov/2010/2010-30201.htm or http://edocket.access.gpo.gov/2010/pdf/2010-30201.pdf. ■

## 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

■ Do questions about troubling topics upset subjects?

■ Re-engineer your human subjects education

■ Achieving harmony: Overcoming IRB obstacles to international trials

■ Try this best practice for internal reviews

■ Make the grade! Get the highest score on sponsor grade cards

■ Improve your corrective action responses

■ Tips for handling FDA audits

# CNE/CME QUESTIONS

5. Which of the following is a good example of what IRBs should include in their policies and procedures?
A. How the IRB appoints members
B. Policies on how submissions are handled and who receives these
C. How reviews are assigned – whether they are rotated or whether there's a primary reviewer system
D. All of the above

6. Who typically has the role of facilitating an IRB review discussion that includes all voices and fosters a cooperative environment?
A. IRB director
B. IRB staff taking minutes
C. IRB chair
D. Research administrator

7. How many of the mothers involved in an environmental biomarker study said they wanted to receive information about levels of pesticides in their own or their children's blood?
a. Less than a quarter
b. Almost half
c. Nearly 75 percent
d. Nearly all

8. What strategy helped depressive patients with neurocognitive impairments better understand informed consent disclosures?
a. Presenting informed consent on a computer screen
b. Providing frequent cues and repetition of information
c. Speaking very slowly
d. None of the above

**Answers: 5. D; 6. C; 7. D; 8. B**