IRB ADVISOR

Your Practical Guide To Institutional Review Board Management

AHC Media LLC

IN THIS ISSUE

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Bioethics training program for Africans helps professionals bring expertise home

Students include doctors, nurses, others

Major corporate research sponsors and large institutional sponsors in the United States increasingly are conducting clinical trial research overseas. Sometimes this raises concerns among IRBs and human subjects protection leaders about human subjects protection measures taken by these organizations.

These international trials establish ethics review boards and seek community input, but how well do these fledging board members and new researchers understand human subjects protection?

This question is being answered in part by bioethics training programs funded through the International Bioethics Education and Career Development Award of the Fogarty International Center of the National Institutes of Health (NIH).

One of the first five recipients of the Fogarty award led to the development of the Johns Hopkins Fogarty African Research Ethics Training Program at Johns Hopkins Bloomberg School of Public Health in Baltimore, MD. Now in its seventh year, the program has been training African professionals in bioethics, so they can bring their experience and knowledge back to their home countries and peers.

"It is critical for African professionals to know where their international collaborators are coming from and what perspectives they have," says **Adnan A. Hyder**, MD, MPH, PhD, an associate professor in the departments of international health and health policy & management at the Center for Injury Research & Policy and Berman Institute of Bioethics at Johns Hopkins University Bloomberg School of Public Health.

"Training in the U.S. makes our colleagues in Africa understand the bioethical perspectives taught here and how they are used to analyze issues internationally," Hyder says. "It will develop their capacity to discuss and contribute to the global dialogue on this issue."

The Johns Hopkins bioethics training program has trained 23 professionals from Africa, including a dentist trainee from Nigeria, a nurse from Uganda, and a pediatrician from South Africa, says **Nancy E. Kass**,

ScD, a Phoebe R. Berman professor of bioethics and public health in the Johns Hopkins Berman Institute of Bioethics.

"The only restrictions on eligibility are that trainees come from Africa, which is the focus of our training program, and that they have finished college or what most people call university," Kass says. "Beyond that, what we look for is not only someone who is talented, but someone who is committed to making a difference in improving an area of Africa."

In terms of commitment and enthusiasm, the program would appear to be a great success.

At the recent seventh-year reunion, 19 out of the 23 trainees returned to Johns Hopkins and took part in a public health community discussion that centered on a viewing of the controversial film "The Constant Gardener," in which HIV/AIDS research in Africa is portrayed as politically and financially corrupt.

"We had the panel of experts, including alumni trainees, discuss what in the movie seemed truthful, and what did not," Kass says.

Other evidence of the trainees' enthusiasm includes these examples of what they've done since they completed the one-year bioethics training program:

• Several trainees established their own IRBs or research ethics boards in their home countries, filling a void; these include one person from the Democratic Republic of Congo who established an IRB in the DRC and a second IRB in Kenya, Kass says.

"He got a federal-wide assurance from the U.S. government so the IRB could be recognized and get funding, and he did it all by himself," Kass notes.

• The Ugandan nurse trainee developed a two-week ethics training workshop for nurses in her home country.

"She developed one week on clinical ethics and one week on research ethics and did an evaluation to see if people learned things and made changes in their practice," Kass says.

• Another trainee now is a speaker and consultant for international organizations when they have a project and need an ethicist to say whether it's ethical, Kass says.

"All of these people have returned to their countries," Kass says. "A few went on to get other advanced degrees, and three have finished their degrees and then returned to Africa."

So far, none of the trainees have chosen to leave their native African nation, which is another positive aspect of the program: it seems to reverse the trend of the mostly trained and educated professionals leaving their developing world nation to live in resource-affluent countries.

One of the reasons the trainees have brought their knowledge back home is because of the way the program is set up. The first half is in the United States, but the second half is in their home country.

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It's intensive, and for the first six months, trainees live in Baltimore and take three graduate courses in ethics at Johns Hopkins, Kass says.

"They take one course in public health ethics, one in ethics of research, and one in ethics issues that come up in public health in developing countries," she explains. "And they take three special seminar series courses, including one in quantitative research methods, qualitative research methods, and one seminar course that is designed just for the trainees."

The special seminar series is run by Kass and Hyder, and it's a combination of having trainees read more core literature related to research, writing case studies for ethical issues in Africa, and listening to guest speakers, Kass explains.

"We bring in guest speakers who are relevant to the trainees," she adds. "So one year we have someone who is a malaria researcher talk about ethical issues in conducting clinical trials."

There also have been several speakers who talk about the ethics of conducting HIV protocols in Africa, the ethics of nutrition studies, etc.

Also, as part of their first six months of training, the students are required to observe four to six meetings of an IRB, Kass notes.

Trainees do all of this and one more task during their first six months: they develop and write a practicum for a big project they'll do during the second six months of the bioethics training program, Kass says.

"The second six months is back in Africa, and we give them a seed grant in order to jump-start their professional life as an ethicist when they go back," Kass says.

While at Johns Hopkins, the trainees meet regularly with Kass and Hyder as they develop the 40-page protocol for their special project, Kass adds.

"Many of our trainees are deeply committed to training their colleagues in ethics, and many have undertaken that as a full focus of their practicum," Kass says. "They're clearly committed to bringing more knowledge to their colleagues."

And it's this commitment that has kept the trainees focused on staying in their home countries, despite the more limited resources.

Although the bioethics training program directly impacts only a few people each year, its indirect impact can be felt across Africa, Kass and Hyder say.

"Each person is a stone in the pond, and his or her ripples are already being felt in their countries and regions," Hyder says. "As one of the fellows said, they are not only working locally and nationally, but they are also 'going global.'"

The program's and the trainees' influence also might help keep other African professionals in their native continent, where their expertise is badly needed.

"In Africa 10 years ago, it was hard to find bioethics training in Africa," Kass says. "But now, partly through our program and others similar to ours, there are five training programs in bioethics that are on the African continent."

The NIH funding has grown to about two dozen similar programs that train people in developing countries in bioethics, Kass notes.

Bioethics trainees have a personal impact on a one-by-one basis, Hyder says.

"And it is as a community that they will affect regional dialogue," he adds. "The hope of Africa must rest with Africans." ■

Improve quality control following expert suggestions

Independent IRB grows with quality

One of the most important services an IRB can provide is rapid turnaround on protocol reviews. The next most important service is providing quality documents, says the president of a large independent IRB in Austin, TX.

At least one IRB organization has achieved both services by incorporating quality assurance processes from the start to finish of the protocol review process.

"As we've grown, we've identified the need for a quality department, which is our regulatory compliance department," says **Lynn Meyer**, CIP, CIM, president and founder of IntegReview Ethical Review Board of Austin.

Meyer formed IntegReview in 1999, and in the last eight years it's grown from having one employee to having a staff of 30 full time employees and one part-time employee. Also, there now are four independent review committees, two of which were created for specific clients who submit a large volume of protocols on a weekly basis, Meyer says.

IntegReview recently received full accreditation from the Association for the Accreditation of Human Research Protection Programs Inc. in Washington, DC. And the company was one of three small business finalists for the Greater Austin Business Award for customer service.

QUALITY CONTROL CHECKLIST FOR NEW STUDIES

MARKED DOCUMENT	
Pharmaceutical/Device Company Name:	
Protocol Number:	Investigator:
Person Performing QC:	Date of QC:

Check upon completion	ITEM
☐	Check to see if IntegReview has an approved "template" IC for the Sponsor/Company Submitting. To check go to group/sample IC's/choose appropriate client folder. If there is a template IC: • ***ensure the information below is present*** • ***do not edit legal sections***
☐	Check Client Requirements (groups/forms/checklists/qc checklists/qc client requirements)
	STUDY INFORMATION (1st page)
☐	**Compare to protocol:** Sponsor/Drug/Device/Testing Company and City and State is correct (If the term "Sponsor" is used, ensure it is defined somewhere in the IC as follows: "The Sponsor is the company who is paying for the study"
☐	Protocol number is correct
☐	Title of study matches protocol exactly, add quotation marks before & after title, delete any periods
☐	Investigator name is correct, if applicable
☐	• Ensure the 1st page identifies the PI as "Name of Person Conducting Study (Investigator or Study Doctor)"
☐	**Compare to database**: Study site addresses are correct, if applicable Study site contact numbers are correct, if applicable • If daytime and after hours phone number is the same, combine
	HEADER (beginning on page 2):
☐	Protocol number is correct
☐	Investigator name and title are present & correct, if applicable
☐	Page numbering is correct
☐	**NOT TO BE USED FOR SUBJECT ENROLLMENT** is present on all pages (including page 1)
	FOOTER:
☐	**THIS IS AN IMPORTANT DOCUMENT-KEEP FOR FUTURE REFERENCE** is present on all pages
☐	Sponsor name/protocol number/marked IC are present and correct
☐	Text Version Box is present & complete & should be formatted as follows: • Multi-site study: initials/master: approval date • Single-site study: initials/approval date

Source: IntegReview Ethical Review Board of Austin, TX

The quality department's role is to perform quality assurance and quality control on all documents the IRB office handles, Meyer says.

"As a result of that, we've implemented a CAPA [corrective and preventative action] program, and through that program, as errors or oversights are discovered, we evaluate our processes to identify if we need to strengthen a particular policy or process," she explains. "Or if there isn't anything existing at this time, then we will need to create a process to strengthen our quality."

When an error or oversight is discovered, a CAPA report is created and it's reviewed at the monthly managers' meeting.

"At the meeting we determine whether or not it was handled appropriately, or if there is something more we can do to take action," Meyer says.

IntegReview also uses a variety of tools, forms, and checklists to assist in improving quality.

For example, the single site review process is summarized in a one-page flow chart that begins with these steps:

- Submit IntegReview New Study Submission forms for single site studies; Submission deadline — Wednesday 12:00 p.m. Central Time;
- Quality assurance performed;
- Data entry;
- Quality control;
- Document distribution to board members;
- Board review Tuesday evening;
- Board action distributed to client within 48 hours of review…

"Any new study submissions are submitted to the senior quality assurance associate," Meyer says. "She goes through the document to ensure all questions are answered and that they're answered appropriately and that accompanying documents have been received and so on."

There are checklists for all documents processed at IntegReview, Meyer notes. **(See sample quality control checklist, p. 100.)**

"Checklists are time-consuming, but it helps you keep on track," she says. "The checklists can vary up to a dozen pages for a new study admission form, and whatever quality assurance person performs the function will use the checklist."

Checklists usually are developed by the director of operations, using input from coordinators, and the regulatory compliance manager helps to maintain and revise documents, Meyer says.

"They're discussed at weekly staff meetings, and sometimes they are a work in progress," Meyer says. "We're forever changing our checklists."

The senior quality assurance associate checks for omissions and mistakes, following the checklist.

If there are missing pieces, the QA associate and her assistant follow-up on this, and all documents stay in the QA department until they're complete and ready to be assigned to an IRB, Meyer says.

One of the IRB's co-chairs is an IRB coordinator, who also is a voting IRB member, Meyer says.

The other board members are consultants to IntegReview, she adds.

After the protocol is assigned to a board, it goes to a team manager, who looks over the study with regard to its therapeutic area and whether the drug has been reviewed by IntegReview in the past, she says.

If the drug has been studied before, it's assigned to the same board that reviewed it previously, she notes.

The team manager assigns new studies to one of the boards, based on the members' knowledge and expertise. If the study review will require a scientific specialist, then there is a list of consultants who can be called to provide comments.

"Once a study is assigned to a particular board, the coordinator/co-chair notifies our client that the study is put on the agenda," Meyer says. "The co-chairs basically introduce themselves and say they will be the main contact for any future communications."

IRB members receive study documents prior to the meeting, and they are provided a checklist that will assist them with their review, Meyer says.

"This helps them stay on track and it helps them look for certain documents that need clarification," Meyer says. "They come into our facility for a meeting, and the first quality control point happens after the meeting."

An IRB assistant uses an overhead projector at the IRB meeting to show board members the informed consent form. The IRBs use a primary reviewer system, so one person is assigned the task of facilitating the study review, Meyer says.

After the IRB meeting, the coordinator/co-chair formats the document and looks at its pagination, putting headers and footers on the document.

"Then they give the document to someone in the regulatory department who will perform another quality control check, reading through the entire document to see if there are any questions and to use the protocol as a reference, Meyer says.

"Sometimes they find things in the consent forms that need to be changed to match the protocol, and these possibly were missed during the study review," she explains. "They're also looking

IntegReview's expectation for informed consent documents

Here's a small sample of required language

Sample Informed Consent Agreement

Required wording to describe an equivalence study:

It is not known which drug is better or even if the drug(s) are the same. The purpose of this study is to help find out. The new drug might be better than the old drug, but it might be the same or might even be worse.

If you qualify for this study, you will receive describe study drug administration using bullet points for ease of reading. Include dose per day and on what study days.

Include this statement when placebo is part of the study design. All subjects will receive placebo sometime during the study. Placebo is like a sugar pill and contains no active ingredient.

Include this statement if appropriate to study design. The study drug you receive will be assigned by chance, like the flip of a coin.

How long the study will last and how many people will be in the study

The study will last oabout # of days, weeks, months, etc. and involve up to o# visits (or nights at the facility). About o# people, ages oX through oX, are expected to be in this study.

When are you eligible to participate in another drug study?

The decision for when it is safe for you to participate in another study is determined by the drug safety information gathered from the previous study. Typically, it is safe to participate in another study as soon as 30 days after the last dose of drug received in the study you are enrolled in. This information is true for most drugs, however, some drugs may be present in your body longer and that may mean you may have to wait before entering into another study. These results are usually only known after the last blood sample taken from you is analyzed to look for left-over drug levels. Our goal is to keep you from doing anything that may be potentially harmful to you. Your safety while participating in these studies is our primary concern. ■

to see whether our required wording is included, as well." **(See sample required wording for informed consent forms, p. 102.)**

"We try to capture a wide range of situations," Meyer says. "For example, there are pregnancy precautions, and the quality control person is making sure those are included in the consent form."

IntegReview staff spent a lot of time working on the sample informed consent form, she notes.

"We wanted to make sure that all the basic elements were there and that it included the board's required wording," Meyer says. "We also need to be sure that consent forms are written below a ninth grade reading level, and sometimes that's a challenge."

IntegReview's staff will write an informed consent document for clients who choose to pay for the service rather than write or modify their own forms according to the IRB requirements, she says.

Once all the changes have been made, the document is sent to the client with a tracking feature so the client can see what was changed from the original document.

"They are receiving from us an approved document, and if they have issues with that, then they can request another review for an approval request to show what changes they'd like to have made," Meyer says. "The coordinators/co-chairs go through these requests because they can be processed quickly if they're minor and pose no additional risk to study subjects."

The final quality improvement process involves identifying errors and beginning a CAPA process.

"If we find a problem internally, it's during the quality assurance processs and it's not reported as an oversight," Meyer says. "If things are sent out to clients and there are errors or oversights, then it's reported, and a CAPA begins."

The staff find out what happened and what on the checklist wasn't followed. If the mistake was due to a process not being in place, then a new process is created to fill that gap, she adds. ■

Heading off headaches with multisite IRB review

Use "pre-conferences" and flexible application templates

Reams have been written about the logistical problems of dealing with local IRBs on multisite trials - the delays, the countless changes demanded by individual boards, the overall hassle.

What's rarer is to find someone who's worked out a practical strategy for dealing with this problem — one that's been proven to work.

That was the challenge taken on by **Jan Blustein**, MD, PhD, associate professor of health policy and medicine at New York University, New York City, and her colleagues.

Blustein, herself the chair of a social science IRB at NYU, was named in 2004 to a team conducting a multisite study as part of the Robert Wood Johnson Foundation's "Expecting Success" program. The program seeks to use quality improvement techniques to improve care to African-American and Latino heart patients.

In taking on the project, which would require individual IRB reviews at 10 sites, Blustein knew that her group could encounter problems — lengthy delays, back-and-forth negotiations with boards over consent documents and privacy concerns, differing estimations of participant risk.

Her group hit upon a novel means of addressing those problems before they came up — working with researchers and IRB representatives at each site before the applications ever were submitted, to try to work out potential problems and address IRB concerns.

"In watching the [IRB] process, it always strikes me that it's bad when people come up with a whole plan and then get shot down at the meeting," Blustein says. "The IRB world can be so capricious and so arbitrary — there's no predicting anything. Everything is so cockeyed out there, why not try to have a direct conversation first thing?"

To her surprise, IRBs were willing to have those conversations, even before their institutions had been chosen as sites for the study. And the approach helped paved the way to a smoother approval process: All 10 sites received approval within 180 days of notification of funding.

Blustein says her team's approach could work with just about any multisite protocol, as long as sites were willing to participate.

"I'm amazed that they were willing to do this," she says. "Nobody said, 'I'm too busy. I don't do stuff like that.' I was impressed by that. I think it shows a lot of effort on the part of people who are putting in their time for free."

Flexible template

The Expecting Success protocol would require post-discharge surveys of patients, patient clinical data, focus group discussions, questionnaires and interviews with physicians, other clinicians and hospital staff. Seriously debilitated patients were excluded from being contacted, and questionnaires did not ask about sensitive subjects such as illegal or stigmatizing behavior.

As a result, the greatest risks posed by the research involved the use and protection of patient data. Blustein notes that at the time of the study, IRBs still were wrapping their arms around the requirements of the Health Insurance Portability and Accountability Act (HIPAA), which put new restrictions on use of patient information.

The group contacted 16 sites that had been chosen as finalists for the protocol. They first provided a model application that researchers at the sites could tailor to meet IRB needs at their own institutions. The templates addressed the usual questions that might come up during IRB review, and included model consent forms, early drafts of the survey instruments and schedules for interviews.

Blustein's team went into great detail about potentially problematic aspects of the study, and provided some alternative approaches for dealing with them. For example, the protocol called for linking patient survey responses to clinical information, which the team knew might raise red flags at some IRBs. So sites were given the option of making those links in-house, and then sending deidentified data to the team.

The research also was broken down into modules or sub-studies, breaking apart the research questions, study design, sampling strategy, recruitment and consent process. Researchers could bind them together into one application or several.

Giving sites those alternatives helped speed the process, and, Blustein says, signaled to IRBs that her team wasn't trying to ride roughshod over individual boards.

"This was about relationship-building," she says. "I think there's a dynamic in IRBs where people start to find things [to oppose]. I think the value here is in establishing some kind of non-adversarial relationship."

Once the sites had had an opportunity to review the written packets, but before they'd actually prepared their IRB applications — and before the foundation board had begun announcing the awards to the 10 sites chosen — the team scheduled a round of conference calls with the finalist sites. Eleven calls were made before the final 10 sites were named, so the rest were discontinued as unnecessary.

Those participating in the conference calls included the site's principal investigator, project director, a member of the IRB and their legal counsel. Although one-hour calls were scheduled with each

site, the calls rarely lasted more than a half hour.

In most cases, Blustein says, the project director led the conversation, with occasional input from the IRB representative.

"We would say, 'This is really for you, tell us what you need to know and what you're thinking,'" Blustein says. "And then the project director would take it from there. In some cases, the IRB person was really dominant, and in other cases, they weren't. The project director might say, 'Does this sound OK to you?' and the IRB person would say yes or no."

The calls gave Blustein's team a chance to deal with potential IRB concerns upfront, rather than submitting a proposal and having it denied.

"In one case, one [IRB representative] was absolutely convinced that there was a federal directive that was contrary to what we were suggesting," she says. "The attitude was, 'You've got to convince us.' But at least we were able to make the case on the phone, instead of just getting a letter saying: 'You've got to be crazy. Have you read Statute blah, blah, blah of Regulation blah, blah, blah?'"

'Concentrating effort'

Blustein says putting together a more flexible application and speaking with sites didn't really take more time than it would have taken had they handled the proposal in a more conventional way.

"I think it concentrated the effort we had to make into a particular time period," she says, noting that much of the template work would have been required by her team's own IRB. "I remember there was sort of this frantic week of writing all this stuff. It was a lot of work, concentrated, but in the end I'm sure it was a lot less work. And it was really worth it.

"This helped the sites to think about what they were getting into and helped us to think about what we were getting into," Blustein says. "That's not the intent of it, but it really had that effect. In that sense, it's really efficient. You sort of say, 'What? Hold it — What are we thinking about doing?'"

She notes that it would have been much more difficult to use this approach with a finished protocol already in hand.

Blustein concedes that the attraction of the foundation grant may have influenced sites to participate in the extra pre-award work.

"I think the incentive of the grant was a big deal," she says. "As a rule, the hospitals we were dealing with are not big teaching hospitals. For them, the fact that they were applying for a grant was a really big deal for them." But she notes that at least a few of the sites were at larger institutions, which presumably would be less influenced by the grant.

Blustein believes this approach could have application for other multisite studies.

"Maybe it's most useful if the [research] you're talking about is not business as usual, if it's something a little unusual for that institution."

But Blustein says IRBs in general need to think about what it's like being on the receiving end of IRB review, and to look at research, particularly multisite studies, differently.

She says that on her own IRB, she resists making changes to multisite study proposals unless she feels they're absolutely necessary.

"Because it just makes it too complicated for people," Blustein says. "We get multisite stuff and we say how much are we going to get by making things different? Are we really going to make things better or are we just going to make them marginally better?

"Maybe the message is that people who are involved in this kind of work really need to be involved in IRBs and IRBs really need to consider these as a separate class of review." ■

Resource

Blustein J, et al. Notes from the field: Jumpstarting the IRB approval process in multicenter studies. *Health Services Research*. 2007;42:1773-1782.

Consent monitoring proposed to improve informed consent

Supporters argue it could decrease IRB burden

Many IRBs spend countless hours of review focusing on the consent documents needed for research studies. Are they too technical? Written at too high a level of readability? Too vague? Not extensive enough in their description of potential risks?

Many The major challenge of getting a consent document right is balancing the twin needs of comprehensibility and comprehensiveness, say **Thomas May**, PhD, associate professor of bioethics, and Ryan Spellecy, PhD, an assistant professor of bioethics, both at the Medical College of Wisconsin in Milwaukee.

"These two goals really are at odds in many ways," May says. "If it's complete and has too

much information, it starts to lack comprehensibility, or certain aspects of the consent form begin to lose their meaning for those who are reading those forms."

May and Spellecy also note that deficiencies in consent document review make up a large number of the violations cited in warning letters to IRBs from the Food and Drug Administration and Office for Human Research Protections.

They have proposed a novel solution for this problem, drawing on the example of hospital ethics boards (HECs) at academic medical centers.

They recommend that IRBs move toward a system of routine monitoring of the informed consent process to be sure that participants understand the research. They argue that that would leave the consent document to be as complete and detailed as it needed to be, while ensuring subjects' understanding of the study itself.

At the same time, they note, the new system could ease the workload of overburdened IRBs.

"I think moving the comprehensibility issue to this system that we're proposing would allow the documents to become even more complete than they currently are," Spellecy says. "Because the primary concern of the document would no longer be this dual goal of completeness and comprehensibility.

Although such a system would increase staffing costs, May and Spellecy believe that cost could be covered by funding from the National Institutes of Health. In fact, they've identified a possible funding source for a pilot consent monitoring project, through newly created NIH Clinical and Translational Science Awards (CTSA).

HECs vs. IRBs: A different focus

Both May and Spellecy have experience serving on both hospital ethics boards and IRBs; Spellecy is currently chairman of an IRB at the Medical College of Wisconsin.

"It was really our discussions about how the approach to informed consent was so different [on HECs] than it was with IRBs that really motivated a solution to this problem we see," May says.

Hospital ethics boards address ethical problems that arise in clinical treatment of patients at their institutions. In that role, they also deal with informed consent issues — for example, ensuring that a patient understands his or her treatment options, or that family members understand the ramifications of withdrawing life support from a patient.

Although these decisions often involve signing informed consent documents, May and Spellecy argue that those documents are not viewed as the ultimate proof of patient comprehension.

They note that hospitals have been successfully sued by patients who say they weren't properly informed, even when they have signed consent documents to that effect.

At many institutions, ethics consultation is offered as an arm of the HEC, and usually is conducted by members of the committee.

They are called in on particularly difficult or unusual cases, May says.

"They usually involve questions about the patient or family's understanding of the proposed procedures or approach to care, as well as matching those proposals to the values of the patient," he says. "That's really what informed consent is all about."

It's that consultation function that May and Spellecy would like to see emulated in a research setting. They suggest that teams of monitors could oversee all informed consent in studies approved by an IRB, and report back to the board as part of their duties.

Spellecy says it's possible that this type of consent monitoring could be used even before a protocol is submitted to an IRB, to help researchers with potentially thorny consent challenges.

"It could work that way, if it was a particularly difficult question," he says. "But we also envision that informed consent teams would go out and observe consent and report back to the IRB, so enabling the IRB to do its job and ensuring that informed consent really is informed, is voluntary and so forth."

Under such a monitoring system, Spellecy says the consent document itself would function much like the package insert for a drug — as a reference material that supplements the actual process of informed consent.

"It could be a useful tool for research participants to refer back to," Spellecy says. "I've got another research visit coming up; am I supposed to fast for this visit? I'm experiencing this side effect, should I be concerned? Should I report it to my study doctor?"

He says he thinks the document could become even more complete than it currently is, because IRBs no longer would have to worry about keeping the length short enough for comprehensibility.

Spellecy says IRBs still would have to receive the reports from the consent monitors to oversee consent, much as they currently receive reports from quality assurance and compliance monitors.

But he believes IRBs would prefer that to the

continued burden of wrestling with consent documents. As a researcher, he also thinks investigators would welcome the change.

"One of the things that researchers often complain about is the length and complexity and cumbersomeness of these consent forms — going back and forth with the IRB with modifications," Spellecy says. "That aspect would largely diminish under our proposal. As a researcher, I would appreciate that."

Both men say that while they haven't completely worked out the details, they could see the consent monitoring system being used in social-behavioral research, as well as biomedical studies.

"With much of social-behavioral and public health research, it's going on in the field and might be harder to monitor," Spellecy says. "But there are ways around that. If you're doing focus groups or semi-structured qualitative interviews, you can just record the consent process and someone could review that."

Finding funding

A system such as the one May and Spellecy suggest obviously would require more staffing - they estimate anywhere from one to 20 staffers, depending upon the workload of a particular IRB.

May says that it would be unlikely that already under-funded, overworked IRBs could afford to try it without a new source of funding.

"I would envision that this service would be written into NIH grants and funded in this way," he says.

They have suggested that the proposal could be piloted through the new NIH CTSA initiative.

The CTSA program works through a national consortium of 12 academic health centers, with plans to increase to about 60 institutions by 2012. The institutions will be linked together to improve the discipline of clinical and translational science. Applicants at the centers can request funding for pilot projects, including those that "seek to improve clinical design, biostatistics, clinical research ethics, informatics or regulatory pathways…"

May and Spellecy describe their idea as being in its "infancy," but say that through a pilot program, it could be strengthened into a viable way for IRBs to improve consent in research studies.

"We think we've isolated this problem of the competing goals of comprehensibility and completeness that IRBs and investigators alike struggle with," Spellecy says. "And we've tried to come up with a novel solution, borrowing from hospital ethics committees and even coming up with a possible funding stream." ■

Reference

May T, et al. Viewpoint: IRBs, Hospital Ethics Committees and the Need for "Translational Informed Consent." *Acad Med*. 2007;82:670-674.

CTSA Web site: www.ctsaweb.org

Preventive misconception: Study shows misunderstanding

Misconception could lead participants to take risks

IRBs already are attuned to the dangers of therapeutic misconception, in which research subjects confuse research interventions with personalized medical care. Meaningful informed consent — explaining clearly the potential risks and benefits of participation in a study — is believed to be the best method of combating the problem.

Now researchers are looking at the potential misconceptions surrounding preventive research, and how a false belief in the benefits of a prevention trial may lead participants to take undue risks with their health.

They've coined the phrase preventive misconception to describe the phenomenon and have demonstrated the existence of preventive misconception in a study of patients participating in a vaccine trial.

The results were published earlier this year in the *American Journal of Preventive Medicine*.

"We wanted to see if a prevention misconception exists and in fact we found one," says **Jeremy Sugarman**, MD, MPH, MA, Harvey M. Meyerhoff Professor of Bioethics and Medicine at Johns Hopkins University, Baltimore, MD. "We coined the term because we think there are distinctions between therapy and prevention. They seem to have similar manifestations, but we wanted to have a better way of talking about it."

Sugarman says preventive misconception carries very real risks to participants, if they "disinhibit," or refrain from taking preventive care of themselves because of their participation in a prevention trial.

HIV prevention trials

He first began looking at this issue through his work as chairman of the ethics working group of

the HIV Prevention Trials Network, which conducts international HIV prevention research.

"If participants believe that an HIV prevention vaccine is going to work, even an experimental one, then they may engage in unsafe behaviors," he says. "When in fact the reason you're doing the trial is because you don't know if it's going to work or not."

Similarly, Sugarman says, preventive misconception could lead patients on an experimental lipid lowering agent to ignore dietary restrictions, or cause participants in a prevention trial for nosocomial infections to slack off on everyday measures such as hand-washing.

Preventive misconception can take two forms:

• A patient may erroneously believe that he or she is taking the experimental intervention, rather than, say, a placebo vaccine.

• A patient may overestimate the effectiveness of the intervention.

Subjects can harbor one or both misconceptions about their participation in a prevention trial, Sugarman says.

Finding misconception in a study

In order to test their theory of preventive misconception, Sugarman's team looked at a shingles vaccine trial conducted at Veterans Administration centers across the U.S. They examined the responses to a telephone-based evaluation conducted with subjects who had just completed informed consent in the trial.

They focused on the answers given to two questions: 1) "What are the benefits to you of participating in this study?" and 2) "What is the primary purpose of this study?" The belief was that the answers to those two questions would help determine whether a subject harbored a preventive misconception.

The team developed a tool that raters could use to identify preventive misconception in the subjects' responses. If it was identified, the rater then tried to decide whether the misconception stemmed from an overestimation of receiving the experimental vaccine, or from an overestimation of the vaccine's effectiveness, or both.

Out of a group of 50 participants whose responses were examined, raters identified a clear preventive misconception in 16, or 32 percent. Of that group, six participants were found to have underestimated the likelihood that they would receive a placebo. Twelve overestimated the effectiveness of the experimental intervention.

Sugarman believes that the relatively high rate of preventive misconception is plausible, given estimates of therapeutic misconception that have been made in previous studies.

Having now identified preventive misconception retrospectively in an existing trial, Sugarman says he now wants to find a way to test the theory in prospective studies, and try to link it to disinhibition.

"We're searching for opportunities in which to use this approach," he says.

He says there's little information now about how preventive misconception may cause disin-

CE/CME Objectives

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

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

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

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

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

COMING IN FUTURE MONTHS

- Here's a case study of overzealous IRB request
- IRB uses fully integrated electronic process
- A novel approach to educating community IRB members
- Decision aids in clinical trials

hibition, let alone what strategies might be best for dealing with the problem.

"We know there is some disinhibition in trials," Sugarman says. "But at the same time, we don't know the root causes of it."

It's possible that the same sort of informed consent improvements used to deal with therapeutic misconception might work in this case, but Sugarman says it's too soon to tell.

However, he says, it's not too early for IRBs to be looking at this issue and considering the potential for preventive misconception in the prevention trials they review.

"I think what's really important, if we do nothing else, is that we now provide a language with which people can articulate their concerns and assess whether it exists in other settings —- and if so, what role it might play in building a robust consent process," Sugarman says.

"We want to encourage IRBs to take a look at this so that they can carry out their obligation to protect the rights and welfare of research participants." ■

Resource

Simon AE, et al. Preventive misconception: Its nature, presence and ethical implications for research. *Am J Prev Med*. 2007;32:370-374.

CE/CME *questions*

9. *True or False*: Using consent monitors for research studies, IRBs no longer would have to review consent documents.

10. What percentage of participants in a VA prevention trial were found to harbor preventive misconception?
A. Nearly a third
B. More than half
C. Up to 90 percent

11. Which of the following is a benefit of a federally-funded program to train African professionals in bioethics?
A. The students can return home to start new IRBs.
B. The students can use their knowledge to train other health care/researcher professionals in their native countries.
C. The students can become consultants and experts on the international health care stage.
D. All of the above

12. Which of the following is a useful tool to use when performing quality assurance checks on IRB processes?
A. A sample protocol form
B. A quality assurance protocol review checklist
C. A CAPA post-it note
D. None of the above

Answers: 9. (False); 10. (a); 11 (d); 12. (b)