IRB ADVISOR

Your Practical Guide To Institutional Review Board Management

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IN THIS ISSUE

Special Report:
Improving IRB/PI Communication

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Special Report: Improving IRB/PI Communication

(Editor's note: Attendees to the 2004 Annual IRB Conference, sponsored by the Public Responsibility in Medicine and Research and held Oct. 28-31 in San Diego found a great deal of discussion about improving communication between IRBs and principal investigators in both biomedical and social-behavioral research areas. This issue of IRB Advisor *features stories that explore how to remove communication barriers and strategies for improving the relationship between PIs and IRBs, as well as strategies for helping the IRB process run more smoothly.)*

Eliminating barriers to effective discussion between PIs and IRBs

Here's what works and what doesn't

Human subject protection is an evolving system that occasionally encounters obstacles in the form of old attitudes and bureaucratic rules. One way to overcome these barriers is through improving relationships and communication between IRBs and principal investigators (PIs), research experts say.

"If you look at what was required 10-15 years ago, you would see the process has undergone dramatic changes since then," says **Jonathan Woodson**, MD, an associate professor of surgery at the Boston University Medical Center. He was part of a panel discussing enhancing communication between IRBs and PIs, held during the 2004 Annual IRB Conference, sponsored by the Public Responsibility in Medicine and Research (PRIM&R) Oct. 28-31 in San Diego.

"Admittedly, there have been bureaucratic types of changes, but the bottom line is that the whole issue of ethics and human subjects research and human protection is an evolving area," Woodson says. "So what was true 15 years ago may not be true today."

The evolution has contributed to an IRB's difficulty with PIs, who may not understand why they are being required to do things differently for

research they've always conducted another way, he notes.

"I think one of the biggest barriers is how researchers think this is one more piece of bureaucracy to get through," says **E. Helen Berry**, PhD, professor of sociology at Utah State University in Logan. She also is the former chair of the USU IRB, and also spoke about improving communication at the recent PRIM&R conference.

"You've written a grant and made sure you dotted all I's and crossed all T's for the grant and sent it off to the granting agency, who asks you to change certain things," Berry says. "And then there's still the IRB — one more barrier to doing research."

The process gives PIs the impression that IRBs are just another group of people from whom the investigator needs to get approval, she says.

"It makes the IRB seem like they have an adversarial relationship with the researcher, and that's not the goal; but that's the way it feels," Berry says. "That's what makes the relationship so negative."

The chief barriers to communication between IRBs and PIs are two-way streets, says **Robert Larsen**, MD, an associate professor and vice chair of Health Science Campus IRBs at the University of Southern California, Keck School of Medicine, in Los Angeles. Larsen joined Woodson in speaking about this topic at the recent PRIM&R conference.

"IRBs demand certain things of investigators; when they don't do these or are confused about them, that will delay the process," he explains. "Investigators want IRBs to be prompt in their evaluations because it's no good submitting protocols and waiting forever."

Taking a look from a broader perspective, this type of communication problem is predictable whenever two groups come to an issue with very different perspectives, says **C. Kristina Gunsalus**, JD, special counsel and adjunct professor in the College of Law at the University of Illinois in Champaign. She was on the PRIM&R conference panel with Berry.

"I think it has roots in how we're all busy and deeply rooted in our own perspective, and there's a lot of social psychology that talks about why it's hard for us to listen well, hear completely, and understand — much less, empathize with others," Gunsalus says. "This is true particularly if we don't have good personal connections with them in advance."

Woodson, Berry, and Larsen provide this look at the barriers IRBs experience in the quest for better communication with PIs:

• **Encountering duplication and delays:** "One thing that frustrates investigators is the amount of duplication that is necessary to get something done," Larsen says.

For example, most centers require investigators

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Vice President/Group Publisher: **Brenda Mooney**, (404) 262-5403, (brenda.mooney@thomson.com).
Editorial Group Head: **Lee Landenberger**, (404) 262- 5483, (lee.landenberger @thomson.com).
Managing Editor: **Alison Allen**, (404) 262-5431, (alison.allen@thomson.com).
Senior Production Editor: **Nancy McCreary**.

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Editorial Questions

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to summarize the clinical protocol they're proposing and then have them submit the complete clinical protocol and grant application where the information already is present, he notes.

"So we're asking investigators to cut and paste because we don't want to read both documents," Larsen says.

Instead, IRBs should ask PIs for background information references, he suggests.

"You could say where there is background information, saying, 'Clinical protocol — page seven,'" Larsen says. "That solves a whole lot of problems."

It also frees the IRB to concentrate on what's important, such as these issues, he says:

— How is the PI going to implement the trial at the institution?

— What are the PI's qualifications?

— Is the research environment supportive enough to get it done?

— Is the budget sufficient to do what the PI intends to do?

— Does the PI have access to patients, and can they make good judgments about whether they should be in research?

— How does the PI implement the trial at this site and make it acceptable?

— What are some risks, benefits, and procedures that will be the same across centers?

• **Having different perspectives:** "PIs grow up in an environment of academics and investigation, focusing on exploring new concepts and discovery, and they almost take it as a given that in the process good people are trying to do good work that will protect human subjects," Woodson says.

"To a certain extent, it's laudable and understandable," he says. "On the other hand, it's the IRB whose job it is, in a very diligent way, to examine protocols for compliance with human protection regulations."

So PIs and IRBs are approaching research from two different perspectives, Woodson adds.

"What makes it worse is that the investigator community doesn't have, by and large, a fundamental knowledge base about what the regulations are and their intent," he says. "That's not to be overly critical, but that's just the way they grew up — they don't know chapter and verse of what's required."

Another characteristic that leads to communication problems is that IRBs are by design eclectic, Woodson says.

"These are a group of individuals convened from different perspectives to examine those protocols," he says. "So you have scientists on the panel, legal people on the panel, and lay people on the panel, and so there should be no expectation that they will all see the protocol the same way."

This diversity of opinion and approach naturally will lead to disagreement and some misunderstandings, Woodson notes.

Likewise, the common experience and perspective of many investigators could lead to communication problems, such as writing protocols in a language that is well understood by the experts in that field, but confusing to some IRB members, he says.

"The PI can't communicate the general idea or intent of what they wish to do and what the PI is intending to send if the message is not received," Woodson says.

• **Attending to documentation details:** PIs often fail to write down everything they intend to do in a protocol, Berry notes.

"The IRB has to consider whatever the PIs wrote and not what they didn't write, but would do anyway," she explains.

For example, researchers might describe a drug trial with three groups of children, including one that would receive the study medication, one that would receive another medication, and a third group that would receive no medication, but would be treated with behavioral therapy, she says.

The children participating in the trial might all have a diagnosis of a behavioral problem. In the protocol, researchers might have neglected to say what would happen if the children who were receiving medication began to experience problems and at which point this would result in a change, Berry says.

However, the IRB catches this omission and asks the researcher if he or she intends to keep children on the study medication even if it is causing problems, she points out.

"The researcher says, 'Obviously, we'd pull the children from the study and find other ways to treat them,'" Berry says. "But if the PI doesn't tell us this in the protocol, we don't know."

• **Knowing the regs:** "One issue that came up recently was the issue of when an IRB could grant a waiver of informed consent," Woodson says. "Again, it related to an industry-sponsored study in which there was promising new therapy for blood replacement, and the federal regulations has specific guidance about when a waiver of consent can be granted."

In this situation, the PIs didn't quite understand that if another model of investigation could be

constructed to obtain the desired information, then they are obligated to investigate the treatment in that way rather than in the model that would require a waiver of consent, Woodson says.

"People have a right to say, 'I do or do not want to be involved as a subject in this study,'" Woodson says. "And just because a study is hard to do in another model where consent can be obtained does not mean it cannot be done that way."

In the blood replacement study example, there was the possibility of constructing a model in which patients could provide informed consent right before surgery so if they were to begin to hemorrhage during surgery, the surgeon could use the blood substitute, Woodson says.

The model the investigators had proposed would have used subjects involved in emergencies that resulted in blood loss, and since those emergencies could not be anticipated, there would be a waiver of informed consent. However, the study could be conducted based on the surgery model, instead, Woodson says.

Most importantly, IRBs need to find ways to improve communication between PIs and IRB members, so when a PI submits a protocol such as the blood substitute study, he or she will understand that the IRB may require a major change in how the study is conducted and be able to address that issue.

"It seems to me that we can be suspicious of PIs and PIs can argue we're trying to keep them from getting research done," Berry says. "But if both sides don't communicate and explain what's needed, then neither side will be happy." ■

Special Report:
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How you can fix common problems

Simple strategies improve process

The relationship between IRBs and principal investigators often seems strained and adversarial, but IRB and research experts say the problems mostly can be solved with a few creative changes.

Here are some suggestions for reducing protocol submission problems and improving communication between IRBs and PIs:

1. Turn an obstacle into an IRB member or speaker.

"The person who complains the most is a really good candidate for being on the IRB for a couple of reasons," says **E. Helen Berry**, PhD, professor of sociology at Utah State University in Logan. Berry is a former chair of the USU IRB.

"The first reason is that the person who complains can tell the IRB what the IRB is doing that makes them crazy," she says. "The PI can tell the IRB where they're being inconsiderate or acting rude when there should be a door opening rather than a wall."

The other reason to invite a PI with complaints to join the board is because he or she will gain a greater understanding of the regulations and IRB process and be able to pass on some of this knowledge and change of mindset to other investigators.

"We're all on the same team," Berry notes. "The PI, IRB, participants, and the university are on the same side — we want research to be done."

2. Change your own behavior first.

"One of the realities in life that is tedious, but important to accept, is you cannot force the other person to change," says **C. Kristina Gunsalus**, JD, special counsel and adjunct professor in the College of Law at the University of Illinois in Champaign.

"But you can control your own conduct, and you can change your conduct so that you improve the way the interaction proceeds," she says. "As much as it's gratifying to sit around and talk about what's wrong with the other guy, what you can change is yourself."

By improving one's own professional skills and approach to problem solving, a person can change the outcome for the better, Gunsalus points out. For example, if the problem is that PIs are not completing documentation effectively, the question is this: "What can I do differently that would help?" she says.

"It's easy to say, 'We put out educational materials and did this, but they didn't take advantage of it,'" Gunsalus says. "But the reality is that all of us in our lives are in information overload."

So the road to a solution is to find a way to provide educational information and support to PIs at the moment that they need it, such as when they are filling out the protocol submission form, she says.

"Make it accessible, understandable, and recognize that people are deadline-driven, so you should schedule some time into the process," Gunsalus adds.

"If our goal is to assist the public and to improve the state of knowledge and be an asset to the university, rather than struggle against human nature all the time, one way to do things is to say, 'There will be people who are frantic at the last minute, so what can I do to keep me from being behind in my work because of them,'" she says.

3. Put the chair in charge of building bridges.

IRB chairs are responsible for airing and reconciling various IRB members' opinions before the board's findings and concerns are reported to investigators, says **Jonathan Woodson**, MD, associate professor of surgery at the Boston University Medical Center.

"If there's any sort of expertise assigned to the IRB chair it's that they have to work the interface between controversies within the committee and between the IRB and PIs," he explains. "The chair needs to be well versed with the protocol and should do his or her own examination of the protocol before walking into the meeting."

While reviewing the protocol, the chair should anticipate friction points and facilitate the discussion of these issues, Woodson adds.

"Where there's a breakdown in understanding between one perspective and another, the chair needs to build bridges and links so various constituents can understand what's being said," he explains.

For instance, if the PI has written the protocol in a way that may lead to misunderstandings among some IRB members, it's the chair's responsibility to provide the background and intent of the protocol in an effort to clarify the proposal and build consensus at the committee, Woodson says.

Then when the IRB's decision and comments are sent to the PI, the IRB chair could help the PI understand what the IRB wants done in the interest of further protecting human subjects, Woodson says.

4. Provide natural consequences.

IRBs sometimes establish deadlines and rules for submission, but then let investigators get away with being late or breaking a few rules. This sends the message to the investigator that it's not important to be efficient and timely and soon, the investigator becomes a chronic noncomplier, Gunsalus notes.

"You need to say, 'Here are the rules and here are some natural consequences for not following them,'" she says.

The chief goal is to make the IRB's own system efficient and professional and to have IRB staff and members hone their own professional skills at communication and negotiation, Gunsalus says.

Once the IRB has become as professional as possible, then it's important to enforce deadlines and rules, she says.

However, if an IRB has allowed an investigator to be late with applications continually, then when the IRB suddenly clamps down, the PI will feel as though the decision is arbitrary, irrational, and unfair, Gunsalus explains.

But PIs will respect an IRB and its deadlines if the IRB is clear from the beginning about what is expected and what will be done if the PI doesn't adhere to the rules, she says.

5. Try different educational approaches.

Web-based education is popular now, and training lectures remain a common way of teaching IRB members, investigators, and research professionals. However, these may not be the most effective ways to teach people, Gunsalus says.

If an IRB continuously finds that its education has not produced the desired results of having better informed and more cooperative PIs, then it's likely the way the education is conducted needs to be changed, she adds.

For example, most people learn more readily by doing rather than listening, so perhaps the best way to teach investigators about the IRB process is by setting up a mock IRB meeting for PIs and others to attend, Gunsalus suggests.

6. Use a language dictionary and templates for informed consent.

"We adapted a language dictionary from the University of Texas in San Antonio," reports **Robert Larsen**, MD, associate professor and vice chair of the Health Science Campus IRB at the University of Southern California, Keck School of Medicine in Los Angeles.

The language dictionary gives PIs a quick reference for using substitute words and phrases in informed consent documents with the goal of making them easier to understand by subjects, he says.

Since the IRB is familiar with the dictionary and its terms, this also helps to make the protocol review process more efficient. Now when an investigator is struggling to come up with a substitute word for medical term, he or she can use a term that the committee agrees to rather than guess incorrectly and have to change it per IRB orders, Larsen says.

Likewise, IRB staff could develop a template for an informed consent document and make this readily available to PIs who are writing informed consent documents for their own protocols, Woodson suggests.

"After so many years of doing this, we know what kinds of language work best in terms of creating reading levels that are best for subjects," he says. "We know exactly what will pass the board, and we know what the federal regulations require, so it helps PIs understand what is required by providing the templated language." ■

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Working with social-behavioral researchers

Try a meeting of the minds

One possible explanation for why IRB reviews of social-behavioral research pose complications and some confusion among IRBs and researchers can be found in the very different mindsets of the two parties.

For their part, social scientists believe they have a right to research, and their work should not be impeded by IRBs. Alternately, IRBs believe it's their job to anticipate any imaginable harm that a social-behavioral study might inflict on participants, explains **J. Michael Oakes**, PhD, assistant professor of epidemiology at the University of Minnesota in Minneapolis.

The problem is that both sides have dated mindsets, he notes.

Until recent years, social behavioral research has been free of most oversight, and the more experienced researchers have difficulty accepting that their corner of the universe has changed, Oakes says.

"There's a lot of entrenchment and anger among social scientists because often the most distinguished social scientists have had illustrious careers, but only 10 years ago, never had to submit to an IRB," he explains. "And now they do, so there's an attitude of, 'Who are these bureaucrats telling me what to do?'"

The tension lies on the balance between conducting important social science research while also protecting human subjects, Oakes notes.

"As a social scientist, I fully empathize with them," he says. "The right to research is very different for biomedical researchers who are so used to having oversight."

However, when an institution and IRB members work with social scientists, it's important to reframe the issue. For example, IRB members might explain to social scientists that the IRB is no different from any other peer review, including obtaining a grant or publishing a paper, Oakes suggests.

"Just like the old, distinguished social scientist would submit a paper to a journal with no peer review years ago, now it's hard to get papers published in distinguished journals — the bar has been raised," he says.

Likewise, the IRB review of social-behavioral research is the new standard, and there is no reason for social scientists to believe their old methods and lack of oversight are rights that should continue into the 21st century, Oakes says.

The typical IRB's mindset also needs some adjustment, he notes.

"We don't understand the risks of social science research," Oakes says. "We don't empirically or scientifically understand them, and that's so obvious we forget about it."

This lack of understanding creates conflicts between social-behavioral researchers and IRB members and may reinforce the investigators' perception that they are being subjected to unnecessary oversight, he explains.

"When I sit on medical IRBs and panels, the physicians and psychologists know what effect the increased dose of medication will have at this point in an experiment, and they know through animal models or other quantifiable means what is going to happen," Oakes says. "In the social science world, we have no empirical idea of what will happen if you ask a sad person if they've ever thought about killing themselves."

IRBs may assume it's possible that such a question could lead to a person committing suicide, but there is no evidence that such an outcome has ever occurred, Oakes says.

"In my own work, subjects who are depressed or at a tough time in their lives find it therapeutic to talk about their depression," he says.

Given the lack of data, it's unclear how any IRB can predict costs and benefits of a social-behavioral study, Oakes notes.

"This can drive a social scientist crazy because

the IRB, with the best intentions, will say, 'This is the worst-case scenario,'" Oakes says. "But it's so different from medical research where they can say, 'I know this might happen.'"

IRBs when reviewing social-behavioral research will base their decisions on imagined worst-case scenarios and then require investigators to jump hurdles and follow stipulations designed to prevent these imagined consequences, Oakes says.

"Then you have a social scientist who is very angry," he notes. "And yet, the IRB is doing its job because without empirical or scientific information, it has to be ethical, worrying about the worst possible case."

There are a variety of potential solutions to this problem, although some will require changes within the research field, Oakes says.

Here is what can be done, both by individual IRBs and by the research industry, in general:

1. IRBs should make certain social-behavioral research experts are on the board if that kind of research is reviewed.

Many institutions have physicians and biomedical researchers and experts on their IRBs, but fail to have members who are experts in survey or social-behavioral research, Oakes notes.

"First ensure that people reviewing studies are experts in the protocols' [field], and make sure you have survey researchers on the panel if there will be survey research to review," he says.

IRB members who are unfamiliar with social science research may tend to err with one of these two attitudes: "They may go by the worst-case scenario out of fear for subjects, or they may say, 'This isn't surgery, so there's no risk here in asking people questions,'" Oakes explains. "Both attitudes are wrong; the truth is someplace in the middle."

However, if an IRB makes an effort to have as social-behavioral expert on the board then that person will be able to help other members put this type of research into the proper context, Oakes explains. "How can IRB members legitimately say they have the proper expertise without having a [social scientist] on the medical panel?"

2. The federal government should invest money into understanding the risks of low-risk studies.

NIH and OHRP need to invest some money into learning more about the risks of social science and other low-risk research, Oakes says.

"We'd never do surgical or pharmacy trials without understanding the risk, but we do it in social science research all the time," he says.

It's possible that such an investigation would show that there are not any real risks to social science work and this would mean that the IRB should refrain from imposing barriers and restrictions to such work, on a case-by-case basis, Oakes says. "Armed with the right information the IRB can use the intentional flexibility in 45 CFR to back off, to waive signatures on informed consent, which often is onerous in a simple survey study."

3. Upcoming social scientists should be taught respect for IRBs and human subject protection.

"I tell IRB administrators and social scientists that it's up to the social scientists themselves to help themselves," Oakes says. "When we train young scientists I think they need to be taught by professors about research ethics and how the IRB works."

Unfortunately, the prevalent social scientist attitude about IRBs leads to faculty giving students the wrong kind of lesson, he notes. "Faculty will say the IRB is a hassle, and it will be four months before you get your answer," Oakes says.

So perhaps the solution is for IRB members to talk with senior social scientists on a one-on-one basis, where they'll more likely develop mutual respect, and through this process change the attitudes underlying the conflict between social science research and IRB review, he suggests.

4. Social scientists could conduct their own risk analysis research.

Rather than waiting for NIH to fund a major risk-analysis project, social scientists easily could conduct their own studies, Oakes says.

For example, individual researchers could assess risk of a sexual behavior survey study by having someone follow up the social scientist's sexual behavior survey by asking these questions:

- What were you worried about?
- Did you understand the informed consent?
- Are you worried about confidentiality?
- Do you feel sad that you answered these questions?
- Do you feel happy that you could express yourself?

"That's very simple, but it can be an expensive approach," Oakes says.

Another approach would be to send out surveys with highly sensitive questions and then sending out the same survey without those questions and then asking both groups what they thought about the IRB's human subject protection and research risk issues, he adds.

"If there's no difference between the groups in their perceptions, then I would say these couple of offensive or scary questions had no impact," Oakes says. ■

Self-assessment can point to needed changes

Full accreditation end reward for one organization

Copernicus Group IRB of Cary, NC, sought accreditation to validate that the 8-year-old, independent IRB and human research protection program was on the right track with its human research protection program.

The organization has grown from a two-person office to a support staff of 35. Its IRB meets twice a week, reviewing 200-500 studies each year, reports **Sharon Hill Price**, BSN, MS, CIP, chief executive officer.

"I think the main reason we wanted to seek accreditation was to get validation that we're doing the right thing and protecting human subjects in the best way possible," Price says. "We learned a lot, and we obviously thought we were doing the right thing, but during the self-assessment process we picked out potential areas that needed improvement, and we built on those areas."

Copernicus Group IRB began the process of seeking accreditation in May 2003 and, by the end of July 2004, the organization received full accreditation from the Association for the Accreditation of Human Research Protection Programs (AAHRPP) Inc. of Washington, DC.

"The main area we needed to improve or adjust our focus about was unanticipated problems involving risk to research subjects and others," says **Tammy Sayers Lesko**, CIM, director of quality assurance and regulatory compliance.

"We were primarily looking at serious adverse events and significant protocol deviations and not at the whole unanticipated problem umbrella," she says. "And after talking with representatives at AAHRPP, it was made clear to us what exactly is involved with unanticipated problems involving research subjects and others."

Initially, the organization formed a subcommittee to assist in conducting the self-assessment, Lesko says.

The subcommittee included Lesko, Price, the director of IRB services, IRB chairperson, and other staff and IRB members.

Within four months, the subcommittee had come up with a working draft of the organization's self-assessment, but it lacked consistency, Lesko says. "I had divided up tasks into five domains, and I assigned different groups of people to work on those and get their comments back to me," she says. "I found people had a lot of different writing styles, and even though I had given a lot of direction about what product I needed to have returned to me, people have different ways of doing things."

The five domains evaluated for accreditation were the organization, research review unit, the investigator, the sponsor, and research participants, Lesko says.

After incorporating the varied styles into one working draft, she and Price attended a three-day workshop held by AAHRPP.

Lesko came away from the workshop with the idea that eliminating the subcommittee process and instead working with one expert within the organization at a time could improve the draft. "So if I needed something about a vulnerable population, I contacted the IRB chairperson who had experience in that," she explains. "If I needed IRB meeting minutes, I'd talk to the director of IRB services who helps with meeting minutes."

Lesko and Price discovered that the self-assessment process was more than an opportunity for an organization to take a closer look at policies and procedures.

"It's also a way to explain to an outside group exactly what we do and how we do it," Price says. "After the self-assessment was completed, we sent it to AAHRPP to determine if our processes met federal regulations."

Then AAHRPP conducts the site visit and interviews are held to see if the organization is doing what it said it was doing, Price adds.

Keeping it short and sweet

One of the changes Lesko and Price made to the self-assessment document was reducing each section to what was most succinct.

"Where we might have taken a standard and described it in four or five paragraphs, what they wanted was short and sweet," Price says. "They wouldn't mind if you said, 'This element is addressed in SOP [standard operating procedures] 10,' for example, so we could cut out a lot of stuff that we'd put in it."

Basically, they replaced their initial paragraph form with brief, concise sentences, Lesko notes.

"It took 2½ months to revise the self-assessment," she says. "Part of that time was spent revising our SOPs and reissuing new SOPs, making revisions for a majority of forms and updating the web site."

Their goal was to update and revise everything necessary before submitting the self-assessment

to AAHRPP, Lesko notes.

When the self-assessment was complete, it numbered nearly 1,000 pages, most of which involved reference material such as the entire list of SOPs and a list of active protocols and investigators, she says.

"Our self-assessment with the five domains was 35 pages, but the references were 919 pages," Lesko adds.

Any checklists and resource materials normally provided to IRB members were included in the packet sent to AAHRPP, Price notes.

The accrediting organization required the IRB to submit an electronic PDF file document on disk along with hard copies for site visitors to review, she says.

A long and arduous journey

Reaching the point to submit the material took seven months, longer than Price had anticipated. "Any organization involved in ethical review of research thinks they've got all their ducks in a row, and we've got SOPs, and it won't be a big deal," she says.

But when the organization became involved in the process, it became clear that considerable work and changes would be needed to make the document as clear as possible, Price adds.

Once the self-assessment was submitted, the IRB waited for a site visit, but the work didn't stop here, Lesko says. "We were training staff and IRB members on the revised SOPs and new forms, and we were making use of that time with interactive sessions."

One of the major changes involved bringing the IRB's focus back to unanticipated problems through determining a process in which investigators would inform the IRB of their situation and whether a problem was unanticipated, Price says."We had to educate investigators to have them feel comfortable making that assessment. It required sending out information to investigator sites, including additional information about unanticipated problems."

Also, the IRB updated its web site with information about unanticipated problems, providing specific details for investigators, Price says.

"We developed a better form for obtaining the information we needed as an IRB," she adds.

Another major change was in beefing up documentation of meeting minutes, Price reports.

"We thought we had very good minutes, but we've improved them through our interactions with AAHRPP and site visitors," she says.

For example, the minutes now include more detail regarding controverted issues.

The term "controverted" always has been confusing, Price says. "It means issues that are discussed for a while."

An AAHRPP site visitor suggested that any issue discussed by the IRB for more than two minutes could be a controverted issue and should be documented as such, Price says.

The IRB also needed to improve on how information is captured about principal investigator qualifications and research experience, Price says.

The investigator site questionnaire was improved with more questions about the informed consent process, including these:

- How long does it take an investigator to conduct an informed consent process?
- Do they understand privacy vs. confidentiality?
- Does the research involve a vulnerable population?
- What types of populations are enrolled in the study?

"We've added information about these on our web site, and our investigator site questionnaire points investigators to our web site if they need more information in any of these areas," Price says.

If investigators indicate that they've enrolled subjects who are economically disadvantaged or who have limited English-speaking skills, then the IRB will ask investigators to describe how they will protect that population with additional safeguards, Lesko says.

Finally, the IRB received an accreditation site visit in April. Interviews with study coordinators, sponsors, contract research organizations, IRB staff and members, and investigators had been scheduled in advance, and everyone knew what to expect, she explains.

After the three accreditation officials met with the IRB for three days, they provided detailed verbal feedback, Lesko adds.

AAHRPP had a deadline of 30 days in which to provide the written feedback, and then the IRB would have 30 days to address and solve any problems that were noted in the report. But the verbal feedback gave the IRB some extra time to prepare, she explains. "We had the benefit of a detailed, closeout meeting."

Price, Lesko, the IRB chair, and the director of IRB services met with the site visitors, while an administrative assistant took notes.

"The notes turned out to be crucial for us," Lesko

says. "We could start working on some of the things that were identified instead of waiting a few weeks to get the report, and we needed the extra time."

When the written report arrived there were no surprises, and the IRB was able to complete all improvements by the 30-day deadline, she says.

"We weren't working in a vacuum with our response," Lesko says. "Every single element we were responding to in our report, we ran past our draft answers with AAHRPP, and they reviewed each item before we submitted the final draft."

Fewer than two months after the final draft was submitted in June 2004, Copernicus Group IRB received its full accreditation, she reports. ■

Journal editors issue new requirements

Industry group moves forward with database

Pharmaceutical researchers will have to register their clinical trials with a publicly accessible database if they expect to ever publish their findings in a top-flight medical journal, according to new requirements issued Sept. 8 by the International Committee of Medical Journal Editors (ICMJE).

In an editorial published jointly by all 11 member journals, committee members announced that they would require all clinical trials initiating enrollment after July 1, 2005, to be registered with an independent, publicly accessible trials registry to have their reports considered for publication.

For trials that have already initiated enrollment, researchers have until Sept. 13, 2005, to register if they want to be considered for publication.

"In return for the altruism and trust that make clinical research possible, the research enterprise has an obligation to conduct research ethically and to report it honestly," the committee wrote in a joint editorial. "Honest reporting begins with revealing the existence of all clinical studies, even those that might reflect unfavorably on a research sponsor's product."

The ICMJE is not requiring all drug trials to be registered, but only those that "prospectively assign human subjects to intervention or comparison study groups to study the cause-and-effect relationship between medical intervention and outcome." Phase I trials, which study dose toxicity, and other studies that don't study cause-and-effect will be exempt from the new policy.

The committee did not require publication in a specific registry, but noted that currently, only the NIH-administered site ClinicalTrials.gov meets all of the criteria they name. To qualify, a registry must meet the following criteria:

- accessible to the public at no charge;
- open to all prospective registrants and managed by a not-for-profit organization;
- contain a mechanism to ensure the validity of the registration data;
- be electronically searchable.

The information in the registry should contain, at a minimum, a unique identifying number for each study, a statement of the intervention or interventions and comparisons studied; a statement of the study hypothesis, definitions of the primary and secondary outcome measures; eligibility criteria; key trial dates (e.g., registration date, anticipated or actual start date, date of last follow-up, planned or actual date of closure to data entry, and date the trial data are considered complete); the target number of subjects; funding source; and contact information for the principal investigator.

The drive for a national clinical trials registry began this past June when the American Medical Association's House of Delegates passed a measure recommending that the Department of Health and Human Services establish a centralized registry and that local institutional review boards be required to make registration a condition of study approval.

Lawmakers in both houses of Congress have proposed legislation to increase compliance with existing federal regulations requiring some trial data to be submitted to ClinicalTrials.gov, and many expect any such legislation to include the AMA's recommendation to require registration for all trials in its final version.

In a separate attempt to address concerns about publication bias, the trade group Pharmaceutical Research and Manufacturers of America (PhRMA) announced the formation of an on-line database that would contain information about the clinical trial results of studies sponsored by its member companies.

The database, available on-line at www.clinicalstudyresults.org, will contain the results of all controlled clinical trials (mainly Phase III and Phase IV studies), both positive and negative, completed since October 2002 for PhRMA-member company drug products approved in the United States, according to a PhRMA statement.

For more information, visit the PhRMA web site at www.phrma.org. ■

COI disclosure not a surefire remedy

Coming clean may make matters worse

IRBs may want to re-think their policies on evaluating research conflicts of interest in light of new studies indicating disclosure may not have its intended effect.

"Our research shows that disclosure, may, in fact make the impact [of conflicts of interest] worse," says **Don Moore**, PhD, assistant professor of organizational behavior and theory in the Tepper School of Business at Carnegie Mellon University in Pittsburgh. "In our study, participants felt less responsibility to provide unbiased advice, not more."

Moore, along with fellow Carnegie business school researchers Daylian Cain and George Loewenstein, is researching conflicts of interest and their impact on behavior.

In one particularly telling experiment, they divided a volunteer group of 146 Carnegie-Mellon students into two groups — advisors and estimators — and asked them to estimate the value of cash in six jars containing amounts ranging from $10.01 to $27.06.

The advisors were permitted to handle, but not open, each jar and study it for as long as they liked. They then recorded their estimate of the amount in each jar, which was delivered on a piece of paper as a suggestion to an estimator.

The estimators then got a 10-second look at each of the jars and made their own estimates.

Participants earned small sums of money based on their performance. The estimators' pay solely depended on how accurate their guesses were, while the payoff to the advisors varied. The researchers used three different scenarios:

- **Scenario 1:** Advisors and estimators were told they would be paid based on the accuracy of the estimators' assessments — conditions encouraging both groups to make their guesses as accurate as possible.
- **Scenario 2:** Advisors were told they would be paid based on how high the estimators' guesses were, while estimators still were paid based on accuracy. The conflict was not told to the estimators.
- **Scenario 3:** Advisors and estimators were paid on the same basis as the second scenario, but, this time, the estimators were made aware of the advisors' conflict of interest.

Before any of the scenarios were initiated, researchers asked advisors to write down their personal best estimates of the amount in each jar.

The researchers were surprised to learn that disclosure encouraged even greater distortion in the advisors' accuracy than the addition of the conflicting incentive alone.

After the first scenario, advisors made suggestions that were, on average, within a dollar of their personal estimates. In the second scenario, the advisors' suggestions were, on average, $3 greater than their personal estimates. But the average went up to around $7 greater in the third scenario, when both sides knew the advisor could profit from an inflated estimate.

While the estimators' guesses differed slightly depending on the disclosures, those differences were not as substantial as the advisors' behavior.

Many behavioral researchers already know that people have difficulty using information about conflicts of interest, Moore explains.

Psychological traits a factor

Certain psychological traits interfere with the average person's ability to use disclosure information, he adds.

An observable phenomenon known as "anchoring" demonstrates that most people will focus on a given piece of information and allow that to influence future decisions even when told to disregard that information. And it's obviously very difficult to how to discount information in light of a disclosure of a conflict.

"For example, your doctor tells you, 'You need to have surgery right away before this condition gets serious,'" Moore says. "But then he tells you that he owns a stake in the company making the particular device or instrument that will be used in the procedure."

So, do you proceed and have the surgery, or not? Moore asks. Is the physician influenced by

COMING IN FUTURE MONTHS

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his external relationship? Probably, one might reason, but to what extent?

Consumers of expert information — whether they are businesses consulting experts, patients consulting physicians, or the medical community reading about clinical research — have a very difficult time giving meaning to disclosures of conflicts, Moore notes.

Even more compelling is the indication that just disclosure of the conflicts, in addition to the conflicts themselves, may also adversely affect the quality of information given.

"It seems to suggest that the real problems are the conflicts themselves and we really ought to look more at eliminating them and not just disclosing them," Moore says.

Reference

1. Cain D, Loewenstein G, Moore D. The dirt on coming clean: The perverse effects of disclosing conflicts of interest. Available on the Social Science Research Network (SSRN) Electronic Library at: http://papers.ssrn.com/sol3/papers.cfm?abstract_id=480121. ■

CE/CME *questions*

Physicians, nurses, and others participate in this continuing education program by reading the article, 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 certificate of completion. When your evaluation is received, a certificate will be mailed to you.

17. Which of the following is a major barrier to better communication between IRBs and principal investigators and more effective IRB review processes?
A. The IRB application process may include duplication, which can frustrate investigators.
B. Investigators sometimes lack a full understanding of federal regulations regarding research and informed consent.
C. Sometimes, IRB members and investigators approach research with different backgrounds and perspectives.
D. All of the above

18. What strategy could be employed to improve the way IRBs assess risk and benefit for social-behavioral research studies?
A. IRBs could offer members the opportunity to conduct a mock social science study.
B. Investigators could invite IRB members to attend an oral history session to observe first-hand the potential risks and benefits.
C. The federal government and scientists could begin to study actual risks and benefits derived from social science research and use these findings as the basis for risk assumptions.
D. All of the above

19. During the course of preparing for an accreditation survey, an IRB learned that its minutes needed more detail regarding controverted issues. What is one suggestion for determining which items are controverted issues?
A. Any issue that has been discussed for more than two minutes.
B. Any issue that has been debated by IRB members.
C. Any issue that a community member has raised concerns about.
D. None of the above

20. The study on disclosing conflicts of interest suggest that disclosure itself will eliminate bias in behavior.
A. True
B. False

Answers: 17-D; 18-C; 19-A; 20-B.