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OHRP move might increase trend of research sites using centralized IRBs

'Many organizations are reluctant to go outside their four walls'

Research institutions increasingly are turning to central IRBs for multisite clinical trials, and this trend probably will accelerate due to recent news that federal regulators are encouraging the change, experts say.

The Office for Human Research Protections (OHRP) in Washington, DC, recently posted a letter that clarifies this philosophical shift by the agency. Essentially, the letter states that OHRP fully agrees with the Food and Drug Administration's position on the benefits of using a single central IRB for multisite research. IRBs and others can post comments on the change. *(See story about OHRP letters, p. 88.)*

The letter was written April 30, 2010, to Carolinas Medical Center of Charlotte, NC, in response to a letter asking whether research institutions using an external IRB would be held liable for non-compliance on the part of the independent IRB.

"As the letter noted, for a while we've been trying to send a message on changing accountability rules," says **Jerry A. Menikoff**, MD, JD, director of OHRP. Menikoff signed the OHRP letter to Carolinas Medical Center. *(See Ask2-4U with more Menikoff comments, p. 87.)*

"OHRP has in a sense been trying to send the message that there are benefits from having a more centralized IRB review," Menikoff says.

"We recognize there can be inappropriate administrative burdens by having multiple reviews, and that can slow down research," he explains. "You can get appropriate protections for subjects through the use of a central IRB, so it really could be a win-win situation."

Even before OHRP published its letter, there had been a growing trend toward the use of central IRBs, experts say.

"Somewhere around half of academic medical centers are outsourcing IRB review almost exclusively on industry-sponsored trials," says **John Isidor**, JD, chief executive officer of Schulman Associates IRB of Cincinnati, OH.

And more than half of community hospitals outsource their IRB reviews, he adds.

"We've been around for 22 years and are among the oldest central IRBs, and we are seeing more and more interest on the part of organizations to use an external IRB," says **Jim Saunders**, MBA, vice president of the New England Institutional Review Board (NEIRB) of Newton, MA.

Does trend threaten internal IRBs?

Some research institutions that have their own internal IRB might opt to use an external, central IRB for industry-sponsored studies. Another model is that some research sites might decide to disband their own IRB and rely on an external IRB for all study reviews, Saunders explains.

"We are seeing a lot of activity along those lines, and I think institutions are realizing that it's very expensive to have one's own internal IRB," he adds. "It's very resource consuming and challenging to keep track of all of the regulatory changes and to have good systems in place that meet the requirements one has to meet."

The OHRP letter could shift more research sites to using a central IRB, although there remains the regulatory roadblock, he adds.

Most people would interpret current regulations to mean that an organization that uses an external IRB is responsible for any noncompliance issues that IRB has, Saunders says.

"Many organizations are reluctant to go outside their four walls and seek external IRB review because they feel they can't always guarantee that everything will be done completely appropriately by an external IRB," he says.

"So they're worried they'll end up being in trouble with OHRP for reasons not of their own doing," he adds.

The regulations date back to the days when most human subjects research was done by a single institution and reviewed by a single IRB. Now research investigators and sponsors have to coordinate a trial across a number of different institutions, juggling many IRB reviews of the same protocol, Saunders notes.

"People weren't thinking about multisite studies when the regulations were written, so there's a huge emphasis on local context," Menikoff says. "That has changed over time, and today there are large numbers of multisite studies."

However, as the research industry has evolved to increasing numbers of multisite studies, the regulations remained the same.

Still, OHRP sees flexibility in the regulations, Menikoff says.

"It's a very different research world today versus 30 to 40 years ago, and we believe the regulations are flexible enough to recognize it," he adds.

Menikoff's letter to Carolinas Medical Center acknowledges the regulatory roadblock, but refers

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Editors: Suzanne Koziatek and Melinda Young.
Executive Editor: Coles McKagen, (404) 262-5420 (coles.mckagen@ahcmedia.com).
Managing Editor: Gary Evans, (706) 310-1727, (gary.evans@ahcmedia.com).
Director of Marketing: Schandale Kornegay.
Production Editor: Ami Sutaria.

Editorial Questions

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the research institution to a letter written last year as an example of how OHRP interprets the regulations in a way that's favorable to the institution.

"Obviously, the best action of all would be to change the regulation," Saunders says. "I could see that within institutions there are folks who would say, 'We don't care what this letter says, if the regulations say something different then we still don't feel comfortable utilizing an external IRB, and we won't until the regulations are formally changed.'"

There's interest in the research community to improve the system, Menikoff acknowledges.

"I can't comment on whatever people will be looking at internally in the government," he adds. "We certainly want to improve the system, and nothing is off the table, in general."

From a research institution's perspective, even a regulatory change might not alleviate all liability fears.

"They could still be sued by a subject," Isidor says.

"Any lawsuit about a personal injury case will be governed under state law," he adds. "And in most instances, the lawyers for the plaintiff will prefer to sue in state court because they assume they'll get a more sympathetic jury and judge."

Still, OHRP's public move toward encouraging the use of central IRBs is likely to have a positive impact on the trend. At the very least, research institutions that are already using external IRBs will view this as affirmation that they've made the right decision, Isidor says.

"For those who have not chosen to use them, it will create more pressure in the institution to start using them," he adds. "Investigators will want to speed up their IRB review process, and institutions will have a more reasoned basis for making outsourcing decisions."

Accreditation driving trend

Also, the trend toward IRB accreditation is helping move more institutions toward central or external IRBs, he notes.

"All the major IRBs are accredited now," Isidor says.

Institutions can use the Association for the Accreditation of Human Research Protection Programs (AAHRPP) as a due diligence standard, he notes.

'They might feel comfortable outsourcing to accredited IRBs because that provides a reliable third-party oversight mechanism," Isidor adds. "Accreditation shows that an IRB is functioning appropriately and that it will provide the same level of protection as your own institution's IRB."

Research institutions can rely on accreditation information, OHRP compliance data, and the status of an independent IRB serving as a central IRB for a multisite study as standards for their decision to outsource the IRB review, he says.

"In addition, some institutions will independently visit the IRB to have a higher level of due diligence, and some will do their own audits," Isidor says.

Eventually, the IRB world likely will include more central IRBs, although many larger institutions will maintain their local human subjects review boards, Saunders predicts.

"You won't see a day where everyone decides they'll go with one centralized approach," Saunders adds. "I think the regulations will be modified, and there will be more interest on the part of institutions to look at models of centralized review." ■

ASK2-4U

OHRP director explains shift on central IRBs

'Use of a central IRB can be a very good thing'

The Office for Human Research Protections (OHRP) in Washington, DC, is indicating to research institutions that the agency favors the use of centralized IRBs for multisite studies. Recently, the agency published a letter it had written to a North Carolina hospital system about the use of central IRBs. *IRB Advisor* asked OHRP Director **Jerry A. Menikoff**, MD, JD, about this change. Some of his answer is contained in this "Ask2-4U" below:

IRB Advisor: Who is responsible if an external IRB has a noncompliance issue when reviewing a research site's study?

Menikoff: The bottom line is that if something inappropriate happens in the study due to an outside IRB, whether it's a central or some other IRB doing something wrong, and we take a compliance action related to that, we will certainly make it clear in our findings that the fault was due to the IRB and not to the people in the institution. It's a question of making it as clear as possible so everybody understands who really was at fault.

In that one example of the letter to the University

of Oklahoma, there was one NCI [National Cancer Institute] central IRB that reviewed the study, and Oklahoma was one of the sites. Oklahoma's IRB reviewed the study, and its IRB did not change some of the consent provisions that were approved by the central IRB. The complainant complained about some provisions of the consent form.

We made it clear that Oklahoma wasn't doing anything worse than the other 100 sites using the consent form, which was vetted by the central IRB. We think some of this is common sense. As far as liability goes, [it pertains to] whoever does something wrong.

IRB Advisor: Is there any other message about central IRBs that you'd like to send to research sites?

Menikoff: I don't know the message is any different than what the letter is trying to get out. That is why when we received this query [from Carolinas Medical Center in Charlotte, NC] we viewed it as a good opportunity to make our response public. We do very much think the use of a central IRB can be a very good thing. We do encourage their use, and I want to clarify on this issue there's a great deal of harmony between FDA's and OHRP's viewpoints. Both entities are very much in favor of this. ■

OHRP correspondence on central IRBs

OHRP outlines shift in philosophy

The Office for Human Research Protections (OHRP) in Washington, DC, recently published letters that explain the agency's revised stand on the use of central or external IRBs.

The initial letter was written to OHRP by James T. McDeavitt, MD, senior vice president, of Carolinas Medical Center, Carolinas HealthCare System in Charlotte, NC. It's dated April 13, 2010, and it states, in part:

- "The FDA has held the IRB-of-record, irrespective of the relationship of that IRB with the research institution/site, accountable for compliance with regulations governing IRB activities. The Office of Human Research Protection (OHRP), on the other hand, has held the 'institution' ultimately responsible for IRB activities, and this has led to the concern that an institution using an 'external' IRB would be held regulatorily 'liable' for noncompliance on the part of the independent external IRB. In our vetting process of several external IRBs, we are receiving mixed messages on their interpretations of the current status of the views of OHRP's on this issue."
- "… the signed Federal Wide Assurance (FWA) states that the institution is responsible for ensuring that the 'designated IRB(s) will comply with the Terms of the Federal Wide Assurance for Institutions within the United States and possess appropriate knowledge of the local context in which this Institution's research will be conducted.'"
- "Absent new guidance from OHRP, the existing guidelines thus seem to indicate that OHRP holds the local institution ultimately accountable for IRB oversight. Without any modification of OHRP expectations, the willingness of local IRB's such as ours to be held fully accountable for decisions and actions taken by external IRB's will likely be low and variable."

OHRP Director **Jerry Menikoff**, MD, JD, responded to McDeavitt with a letter, dated April 30, 2010. It states, in part:

- "As you indicated in your letter, concerns about regulatory liability under the Department of Health and Human Services human subject protection regulations appear to be one of the main reasons inhibiting institutions from exercising the regulatory flexibility that currently permits institutions to rely on the review of an IRB operated by another institution or organization."
- "The ANPRM [advance notice of proposed rulemaking] sought public comment on whether OHRP should pursue a notice of proposed rulemaking to enable OHRP to hold IRBs and the institutions or organizations operating the IRBs directly accountable for meeting certain regulatory requirements of the HHS regulations for the protection of human subjects."
- "The majority of public comments we received supported this regulatory change, and we are continuing to consider whether to pursue this change in order to further encourage institutions to rely on IRBs that are operated by another institution or organization, when appropriate."
- "… As you indicated, we have archived prior guidance documents that suggested OHRP favors local IRB review over review by a non-local IRB, a position that OHRP no longer holds."
- "Also, in our recent compliance evaluations, we have taken into consideration whether a single

central IRB external to the institution was responsible for any identified regulatory noncompliance with 45 CFR part 46."

- "An example of how OHRP addresses this issue can be found in a recent compliance determination letter (see http://www.hhs.gov/ohrp/detrm_letrs/YR09/jun09c.pdf, section A(2) regarding the discussion of corrective actions)." ■

Drama queens (and kings) help IRB training

Office was informed by participant survey

A Los Angeles, CA, research institution has found a way to bring a little Hollywood flare into the otherwise dry informed consent process by making use of local acting talent, video directing, and role-playing.

"We found it's useful to do mock sessions where we play out what can happen in the informed consent process," says **Rebecca Flores Stella**, CIP, manager for operations and education in the office of research compliance and quality improvement at Cedars-Sinai Medical Center in Los Angeles, CA.

The facility's quality improvement (QI) team administered various surveys at Cedars-Sinai, asking research participants about their backgrounds, experiences, and comments on informed consent, Stella says.

The survey broke down the elements of informed consent and asked participants to rate whether they felt the information they received addressed these, Stella says.

None of the ratings were lower than 75%, but those that were not as high as desired tended to be items that participants had difficulty understanding and would need to be addressed.

Based on the survey, some questions they determined needed to be better understood by research participants included these:

- Why is the doctor/investigator talking to me about a research study?
- What do I hope to learn from this study?
- How is this study different from the care I would normally receive?
- Is this a treatment, and can I expect it to help me?
- What are my options if I don't wish to participate?
- What will my participation involve?
- What are the possible risks and benefits?

Unmixing the message

"Based on survey results from the prior year, we felt these were questions and areas we could improve on," Stella explains. "We thought we could get our research community to better focus on these issues and concerns that our subjects really wanted to know."

For example, a research physician's good intentions could result in mixed or confusing messages, crossing the line between clinical research and medical care, Stella notes.

When the research compliance office asked staff for ideas of how they could educate IRB members and staff about ethical nuances in informed consent (IC), **Jessica Spotts**, an IRB analyst, who also was an aspiring actress and director, suggested they create a short film.

"We had our staff think about difficult consent situations or studies that had challenging consent situations," Stella says.

These challenges might involve new technology, therapeutic misconception, or highly sensitive research data.

"Our staff members helped us come up with scenarios for challenging consent processes," Stella says. "We asked coordinators to think of the best way they did informed consent, incorporating all of the elements of consent."

The IC team used consent forms that had been approved by the IRB to prepare for the mock informed consent session. Also, they brought in four IRB community members to serve as prospective subjects. Two principal investigators and two research coordinators also participated, using one of their own study informed consent documents in the mock session, Stella adds.

Spotts directed the video of mock informed consent sessions.

For the video vignettes, Stella asked the investigators to blur the lines between their roles as a research investigator and as a clinical care physician.

"We asked them to make that as blurry as possible," she says.

"For each study we did a 'good take' and a 'bad take,'" Stella says. "As part of the education, we identified four key areas which we felt should be part of any comprehensive informed consent process, and we let them know this is what we were focusing on." *(See story on four key areas of IC, above.)*

Research staff proved to be naturals as the cam-

What are four key areas to teach in informed consent?

Step 1: Make sure it's clear

Based on a survey of research participants, the office of research compliance and quality improvement at Cedars-Sinai Medical Center in Los Angeles, CA, has come up with these four key areas to demonstrate informed consent.

These four areas can be taught to IRB staff through the use of "good" and "bad" mock IC scenarios. Here they are:

1. Distinguish standard of care from research participation.

"This needs to be made very clear to research subjects," says **Rebecca Flores Stella**, CIP, manager for operations and education in the office of research compliance and quality improvement at Cedars-Sinai Medical Center in Los Angeles, CA.

Researchers need to do a better job of explaining the purpose of a study, she says.

In a mock informed consent scenario, the principal investigator should talk with the subject about what a phase I study means and what could be expected, Stella explains.

"You should talk about how this is the first time the investigational product is used in humans, and talk about the unknown nature of this product," she says.

In a bad IC scenario, the investigator might say, "You've used up all your options. This is pretty much all that's left for you," she adds.

2. Make sure the study's purpose is clearly communicated.

An IC scenario might have an investigator discussing how the subject's tissue sample will assist with research that might lead to an innovative treatment for a particular disease. The investigator would clearly explain how the study's purpose is to collect data for use later.

"Give the subject a better picture of the overall purpose of research," Stella advises.

In the bad IC scenario, the investigator might say, "If you give me your tissue, we'll find a new treatment for your disease," she adds.

3. Answer all logistical questions clearly.

Research participants often want to know the details of their participation in a study, including these questions:

- How long will the appointments be?
- Where do I park?
- How many study visits will I have to make?

In a good scenario, the investigator will clearly answer these questions within the informed consent document and then also address them when meeting with the potential subject.

"The investigator will say, 'You'll have 22 appointments and six will be very detailed and long — up to four hours long,'" Stella says.

In a bad IC scenario, a study might entail 22 study visits, which would be a burden for most research participants. But instead of being straightforward with potential subjects, the study coordinator might say, "You'll come in and have a regular office visit, and that'll be that."

4. Clear up any confusion about who pays the bill.

"This is a huge issue," Stella notes.

The investigator could say to a patient, "These are the things we'd do with you as a patient, regardless of whether you're in the study," she says. "And these are the things that will be repeated or done additionally for the research so they won't be billed to you." ■

era rolled.

"We interrupted very minimally," Stella says. "On the first session we offered a little more guidance, but they took it from there."

The end result was an informed consent teaching video that has been well-received when used to instruct staff and IRB members, she says.

"We're sure there are better quality professional videos out there, but the feedback we received is that people were seeing their peers walk through the consent process, and this helped make the information resonate a little bit more," Stella says. "We repeated this workshop three times, and it was received very well."

Now the video also is available for staff online, and more than 300 people have seen the informed consent video, she adds. ■

Biobank uses opt-out approach to gathering blood samples

Bank not technically human subjects research

When Vanderbilt University Medical Center set about creating its BioVU biobank, it went in a different direction than most institutions.

Instead of using an opt-in approach that recruited patients to submit blood samples, the institution instead decided to collect discarded blood samples from routine clinical testing.[1]

Samples are linked to a deidentified version of the hospital's electronic medical record, so they can be used to look at how genetic differences affect health without involving individually identifiable health information.

Under the federal regulations, this does not constitute human subjects research, so the Office for Human Research Protections (OHRP) did not require prospective informed consent from patients for the use of their samples, says **Daniel R. Masys**, MD, chairman of the department of biomedical informatics at Vanderbilt University Medical Center (VUMC) in Nashville, TN.

But Masys says the Vanderbilt IRB determined early on that the institution should go further in giving people information about the program and the ability to opt out if they chose. Vanderbilt has conducted education about BioVU using brochures and advertising. A notification on all of its treatment consent forms tells patients about the collection and allows them to check a box to refuse to have their samples stored.

"Both the educational campaign and the opt-out were directly the result of the IRB believing and asserting that the current protections provided by 45 CFR 46 are not in sync with community expectations about genetic research," Masys says.

"We have two, separate thoughtful opinions in writing from OHRP that told us 'You can do this opt-out thing but it's not required by federal regulations,'" he says. "But IRB just didn't think it was right to run it as an invisible, behind-the-scenes program."

The IRB reviews any changes to BioVU and reviews the entire program annually.

After three years of operation, the biobank contains more than 80,000 samples, and Masys expects it to hold a quarter of a million samples by 2014. After years of discussion and surveys of parents, the bank also began collecting pediatric specimens.

The opt-out rate currently stands at about 5%, he says.

"Interestingly, that was predicted by our opinion surveys done ahead of time, which told us that about one out of five people have some concerns about doing this kind of approach, but only one out of 20 have sufficiently held opinions that they actually want to be opted out," he says.

Opt-out contained in consent-to-treat form

When a patient is treated at VUMC, he or she is presented with a Consent to Treatment/Agreement to Pay form that contains a section briefly describing the sample collection:

"I understand and agree that any specimens or tissues normally removed from my body by VUMC in the course of any diagnostic procedures, surgery or medical treatment that would otherwise be disposed of may be retained, used for educational purposes or research, including research on the genetic material (DNA) or other information contained in those tissues or specimens."

The form also notes that any research done will not identify the patient personally and that patients will not benefit financially from any resulting invention or drug.

The patient may check a box that states: "Do not use my leftover blood for the DNA databank."

Masys says patients receive this consent form annually and can withdraw consent at any time for future use of their data.

Once samples are in the system, they are linked to a deidentified version of Vanderbilt's electronic medical record called the synthetic device (SD). Because this system does not allow for recontact of patients, the usefulness of the samples depends upon the usefulness of the medical records system, Masys says.

"We have a very rich EMR and I think that's the cornerstone," he says. "And the IRB as well had to have confidence in our ability to deidentify data in the EMR."

The deidentification process removes or changes all of the required HIPAA identifiers – for example, dates of clinical events are changed, while still preserving the time that passes between events. Masys says the SD is treated as a limited data set, and has strict rules regarding its use.

Users must be Vanderbilt employees, research faculty or staff, and must get IRB approval for any use of individual records – through a streamlined process that can be turned around in about a day.

Anyone with a university login may use a version of the SD that shows information about groups of records.

"For example, if you were a cardiologist and you wanted to know how many people were on Plavix and had had a myocardial infarction, you can get numbers back from that," he says. "But if you want to actually get access to clinical data, you have to go through the IRB review."

He says that if a search turns up only a few records, the system won't allow those individual records to be shown.

"So you couldn't, for example, triangulate and find a single individual because you know they have this rare combination of diseases."

Despite the deidentification process, Masys says there's a possibility that information in the written portions of the records may inadvertently identify a patient. Users are directed to tell the institution about any instances they find so that they can be removed.

He says that users of the SD know that if they misuse data they're at risk for sanctions up to and including losing their jobs.

"We are very sensitive to those issues in the protections around use of the data and we never assume that we have eliminated the risk of reidentification entirely. As much as our lawyers would like us to give that guarantee, we just cannot give that guarantee."

A special community advisory board, drawn from local organizations and patient advocacy groups, was created to guide the institution in its development of the biobank.

"They meet two or three times a year, face to face, only to discuss this project," Masys says. "It is actually a remarkably outspoken, independent, effective board. It's headed by a lawyer who works in the State of Tennessee Office of Disability and is very conversant with issues not only of public perception but of possible scenarios of misuse."

Masys says the advisory board sometimes is at odds with Vanderbilt's own bioethics committee, which can take a more cautious approach.

"The bioethics committee is very concerned about scenarios that might be very rare – they just want to make sure that there's no possibility that something might happen," he says. "And the community advisory board can be a lot more commonsense about that. As the community board has learned more about the project, they sort of want us to go faster – they want us to make more progress with more diseases."

He says the board has given practical advice about educating the public, helping rewrite the education brochures in both English and Spanish and asking that certain questions be addressed such as whether companies have access to the data or in one case, whether DNA in the samples could be used for cloning.

"We would have thought that was a little bit scientifically farfetched, but they said you should address that," Masys says. "They serve as an ongoing reality check for 'Are we missing anything big?' and 'Are we headed in the right direction?'"

Despite the educational efforts and other public outreach, Masys says Vanderbilt does get occasional phone calls from people who learn about the biobank and have concerns. If those people still are unsatisfied after talking to patient services representatives, they talk to Masys.

"So I get the people at the tail end of the curve who are absolutely outraged and believe there should be laws against this sort of thing and believe that this couldn't possibly be legal," he says. "They never realized that federal research regulations have allowed use of existing tissue and data for 40 years now."

Masys says that aside from the sheer number of samples being collected for BioVU, its success can be measured in the types of samples being gleaned – from minorities and other underserved populations who often do not contribute to opt-in biobanks.

"For those of our faculty who are interested in diseases that are preferentially found in minority populations, it's actually become an unexpectedly rich resource to do science they couldn't otherwise do," he says. "At least we're generating hypotheses and gathering preliminary data. And that was a very nice endorsement of building an all-comers biobank in this deidentified space."

Masys believes that close involvement by the IRB throughout the process has been crucial to the success of this approach.

"I think it's a good thing, especially when you're trying to develop a novel research resource, where it is a moving target," Masys says. "The power of genomic technologies is raising ethical issues every week, if not every day. So having the IRB as a participant in the design and operation is not just one of those things you do because of structural necessity, but to actually enhance the project."

REFERENCE

1. Pulley J, Clayton E, Bernard GR et al. Principles of human subjects protection applied in an opt-out, deidentified biobank. *Clin Transl Sci* 2010 Feb;3(1):42-8. ■

Survey shows QI projects do get some oversight

However, ethics training, independence lacking

When the federal Office of Human Research Protections raised questions about a quality improvement (QI) initiative to reduce catheter infections in Michigan hospitals in 2007, it reignited a debate over the line between QI and human subjects research necessitating IRB review.

The project, an assessment of infection control practices in hospital ICUs, had been granted exempt status by the IRB at Johns Hopkins School of Medicine in Baltimore, MD, where the project was developed. But OHRP initially ruled that IRBs at all the participating hospitals should have reviewed it and that informed consent should have been obtained from patients.

Although the project eventually was allowed to continue, the incident left QI advocates concerned that they face increased IRB review requirements for their work. They say such reviews will hamper their efforts to protect patients using interventions that already have been proven successful and thus, aren't really human subjects research.

In an effort to move the discussion along, a team from Johns Hopkins wanted to see exactly what review QI projects currently undergo – by IRBs, by QI departments or by other institutional entities. What ethical considerations are examined? What ethical training do QI practitioners have?

The results, published in a recent issue of the journal *Quality and Safety in Health Care* show that while QI projects generally have some sort of oversight, they often are not reviewed by someone with ethical training or who is independent of those conducting the intervention.

Holly Taylor, PhD, MPH, a core faculty member at the John Hopkins Berman Institute of Bioethics, says there's not enough information yet about the practice of QI to know what kinds of policy recommendations should be made for the ethical review of these projects.

"Our goal was to describe what we know about what happens," she says. "We wanted to find out whether quality improvement initiatives were systematically reviewed in any way, period."

Asked about effectiveness

Taylor's group surveyed 132 quality improvement practitioners from hospitals and healthcare systems.

Respondents were asked about oversight mechanisms used at their institutions, their opinions about the effectiveness of those mechanisms and factors that they thought were relevant to the ethical review of QI:

Type of review – 83% of all respondents said that QI initiatives at their institutions were subject to some kind of review prior to implementation.

Among that group, the most common QI oversight mechanisms reported were (in order): review by the QI management team; oversight by the clinical leadership conducting the QI intervention; and review by an advisory board set up specifically to look at QI initiatives.

Only 15% of QI practitioners who reported any kind of review said that their IRBs were involved in the review of QI.

Quality of review — For each mechanism, almost all respondents reported that they believed it to be either 'very' or 'somewhat' effective.

Nearly 70% of the respondents said their QI oversight mechanisms identified and considered ethical issues either 'well' or 'very well.'

Ethical considerations — When asked what considerations were important to the ethical conduct of QI, respondents listed human subjects protection issues – minimal risk to patients and privacy and confidentiality – as most important.

Taylor says that despite their differences, the ethical review of QI is closely related to the ethical review of human subjects research.

"Both groups would recognize their responsibility to protect the welfare of their patients and participants," she says. "For example, they both clearly recognize the importance of privacy and confidentiality. The culture in health care is such that privacy and confidentiality are always a concern."

At the same time, however, only a third of the 102 respondents who answered demographic questions had completed any course in the ethics of human subjects research.

Taylor says there still are a lot of unanswered questions about the role that ethical considerations play in the review of QI initiatives. The role of special QI advisory boards, for example could be fleshed out more, comparing their work to the work of IRBs, especially since they're set up to be independent of those actually carrying out the QI interventions.

She says that while conflict of interest questions may be slightly different for QI professionals than they are for typical researchers, the existence of an independent body may be a good approach to review of QI projects.

"The question is still open as to whether that's the best mechanism," she says. "If I was making a recommendation, a next good step would be to answer the question of how do these advisory boards operate? How are the ethics of it looked at in the review of the project?"

In the meantime, Taylor says, IRBs should take the opportunity to reach out to quality improvement professionals at their institutions and find how QI initiatives are handled there.

"If I were an IRB administrator or an IRB chair, I might want to pursue a conversation with them about whether there's a way we can work together," she says.

"Say an investigator submits a project that really looks like quality improvement or practice improvement. The IRB isn't really an expert in that. If I had a contract with someone who does this every day, I could pick up the phone and say, 'We have a project we think is QI – can you look at it.' If there is such a mechanism for review."

Likewise, she says, a quality improvement officer could look at a proposed QI intervention and see a potential for patient risk. "Then, they can reach out to the IRB chair," Taylor says.

Taylor says she would not want to see a requirement that any intervention labeled as quality improvement be reviewed by an IRB.

"My worry would be that IRBs would be overwhelmed and that QI staff would choose not to collect data because they do not want to go through that process," she says. "It would stymie their ability to make progress. We want to facilitate moving the agenda forward."

REFERENCE

1. Taylor HA, Pronovost PJ and Sugarman J. Ethics, oversight and quality improvement initiatives. *Qual Saf Health Care* 2010 May 27 (epub). ■

Informed consent when the victim is a black male

Legalese may heighten subjects' fears

Young black men are disproportionately more likely than other groups to be victims of violent crime. But when researchers set out to study this group, they encounter difficulty in recruiting and retaining subjects.

There are a variety of reasons for that difficulty, says **Jane Liebschutz**, MD, MPH, FACP, associate professor of medicine and social and behavioral sciences at Boston University Medical Center. Some are related to black patients' general distrust of research and researchers. In addition, crime victims may be poorer and harder to reach.

But Liebschutz and research assistant **Joel Hoyte** say the experience of crime adds a layer of complexity to recruiting that requires careful thought by researchers and IRBs.

For example, Hoyte notes that patients who've been the victims of crime may have fears about crowds and using public transportation that may make it difficult to show up for appointments. Liebschutz says a victim may lose his job or his place to live as a result of his injuries.

"Some of them have really bad (post-traumatic stress disorder), their days and nights can get reversed," she says. "I don't think it's necessarily that different from other poverty issues. But the violence makes those issues more acute."

Liebschutz says her team ran into these problems when they attempted to recruit subjects for two studies on medical and counseling services extended to victims of crimes in Boston. When they began having difficulty, they started to survey subjects about the barriers to enrolling young black men in this type of research. Results from the survey were published in a recent issue of the journal *Psychological Trauma*.

Problems identified in the survey included a culture that discouraged "snitching" and concerns that researchers might be connected with the police.

But Liebschutz and Hoyte also identify an area that often tripped up potential subjects: The informed consent document, whose language was not only difficult to understand, but had the potential to increase subjects' fears due to poor wording. She says IRBs could help ease this difficulty by allowing flexibility in the language of informed consent.

One obvious example, says Liebschutz: What do you call the person who is leading a study?

"'Principal investigator' is a ridiculous term to use with this particular population," she says. "When else do you use the word 'investigator,' besides in connection with the police?

"Why can't it be 'research director' or 'study director?' That term is really difficult with this population, who already is having some police

involvement (as a result of being the victim of a crime)."

'Freaking out' over document

Hoyte, who conducted informed consent conferences for the studies involved, says that when he discussed the studies with potential participants, he had a script that used more lay language to explain the informed consent elements.

Then, says Liebschutz, "they'd look at the consent form and freak out."

In one case, she says, a 19-year-old man agreed to participate, then took the consent home to his mother and came back the next day because of concerns she had raised. The form explained that his information would be confidential, but included required language that detailed circumstances under which it might have to be released. Further discussions with the man and his mother helped clear up the misunderstanding.

In studies such as this, certificates of confidentiality obtained through the National Institutes of Health can help allay fears about potential disclosures – as long as they're explained carefully to subjects, Hoyte says.

"It helps in the qualitative portion (of a study) where you're disclosing details of the (crime) incident itself," he says. "We really emphasized that in the interviews, that it was completely confidential."

He says IRBs should be looking at the informed consent process to ensure subjects really can understand the information. Are they asked whether they have questions? Does the researcher have them repeat back important information?

"Because sometimes people are actually not very informed," he says. "And it can cause mistrust and questions afterward."

Other issues that IRBs should consider when reviewing studies that involve victims of violent crime, says Liebschutz:

• **Establishing a relationship** — Often, patients wanted much more contact with researchers before signing a consent form, which can be at odds with the usual practice of informed consent. "Usually you have to have them sign a form before they even talk to you, which is very hard to achieve in this particular population," she says. "You don't want to exploit people, but you have to be realistic in terms of wanting to have people involved and developing that relationship."

• **Interaction with other subjects** — Liebschutz says her group originally intended to run focus groups with crime victims, but her IRB raised concerns that some of the participants might have had previous run-ins with one another.

"Gangs are not huge in Boston, but they were concerned that we not be exposing one participant with another with whom he might have some history," she says. "In those cases, there can be concerns about individual safety."

REFERENCE

1. Schwartz S, Hoyte J, Conoscenti JT, et al. Challenges to Engaging Black Male Victims of Community Violence in Healthcare Research: Lessons Learned from Two Studies. *Psychol Trauma* 2010 Mar 1;2(1):54-62. ■

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

■ Web-based compliance database helps with trial management

■ Researchers surveyed about engaging the community in NIH studies

■ Follow these best practice strategies to implement or improve electronic IRB system

■ Working as a team to improve community participation in research

CNE/CME QUESTIONS

5. The Office for Human Research Protections (OHRP) in Washington, DC, recently posted a letter that discusses how the agency views using a central IRB in the case of multisite studies. Which of the following best describes the OHRP's new position?
   A. OHRP discourages the use of central IRB reviews
   B. OHRP has sent the message that there are benefits from having a more centralized IRB review
   C. OHRP believes centralized IRB review should be used in conjunction with local IRB review when studies are multisite
   D. OHRP strongly advocates research sites moving toward central IRB reviews for all studies

6. Based on a recent survey, which of the following is <u>not</u> one of the questions research subjects need to learn more about in the informed consent process?
   A. What do I hope to learn from this study?
   B. How is this study different from the care I would normally receive?
   C. What are my options if I don't wish to participate?
   D. All of the above are questions subjects need to have clearly answered

7. True or False: A opt-out biobank that collects discarded blood samples from an institution and links them to a deidentified electronic medical record must obtain informed consent from patients, according to federal regulations.
   A. true
   B. false

8. In a survey of QI professionals, how many had completed ethical training in human subjects research?
   A. A third of respondents
   B. Half of respondents
   C. Three-quarters of respondents
   D. All of them

Answers: 5. B; 6. D; 7. B; 8. A.