IRB ADVISOR

Your Practical Guide To Institutional Review Board Management

AHC Media LLC

IN THIS ISSUE

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Building an IRB to ensure rights of subjects in a developing nation

Team uses experience setting up IRB in Haiti as basis of handbook

Medical research in developing countries often is conducted by Western institutions, using their own IRBs to ensure the rights of participants who could be half a world away.

It's a process that can fail to take local input into account, and that fails to give credit to the institutions on the ground who are committed to providing care in these countries, says **Ellen L. Palmer**, RN, MSN, PhD, an assistant professor of nursing at the University of Texas in Arlington and board member of International Child Care (ICC), a Christian health development agency that operates a hospital and clinics in Haiti and the Dominican Republic.

Palmer and **Cheryl Rowder**, RN, PhD, CCRC, an associate professor of nursing at the University of Mary Hardin-Baylor in Belton, TX, are collaborating to change that model, starting an IRB at an ICC hospital in Port-au-Prince, Haiti. In the process, they're literally writing the book on how to start up IRBs in developing countries.

While many smaller countries currently don't have regulations requiring human subjects protection for research conducted within their borders, Palmer foresees a time in the not-too-distant future when all international research projects will require local IRB approval.

"The United Nations and World Health Organization — and some of our big grants in the future — are going to require that," she says. "I think we're going to have to show that we have in place some kind of ethical committee, rather than work off the [IRB] from the country that comes in."

The IRB Palmer and Rowder are creating will be based at Grace Children's Hospital, ICC's 40-year-old tuberculosis hospital in Port-au-Prince that serves as the command center for all of the organization's Haitian clinics. The hospital provides TB, HIV, and AIDS treatment services to children and adults, as well as a nutrition clinic and other health services.

While some clinical trials have been conducted at Grace, much of the research involves measuring the effectiveness of various treatments for

disease or nutritional interventions rather than testing new drugs.

Palmer says that while outside groups come to the hospital to look at data, Grace currently does not have a system in place to initiate or review research locally.

"My concern is that without [the hospital], they wouldn't have a place to do the research," Palmer says. "And we don't get the credit — 'we' meaning me as a Caribbean Haitian. Seeing that our organization is there for them to do their research, I don't think we get the recognition we deserve."

Unique issues

Palmer has volunteered in Haiti for more than 30 years and currently serves on ICC's U.S. board (in addition to clinics in Haiti and the Dominican Republic, ICC has offices in Columbus, OH, and Mississauga, Ontario).

She pitched the idea of an IRB associated with Grace Children's Hospital to the ICC board and began working on the project in November 2006. She tapped Rowder, who has conducted clinical research and helped create a university IRB in the United States, to provide her expertise in dealing with IRB policies and procedures.

Rowder says she has drawn upon her experiences with IRBs — both good and bad — to help come up with an effective plan for a new IRB at Grace. Because Haiti has no human subjects protection regulations, she's using modified forms and policies from American IRBs while addressing some of the ethical issues that are unique to international research in developing countries.

For example, Rowder says, an IRB in a developing country would have to consider whether to allow placebos to be used for research on diseases for which the country currently has no standard of care, although a treatment may be available elsewhere.

"To say we're going to have a placebo group, even though there's a known treatment in another country, when it doesn't exist in this country — that's a pretty major ethical issue," Rowder says.

An IRB also must weigh whether proposed research will provide real benefit to its local population, especially if the treatments being tested ultimately wouldn't be affordable there.

"Institutions need to know how to evaluate a project and the impact it's going to have on their population — whether it's appropriate for their population and whether they're actually going to gain anything," Rowder says.

The IRB's membership will include several ICC leaders, including Harry Geffrard, the organization's national director in Haiti, and Jean Marius Lafond, a maxillofacial surgeon in Haiti and president of ICC's board in that country.

Palmer says the Methodist Church in Haiti will provide members that will offer an ethical perspective, and says she knows of people who

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can serve as community members of the IRB.

"There are wonderful people in these countries just waiting for people like Cheryl and I to come through and help them write the manual, and get this started," Palmer says.

Although these types of projects in developing countries always require the consent of the government, Palmer foresees no difficulty in getting approval from the Haitian government, thanks to ICC's long track record in that country.

"I have no doubt that they'll agree," she says. "We have the credibility and reliability with the Ministry of Health. There are several people down there at the medical university in Port-au-Prince who want to talk to me. They realize we need to do this."

Trust essential

Palmer says that kind of trust relationship can be essential in countries where there has been past exploitation.

"The reason I'm able to do this is that I've been there for many years," she says. "They're trusting me. They trust that I'm not going to put something out to make them look bad."

Rowder says her years of working with IRBs have helped her come up with the multitude of templates that will be needed for the Grace Children's Hospital IRB. But the training manual will be of prime importance, because many of the people who will be involved in this process know little about IRB review.

"It's going to require something almost like an introduction to research," Rowder says.

The IRB manual and supporting documents all will be translated into Spanish and French, and back-translated into English to double-check the accuracy of the translations.

One vital factor in creating an IRB that is responsive and builds good relationships with researchers is the selection of an administrator who can keep in contact with researchers, monitor projects, and keep the IRB organized, Rowder says. But she also wants to ensure that researchers can communicate directly with the IRB if they have problems.

"That's one of the biggest stumbling blocks, if the researcher is having difficulty with the administrator and there's no way for them to speak to the chair of the IRB or to present their quandary to the IRB — that can really be an issue," she says. "There have to be open lines of communication and real assistance to researchers. Some of them are going to be new to this, and other groups will be used to it already and will pick right up on using the templates.

"But I think it really can hinge on having a really good administrator," Rowder says.

That IRB's records probably will be kept at the ICC's Ohio office, because communications and other systems in Haiti sometimes can be sketchy, Palmer says.

Palmer estimates that the committee will be put in place in March 2008. She and Rowder already have arranged for a nursing research project to be used as a trial run for the new IRB.

"We want to put in an application to show how this works," she says.

In the meantime, they say they've received a lot of interest about their project, particularly the manual they're creating on how to develop an IRB. The manual should be completed in the next year.

Palmer says that when she created a poster presentation for Sigma Theta Tau's International Nursing Research Congress in Vienna, Austria, last summer, "I was busy every minute I was there with inquiries about how to do this. I'm much aware that it's needed."

Palmer says that in the future, she'd like to look for grants that could help start an IRB process in different countries.

"It isn't meant to be tied just to Haiti."

[Editor's note: For information about the manual that Palmer and Rowder are creating on starting IRBs in developing countries, contact Palmer at ellenlpalmer@tx.rr.com or Rowder at cherierowder@yahoo.com.] ■

Rare diseases research brings special challenges

Confidentiality, expertise key to protocol review

Those advocating research into rare diseases often have an uphill battle, searching for funding and trying to garner public support for treating conditions that don't have the same widespread recognition as HIV or breast cancer.

The research also comes with unique challenges for protecting human subjects — both because of the rarity of the conditions being studied and the greater concern about confidentiality, says **Kathleen Paulus**, CIP, protocol manager for the Rare Diseases Clinical Research Network at the University of South Florida, Tampa.

"If you're looking at dots on a map [that

represent patients with rare diseases in the United States], you could theoretically identify somebody by their dot on the map," she says. "If you were a physician who lived and worked in Texas and saw a dot on the map in Texas for, say, a genetic steroid disorder, then it would be pretty obvious to you if you had ever had contact with that one person in Texas who had that disorder who that person was."

Paulus says people suffering from rare diseases, many of which are genetic in origin, have understandable fears about potential loss of health insurance or employability if others learned about their conditions.

"We're extraordinarily careful and use the most cutting-edge practices," Paulus says of the research network, which includes 10 consortia, each representing a group of similar rare diseases such as bone marrow failure diseases, rare lung diseases, or various forms of vasculitis.

"We have sites in Japan, Canada, Europe, and South America," she says. "Since we are storing all these data from all over the world, we have to ensure that it's stored appropriately and getting to us [in a secure way]. We have these electronic on-line data capture forms that go directly into our systems here."

But she notes that beyond secure computers and proper data storage techniques, her network must consider issues that pharmaceutical companies or researchers with large patient populations may take for granted — for example, the confidentiality problems raised by plotting their subjects on a map.

"If someone wanted to show on a map how many individuals they have in their study of heart disease, it wouldn't make any difference, because so many Americans have heart disease," Paulus points out.

Expertise sometimes lacking

In addition to issues of confidentiality and HIPAA compliance, Paulus says reviewing rare diseases research raises other issues in IRB review:

• **Lack of expertise.** Because the disorders involved are so rare and not particularly lucrative for the pharmaceutical industry, there is a dearth of scientists who specialize in them. As a result, IRBs may have not have members on their boards with expertise in the condition being studied.

"So investigators will run into IRBs that don't truly understand the nature of the disease or the science behind what the investigator is proposing," she says.

• **International reach.** Most studies in this field must be international endeavors to recruit enough subjects. Paulus says IRBs that want to make minor changes to protocols can end up causing serious delays.

"Changing a protocol that's been thoroughly reviewed by, let's say, the National Institutes of Health and multiple government agencies around the world, for minor issues really does hold up the research endeavor for these rare diseases," she says. "I'm a certified IRB professional, so I know where the IRBs are coming from, but they need to work with investigators to make sure that only really necessary changes to the protocol are made at the time of review. Other changes could really be held until the next amendment."

Paulus says that in her experience, the vast majority of IRBs understand this issue.

"They understand that this is a truly rare disease and that this is real progress being made by [NIH's] Office of Rare Diseases towards serving these patient populations," she says. "They're not willing to be bulldozed, nor should they be. But then there are one or two IRBs that don't quite understand how imperative it is for this to move forward without perhaps the level of bureaucracy that is standard with pharmaceutical studies."

• **Protecting subjects from unnecessary research.** Paulus says IRBs she deals with often are concerned as to whether the research being proposed is truly of value.

"They're concerned with the protection of their local subject population," she says. "Because the diseases are so rare there is no standard of care. And is putting these families and these patients through this particular research endeavor really worth it, even if it's just a longitudinal study?"

As an example, she says an IRB may question whether it's necessary to ask extremely personal questions in a survey.

"They'll ask whether maybe the discomfort of asking this question may be inappropriate," Paulus says. "And it may be absolutely appropriate, because it speaks to the progression and history of the disease — it's a very important data point."

She notes that because there is limited funding for rare diseases research, experts in the field are careful to spend that money wisely.

"Much less with rare diseases research would you find a [study] that isn't really important to the cause of the disease," she says. "In rare diseases research, they're really focused on curative

research or understanding the progression of the disease."

Recruiting a geneticist to the IRB

Because of the complexity of the diseases being studied, "the terminology becomes exponentially more technical," Paulus says. "The majority of rare diseases have a genetic basis, so you're talking a lot about genotypes and phenotypes."

• **Informed consent challenges.** Paulus says IRBs could benefit from having a member who is a geneticist, to help sort through the scientific terminology and make sure informed consent is accurate and understandable.

She says much of the research is done on children, so IRBs also must carefully examine the consent/assent process for parents and their children.

"You have to make sure that you weigh the parents' eagerness against what the child would actually be willing to do, if they were of consenting age," Paulus says.

Although the diseases themselves are rare, there are so many of them that Paulus estimates that nearly every IRB should encounter at least one rare disease proposal at some point.

In addition to having a geneticist on board, she advises that IRBs learn where to go for specialized help should such a proposal come before them.

"They need to be aware of who are the leaders in the field," Paulus says. "They could approach a patient advocacy group — they will always know who the leading expert is. Or if it's one of our diseases [in the Rare Diseases Clinical Research Network] they could always come to us.

"There's nothing these researchers want more than to make sure that high-quality excellent research is being conducted on these areas where these populations are underserved."

Paulus says IRBs dealing with rare diseases research also should have a good understanding of certificates of confidentiality, which are issued by the NIH and other Health and Human Services agencies to protect identifiable research information from forced disclosure in civil or criminal legal actions.

"It's not an absolute catch-all — lawyers have been able to poke holes in it in the past, but it does provide some level of protection," she says. "It can provide a layer of assurance to investigators who may be reluctant to perform specific tests because of the risks to the patient. And we should use any tools at our disposal." ■

IRB staff and managers need these survival skills

Bright lights can burn out

One of the truest sayings an IRB professional might hear is that you can't have burnout unless it's a really bright light to begin with, an expert says.

"Our IRB employees are incredibly dedicated people," says **Michelle Christiano**, CCRC, CIP, director of the office of human research protection at the Medical College of Georgia in Augusta, GA.

Christiano learned first-hand how terrific her staff was when the staff shrunk from nine employees to four full-time and one part-time person last summer due to maternity leave and other issues.

"We made it through the last week of June until Oct. 8, before we were back to full staff," Christiano says.

With only half the necessary staff, the IRB team bunkered down and got the work done: skipping vacations, and even bringing their children into the office to help with trivial tasks.

"I bought the kids gift cards," Christiano says, adding that she used her personal funds since the state-funded institution doesn't provide enough discretionary funds for thank-you gifts.

Christiano also recognized her hard-working staff's efforts as much as they would allow her, but there's always the prospect that people will experience burn out after such intense workloads.

So as an IRB director, Christiano has devised these strategies for preventing staff and personal professional burnout:

1. Have a passion besides work.

"Part of what you have to do is have a strong enough personality outside of the office and have something else in your life that you're passionate about," Christiano says. "You have to have a hobby and something that takes you completely away from the IRB world."

Christiano's first passion is her family, but she also has carried her IRB organizational skills and passion for protecting people to volunteer work.

Participating in volunteer work can be time-consuming, but it also can be rewarding and a way to be recognized in a more positive way than an IRB professional might experience at the job, she notes.

"So much of what we hear in the IRB office is negative," Christiano says. "We might not hear people say, 'Thank you for saving this protocol.'"

Also, volunteering can help people learn new skills.

"One of the best things I did was participate on a task force about informational technology [IT]," she says. "I volunteered even though I didn't have the time."

"When I got into it, I found that the IRB office could use information technology, and it would make our jobs so much easier than they were," Christiano says.

2. Make sure your IRB office has the right tools.

IRB offices, no matter how small, need the right tools. Some community-based IRBs don't even have a dedicated copier and/or scanner, Christiano says.

They lack the technology and software to make documentation easier, and they lack IT support when electronic documentation upgrades are needed, she adds.

Sometimes an IRB office already has the right tools, but the staff has not been informed or educated on using them, Christiano says.

Other times the institution's administrators need to be convinced that investing in new equipment is a worthwhile venture.

In either case, Christiano says the best strategy is to gather data and look for the simplest solutions. For example, the staff complained of wasting too much time walking down the hall to use the only working scanner.

The solution turned out to be a workable copier/scanner that was in the office and not being used, Christiano says. "So we called IT to have it hooked up," she says.

3. Collect data to show staff and administration.

Christiano had staff members track how much time they spent on the telephone handling certain issues. Workers had complained that these phone calls shaved hours off their days.

But when the logs were kept and the data analyzed, Christiano found that the phone calls used up far less of their time than they perceived.

So it was their perceptions that she worked on changing, armed with the data, she says.

Also, the office changed its internal forms, which caused the intake time to increase significantly, so Christiano had the staff track it.

"We're all creatures of habit, so when there's a change we say it's much easier the old way," she notes. "But when we track the data we see that the new way is much easier."

It's also important to track the time spent on protocols to see where the process is bogged down, Christiano suggests.

The IRB office is collecting three years of data that will be posted on its web site next year.

"The biggest trend is the investigators are not getting back to us in a timely manner," Christiano says. "We give them 30 days to get it back, and they take it to the 29th day."

For instance, at 3:21 p.m. on a Tuesday afternoon, Christiano notes that two protocols have been submitted for that day's 4 p.m. deadline.

"By 4 p.m., we'll have six or seven in because they wait until the last minute," she says.

4. Have managers and administrators stand behind staff decisions.

IRB workers tend to want to help out investigators by offering them breaks on deadlines, but they quickly find that the occasional one-hour late becomes a day late, and not just the rare emergency, but a trend.

This can lead to burnout.

"People have a hard time recognizing when they're burned out, and they have to say that for their own sanity the answer is 'No,'" Christiano says. "That's so hard for people to do, especially for women."

But they need to set their priorities, set their limits, she adds.

So the IRB began to enforce its deadlines to the hour, except in cases of true emergencies involving patient safety.

"When an investigator is late, the staff will say, 'I'm sorry but the deadline is 4 p.m., posted here and here — but we'll be happy to take it for next month,'" Christiano says.

Then the investigator will call the vice president of research to complain.

At the Medical College of Georgia, the top research administration and IRB officials will stand behind the staff decisions, Christiano says.

When these deadlines are enforced consistently, investigators soon will learn to respect them, and it takes unnecessary pressure off the IRB staff, she adds.

"You have to be fair and consistent — just like when raising children," Christiano says.

5. Provide whatever incentives are possible.

Even in government-funded institutions where discretionary funds are limited, there are ways to

provide staff pick-me-ups.

Christiano will bring in donuts, and there's a monthly luncheon where the staff exchange recipes.

On Fridays, the office holds a "funky 15," where for 15 minutes they can listen to old music that one person selects. Everyone can sing along, Christiano says.

Also, Christiano encourages the staff to attend study coordinator meetings, which are held regularly. They can attend these for their own training purposes if they need to, or they can serve as greeters to new coordinators for the first few minutes as people enter the class.

"This way they can meet the new coordinators and put a name with the face of the person they've been talking with on the telephone," Christiano says.

When an investigator or study coordinator sends her an e-mail complimenting one of the IRB workers, she'll pass on the compliment at the staff meeting and keep the compliment in the employee's file where it will be used during the annual review.

Sometimes, all it takes is a compliment and telling a worker that she or he has done a good job, Christiano says. ■

Starting or expanding an IRB office? It helps to know size, scope, culture

Expert offers this advice

When planning to expand an IRB office or start a new one to support one or more IRBs, the key principle to keep in mind is that one size does not fit all when it comes to IRBs, an expert says.

"Look at your own institution and the size of it, scope of it, and culture," advises **Susan Kornetsky**, MPH, CIP, director, clinical research compliance of Children's Hospital of Boston in Boston, MA.

"There's no one way that's better than the other," Kornetsky says. "That's the beauty of the IRB world — there are lots of different ways of doing things."

For a start, it's important to understand the role of the IRB administrative office and the role of the IRB chair, Kornetsky says.

"This varies from institution to institution," she explains. "Some IRB chairs are very involved in everyday processing and decision making, and other IRB chairs are not so involved."

The IRB administrative office's support role would be directed by how much involvement the IRB chair has in the day-to-day operations.

Cross-train or specialize?

Another decision to make involves how to structure the IRB office.

In some institutions, the IRB office follows the model of having each IRB professional learn all of the necessary tasks involved in IRB review: handling new protocols, continuing reviews, unanticipated problems, policies and procedures, amendments, revisions, informed consent changes, etc.

If the institution is small, then one person might handle everything for all protocols. If the office is large, then each IRB professional would be responsible for everything that needs to be done, but only for the protocols submitted by a particular department, Kornetsky suggests.

"The advantage of that is you'd become a resource to a group of individuals and departments and could understand and support the scope of research in that department, Kornetsky says. "You might realize when there are competing protocols, and you might become an expert in particular areas."

The other common model used by larger IRB offices is one in which each member of the staff is specialized in handling certain aspects of the office work.

"Each person is hired for a particular function," Kornetsky explains. "Work is divvied up among specific functions in that office."

This model is common in larger institutions where the IRB office's staff is large and there is a need for more defined roles and responsibilities, Kornetsky says.

"The model we have is having people [assigned to] different departments," she notes. "For right now, we'll keep our model of having each person do everything, but that may change as we do more clinical research."

When expanding or starting an IRB office, it's important to discuss these different models and their pros and cons with people at the research institution, including the IRB chair.

IRB office may offer investigator support

Another aspect of the IRB office involves its support role.

"There has to be some thoughts about whether your IRB office is just there to support the IRB, meaning your work begins once the investigator submits the protocol," Kornetsky says. "Or are you an office that provides a lot of information before the protocol is submitted?"

For example, ask these questions:

- Will investigators be encouraged to call the office to ask questions before submitting protocols?
- Will the IRB office pre-review the protocol before forwarding it to the IRB?

An IRB office that is designed to provide some educational support to investigators might invest time in new protocols and get back to the investigator with questions that he or she should answer before submitting the protocol to the board.

For example, a protocol might not spell out how subjects will be recruited, Kornetsky says.

"The IRB office can get back to the investigator and say, 'You don't have enough details about recruitment, and you didn't provide us with posters or letters, and we hope you will collect that information before this protocol comes to the IRB,'" she says.

The goal is to get the protocol into the best possible shape before it's reviewed by the IRB, Kornetsky says.

This is extra work for the IRB office staff, and this is where the institution should know its cultural issues and whether the resources and time will be adequate for this extra work, she adds.

Some institutions might decide the IRB itself should handle all of this type of education and that the IRB staff is too limited in time and manpower to handle the extra load of work.

On the other hand, some institutions have found that giving an IRB office this responsibility, along with the resources to handle it, has led to improved relationships with investigators and better response times on protocol reviews.

A research institution should consider budgetary issues, such as how much money will be available for training, conferences, educational materials, and even the occasional staff lunch, Kornetsky says.

And institutions should examine privacy concerns, which are particularly important when an office's physical structure involves cubicles and not offices, she adds.

"You also need to think about electronic versus paper systems," she says. "More and more IRB offices are moving toward electronic systems, but they're expensive and you have to decide whether to buy one or develop one in house." ■

Illegal drug-using subjects pose unique ethical challenges

Even collecting syringes is problematic

IRBs reviewing protocols involving HIV drug-using populations sometimes find that it's impossible to anticipate all of the ethical issues that will arise during the trials.

HIV investigators also might not have imagined certain ethical difficulties, and so additional human subjects protection measures have to be created at the site as the trial is ongoing, an expert says.

"When dealing with a population with a stigmatized behavior there are bound to be ethical issues, especially when this is a population of drug users who are actively using and not in any formal treatment program," says **Kaveh Khoshnood**, PhD, an assistant professor of epidemiology in the Yale School of Public Health in New Haven, CT.

"I'm not a bioethicist," Khoshnood notes. "I'm an infectious disease epidemiologist, and my research has focused on trying to prevent HIV infection among active drug users."

In the course of interviewing drug-using participants and enrolling them in studies, Khoshnood was bothered by the ethical issues that arose.

"Many of which we had not anticipated, frankly," he says. These ethical issues also weren't on the IRB's protocol as they were brought to light during the field experience.

"I was looking for answers, ways to resolve these ethical issues," Khoshnood says. "I looked in the literature and could not find documents that were helpful and which directly addressed some of the ethical issues that come up in HIV prevention research."

Needle exchange bans

One striking example involved a protocol that called for staff to collect used syringes and test them for HIV and hepatitis infection.

Researchers found that drug users were requesting a replacement syringe. The syringe they gave up was their only one, and they needed a new one or they would be compelled to use a shared syringe. Needle sharing is a major risk factor for HIV and other blood-borne pathogen infections.

So if researchers took subjects' used needles and didn't replace them with clean new ones, they would be indirectly placing these study participants at risk for major illness and/or death.

The ethical answer would be for the trial to include clean syringes to exchange for the used ones, Khoshnood says.

But since the study was funded through a federal grant, and there is a federal ban on needle exchange, investigators were not allowed to use the study's funds for clean needles, he explains.

"The IRB didn't raise that issue," Khoshnood says. "Many IRBs don't have that expertise, and that's not something we thought of putting in the protocol."

So what happened was that investigators, in the interest of protecting their human subjects, paid for clean needles out of their personal finances initially. Eventually, some sites collaborated with existing state or local needle exchange programs, Khoshnood says.

"In one location, needle exchange was not allowed, so investigators decided to use personal funds to make sure the drug users had access to clean syringes," Khoshnood says. "We didn't want to break the law or endanger the life of human subjects."

Confidentiality is another issue that is of particular concern when researchers are dealing with a population that uses illegal drugs, he says.

"Breach of confidentiality is a concern for all human subjects, but for someone who is using drugs the consequences could be far greater if their drug use status becomes known to their family members and community," Khoshnood says.

Since the participants' substance use involves illicit drugs, as opposed to alcohol or nicotine, there are more severe consequences if confidentiality protection is breached, he adds.

For example, if a trial subject is pregnant and actively using drugs, there is a risk that she could be arrested for endangering the fetus, he says.

Obtaining informed consent

IRBs reviewing these protocols might also have to consider the informed consent process differently, Khoshnood suggests.

For years, Khoshnood would provide subjects the informed consent document, read it to them, obtain their signature, and move on, he notes.

"Then I began to ask the question, 'What does it really mean?'" he says. "If someone is dependent on a substance and they approach you when they're craving street medication or are going through withdrawal, is that truly informed consent?"

Khoshnood had to admit that he didn't have a good answer for that question.

"The way we deal with this situation is pragmatic," he says. "If someone is so high they can't think straight, we say, 'Thanks for coming today, but today is not a good day for us to do this. Why don't you come back tomorrow?'"

Enrolling subjects who are obviously high might make a mockery of the informed consent process, Khoshnood says.

"People may get upset when we ask them to come back, but what do you do?" he says. "Do you get their signature knowing their cognitive function is compromised, or do you bring them back at a time when they're more alert?"

This issue isn't unique to people using illegal substances, and a lot of IRBs are raising these issues, Khoshnood says.

"I'm doing a study of IRBs to understand how they handle research protocols that have active drug users," he notes.

"I'm in the beginning phase of the study and have interviewed 15 chairs of IRBs and IRB staff members," Khoshnood says. "And what is beginning to emerge is there is a lot of misinformation about what drug users are and what they look like and how they act and behave and what they are capable of doing."

Drug users cannot be grouped together when it comes to their behaviors.

"If someone is using psychoactive drugs, it is very different than someone using heroin," Khoshnood says. "I find that IRB members, especially those who don't have substance abuse protocols, are not aware of fundamental differences," he adds.

"Many IRB members who are not familiar with the pharmacology of these drugs may put them all into one category, and say that if you as an investigator put them into your study they may not be able to consent." However, the ability to consent varies from drug to drug and person to person, Khoshnood says.

"Many of these people have full-time jobs and families, and clearly are making decisions every day," he adds. "I have found a gap in knowledge of some IRBs about this particular issue."

Compensation concerns

A third issue that often arises involves compensation to subjects.

"Many IRBs have expressed discomfort when

the investigator suggests payment of cash to a known drug user in a study," Khoshnood says. "We try to get at what's behind that discomfort."

IRB members will say that they don't want to contribute to the subject's drug use. But is this an ethical or human subjects protection issue?

Is giving a $20 or $50 cash compensation to a heroin user any different than giving the same amount to a college student who will use the money to get drunk on the weekend, he asks?

"It's interesting that IRBs raise this issue exclusively for a drug-using population," Khoshnood says. "They're not concerned about the payment being a risk; they're making a judgment based on their own comfort level and not on any regulation."

Some IRB members might say that cash payment to illegal drug users is coercive and undue inducement, assuming the participant wouldn't enroll in the trial for any other reason, he says.

"If you offer someone hundreds of dollars for an interview then, yes, it could be undue inducement," Khoshnood says.

But if the cash payment is minor and if the study poses no risk other than having subjects answer questions, then there is no increased risk to the subject, he says. ■

Organ transplant research: Do we need a central IRB?

Nationwide IRB may facilitate studies

A patient needing a transplant for a vital human organ often waits months or even years before one becomes available. Advocates for transplant research contend that someday, that wait could be shortened by new research into ways to better keep organs viable for transplant to improve their function.

But for that to happen, IRBs must allow research with organs currently being transplanted into patients, a practice that raises ethical and practical issues.

Eric Grossman, MD, FACP, medical director of the New York Organ Donor Network, New York City, spoke to an IRB conference earlier this year about his concerns that transplant research could be stymied by the process by which organs are distributed across the country and the necessity of obtaining individual IRB approval at those sites.

Grossman says there has been a great deal of research done on post-transplant interventions such as the use of immunosuppressive drugs by recipients. However, he says interventions that take place with the donor or with the pre-transplant organ pose unique problems.

A hypothetical example might involve a drug given to a patient after brain death has occurred to improve the donor's liver function. The patient's family gives permission for the administration of the drug and the donation of the liver.

"The drug is given and then the organ is allocated to a person after that point," Grossman says. "Often it takes hours to allocate an organ, because we have a list, and we have to communicate with each surgeon for each patient on that list.

"So now, you have a recipient, who has been waiting for an organ, maybe for months, maybe for years," he says. "And you're offering them an organ, but the organ has had an intervention. The question is: How is appropriate informed consent obtained?"

In some cases, the recipient must be told that his or her organ may have had the intervention or may have had a placebo instead.

A recipient in any state

Grossman notes that because of the way organs are distributed throughout networks, the organ could end up with a recipient in any state in the country.

"It is practically difficult to obtain IRB approval from every transplant center in every state in the U.S.," he says.

In the past, this type of research may have occurred without seeking such approvals. But in this era of IRB review, Grossman says he believes promising research is being hampered.

"I think what's happened, by and large, is that the research hasn't occurred," he says.

Grossman notes that nearly 100,000 people are currently on a waiting list for an organ transplant, while only 29,000 deceased-donor transplants were accomplished in 2006.

According to the United Network for Organ Sharing, about 17 people die each day waiting for a transplant of a vital organ, such as a liver, heart, lung, or kidney.

"And the type of research that we're talking about potentially could increase the number of donors by allowing them to survive long enough to the recovery procedure," Grossman says. "It could increase the number of organs that could result by interventions that improve organ

function while they're still inside the donor or once they're removed from the donor.

"That's why it's really critical that we figure out how to make this research happen," he says.

During his presentation at Columbia University's annual IRB education conference, Grossman says participants discussed some possible solutions to the problem of obtaining IRB review of transplants throughout the country.

Most promising, he says, was the suggestion of a nationwide IRB devoted solely to transplant protocols. He acknowledges that the challenge would be gaining acceptance for such an overarching IRB by all of the IRBs at the various transplant centers across the country.

Joel Frader, MD, a professor of medical humanities and bioethics at Northwestern University's Feinberg School of Medicine in Chicago, is a member of the Chicago Transplant Ethics Consortium.

He says there are existing models for centralized IRBs, including the National Cancer Institute's Centralized IRB program, which allows for facilitated review of multisite studies.

"IRBs can sign on to the process and say 'Yes, we'd like to participate.' They get a copy of the central IRB's review when the protocol is submitted to the local institution," Frader says. "One person at the local IRB is responsible for reviewing what the central IRB has done and saying, 'Yes, we accept this,' or 'No, it requires full IRB review.'"

He says many local transplant centers' IRBs probably would be comfortable with a central IRB associated with a well-known organization such as UNOS. But Frader worries that even a central IRB with impeccable credentials raises the potential for conflict of interest.

"Whether we're talking about the NCI or a hypothetical UNOS IRB, these obviously would be review boards that would have a stake in having this research conducted and whether they could over time retain objectivity is an open question," Frader says.

Putting protocols on-line

Grossman says another possibility to aid — and speed — informed consent in transplant research would be to make the various protocols available on-line to potential recipients on the waiting list, so that they have a chance to review them before faced with the life-or-death decision of accepting or rejecting an organ. Patients could be reminded by their physicians during medical visits to review the protocols.

"It would take a lot of commitment on the part of each transplant center," he says. "There are a lot of other things that need to occur at those (medical) visits and we would have to develop a real commitment on the part of the transplant centers to do that. It would require a real cultural change."

The actual decision of whether to accept an organ that has undergone an experimental intervention, Grossman says, isn't all that different from other decisions recipients often must make. Some recipients, for example, must decide whether to accept an organ from a donor who had a disease such as hepatitis B or hepatitis C,

CE/CME Objectives

The CE/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

- Advice on handling incidental findings
- American Psychological Association task force seeks to ease tensions between IRBs, researchers
- Follow these tips in writing IRB meeting minutes
- Handle continuing reviews following these best practices

which could affect the function of that organ.

Grossman says that many organizations involved in improving organ transplants are anxious for a resolution that will better enable transplant research. He hopes that outreach efforts such as his will help push the issue into wider discussion and bring about a faster solution.

"I think given how many people's lives are held in the balance, how much money is spent in procuring organs and in transplanting organs, that we ought to make whatever additional investment it would take to solve this issue," he says. "The amount would be minuscule compared to the amount that's spent in this area.

"If leadership is shown, people will respond to that. I think people will be receptive if we lay out a road map." ■

CE/CME *questions*

21. Which of the following is a suggested source for finding an expert to aid in an IRB review of a rare diseases protocol?
    A. Wikipedia
    B. Patient advocacy groups
    C. On-line advertising
    D. None of the above

22. How many people currently are waiting for a transplant of a vital organ?
    A. 29,000
    B. Less than 2,000
    C. Nearly 100,000
    D. More than 200,000

23. Which of the following is an ethical issue that might arise when reviewing a protocol that involves injection drug-using participants?
    A. If their needles are collected to check for viral infections, is it ethical to not replace the needles?
    B. Is it any different to provide a $50 cash fee to participants who are known users of illegal drugs as opposed to any other research participant?
    C. Can participants who abuse illegal drugs provide adequate informed consent?
    D. All of the above are ethical issues an IRB might discuss.

24. What is a good strategy for preventing burnout among IRB staff and managers?
    A. Have top level administrators stand behind decisions made in the IRB office.
    B. Provide incentives, no matter how small.
    C. Make sure the office has the right tools and electronic equipment to conduct business efficiently.
    D. All of the above

Answers: 21. (b); 22. (c); 23. (d); 24. (d)

IRB ADVISOR

Your Practical Guide To Institutional Review Board Management

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