IRB ADVISOR

Your Practical Guide To Institutional Review Board Management

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Medical librarians can be a bridge between IRBs and researchers

Non-scientist perspective, attention to detail

An IRB looking to recruit a good non-scientist to the board may have to look no further than its own institution's medical library. Medical or health services librarians can bring a unique perspective and useful expertise in searching medical literature to the process of IRB review, say librarians who have served for years on their own institutions' boards.

"I think librarians, not only by training, but by some more inherent characteristics, make very good IRB members," says **Deborah Klein**, MSLS, AHIP, medical librarian at Pomona Valley Hospital Medical Center, who serves on IRBs at two institutions. "We have a service mentality, so we tend to be willing to volunteer for this kind of thing."

While some librarians approach volunteer service with the idea of primarily conducting literature searches, their IRB roles have increased to include assessing informed consent documents, voting on protocols and in some cases even conducting primary reviews. They say they enjoy their service on the IRB, despite the extra workload it can require.

"I think this is one of the few times that you actually have a chance of having an impact on the lives of people," says **Carlos Rodriguez**, BA, MS, medical school liaison at the University of Pennsylvania Biomedical Library in Philadelphia. "The fact that you may be looking at a study that 10 years down the road may affect somebody's life for the better, makes all the angst and anxiety that I have when I'm trying to finish all the work worthwhile."

Interest triggered by tragedy

The push by medical librarians across the country to become a more integral part of the research process was triggered in part by the 2001 death of Ellen Roche, a healthy volunteer in a study conducted at Johns Hopkins University. Roche died after inhaling the chemical hexamethonium during a study designed to help researchers better understand the

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underlying causes of asthma attacks.

Reports on the incident noted that initial literature searches conducted about hexamethonium failed to turn up articles from the 1950s that contained information about its potential toxicity. In its own effort to improve research oversight in the wake of Roche's death, Johns Hopkins committed to requiring investigators to collaborate with a librarian and a pharmacist to strengthen literature searches.

While expertise in combing medical literature is a big part of the appeal of recruiting a medical or health services librarian to an IRB, librarians bring other advantages to the board table. "I think librarians are knowledgeable about a wide range of subjects," Klein says. "I don't have a degree in biochemistry, but I know more than a layperson does about it and other subjects.

"We are analytical thinkers; we are very detail-orientated. On an IRB, you need to pay attention to details and structure, primarily because of the federal regulations. You have to pay a lot of attention to form, to making sure that a whole bunch of elements are included in the consent form. We're used to double-checking that kind of thing."

Klein and other librarians note that they can fulfill the requirements for a non-scientist member, who often can be hard to recruit to the IRB. And in some cases, they can serve as community members.

Klein is a non-scientist member of the IRB at the Pomona Valley Hospital Medical Center, where she works. A few years ago, she was approached by nearby California State Polytechnic University (Cal Poly) in Pomona to join their board as a community member.

"Cal Poly is a big university that does very different kinds of research (from the medical center)," she says. "They have a lot of social science programs, educational programs, food and nutrition, exercise science. It's a whole different thing than cancer trials. But their IRB was looking for a community member and because I'm not affiliated with the university, I could (fulfill that role)."

As she had already been serving on an IRB, Klein did not have to undergo as much training to begin work with the Cal Poly committee.

Many medical librarians felt they could also help improve human subjects protection by volunteering to work with IRBs. **Nancy Harger**, RN, MS LIS, librarian at the University of Massachusetts Medical School in Worcester, was one of two library staff members who began serving on the university's Committee for the Protection of Human Subjects in 2002 shortly after the Johns Hopkins case.

"Initially, we just took our laptops into the meetings and we'd be available to answer questions that came up in the course of the meetings," Harger says. "And the two of us sat there

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Editors: **Suzanne Koziatek and Melinda Young**.
Executive Editor: **Coles McKagen**, (404) 262-5420 (coles.mckagen@ahcmedia.com).
Senior Managing Editor: **Gary Evans**, (706) 310-1727, (gary.evans@ahcmedia.com).
Production Editor: **Neill L. Kimball.**

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for the whole year and hardly anyone asked us any questions."

So they began looking at other ways they could contribute, and realized that some protocols were being submitted with few references to medical literature on the subject being studied. In other cases, they knew from their own work that some of the citations were not the most current. So they began doing their own literature searches on each protocol.

"We would submit the results of those searches to the two reviewers," Harger says. "At first, we'd just send them the citations and then we decided it would be more useful if we sent them the full text. We'd send a few articles that would give them background to help the reviewer. It's actually come about that they like that a lot. I think our biggest contribution is really to the reviewers, to provide them with information on the topic when they're reviewing the protocol."

Harger and **Judy Nordberg**, BA, MLIS, another University of Massachusetts medical librarian who joined one of the IRB committees more recently, are both voting members of their committees. They've been called upon to read through informed consent documents for clarity and readability.

"We're in a good position to read a consent form and from our own perspective say that we understand it or we don't understand it," Nordberg says. "If we can't understand it, it's a pretty good indication that (it could be improved)."

Knowing the researchers

Ellen Schellhause, MSLS, currently serves as a community member on the IRB at the University of Illinois College of Medicine at Rockford. She used to serve on the board as a non-scientist member, before she left her job as director at the university's Crawford Library.

She describes the library as a "bridge" between researchers and the IRB at an institution, and believes librarians can bring that same quality to review.

"You can make things flow more smoothly for everybody, because you've already worked with the researchers as clients," Schellhause says. "When you're on the committee, you separate yourself from the personal, but you also know enough about research that when it's discussed, you have some input and understanding of what the research is about. You can help with clarity and explanation."

In addition, her work with a campus health literacy group led her to look at the readability of informed consent documents.

"We noticed that the consent forms were just horrible for people to read," she says. "They'd be written at a 12th-grade level. Our group passed a rule that said consents and assents written on our campus for local studies had to be written at a fifth- to eighth-grade reading level."

Schellhause says she believes the focus on literacy in consent documents was her most valuable contribution to the IRB. Librarians also can be useful to an IRB that uses electronic submissions, she says.

"Librarians are very into databases and have a good understanding of this kind of a system. They have technical expertise in electronics and in forms posted online. They understand how the Internet works. I think that can also be a very valuable contribution."

Despite their technical expertise, librarians also bring something of an outside perspective, Rodriguez says. While other IRB members have much more technical and medical knowledge, he can provide a point of view that they may overlook.

"It has to do with being immersed in a certain environment, so that (other perspective) doesn't even occur to you, or it becomes invisible," Rodriguez says. "That is really, in many respects, the value of having a non-scientist on the board."

Seeking a meaningful role

At the University of Pennsylvania, Rodriguez says the associate director of his library spoke with the Office of Regulatory Affairs, offering the services of the librarians. Rodriguez says he and other librarians who joined the IRB committees originally viewed their role as offering a literature search service — "sort of like a private librarian to the IRB." In the meantime, he completed the necessary IRB training, observed meetings and began reviewing informed consent documents.

Now, Rodriguez conducts continuing reviews, reviews amendments, and sometimes acts as a secondary reviewer for new protocols. Though he'd love to be a primary reviewer, Rodriguez knows that he doesn't have the necessary expertise.

"If I had a science background, maybe, but I don't," he says. "When you're a secondary

reviewer, the real hard work has been done, everything in the protocol, all the science has been worked out."

Rodriguez's library background enabled him to create a list of resources that other non-scientist IRB members could use for looking up things they didn't understand. "There were people on the board as well as people in the Office of Regulatory Affairs who had never seen some of these resources," Rodriguez says. "So it was a win-win situation for everybody all around."

The librarians say that their service on the IRB adds to their existing workloads, and much of that work must be done on their own time.

"My family will tell you, 'Oh, Dad's doing the IRB — we won't see him until Wednesday night after the IRB meeting,'" Rodriguez says. "I dedicate myself to looking at the protocols and there's a lot of stuff that I don't know, so I have to look up a lot of things." ■

Start-up consultations improve site compliance

Ensure informed consent, documentation correct

Researchers often criticize IRBs and see them as barriers to research. One way to turn that attitude around is through the creation of a study start-up consultation. This has another advantage: it can improve clinical trial site compliance with human subjects protection regulations and policies.

This type of consultation has human subjects research (HSR) regulatory experts working with researchers to ensure their study site's documentation and consent processes are in order.

"We've worked hard to collaborate with researchers and work with our research community to provide sound, ethical research," says **Sandra L. Alfano**, PharmD, FASHP, CIP, chair of the human investigation committee I and III, and co-chair of the embryonic stem cell research oversight committee at Yale University in New Haven, CT.

"We view ourselves as facilitators of human subjects research and not as barriers or hurdles that researchers have to get over," Alfano says. "The study start-up consultation is clearly an illustration of that collaborative effort."

Yale started the study start-up consultation with the idea that new and inexperienced investigators would benefit from regulatory assistance before they start their study. From a compliance perspective, a preventive effort is preferable to an audit and punitive action when mistakes are found, she notes.

"We'd like to work with people early on to help them think through different issues and put processes in place at the outset," Alfano says.

While the initial focus was on new investigators, the consultation also has proven popular with experienced investigators, says **Tracy Rightmer**, JD, CIP, compliance manager of the human research protection program at Yale University in New Haven, CT.

"Experienced investigators are asking for it as well," she says. "They say they want to get a better handle on various regulations and policies and requirements."

Investigators want to do the right thing, but they're not always sure they are in full compliance, Rightmer adds.

Typically a researcher will request the study start-up consultation after seeing an educational session where it is mentioned. Sometimes Rightmer might recommend the consultation when an investigator demonstrates the need for closer oversight after study problems arise.

Here's how the study start-up consultation process works:

1. Compliance manager reviews protocol and IC paperwork. "Before the start-up visit, I look at the protocol and consent documents to get an understanding of the study and to identify areas of potential noncompliance," Rightmer says.

For instance, some common problem areas involve the informed consent process, subject payments, medication compliance and storage, she says.

"I encourage investigators to come up with questions, and I have templates and forms for them that are available on our website," she adds. "These include enrollment logs, inclusion/exclusion criteria, checklists, staff responsibility log, regulatory documentation sheets, staff training checklist, and a few others."

2. Consultation visits provide education, advice. Rightmer and a coordinator who works part-time on compliance issues typically conduct start-up consultation visits within a few weeks of the request from investigators.

"We want to have this consultation before they have their first study visit," Rightmer says. "We will take one to two hours on the consultation,

depending on the study's complexity."

The consultants will ask to see checklists and other documents, including source documents, case report forms, enrollment logs, inclusion/exclusion criteria, site signature and responsibility logs, etc.

"Then we go over areas that might be problematic for their particular study," she says.

When the consultant finds a potential problem, she discusses it with the investigator.

For example, in one study start-up consultation, Rightmer asked the investigator and study staff how they would verify medication adherence since they didn't have a process in place.

"I asked, 'How are you going to count pills, use a subject diary?'" she says. "I provided them with information about medication adherence."

3. Look closely at informed consent. The study start-up consultation almost always focuses on informed consent.

"If the study involves minors or those with decisional impairment then you certainly want to go over the consent process and safeguards for those vulnerable populations with investigators," Rightmer says. "If it's a medication study, then I'd want to know how they store medications and verify it."

Another important area involves subject payment. Consultants want to ensure study staff and investigators are documenting when subjects are paid.

"We take a good close look at the protocol," Rightmer says. "Then we identify areas that are problematic for investigators and address those during the meeting."

4. Educate CT staff on adverse events and unanticipated problems. During the consultation, Rightmer will define unanticipated problems and serious adverse events (SAEs) for investigators and study staff.

"A lot of industry studies want all adverse events reported, while the Office for Human Research Protection (OHRP) wants only serious and related events reported," Rightmer says. "There can be discrepancies between the two."

The IRB follows OHRP's guidance on the issue, but sometimes receives too many reported unanticipated problems, she notes.

"So if I'm meeting with an investigator who has an industry sponsor, I find out what the sponsor wants and what is required by the IRB," Rightmer explains. "Sometimes the investigator will have to report the AE to the sponsor but won't have to report it to the IRB." ■

Facebook research poses unique ethical concerns

Consent extends to friends & family

Researchers might find it tempting to collect data for socio-behavioral studies from social websites like Facebook. Their appeal is having fairly easy access and viewing a broad range of behavioral information. However, there are big ethical issues with regard to informed consent and privacy, an expert says.

"There are so many people doing research on sites like Facebook, and they're kind of blithely telling the IRB that 'People put this out there on their Facebook site and on their wall where I can see it, so it's fair game for me,'" says **Montana Miller**, PhD, an assistant professor at Bowling Green State University in Bowling Green, OH. Miller is a popular culture expert.

This attitude is not sound from an ethical perspective, Miller says.

The words people write on their social website walls and the photos they post are not a free-for-all. Researchers will need to obtain informed consent from the people who own the walls and photos, and their responsibility doesn't end there, she adds.

"Maybe you have decided in your study you'll get consent from all the people whose Facebook sites you include in your study, and then you start collecting data," Miller says. "What about all the people you didn't get consent from who are writing stuff on the sites of their friends?"

This is a huge third-party issue that is not being dealt with by most researchers and IRBs, she adds.

The informed consent process in other types of socio-behavioral studies are less complex because the study subject's friends and family members will have to know about the study before they can be inadvertently drawn into it. But when researchers collect data from an Internet website, this is a passive activity that can be invisible to the subject's friends and family members.

"On sites like Facebook, I have no idea if my friend is participating in some study, so I might say something embarrassing or personal or sensitive on the friend's wall, and I do this impulsively," Miller explains. "This happens all the time; people don't want the whole world to know about it, but they don't think anybody significant is watching or that the writings on the wall are collected and analyzed as data."

These third parties have not consented to be included in the study, but their information is recorded because of their friend having provided informed consent.

"The same is true of photos posted online," Miller says. "A lot of people are doing studies of images posted on social networking sites, but what if I'm in those photos? It's a very murky and tricky area."

A changing reality

Further complicating the issue is the reality that protocols and privacy boundaries change regularly on these types of websites.

"Even an expert on the subject can't keep up with the changes," Miller says. "The privacy policies of these sites can be so difficult to read through they're almost deliberately inaccessible to the public."

IRBs need to consider and address these kinds of new technology issues by having at least one IRB member who is concerned about electronic privacy and who keeps up-to-date on this topic, she suggests.

"I get huge numbers of emails from around the country asking for advice about these issues, and I don't have time to answer all of them," Miller notes. "I go to the PRIM&R conference and try to educate people."

IRBs should send members to these sorts of workshops and lectures or at least have them check out discussion boards where these questions are raised.

"There aren't good updated guidelines readily available to people who need help," Miller says. "But there's an Association of Internet Researchers at aoir.org who discuss these things."

It's probably too much to ask the entire IRB to become educated on ethical issues related to technology and the Internet, but at least one or two members could be the point persons when these issues arise, she adds. ■

Privacy issues when reviewing sensitive work

Ask for details about safeguards

IRBs at academic research centers often review international infectious diseases research that can raise red flags regarding privacy, confidentiality, and vulnerability. One example might be a study conducted in the Dominican Republic and involving HIV prevention and sex workers. IRB members might question how researchers will collect and store sensitive data, and whether a potential breach of confidentiality poses a serious risk to subjects.

"If data are transferred from other countries, you need to look at how that transfer is being done, whether the identifiers are being destroyed or de-identified," says **Joyce Plaza**, manager of Columbia University's Morningside IRB in New York, NY.

"Two issues we look at are confidentiality and privacy," she adds.

To address both of these concerns, Plaza suggests IRBs should ask these questions during the application and review process:

- "Is the interview done in a private location?"
- "Are subjects cautioned they don't have to answer if they don't want to answer?"
- "Once researchers have collected the data, what steps are they taking to protect that data?"
- "Are they defining who has access to data?"
- "Are staff trained in confidentiality procedures?"
- "Are data sent electronically? Is there encryption?"
- "Is information being hand-delivered? Is it coded?"
- "Are the data collected or stored with the names of subjects, or are they coded?"
- "Are they transferring codes, linking names with study numbers in separate files than research data?"

Electronic submission recommended

An efficient way to collect answers to these concerns would be to have an electronic submission system for IRB submission that walks investigators through sensitive data questions, making suggestions for what needs to be done, Plaza says.

This serves as both education and a way to ensure all protocol review concerns are addressed.

"Privacy and confidentiality need to be explained in the submission process," Plaza says. "We call it the study description that collects details about the study protocol, and we prompt investigators to enter information about privacy and confidentiality and to be explicit with their answers when they're submitting an application."

The IRB also has continuous education programs for principal investigators and their research staff.

"During the review process, if there are items missing from a protocol that we need to consider, then we return the submissions to the

investigator and obtain these specific details," Plaza says.

The Columbia University IRB electronic submission system requires investigators to describe and explain the privacy and confidentiality protections plan for the study, she adds.

"We ask about the privacy and confidentiality procedures they will implement in the study description," she says. "For example, we ask them to describe how subject privacy will be protected and the limits to that protection."

The electronic form could summarize privacy protection as safeguarding an individual's expectation that the information the individual provides will be offered in confidence. Also, IRBs can inform investigators that privacy protection should cover all screening activities, HIPAA provisions, forums like focus groups where private information may be shared, and recordings of research activities where applicable, Plaza says. "Limitations such as compelled disclosure and mandatory reporting also should be described," she adds.

In the Columbia IRB's electronic protocol submission process, there is also a section called "Confidentiality of the data." In this section, investigators are told to describe how confidentiality will be maintained locally and during transmission to another site.

"We have them include a clear description of how data will be stored, specifically indicating whether the data will contain direct or indirect identifiers," Plaza says. "We ask them to describe protections related to accessing the study data, whether in electronic or paper form."

The IRB's website also provides definitions and descriptions of identifiable, coded data, de-identified data, anonymous data, and confidential data so the IRB and investigators are using the same terminology.

"We're always reviewing our language on the website to eliminate areas of confusion," Plaza explains. "I'm always referring investigators to our website for the definition of the different types of data, and we have FAQs [frequently asked questions] on our website that define what 'coded' means, 'anonymous' means, and 'confidential' means because sometimes investigators use the words 'anonymous' and 'confidential' synonymously, and we need them to clarify what they mean."

Investigators also confuse the terms "privacy" and "confidentiality," she notes.

Privacy can refer to the location of the subject when investigators are obtaining sensitive information from them. This location might be a private place of the subject's choice. Confidentiality refers to how data are protected once collected, whether data are kept in an identifiable manner, anonymous, de-identified, or coded.

"This is becoming more complicated with all the research activity going on these days, and it is a concern," Plaza says.

The protocol submission process also asks investigators about their staff training and confidentiality procedures that are included in the consent form. Plaza says the process asks these questions:

- "What will happen to identifiable data at the study's end, after publication?"
- "Are data destroyed, including photographs and recordings and tissue samples?"

Secondary use issues

Another issue involves the secondary use of confidential data.

"We have a lot of faculty obtaining secondary data to do an analysis, and often the owners of that data require a data protection agreement, and it may require the signature of an IT person in that department who has reviewed the data protection plan and made sure it's secure," Plaza says.

International research particularly has privacy and confidentiality nuances.

For example, a study that is enrolling women in a country with customs that are different from the United States and Europe might follow local custom and have the women's male heads of household provide consent for the women's study participation, Plaza says.

"But what if the woman doesn't want the male to know about the study?" she says. "We ask the person with knowledge of the local context to guide us."

This is where it's important to have a local review committee or a consultant knowledgeable of the local customs and norms to also address the same privacy and confidentiality issues in the context of their region's traditions and beliefs.

"The consent form should specify what the procedures to protect confidentiality are going to be, and the board could grant a waiver of documentation of written consent so subjects don't have to sign a consent form in order to protect their privacy," Plaza says. "Investigators still have to go through the whole consent process, but they waive the need for the person to sign the form in the event the principle risk of harm may result from a breach of confidentiality." ■

Revised GPP guidelines improve user engagement

International studies can avoid trust problems

IRBs dealing with international or high-risk research can find some guidance on how to handle all stakeholders in studies in the recently-revised Good Participatory Practice Guidelines for Biomedical HIV Prevention Trials (GPP).

The GPP guidelines offer insight into strategies for improving human subjects protection in studies involving international and/or vulnerable populations. They were developed by a working group formed by the AIDS Vaccine Advocacy Coalition (AVAC) and UNAIDS after two international trials of pre-exposure prophylaxis tenofovir were closed due to activist pressure in Cambodia and Cameroon. The incident raised concerns among researchers, IRBs, and others in the human subjects research community that many other international studies could be similarly impacted by negative publicity and activist pressure.

"These two trials were suspended following regulatory approval by the highest political leaders in their countries," says **Catherine Hankins**, chief scientific advisor to UNAIDS. "There was concern that the issues raised during these suspensions could jeopardize all HIV prevention trials," she adds. "What became evident to everyone was we were not operating in a silo; what could happen at one site in one field could happen to all of us."

The good news was the Cambodian/Cameroon trial problem led to the formation of the GPP guidelines in 2007, which serve as a thorough and thoughtful roadmap to engaging study stakeholders in preparation of a new study.

IRBs can use the GPP guidelines to discuss with investigators how they'll address issues raised in international studies, suggests **Lori Miller**, MHS, senior program manager of AVAC in New York, NY.

The guidelines also provide detailed information for how investigators can raise awareness of their studies and engage with members of the community.

Twelve organizations were involved in a year-long process of sharing the guidelines, holding meetings and consultations about them, and seeing which parts made sense and which parts should be improved and revised, Miller says.

"We compiled all results from the consultation and there was a lot of consistency in the feedback we received," she adds. "The guidelines needed to be revised to have greater human rights perspective and they needed to be simpler and clearer."

The revised guidelines discuss some of the most important issues and, sometimes, sources of contention, between communities and researchers. Here are some examples from the revised guidelines:

- **Power inequalities:** The organizations and nations funding research are perceived by communities to have a power inequality with their leaders who are drawn into the trial start-up process and with their citizens, who are being asked to participate in studies. This perceived inequality can impact the decision-making process, priority setting, control of resources, and recognition of input. Also, there can be power inequality with regard to literacy, education, economic resources, and the provider-patient relationship.
- **Scientific and ethical integrity:** Human subjects research should maintain the highest standards of scientific and ethical integrity, maximizing the benefits for the trial community and advancing global science, the revised guidelines say.

To achieve this, there should be transparency in the form of open, timely, and clear communication between researchers and stakeholders. And there needs to be accountability to stakeholders through the use of GPP and responding to stakeholders' input.

One of the changes in the revised guidelines is a shift from using the term "community" to the term "stakeholders," Miller notes.

"That was a very purposeful change in response to a lot of feedback we received in consultations," she says. "A number of groups said we have to be thinking about all stakeholders, not just the community stakeholders."

For instance, stakeholders also include the government, the media, and others.

"Trial sites should have a stakeholder engagement plan that addresses who the possible stakeholders are and how best to work with different groups," Miller says.

The guidelines also address how a study might be closed in the event of evidence of harm or for unforeseen circumstances, such as administrative or financial reasons. And, researchers should consult with relevant stakeholders to develop a plan for disclosing study results, the guidelines say.

Study closure is important for researchers and IRBs to consider for a variety of reasons, including one that often is overlooked: the same research

institution might use the particular site again for different studies.

"The conclusion of the GPP guidelines discusses site maintenance between trials, and that's a very important issue," Miller says. "If research teams invest a lot in a site, working with stakeholders, and building a relationship, then it's not ideal to have that relationship dissolve when the trial ends."

Any new trials would have to start all over again, building up trust and rapport with stakeholders, she adds.

"It's important to maintain the relationship and keep core staff to continue those relationships," Miller says. "That's something where we think about applying pressure to sponsors who have the money to make sure that maintenance between trials can happen."

For more information about the GPP guidelines, visit the website at www.avac.org. ■

A closer look at 'incidental findings'

Provisions needed for informing patients

As more sophisticated imaging technologies are used in research, investigators and IRBs must grapple with an unintended side effect – an increase in incidental findings (IF), or new health data unrelated to the study that is revealed about participants.

Common incidental findings turned up by X-rays, MRIs and CT scans can range from minor issues requiring no follow-up action to potentially life-threatening conditions such as a fast-growing cancer or aneurysm. But it's hard for researchers and IRBs to plan to manage such findings without knowing more about their frequency and severity.

In an effort to better understand what to expect from incidental findings in imaging studies, a team of physicians, radiologists, bioethicists and IRB specialists at the Mayo Clinic in Rochester, MN, tracked and analyzed data from three months worth of research imaging exams conducted at the hospital.

They looked at the IFs generated by more than 1,400 imaging exams — tracking follow-up studies, final diagnoses and interventions. The result: Nearly 40% of all exams turned up at least one IF, and nearly 20% had multiple IFs. Results were published recently in the *Archives of Internal Medicine*.[1]

But **Nicholas Orme**, MD, an internal medicine resident at Mayo and lead author of the study, says it's important to look beyond that initial, startling number.

"Incidental findings are common, but they're not commonly significant enough to cause clinical inquiry," he says. "So even though 40% of our research subjects had an incidental finding, only about 6.2% of those went on to have further clinical action."

In cases where there was clinical action, he says, the eventual benefits to the participants were often unclear, or worse, the procedure proved to be an overall burden. A mass might be investigated and found to be benign, causing extra expense, discomfort and stress to the participant in the process.

But in a handful of cases, the IF turned out to be the first clue of an extremely grave condition, such as a brain tumor, necessitating life-saving treatments.

"In three months, there were six cases where there was clear medical benefit — where something was picked up incidentally and then went on to have a significant positive impact," Orme says. "You can't just say, 'Oh, we can't worry about these things because they're so uncommon,' because when they do happen, they can be a big deal for the patient."

Breaking down the data

Orme says that part of the value of this study is that it breaks down IFs by the mode of imaging and area of the body, showing that certain types of imaging are far more likely to produce serious IFs that require follow-up.

As a result, researchers and IRBs can look at a proposed imaging study and estimate how likely it is to generate serious IFs. For example, 9.2% of all the CT scans done of the abdomen and pelvis during the three months of the study resulted in an IF that required further action.

"That's really quite high," Orme says. "If you're going to scan 300 people with this CT abdomen/pelvis (in a study), we may have 30 people who need further workup.

"So the IRB and the research protocol should determine what they are going to do. What's the plan? How quickly are we going to follow these scans up? How quickly are we going to refer them? Are we going to communicate with the primary care physician? There should be a plan in place, because that's going to come up in that study."

On the other hand, the Mayo study found fewer incidental findings from knee X-rays, with almost none requiring follow-up. So in protocols requir-

ing knee X-rays, the IF planning wouldn't need to be as extensive, Orme says.

William Tremaine, MD, director of Mayo's Office of Human Research Protection, who was part of the panel that evaluated the incidental findings for this study, agrees that the results should aid IRBs in modulating their response to the potential for IFs.

"Certainly it was the abdominal and pelvic CT and to a lesser extent the chest CT and head scans that carried the biggest risk," Tremaine says. "I think IRBs would want to see if there are clinically validated studies used in part of the research. And if those studies carry a substantial risk for identifying important unexpected clinical findings, then provisions should be made for informing the participants and dealing with those."

Both he and Orme say that the informed consent for these types of imaging studies must lay out not just the possibility of incidental findings, but the consequences that could flow from them — extra tests, potential side effects and expenses to the participant.

"If there's a spot that's found on the lung and it will require repeat CT scans every several years, depending on how things are set up on this particular study, it may be on (the participant's) own dime, " Orme says. "That's something that they should probably be aware of."

When to review scans?

Since 2003, the policy at Mayo has been to have a trained staff radiologist examine all research images for potential IFs the same day the scans are administered. Orme says he knows that kind of commitment requires resources that not all institutions have.

"But I think this does bring up issues that people should be talking about," he says. "In some places, these scans are taken and then they're not read until a year later when the radiologist on the team has time, and that's a window of opportunity. If you do see a brain cancer that you could resect, a year later it's now metastatic brain cancer."

Tremaine says research scans should be reviewed within the same time frame as the clinical standard of care for the institution.

"For Mayo, that's the same day, but for some places, it might be the same week, or the same two weeks," he says. "If you're using a clinically validated study, it should be held to the same standards as that same test being done for clinical purposes."

Orme says one of the strengths of this study was the diverse team of experts assembled to analyze the results.

"We had a former head of our IRB, we had bioethicists, we had a lawyer, we had all these people who saw it from different angles," he says.

And Tremaine was happy to have the IRB heavily involved in the project.

"I was thrilled to see that the IRB was included in the research process as well as just the research oversight," he says. "I think there's a tremendous opportunity for that. Research deals with crunching data, and the IRB has lots and lots of data at every institution, so it's a huge opportunity for participation in research, not just oversight of research."

REFERENCE

1. Orme NM, Fletcher JG, Siddiki HA, et al. Incidental findings in imaging research: Evaluating incidents, benefits and burden. *Arch Intern Med* 2010;170(17):1525-1532. ■

Helping researchers with a tough topic

Phase 1 recruitment — essential points, pitfalls

Recruiting patients for Phase I oncology studies — which are unlikely to provide therapeutic benefit to participants and which carry the risk of significant side effects — raises unique issues in informed consent.

Patients who are recruited for such studies often have late-stage cancers that have not responded to previous treatments. Although the purpose of Phase I studies is to see if an experimental medication is safe and to establish dosages, studies have shown that patients often have unrealistic hopes for the drug's effectiveness against their illnesses.

Trying to recruit patients without producing this therapeutic misconception can be difficult for clinicians, says **Richard Brown**, PhD, an assistant professor in the department of social and behavioral health at Virginia Commonwealth University School of Medicine in Richmond.

"We know that clinicians commonly rate clinical trial discussions as one of their hardest communications challenges," Brown says. "This is in part because they have to go from being an expert, with an evidence base for the treatment, to being something of a salesperson, having to sell something without that evidence they can use to back up their recommendations."

"There are particular communication issues

that arise in Phase I studies because of when they are conducted and the likelihood of benefit for patients. It's a tricky, challenging area and it's one that's been under-studied."

Analyzing consultations

Because of evidence describing poor communication during informed consent discussions, Brown and his colleagues examined a series of consultations in which patients were recruited to Phase I oncology trials. They looked for the types of information being presented, how the information was presented and the strategy for decision-making used.

Results from the study were published in the journal *Psycho-Oncology*.[1]

Brown says the goal is to develop communications strategies to help clinicians and patients in these types of discussions.

"It seems to me that one of the ways forward with this is for clinicians to understand the challenges and to be given support and suggestions for ways they can address these kinds of issues in more helpful ways," Brown says.

Brown's group recorded and analyzed conversations between six oncologists and 16 patients regarding Phase I trials. They identified six communication themes that arose during these conversations:

— Orienting, in which the physician and patient reach agreement about the diagnosis and extent of the patient's disease. The physician may talk about various other treatments and rule them out as options.

— Educating the patient about Phase I studies in general and a specific study or studies for which the patient may be eligible. The doctor will discuss how the experimental treatment is supposed to work in the body as well as concepts such as dose escalation.

— Describing uncertainty, explaining the rationale for the study, such as providing knowledge to help future cancer patients, as well as noting the possibility of benefit to the patient or side effects.

— Persuading, in which the physician uses one or more strategies to convince the patient to participate. These might include expressing optimism about the trial or urgency to sign up (by saying, for example, that there are limited openings for participants).

— Decision-making, in which the physician and patient come together to make a decision about the trial.

Not all of the themes identified in the study were present in all of the discussions, Brown says. In the recommendations, the group actually looked at ways to avoid some of the persuasive techniques identified.

Shared decision-making

Brown says that "shared decision-making," with the physician and patient contributing equally to the final decision, is considered the gold standard for clinical trial communications. But he says that's not always what every patient wants.

"The literature shows that some patients prefer shared decision-making," he says. "On the other hand, some patients really want to make the decision themselves while taking into account the physician's recommendation. And at the other end of

CNE/CME OBJECTIVES

The CNE/CME objectives for IRB Advisor are to help physicians and nurses be able to:

- establish clinical trial programs using accepted ethical principles for human subject protection;
- apply the mandated regulatory safeguards for patient recruitment, follow-up and reporting of findings for human subject research;
- comply with the necessary educational requirements regarding informed consent and human subject research.

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

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

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

COMING IN FUTURE MONTHS

- Health services research — special issues for IRBs
- Follow this advice to improve mentoring skills
- Strategies for achieving ongoing consent
- Make meeting minutes sing — greater efficiency, clear writing

CNE/CME QUESTIONS

1. The push by medical librarians across the country to become a more integral part of the research process was triggered in part by the 2001 death of a healthy volunteer in a study on:
A. HIV
B. cancer
C. asthma
D. pneumonia

2. During an IRB review of an international trial, which of the following questions would be appropriate to ask of researchers?
A. Are subjects advised that they don't have to answer if they don't want to answer?
B. What steps are you taking to protect data?
C. Are you defining who has access to data?
D. All of the above

3. One of the main motivations of the start-up consultation process is to identify fraud and abuse by investigators.
A. True
B. False

4. A study that included 1,400 research-generated images found that nearly 40% had an incidental finding. What percentage of those required clinical action?
A. Less than 1%
B. 3.7%
C. 6.2%
D. 9%

Answers: 1. C; 2. D; 3. B; 4. C

the spectrum, some patients just want to give the decision to the clinician and say, 'You tell me what you want to do.'"

He says physicians should determine how the patient prefers handling the decision, and check back with him or her frequently to make sure that preference doesn't change as the situation changes.

Likewise, Brown says clinicians should understand how much information patients want to know — about the trial, about potential side effects, about their prognosis — and tailor the consultation to the needs of the patient, checking back periodically to make sure preferences haven't changed.

REFERENCE

1. Brown R, et al. Seeking informed consent to Phase I cancer clinical trials: Identifying oncologists' communication strategies. *Psychooncology* 2010 Apr 7 (Epub). ■

2010 SALARY SURVEY RESULTS

IRB ADVISOR

Your Practical Guide To Institutional Review Board Management

IRBs ride out tough times, see hope for turnaround

Fewer raises, rising workloads cited

As institutions continue to weather the economic downturn, the toll on IRB offices is showing. The trends of previous years — fewer raises, more job cuts, increasing workloads — continued in 2010, according to responses to *IRB Advisor's* annual Salary Survey.

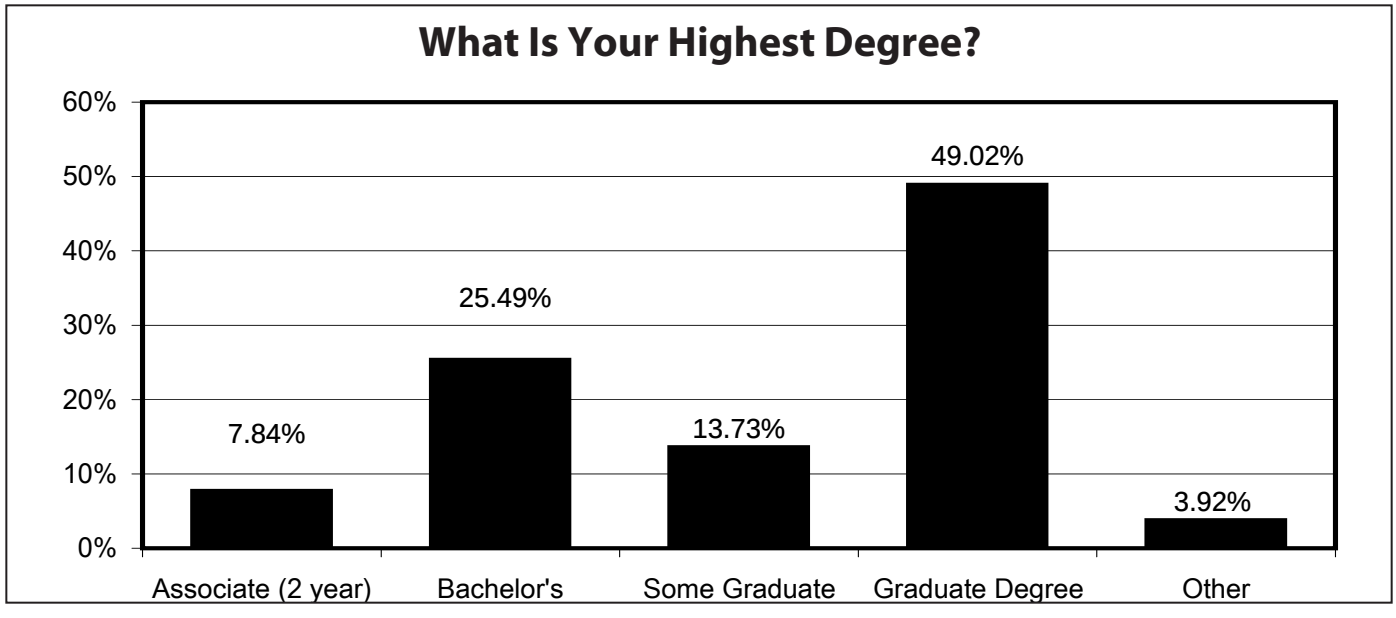
But there's room for optimism in some of the results. Some previous concerns, including pay cuts, seem to have subsided, and more respondents in this year's survey reported higher salaries than in the past.

At Vanderbilt University, **Julie Ozier**, MHL, CHRC, CIP, associate director of the Human Research Protection Program, says she's cautiously optimistic after signs of a modest recovery this year. In 2010, IRB staff members in her office were eligible for raises of up to 3%, after a year in which no raises were given. Another ½% increase was scheduled in January.

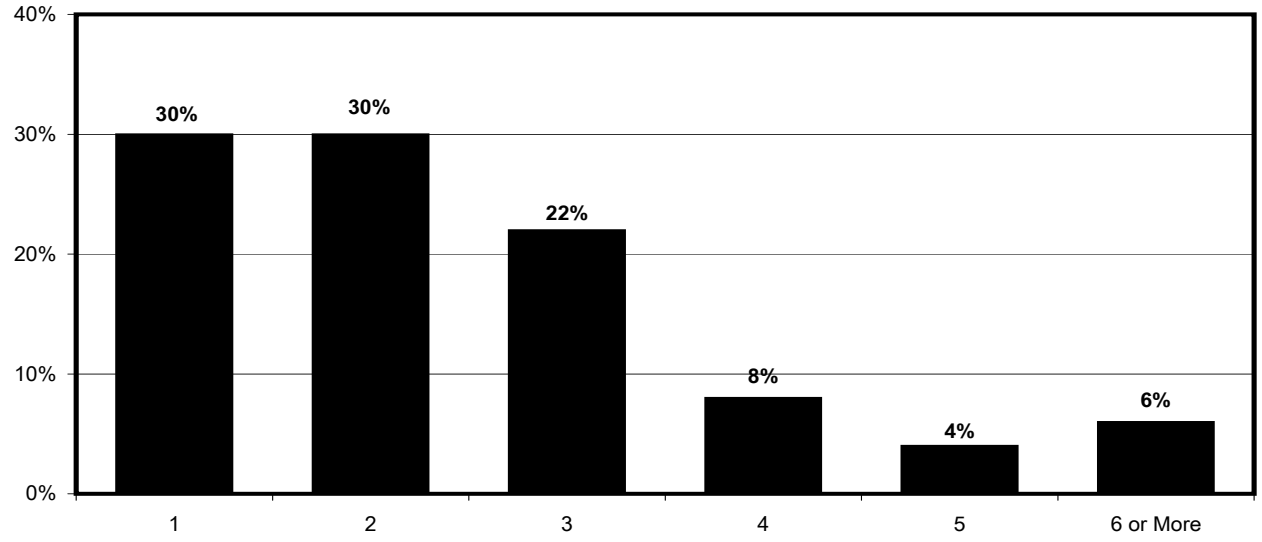
"Our medical center feels like they're recovering a little bit," Ozier says. "I don't know if we're starting to see a turn, but we're very hopeful."

The 2010 salary survey drew responses from 52 people — IRB coordinators, administrators and managers, directors of human research protection and other professionals involved in the oversight of human subjects research.

Those reporting were primarily from smaller offices — 82% reported that three or fewer people worked in IRB administration in their departments. Most institutions reporting were in hospitals (54%) or academia (40%), and were located



How many people work in your department (IRB administrative side)?



in either medium-sized cities (48%) or urban areas (31%).

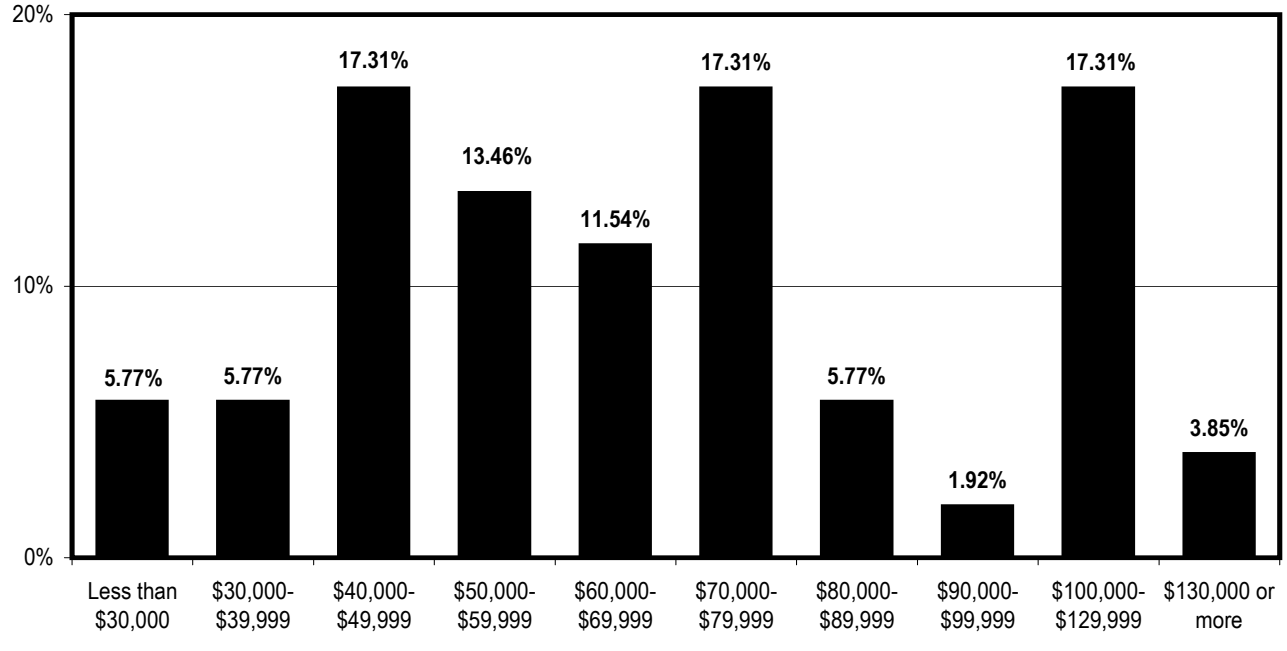
The salary spread in this year's survey appears larger than in the past. Over the past several years, the largest percentage of respondents made between $40,000 and $49,999. This year, there were as many people in that group as there were making $70,000-79,999 and $100,000-$129,999. Overall, a larger percentage of 2010 respondents made more than $50,000 (71%) and more than $70,000 (46%) than had been reported in previous years.

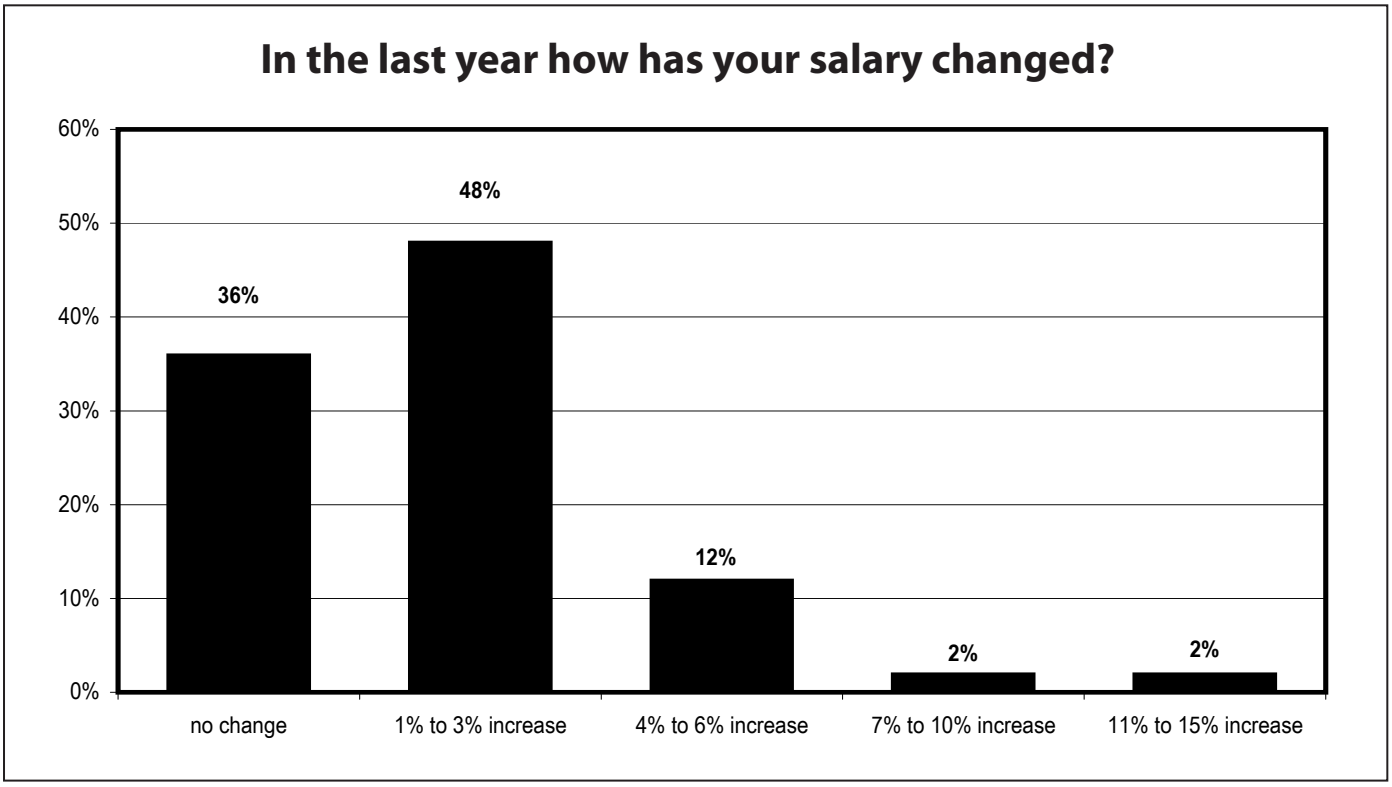
Mixed signals on raises

Nearly half of all respondents reported this year that they received a 1% to 3% raise — about the same percentage who reported a similar raise in 2009 and more than the 44% who received it in 2008. And unlike the previous two years, no 2010 respondents reported a decline in salary.

But the percentage of IRB professionals who reported no change in salary has climbed steadily since 2007, when just 16% said they'd had no change, to 36% this year.

What is your annual gross income?





At the University of Southern California in Los Angeles, staff members have alternated between raises and no raises over the past few years, says **Susan Rose**, PhD, executive director of the Office for the Protection of Research Subjects.

"Last year, we had a 2% raise and the year before that, no raise," she says. "This year, we're looking at none again. But we also kept staff."

Rose says her office has cut back in other areas, including curtailing travel, in order to save jobs. Both she and Ozier say they're trying to continue to provide professional development for their staff, but are focusing on conferences closer to home instead of sending people across the country.

Rose says she was surprised by one of the findings in the salary survey — reports of increased workloads in IRB offices.

Three-quarters of all the IRB professionals surveyed in 2010 reported that their workload had increased in the past year — up from 68% in 2009. Sixty-seven% of 2010 respondents said they worked more than 40 hours a week.

At USC, they've actually seen fewer studies in the past year, particularly big national studies funded by pharmaceutical companies, Rose says.

Vanderbilt's IRB, by comparison, has seen steadily rising numbers of new submissions — more than 800 a year since 2008, Ozier says.

Workload concerns cited in the survey may be partly attributable to lost staff. In 2010, about 22% of all of those surveyed said their offices lost staff, up from 15% in 2009 and 12% in 2008.

Other results from the 2010 salary survey:

• **Demographics** — 85% of respondents were women. Age distribution was fairly wide, with about half of those surveyed between the ages of 26 and 50.

• **Education and experience** — Nearly half of all the respondents have a graduate degree. For another 25%, the highest degree obtained was a bachelor's degree. The most common certification held is a Certified IRB Professional (CIP). More than three-quarters of all those surveyed have been in the human subjects protection field 12 years or less.

Personnel issues abound

Those who responded to the survey also listed some of the biggest personnel issues they face. Among the most common themes:

• Maintaining qualified, educated staff during lean times;

• Lack of resources, even as research programs grow and workloads increase;

• Burnout and lack of morale due to decreasing raises.

Ozier and Rose say there are steps that IRB offices can take to combat these problems.

At Vanderbilt, administrators are looking at

ways to shift resources in order to use protocol analysts more efficiently.

"Currently, analysts are assigned to a committee and work only with that committee," Ozier says. "We're looking at maybe creating a pool of protocol analysts to spread the volume (of work) out more equitably."

To deal with morale issues, she schedules team-building exercises and retreats. When it's not possible to give raises, providing employees with more work options can help soften the financial blow.

"We allow them to do flexible schedules — for example, we allow them to do four 10-hour shifts in a week instead of five eight-hour shifts," Ozier says. "We're doing more things electronically, so it's allowing us to be able to work from home. All the protocol analysts can set a schedule where once a week they can work from home, and that's working pretty well."

Rose says that USC provides free tuition for employees who are working on higher level degrees. "There's a wonderful master's degree in regulatory science that a lot of them take."

Identify the unnecessary

As far as managing an IRB office in tough economic times, Rose says the key is learning not to do what you don't have to do.

For example, at USC, the IRB no longer looks at every adverse event report that comes in.

"If they are internal ones, if they meet the criteria for an unanticipated problem, look at it," she says. "If it's from another site and doesn't (meet those criteria) — don't."

While automating IRB operations can streamline the process and save staff time, Rose notes that it doesn't necessarily result in fewer employees.

"We now have two full-time IT (information technology) people — so it's a trade of types of employees," she says.

Rose advises looking carefully at the regulations and ensuring that the IRB is reviewing studies at the right level.

"If you review everything at full board or expedited when you don't have to, you don't know what you're doing," she says.

She's also working on changing policies regarding exempt studies so that the office doesn't waste time on activities that aren't really human subjects research. In many cases, she says, boards are reviewing things like polls and program evaluations that don't require IRB review.

"For example, USC and The L.A. Times have been involved in polls and none of the exempt categories use the word 'polls,'" Rose says. "We're creating a category for things that are clearly no risk, where there's no federal funding and are clearly exempt." ■