IRB ADVISOR

Your Practical Guide To Institutional Review Board Management

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IN THIS ISSUE

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OHRP & FDA issue new guidance on transferring approved projects

Agencies answer industry's questions

As the hurricane season picks up and the potential for other types of emergencies continues, a research institution might find it necessary to transfer its IRB-approved research to another institution. Or an IRB simply might need to transfer a single study for a variety of reasons. Federal guidance on how to handle these contingencies now is available.

The Office for Human Research Protections (OHRP) and the Food and Drug Administration (FDA) recently issued separate, but collaborative, draft guidance on how research institutions can make this type of transfer as safely and efficiently as possible. IRBs and research institutions can make comments on the proposed guidance through Aug. 13, 2012.

OHRP's draft guidance states the goal is to assure continuous IRB oversight with no lapse in either IRB approval or the protection of human subjects.

"Therefore, we recommend that the original IRB work closely with the investigator, the sponsor, if any, and the receiving IRB, as appropriate, throughout the transfer process to ensure an orderly transition and continued protection of human subjects," the OHRP draft guidance says.

The same language appears in the FDA's draft guidance, which also emphasizes effective communication among the IRBs, sponsors, investigators, FDA, and others.

OHRP developed the draft guidance after receiving numerous questions from the research community about this subject, says **Irene Stith-Coleman**, PhD, director of OHRP's division of policy and assurances.

"I remember back to Hurricane Katrina when there were institutions that were underwater," she explains. "Some of the questions the research institutions had involved what to do about the ongoing need for IRBs in situations like that."

Another event that might trigger a transfer of a research approval is when an institution is involved in a multisite study for the first time and

it doesn't have the resources to create its own IRB, Stith-Coleman says.

Crises can arise and institutions want answers, which is why the guidance was written, she adds.

According to the OHRP draft guidance, the IRBs and institutions involved in a research project transfer should have written procedures and create a written agreement between the original and receiving IRBs, if appropriate. The agreement should address these eight actions:

1. Identify those studies for which IRB oversight is being transferred.
2. Ensure the availability and retention of pertinent records.
3. Establish an effective date for transfer of oversight, including records, for the research project.
4. Conduct a review of the study or studies by the receiving IRB, where appropriate, before it accepts responsibility for the study or studies.
5. Confirm or establish the date for the next continuing review.
6. Determine whether the consent form needs to be revised.
7. Notify the key parties.
8. Address IRB regulatory issues.

IRB authorization agreements have been in place for years, Stith-Coleman notes.

"These are agreements institutions use when they want that grant money but don't have the resources to create their own IRB and have to rely on an external IRB," she explains.

The draft guidance provides a framework for what agreements should address.

The OHRP and FDA guidance offer suggestions that could make these agreements more consistent across the human subjects protection industry.

"Relationships will be different with each IRB, but some of the considerations will be the same," Stith-Coleman says. "Based on OHRP's experience with IRB authorization or reliance agreements, we believe that IRBs are accustomed to entering into written agreements documenting their interactions with other IRBs.

"By clarifying the regulatory requirements and considerations involved in the transfer of a research study to another IRB or another institution, we believe this guidance will help institutions and investigators avoid unnecessary disruptions in their research activities," she adds. "In addition, the guidance should assist institutions that have expressed confusion about how to carry out such transfers and allow them to run their IRB systems in a more flexible way and lead to better protections to subjects."

For instance, OHRP recommends that the original and receiving IRBs have a clear understanding of which studies are being transferred, the risk posed by the studies being transferred, and the circumstances leading to the transfer.

Also, OHRP advises IRBs receiving a transferred

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Editorial Questions

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research project to obtain copies of pertinent records, including sample consent forms, investigator's brochure, IRB meeting minutes, grant proposal and research protocol. And both the original IRB and the receiving IRB should maintain adequate records regarding the research projects affected by the transfer, including records of any written agreement between the two IRBs, the OHRP draft guidance says.

OHRP's draft guidance notes that federal regulations do not require the receiving IRB to review the project prior to the next continuing review date established by the original IRB, but OHRP suggests that this type of review often is and should be done.

"Depending on the circumstances of the transfer and characteristics of the specific research project, the receiving IRB may decide to undertake an initial review or a continuing review [either by the convened IRB or under an expedited review procedure, if appropriate]," OHRP's guidance states.

It's important research institutions make comments on the guidance, Stith-Coleman says.

"I'm anxious for them to start putting some comments in there for the public record so if we have overlooked something we'll hear about it," she adds.

OHRP's draft guidance document was developed and reviewed internally before it was shared with FDA and other HHS agencies for review and comment, Stith-Coleman says.

"It was also shared with non-HHS Common Rule departments and agencies for review and comment," she says. "The draft guidance was then revised by OHRP in response to comments from federal agencies, and OHRP actively worked with FDA to harmonize both documents during the development of its draft document."

For more information about the new draft guidance, visit the OHRP website at http://www.hhs.gov/ohrp/newsroom/rfc/transferdraftdoc.html. ■

Cultural issues should be addressed in IC process

Use IC to tell a story

When research involves an international or multicultural population, there can be informed consent issues that no one anticipates — not even the best-informed IRB.

For example, HIV researchers in Africa discovered that research participants were anxious about having their blood drawn for a totally unexpected reason: "The women didn't know their bodies continually made new blood, and they thought, 'I have a certain amount of blood, and if you keep taking blood out of me it will hurt,'" says **Cynthia Woodsong**, PhD, director of social and behavioral sciences at the International Partnership for Microbicides in Silver Spring, MD.

Woodsong learned of this misconception from a staff member in Rwanda.

"So I developed information, a page and illustrated sheet that can be made into a poster that talks about some of the blood issues," Woodsong says.

The illustrated sheet shows a woman character named Rose who stands next to a five-liter jug, which represents how much blood is in the human body.

"Then we show someone holding a vial, showing how much blood we'll be taking," Woodsong says.

There also is a picture of a sun and moon on the page. These represent day and night, the amount of time it takes for the body to replenish the vial of blood that is drawn.

The educational sheet is as much for the informed consent counselor as it is for the research participant, Woodsong notes.

"The illustrations help the counselor remember what to say," she says.

Researchers guided by their IRBs could anticipate informed consent problems related to cultural misconceptions if they take a few extra steps when developing the informed consent process.

A first step would be to ask local and service delivery staff for assistance. They might know which misconceptions or beliefs are prevalent and could read over informed consent materials to see if there are any potential problems.

"Spend time with local practitioners and talk to local staff," Woodsong suggests. "I've interviewed hospital and clinic staff and community leaders not associated with a trial."

Also, IRBs and investigators should view the informed consent process as a way to tell a story.

"What's on paper is the legal information, but it doesn't tell the story of what a person is getting into, like what you would tell a friend," she says. "The key point is to not develop your materials

from sitting in your office, but from active collaboration with people in the communities and research centers."

The research center staff has a much better idea of what participants will understand. Community advisory boards and other stakeholders also can be helpful with identifying what participants need to hear, and they can be a good sounding board for new informed consent approaches, she adds.

For instance, Woodsong developed illustrated instructions on how women participants in a trial using vaginal rings should insert the rings. She used an illustration of the character Rose putting her ring in to show how it is done. When Woodsong shared this illustration with community advisors, she learned that the illustration gave women and men the wrong impression.

"When the community looked at the picture of her putting the ring in they thought she could be playing with herself," Woodsong says. "It could be misconstrued."

So the drawing was changed to one with Rose holding the ring in her hand, and that drawing was included on an informed consent flip chart that accompanies the IC form.

When researchers obtain feedback from local experts, they should make sure the experts know what they did with the feedback, Woodsong advises.

"Say to them: 'Here's what you told us; here's what we did with what you told us,'" she suggests. "We often take from them and don't give back."

Woodsong's story approach includes an enrollment IC assessment checklist that can be adapted for different types of trials.

"What I've trained staff to do is have the woman tell a story of the trial," Woodsong says. "You ask her, 'If a friend of yours was thinking about joining the study, what are all of the things you think she should know?'"

Then the staff member goes through the checklist as the woman speaks, making sure she understands each important item. If the woman/participant forgets to mention something important, the informed consent staff member can ask about that specific item.

Here are the eight open-ended questions/statements on the enrollment informed consent comprehension checklist:

- Please describe your understanding of the purpose of the study.
- What do you understand that you are being asked to do in this study?
- What do you understand about possible risks that might happen as a result of being in the study?
- What will happen if you do not join the study?
- Please tell me about the different groups of women in the study.
- How will the information about you be protected?
- What are the benefits to you of participating in this study?
- What should you do if you have any questions about what is happening in the study?

The checklist also has a column for comments and a section with checkboxes related to the outcome, such as whether the subject demonstrated comprehension of all required points and decided to enroll in the study.

Woodsong developed the checklist while at Family Health International of Research Triangle Park, NC, where she previously was employed as a scientist. Since then, it's been used by several international research organizations and on various trials.

Another IC checklist is for ongoing IC comprehension, and it can be adapted to assess comprehension of specific clinical trial procedures. For example, the HPTN 035 ongoing IC comprehension checklist has these questions/statements, in addition to some included in the enrollment checklist:

- Please tell me about the different groups of women in the study.
- If a woman always uses study gel, but does not use condoms, can she get HIV?
- What should women do if they have a question about the study or a problem related to being in the study?
- Are women who join the study allowed to leave the study?

When researchers and IRBs follow the "tell a story" approach to informed consent they will find that consent forms can be shortened by several pages, Woodsong notes.

Instead of using a visit-oriented format that details exactly which procedures will be done at each visit, often repeating items, the story approach simplifies the information: "When you come in every month for a visit we'll give you a blood test; when you have a blood test, we'll do the following things," she explains.

The approach can be further simplified with wording that lists how many blood tests and

other procedures will be conducted throughout the study.

"They tell the story about what is of concern to the participants, rather than following a clinical protocol," Woodsong says.

IRBs can sometimes hinder this simplification process by asking for more information, she says.

From the IRB's perspective the informed consent form always is too long, but there also are things that weren't explained well enough, Woodsong says.

"We're told to keep it brief, but get in all of the important points," she adds.

It would facilitate a better informed consent process if IRBs would interpret the regulations regarding informed consent more generously, Woodsong says.

"IRBs are following their interpretation of the letter of the law and not keeping abreast of developments and innovations and research ethics," she says. "So the people living and breathing and debating research ethics may move on to simpler or more generous interpretations of things." ■

BEST PRACTICES SPOTLIGHT

Pre-review process results in faster IRB review process

All submissions are pre-reviewed

IRBs could improve and expedite their review process by hiring someone to pre-review submissions, an expert suggests.

About five years ago, the IRB at the University of Tennessee Graduate School of Medicine (UTGSM) in Knoxville added an office position of research associate, says **Reni Leslie**, CIM, IRB associate director. The IRB has 15 members plus four alternates and mainly handles biomedical studies.

"Our research associate pre-reviews all prospective submissions, whether they are minimal risk, expedited review or full review," Leslie says. "She looks at the applications, works with investigators, and whether or not we need more clarification it is worked out before it's submitted for IRB approval."

This pre-review process speeds up the entire approval process, especially if submissions go to the full board, she adds.

"In general, very rarely do we have a study that is deferred," Leslie says. "Studies usually receive provisional approval pending minor corrections or clarifications that can be reviewed and approved by the chair."

The IRB meets monthly to conduct full board reviews of all studies with more than minimal risk. The board also has an expedited agenda containing annual reviews, expedited reviews, revisions, safety reports, and other items that need to be processed and approved, she says.

With the pre-review process, the hold-ups common at other IRBs almost never happen at UTGSM.

"I hear horror stories of different IRBs, where it can take a month or two to get approval, and that rarely happens here," Leslie says. "Our policy states the approval process takes five to 10 working days after we receive the submission and review the application."

The IRB's research associate's chief role is to assist investigators with submissions. She often works with first-time investigators who have basic questions about completing the submission forms.

"She also does random audits on protocols," Leslie adds.

Here's how the pre-review process works:

• **Submission calendar:** "We send out a submission calendar in October/November for the following year," Leslie says. "It gives the date and deadlines for greater-than-minimal-risk studies that receive full board pre-review, the date it's due to be processed, the date of the IRB meeting, and it's sent out to all IRB members."

• **Electronic submissions:** Investigators submit protocol applications electronically, and the research associate reviews the application and informed consent.

"She makes sure all questions are answered and if something was left out, or if she has an issue with the language in the consent form, she works with the investigator or coordinator," Leslie explains. "When everything is completed and she's satisfied with the explanation, she signs off on it, and this is usually a week to 10 days before it's due to be submitted to the IRB."

Most questions can be answered prior to the IRB meeting, she notes.

The UTGSM website contains a checklist for

IRB applications. It lists items that are part of the IRB submission process, including any or all of these:

- application signed by all study personnel and the principal investigator's department chair;
- protocol;
- investigators brochure;
- consent;
- budget;
- collaboration forms;
- radiation safety review;
- advertisements;
- grants;
- letters of support;
- curriculum vitae for all study personnel (first IRB submission only).

"By doing the pre-review we get most of the kinks worked out," she says.

• **IRB pre-review:** In addition to the research associate's pre-review process, there is a system in which IRB reviewers look at the new protocol or the amendment sent to the full board for review.

"We try to get the reviewer's comments back before the meeting because if there's a question that the investigator can answer before it goes to the board, then this will help cut down on time," Leslie says. "I like to get all of the answers before the board meets."

For instance, the IRB reviewer might have some minor questions about the inclusion criteria, the numbers enrolled, or the lab work.

• **Informed consent:** "It's very helpful for investigators who have never conducted research to have someone work with them to develop an informed consent document," Leslie says. "There are times when she helps them write the consent document and the application because not everyone knows how to do this."

• **Investigator assistance:** Besides expediting the approval process, having a research associate position has been a tremendous help to physicians, residents, and others new to research, Leslie notes.

"To me, it's the best thing that ever happened," she says. "It seems like people really appreciate it."

Each year when new residents arrive, Leslie, the IRB chair, and the research associate speak with the residents and give them an inservice about the IRB.

"We pull up our website and show them the IRB submission flowchart," Leslie says. "We show them which forms to submit." ■

National Children's Study tests shared IRB model

Local sites choose degree of involvement

The first babies brought into the National Children's Study while they were still in utero are now about three years old. And they're not all that's grown.

The project itself — an ambitious long-term observational study that seeks to follow children through age 21 — has enrolled about 7,000 pregnant women at 40 locations across the country, with about 3,000 children enrolled after birth so far, says **Steven Hirschfeld**, MD, PhD, director of the study. The study, still in its early "vanguard" stage, eventually hopes to enroll 100,000 children, collecting information about environmental and health exposures and other factors that may affect childhood development.

The number of IRBs involved in the project has grown as well, leading to a complex network of institutions that must make decisions about the study and its dozens of amendments. In order to cope with this, the study is testing out a form of multisite review called a federated IRB model.

"We implemented it here in the National Children's Study so that first, we could learn about the model, and second, we could simplify our own human subjects oversight and approval process," Hirschfeld says.

A single study location may involve multiple IRBs. For example, The Children's Hospital of Philadelphia (CHOP) is carrying out the study in a multicounty region around the city. Within that area are at least 16 hospitals where babies are being delivered, and where researchers will go to carry out some of the study activities, such as ultrasounds and cord-blood collection, says **Mark Schreiner**, MD, chairman of the Committee for the Protection of Human Subjects at CHOP.

IRBs at each of those facilities may have different ideas about the degree to which they are willing to rely on the IRB of record for the study, the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) IRB.

"We reviewed the study under expedited procedures," Schreiner says of CHOP. "It's a minimal risk study, it had been through extensive review, it qualified for expedited review."

At many of the hospitals in his region, IRBs insisted on reviewing the study themselves, despite the fact that the Office for Human Research Protections (OHRP) had issued a letter stating that these sites were not engaged in human subjects research.

"The CHOP study team went to those sites and performed all of the procedures," he says. "People at their sites are participating in research, but the research activities are being carried out by the investigators' sites.

"We had some sites that agreed that they were not engaged in research, some sites that allowed us to be their IRB of record, which minimized their burden, and some that insisted on their own review."

A tiered model

Schreiner says he participated in an IRB advisory committee to the National Children's Study once it was underway, and saw some of the effects of this varying IRB involvement.

"Some of these sites were taking all of these things to the full board and were editing the consent form every single time [there was an amendment]," he says. "The burden must have been huge.

"At one of the very first meetings, I said that I didn't think our IRB was adding any value and that we should be able to sign an agreement with the [NICHD] IRB to be the IRB of record. And there was enthusiasm for that idea among the members of that committee."

In response, the National Children's Study set up the federated model. Under this arrangement, IRBs can choose one of three tiers of review for the study:

-Tier 1 institutions agree to rely on the NICHD IRB as the IRB of record, handling all reviews, amendments and adverse event reporting. Thirty-seven percent of the study centers opted to join this tier.

-Tier 2 consists of facilitated review, a shared reliance between the NICHD IRB and local IRBs. Only 9% of study centers have signed up for this type of review.

-Tier 3 is for institutions who want their own IRB to be the IRB of record. More than half the study centers are maintaining local review of the study.

"All of this demonstrates the conservatism of a lot of IRBs," says Schreiner. "I think there is a tremendous reluctance to have cooperative review. People are burdened by this research — here's a minimal risk study with all these amendments and they still think they have something to add to protect subjects. I just find it bewildering."

For his part, Schreiner says CHOP would have joined Tier 1 immediately, but first had to work with the eight sites that were relying on its IRB to get them transitioned to the NICHD IRB as well.

Communication key

In addition to the varying levels of reliance, Hirschfeld says the federated model includes mechanisms for IRBs to communicate with one another, including an operations center where they can download documents and then can upload their own reviews.

"So all the other IRBs know what's going on," he says. "Our goal is to build a trusting community among these other IRBs who otherwise would not have a structured way to communicate."

During the study, an institution can switch from one tier to another, although Hirschfeld says there's been little movement within the federation to date.

He says results are expected later this year from a survey of institutions and researchers about their impressions of the federated model. But he says he's heard informally that the process seems to be working well.

One problem that's surfaced is that minor amendments tend to take longer to get through the system than researchers would like.

"For minor amendments, it takes three weeks, because of the structure and the paper trail that we engage in," Hirschfeld says. "For major amendments, it takes about the same time. But we've reduced by at least an order of magnitude the amount of paperwork and time needed to keep the protocol current. And we've improved the communication, we know that."

He says there are plans to apply this federated model to other projects, including studies within the National Institutes of Health's Clinical and Translational Science Awards.

"The model is adaptable and flexible and is going to be rolled out in other venues in the coming months," Hirschfeld says.

For his part, Schreiner would like to see future projects use models that more strongly encourage participating sites to use a central IRB.

"We've seen a number of NIH grants for

research consortia that include a requirement that investigators applying for those grants get a letter from their IRB stating that they would agree to use a central IRB," he says. "That's the way you get people to do it. You have to limit the applications to people who are willing to do that.

"For these huge things, especially if it's a minimal risk study that's been approved by the NIH's IRB, what could we possibly be adding as a site?" ■

Quality improvement study hampered by IRB concerns

Investigator: Resubmissions added to costs

Pay-for-performance initiatives, which provide bonuses for physicians, hospitals and other providers who meet certain performance standards, are increasingly used by insurers such as Medicare to try to improve quality and efficiency.

Yet the actual effectiveness of such incentives hasn't been well studied, says **Laura Petersen**, MD, MPH, director of the Veterans Affairs' Health Services Research and Development Service Center of Excellence in Houston, TX.

Petersen's team set out to test whether VA medical centers would do a better job of adhering to clinical guidelines in their care of hypertension patients if the providers received financial incentives. Medical centers would be assigned to one of four study groups, with incentives received by physicians, health care provider groups, both, or no one.[1]

However, she encountered a significant obstacle in attempting to obtain IRB approval from 17 study sites. Fourteen of the sites eventually approved the study, all determining it minimal risk. But those approvals came only after multiple submissions and a number of concerns raised by various IRBs.[1]

Additional submissions were required at every site, Petersen says, and the total time spent in the IRB approval process before the trial could commence was more than 27 months. She estimates that the staff time spent obtaining IRB review cost nearly $170,000, not counting her own salary and those of the principal investigators at the sites.

"If you add in all the opportunity costs, what we could have done with the time, the energy, the brainpower and money — it's highly costly," she says.

And Petersen notes that the sites left in the study when it finally launched were more likely to be academic medical centers and specialty hospitals, which treat more complex patients. This affects the generalizability of the results, Petersen says.

"We really wanted to have a study that ended up being generalizable to community, rural non-academic sites, because that's where much of the health care is delivered and we don't have a lot of data about what works in those sites," she says.

Ethics, notification of patients questioned

Concerns raised by IRBs over the study were varied. Some directly questioned the ethics of pay-for-performance incentives. "Offering money to people to do what is expected of them is not ethical," one IRB wrote. "Is this legal for a research study? If legal, it seems to lead to unethical behavior similar to paying finder fees," was another IRB response to Petersen's submission.

Petersen notes that pay for performance is already in use in the Medicare system. "We could just go and do like Medicare's doing and just pay everybody to reward them, but I think it's important to know whether that's an effective method or not, because if it's not effective, we're all just wasting time and money," she says.

Despite the fact that physicians and their institutions were the actual subjects of the study, some IRBs required that their patients be notified about it. The study team offered to put flyers in the clinics describing the study, but one IRB insisted that patients be notified individually. Petersen says investigators were worried this would introduce bias and the potential for breach of confidentiality of the physicians in the study.

That IRB eventually disapproved the study, saying, "The potential risk to hypertensive patients is too great to justify their involvement."

"How would there be risks to patients from following a national guideline?" Petersen asks. "This is not a guideline that I made up — these are guidelines that have been around for a long time."

'A huge variation'

Petersen's own IRB had no problems with the proposal. And of the 14 sites that approved the study, one of them did so through an expedited process.

"There was really a huge variation — everything from an IRB saying it was too risky to justify involvement to someone doing an expedited review.

I don't really think there's a good justification for having such variation."

She believes much of the problem lay in IRBs not having enough experience with this type of quality improvement study.

"I think IRBs aren't really used to them," she says. "With all of the patient-centered outcomes, research initiatives and more attention to improving quality, IRBs need to get more expertise on their boards so they can handle these studies without having these kinds of hiccups."

Petersen suggests that IRBs could tap health services researchers, statisticians or epidemiologists to assist them, just as they would seek out experts to consult on other specialized studies.

"There's specific expertise in judging these studies and their methods' strengths and it's not difficult expertise to get," she says.

She also praises proposed changes to the Common Rule that would revise existing review categories to better match the risk levels of different types of research.

"Is the way that we're currently reviewing these studies really justified given this example, where there were actually 14 IRBs that made a determination and they all decided that it was minimal risk?" Petersen says. "Is it really worth putting studies like this through such a rigorous process? Or is there some other sort of streamlined process that they could go though?"

REFERENCE

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Recordings of IRB meetings show gaps in discussions

Don't always discuss all Common Rule criteria

There have been many surveys of IRBs and their operations — gauging how long protocols take in their journey through review, how much it costs to operate a human subjects protection program, and IRB members' attitudes about various aspects of their work.

But it's hard for those types of studies to reveal how protocols are actually reviewed on a day-to-day basis in IRBs across the country.

A recent study published in the journal *Academic Medicine* gives us an unusual look behind the closed doors of IRB meetings, to see what gets discussed in review — and what doesn't.[1]

Charles Lidz, PhD, a professor of psychiatry at the University of Massachusetts Medical School in Worcester, and his colleagues gained permission from 10 academic medical centers to audio-record a total of 20 IRB meetings, along with reviewing the 104 study applications discussed during those meetings.

Lidz's team analyzed the recordings to see whether IRBs were discussing all of the criteria required by the Common Rule: risk minimization; risk/benefit comparison; equitable subject selection; informed consent; data monitoring to ensure safety; privacy protection and confidentiality; and protection of vulnerable subjects. Lidz says the team determined whether the elements were either adequately addressed in the application or discussed during the meeting.

Equitable selection

The results showed that while some elements were routinely addressed, others surfaced less often in discussions. For example, the team found that equitable subject selection was adequately addressed in only half of the submitted applications. IRBs raised the issue in only 40% of the remaining studies.

In contrast, 98% of the reviews included discussion of informed consent.

"I think there are a number of these things that are simply not thought about very much, particularly the equity of including or excluding groups," Lidz says. "Sometimes, for example, the issue of protecting vulnerable populations gets in the way of equitable subject selection."

He notes that studies sometimes exclude a group without explaining why it is necessary to do so and that decision often is not questioned by the IRB.

"We found a number of places where they said, 'We're excluding all vulnerable subjects,'" he says. "That takes thinking. These are complicated questions — do you want to include them in a trial or are we excluding them for the right reason? Those questions about vulnerable subjects and equitable subject selection tend to take a second place, or sometimes simply get ignored. And I think that's too bad."

The team found that only 13 of the 104 total applications adequately addressed a risk/benefit comparison, and IRBs only discussed that criterion in 39 of the remaining studies. Lidz says this generally involved a failure to consider potential benefits of a study alongside its risk.

"A lot of the time, the benefit is taken for granted — that the research is a good thing," he says. "You wish there was a closer look at that: Is this research going to learn anything? But that's a really hard question for an IRB to tackle successfully."

Checklist may help

IRB discussion in the meetings did not always lead to a decision on a particular element.

In the area of risk minimization, for example, the team determined that 82 of the 104 applications lacked enough information about minimizing risks. IRBs discussed it in 65 of those 82 cases, but in two of them, the issue was raised in the meeting without being resolved.

Lidz says his group interviewed the IRB staff about their work on the applications. "But the way we tended to see this was that the committee really needs to assess these things."

He says the solution may be as simple as a checklist kept by the IRB chairman to ensure that each element is addressed and decided before moving on.

"I don't think this is rocket science — it's just making sure we've gone over these things because that's what's expected of us," Lidz says.

And he does believe some of the work of addressing these criteria can be handled by staff, as long as there is oversight of some sort by the IRB.

"If they decide, for example, 'We don't want to talk about informed consent, we'll let the staff do that,' that's okay, if they have a policy and a review procedure where the chair reviews it," he says. "You can imagine privacy and confidentiality protections being a carefully designed checklist of what the application has to say, and have that be a staff-reviewed process."

That would leave IRBs with more time to devote to important questions about safety and risk, he says.

Lidz says the team did not set out to compare the IRBs in the study to one another, or to tell the IRBs involved that they're doing a bad job.

"We were consistently impressed with the quality of the discussions — they're thoughtful, they're serious," he says. "They just sometimes don't cover everything."

REFERENCE

1. Lidz CW, Appelbaum PS, Arnold R, et al. How Closely Do Institutional Review Boards Follow the Common Rule? *Acad Med* 2012 May 22. (epub). ■

Lower-income patients less likely to be in cancer trials

Survey shows less participation

A survey of nearly 5,500 cancer patients found that those with lower incomes were less likely to be enrolled in clinical trials, and more likely to be concerned about paying for participation in a trial.

Even when accounting for factors such as education, minority status and co-morbidity status, patients with annual household incomes of less than $50,000 were less likely to be enrolled in a trial than those with an income of $50,000 or more.

The findings held true even for patients over 65, who have access to Medicare, says **Joseph Unger**, MS, PhC, a statistician and health services researcher at the Fred Hutchinson Cancer Research Center in Seattle. Unger is also on the staff of the Statistical Center at the SWOG cancer research cooperative group, which conducted the survey.

"The results may point to a generalized anxiety about how to pay for things, especially when you're dealing with clinical trial participation, about which patients may already feel uncertainty," Unger says. "The additional uncertainty about what it would cost may make it particularly difficult for lower-income patients to decide that a clinical trial might be for them."

In a statistical model accounting for demographic, socioeconomic and co-morbidity factors, patients with incomes less than $50,000 per year were 27% less likely to participate in clinical trials, compared to higher-income patients. When income level was split at $20,000 per year, patients with lower incomes were 44% less likely to participate.

In the end, income level was the only socioeconomic or demographic factor that remained an independent predictor of clinical trial

participation, Unger says. "That was a bit of a surprise."

Unger's group presented their findings in June at the annual meeting of the American Society for Clinical Oncology.

He says that the study results raise concern that clinical trials, an important patient resource for state-of-the-art-therapies, are not equally accessible to patients of all income levels. He says participation by lower-income patients in the trials would make trial results more generalizable and would allow trials to be conducted more quickly.

In examining the data about trial participation, researchers were careful to separate income from other factors, including education and co-morbidity. Unger says patients sometimes have medical conditions in addition to cancer that may make them ineligible to participate in clinical trials.

"Those who have lower socioeconomic status have been shown to have higher rates of conditions such as diabetes or high blood pressure, which could lead them to be ineligible for trials based on that factor alone," he says.

He notes research has shown that the health care costs to patients participating in a trial are not appreciably higher than costs for standard clinical care.

"But patients may still be concerned about co-pays and co-insurance, even if they're not necessarily higher than for non-trial care," Unger says, noting that better communication in the informed consent may help alleviate those concerns.

"There's been some suggestion that consent forms are not very clear about what costs are covered for patients in a clinical trial," he says. "If that is true, then greater clarity in consents could help patients better understand the cost burdens of participation and whether there is an extra burden at all."

He also says that indirect costs of participation — things like transportation and time off from work — may factor into a lower-income patient's decision. Helping relieve those costs could be a step toward lessening the burden on patients.

"Simple things like free bus passes and paid parking could make participation more convenient, especially for lower-income patients," Unger says. "Flexible clinic hours, to allow patients greater convenience, regardless of what type of work they have, might also encourage participation." ■

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

- ■ Learn strategies for better staff management
- ■ Tips for better recordkeeping in electronic era
- ■ Is the proverbial "complaints box" enough?
- ■ Waiting on the ANPRM: Are IRBs putting off plans to improve?
- ■ "Professionalizing" the IRB: One institution's approach

CNE/CME QUESTIONS

1. Which of the following is not one of the eight actions OHRP recommends in its draft guidance that IRBs take when transferring a research project to another IRB?
   A. Ensure the availability and retention of pertinent records
   B. List and include footnotes of all IRB regulatory issues
   C. Conduct a review of the study or studies by the receiving IRB, where appropriate, before it accepts responsibility for the study or studies
   D. Confirm or establish the date for the next continuing review

2. An enrollment informed consent comprehension checklist might include which of the following questions?
   A. What do you understand that you are being asked to do in this study?
   B. What do you understand about possible risks that might happen as a result of being in the study?
   C. What will happen if you do not join the study?
   D. All of the above could be included

3. Under the National Children's Study's federated IRB model, IRBs have the option of conducting local reviews of the study and its amendments, rather than relying on the central IRB.
   A. True
   B. False

4. In a survey of nearly 5,500 cancer patients, the only socioeconomic or demographic factor that remained an independent predictor of clinical trial participation was:
   A. Education
   B. Income level
   C. Co-morbidity status
   D. Minority status