IRB ADVISOR

Your Practical Guide To Institutional Review Board Management

December 2011: Vol. 11, No. 12
Pages 121-132

IN THIS ISSUE

Statement of Financial Disclosure:
Editor **Suzanne Koziatek**, Editor **Melinda Young**, Executive Editor **Michael Harris**, Nurse Planner **Kay Ball**, and Physician Reviewer Mark Schreiner, MD, report no consultant, stockholder, speaker's bureau, research, or other financial relationships with companies related to the content in this CNE/CME activity.

AHC Media

Some see including minorities in CR as an IRB/ethical CR responsibility

IRB's role could be educational

Research ethicists and others have long described the value of recruiting more minorities in clinical research (CR) trials, but the question is whether or not IRBs have a role to play in advancing this goal.

Is it enough to ask investigators to work toward greater inclusion, or should IRBs take part in both clinical research staff education and educating the greater community about the research enterprise and minority participation?

"We do believe there is a role for the IRB to simply monitor the inclusion of the women and minority component of the National Institutes of Health (NIH) guidelines," says **Stephen Thomas**, PhD, professor and founding director of the Maryland Center for Health Equity, and a professor of health services administration at the school of public health, University of Maryland in College Park, MD.

IRBs could ask researchers to outline their efforts to recruit minorities when they submit protocols, but it might be better to address recruitment inclusiveness from an institutional perspective, some experts say.

"I personally have a bias against using the regulatory arm — i.e., the IRB — in terms of telling investigators what to do," he adds. "The IRB has a role to play, but a greater role is needed from the institution."

IRBs can help a research institution with developing a more inclusive recruitment strategy by using their own data to assess the big picture.

For instance, the IRB can see what type of recruitment has taken place at hundreds or thousands of clinical trials, says **Sandra Crouse Quinn**, PhD, professor of family science and associate dean for public health initiatives in the school of public health at the University of Maryland.

"IRBs can have a sense of the big picture," she adds. "Potentially, if they had the resources, they could serve a role at the institution of looking at how successful investigators are in recruiting diverse populations."

IRBs also are in a good position to note best practices and success stories in recruitment.

"A good IRB staff could learn a lot from seeing what's submitted to them — what's successful and what's not," Quinn says.

At the University of Maryland, the IRB director joins other experts in working on a curriculum for educating researchers and minority communities about research participation, says **Mary A. Garza**, PhD, MPh, an assistant professor in the department of behavioral and community health at the University of Maryland School of Public Health and associate director for the Maryland Center for Health Equity.

Also, IRBs could expand to include more community members and make an effort to recruit members of minority communities, Garza suggests.

"IRBs play a very strategic role, and this is their opportunity to make sure they can help the population," she adds.

For research institutions, the key to encouraging more minority participation in CR might be to separate regulatory authority from educational influence. The IRB could be helpful in the realm of educating the research community, but regulatory actions might be left to the government.

"To add a regulatory function might be too much," Quinn says. "But they may have opportunities to spark dialogue because they have the big picture perspective."

IRBs could hold brown bag lunches with investigators to highlight those who are successful at recruiting minorities and to encourage information sharing, she notes.

There is some benefit in putting regulatory teeth to any guidelines regarding minority inclusion in trials. For instance, the NIH exercises some of that clout by giving research sites a lower score if they have fewer women and minorities in their trials, Thomas says.

"We have been struggling in trying to determine where would be the best home for that responsibility [for minority inclusion]," he says. "So we think that current principal investigators and their research staff need formal training in recruitment and retention of racial and ethnic minorities in research."

Online bubble forms are insufficient. The training should be about more than tools and techniques, he adds.

"It should truly be transformative training that also impacts attitudes and beliefs," Thomas says.

"We don't want this area to carry all of the baggage of having the IRB ask researchers to do one more thing," Thomas says. "So we're trying to find an institutional, administrative home for who is responsible for ensuring researchers and research staff get appropriate training in minority recruitment and retention." ■

IRB Advisor (ISSN 1535-2064) is published monthly by AHC Media, a division of Thompson Media Group LLC, 3525 Piedmont Road, Building Six, Suite 400, Atlanta, GA 30305. Telephone: (404) 262-7436. Periodicals Postage Paid at Atlanta, GA 30304 and at additional mailing offices.

POSTMASTER: Send address changes to IRB Advisor, P.O. Box 105109, Atlanta, GA 30348.

AHC Media is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

AHC Media designates this enduring material for a maximum of *18 AMA PRA Category 1 Credits*™. Physicians should claim only credit commensurate with the extent of their participation in the activity.

AHC Media is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center's Commission on Accreditation.

This activity has been approved for 15 nursing contact hours using a 60-minute contact hour.

Provider approved by the California Board of Registered Nursing, Provider #14749, for 15 Contact Hours.

This activity is intended for clinical trial research physicians and nurses. It is in effect for 36 months from the date of publication.

Opinions expressed are not necessarily those of this publication. Mention of products or services does not constitute endorsement. Clinical, legal, tax, and other comments are offered for general guidance only; professional counsel should be sought for specific situations.

SUBSCRIBER INFORMATION

Customer Service: (800) 688-2421 or fax (800) 284-3291, (customerservice@ahcmedia.com). Hours of operation: 8:30 a.m. – 6 p.m. Monday-Thursday; 8:30 a.m. – 4:30 p.m. Friday, EST.
Subscription rates: U.S.A., one year (12 issues), $399. Add $17.95 for shipping & handling. Outside U.S., add $30 per year, total prepaid in U.S. funds. Discounts are available for group subscriptions, multiple copies, site-licenses or electronic distribution. For pricing information, call Tria Kreutzer at 404-262-5482. Back issues, when available, are $65 each. (GST registration number R128870672.)
For recent permission, please contact: Stephen Vance, Telephone: (800) 688-2421, ext. 5511 • Fax: (800) 284-3291 • E-mail: stephen.vance@ahcmedia.com • Address: 3525 Piedmont Road, Building 6, Suite 400, Atlanta, GA 30305

Editors: **Suzanne Koziatek** and **Melinda Young**.
Executive Editor: **Michael Harris**, (404) 262-5443 (michael.harris@ahcmedia.com).
Production Editor: **Kristen Ramsey.**

Editorial Questions

Questions or comments?
Call Michael Harris at (404) 262-5443.

COMPLIANCE CORNER

IRB has CR sites correct errors with action plans

Key is prevent noncompliance

IRBs and research offices need a variety of procedures and tools to ensure compliance. One tool that sometimes is overlooked is requiring research sites to develop corrective action plans (CAPs) when they have problems.

"Often times the principal investigator and research staff want to do the right thing, and they don't want adverse events or violations to continue occurring, but they might not know how to create a corrective action plan," says **Stephanie Gaudreau**, CIP, IRB administrator for the Ochsner Institutional Review Boards at Ochsner Health Systems in New Orleans, LA.

The purpose of the plan is to reinforce the importance of internal controls to prevent harm to research participants, she notes.

"Going through the process helps them look at a root cause of a problem and address it," Gaudreau adds.

This is where an IRB office can assist.

"By having the corrective action plan come through the IRB office, it forces investigators to think about, report it, and respond to it," Gaudreau says. "Without the CAP, research staff might not take time to think about the root cause of the problem and how to fix it and do internal educating and communicating."

Gaudreau offers these tips on creating a thorough compliance process that uses corrective action plans (CAPs):

• **Establish triggers for requiring a CAP:** Research institutions that conduct post-approval monitoring audits can recommend CAPs from research sites that have had findings during these audits.

"We have an internal QA office that does for-cause and not-for-cause audits, and often times they'll go into a department and work with a specific principal investigator, finding a list of protocol violations," Gaudreau says. "The violations could be something we consider minor or others that are not minor," she adds. "For instance, we've had a few where the consent process was not carried out correctly, and the documentation for consent was not done correctly."

If this problem occurs just a couple of times, it could be seen as a minor violation. But in cases where it has occurred repeatedly, the IRB might see that as a compliance problem and would require a corrective action plan from the site, she says.

"We've also had some major issues where we may have had a study drug given outside its window, and that may have occurred with two or more subjects," Gaudreau says. "In that type of case we would definitely want a corrective action plan, and the requirements might be stricter: we might ask for follow-up data in 30 days and ask that the continuing review be submitted quarterly."

Another trigger for a CAP would be if a researcher is noncompliant in terms of submitting continuing review forms or has a large number of violations or events, she says.

"We may request the QA office audit some of their files, but this rarely happens," she adds.

Also, the CAP might be triggered involve reportable event reporting to the IRB and findings during continuing review. If there are trends, a pattern of violations or adverse events, then the IRB office will forward the information to the IRB chair and ask for advice on whether it should go to the full board for review, Gaudreau says.

"About 90% of the time the full board or chair will request an action plan," she says.

Any regulatory agency investigation that produces findings or warning letters would trigger a CAP, as well, she adds.

• **The IRB makes the final CAP decision:** "Sometimes the IRB chair will determine right away that it needs a corrective action plan before it goes to the panel," Gaudreau says. "Sometimes the chair will decide to wait and take it to the full panel, especially if we're trying to determine whether there's continuing or serious noncompliance."

The chair will wait for the full board to make a decision in those cases because the IRB also will have to report these events to other agencies, she adds.

When the IRB decides a corrective action plan is necessary, the IRB's electronic system sends out a formal notification from the IRB requesting corrective action plans.

"The letter provides a link to a sample corrective action plan and guidance," Gaudreau says. "We recommend they contact the IRB office for additional guidance."

• **Provide guidance on creating CAPs:** The IRB has a CAP form that lists the action the research site is go-

ing to take, the due date they expect the action to be met, and whose responsibility the action is plus any additional comments.

"It's not open-ended," Gaudreau says. "We want to see that they're addressing the problem and that there's a submission or end date and we can see who is held responsible in their team to make sure it happens."

The IRB office will suggest researchers check out the online materials, including a tool that outlines how to design corrective action plans for clinical research, she says.

"Education of the study team is key, so we always request they put that in the plan," she adds. "If the site's problem is addressed within the IRB's standard operating procedures or institutional policies, then they'll advise them to go to those policies and review them with their study team."

Ochsner's corrective plan guidance includes these six steps to writing effective CAPs:

1. State the problem or weakness succinctly, including the root cause.
2. Have "owners" who are accountable for results.
3. Break the solution into discrete, measurable actions that address the root cause.
4. Identify accountable person for each action.
5. Set achievable deadlines.
6. Monitor progress.

The Ochsner material also lists some items that the U.S. Food and Drug Administration (FDA) expects to see in corrective action plans, including these:

— Evaluation of the extent of the problem
— assessment of the root cause
— Any corrective actions, including plan to correct, implementation details, training, and assessment of the correction
— supporting documentation
— preventive actions to prevent recurrence.

The guidance material also lists nine helpful hints and provides a one-page sample corrective action plan based on the deficiency of having case report forms that are incomplete.

• **Have the IRB review the completed CAP:** First the IRB office staff review the plan to see if it is complete and contains the items the board would require.

"If something is missing we return it to them and pick up the phone to talk with the investigator or coordinator to give them specifics of what we're looking for," Gaudreau says.

Then the CAP is put on the schedule for the board's next review meeting. These CAP reviews last 10 to 30 minutes, depending on how serious were the events that triggered the plan.

"If it was a serious event that triggered the plan, then the board tends to focus on follow-up information so they will often request a follow-up to the CAP within four months or three months," Gaudreau says. "The follow-up could be a narrative from the principal investigator."

The PI needs to explain whether the CAP is working and how many people have been enrolled since the CAP was reviewed.

"It hasn't happened very often, but in some cases where participants may have potentially been seriously harmed, we'd request the follow-up data," she says. "Also at the time of continuing review, we'd look at the review and remind the panel of the corrective action plan and what the team was supposed to be following."

After comparing the CAP and the past year's events, the IRB would look for red flags that might need to be addressed by the board, she adds. ■

Lean process QI plan can work well for IRBs

Target wasteful processes

Most major corporations and business sectors have adopted business quality improvement (QI) measures like Six Sigma, Lean Process, and others. But in human subjects research, this type of QI approach is fairly new, an expert says.

"The Lean Process involves gathering people who are involved in all phases of research together to define what the current state process is and to analyze which pieces of the research process add value and which add waste," says **William A. Bornstein**, MD, PhD, chief quality and medical officer of Emory Healthcare in Atlanta, GA.

The Lean Process was the basis of the Toyota production system and is used often in manufacturing, he notes.

"The focus on lean is to try to distinguish value from waste," he adds. "This gets into a more disciplined way than most of us are used to thinking about."

While some kinds of waste are necessary, such as waiting in line or waiting for inventory to arrive, many types of waste can be eliminated through process improvements.

The lean process identifies waste through several steps:

— Define value stream
— map current processes
— identify which of the pieces or parts of the process add value and which are waste
— rapid improvement events.

In human subjects research, the value involves a scientific product that advances knowledge and improves patient care, Bornstein says.

"Applying this process to clinical trials, we broke the value stream into parts, beginning with conception of the study and going to the point of actually enrolling patients," Bornstein says. "Clearly there's more to it than that, but that's the first bite we took."

Applying a Lean Process formula to research can be eye-opening: "We found that the process was very complex and there were multiple processes to the same end," Bornstein says.

Emory Healthcare illustrated the research process with a diagram on the wall.

"Then we asked people to use sticky notes to define the kind of waste that can occur," he says. "Waste can include things we do that we don't need to do, and they could also include defects."

The wall was full of sticky notes.

"The next phase of it was to come up with a future state that would eliminate as much of the waste as possible and define a desired state," Bornstein says.

During this process, the people involved with the Lean Process should pause, take an insider's look at the current processes, and think about their findings.

"For the value stream analysis you need to step back because so often we're in the midst of getting things done, and we'll do work-arounds that we know aren't ideal," he explains.

"In manufacturing, you visit the production line," he adds. "In the IRB processes, it's less about physical places and more about having all of your stakeholders present in the room."

So one possibility is to hold a rapid improvement event, in which teams meet for several days to drill down into that area of concern and look at the mechanics and how to redefine the process, he says.

"Another common feature in quality improvement activities is the trial and error process," Bornstein says. "It's like the scientific method where you have a team of people involved in the steps and process."

A team might have identified areas that are not standardized but which could be and other areas that need some focused improvement activity, he says.

"You look at whether you can drill deeper in this area and what the current state is," he adds. "We go in there and try to redesign in real time how the trial works."

This is an ongoing activity.

One example of applying the Lean Process to IRB work would be to take a look at the length of time researchers wait for IRB approval. This form of waiting is a waste and can create delays, and some of it could be improved.

"What can we do to reduce that waiting, streamline the process?" Bornstein says.

There might be some improvements that can be done easily and someone could be assigned to make those changes. Called "just do it," these are the low-hanging fruit.

Other changes are more complex and might require a rapid improvement event in which a group of experts and staff are involved.

Still others could be long-term solutions.

"These might be an area where we won't prioritize it now, but we think it's waste and we may want to come back to it," Bornstein says.

An example is information technology improvement.

"By using information technology we may be able to improve reliability and reduce waste, but it requires longer-term planning," he explains. "So in the meantime, what else can we do to reduce waste?"

Emory Healthcare has used the Lean Process for more than five years as one tool for its quality improvement efforts, and it continues to be a learning process, Bornstein says.

"Many people who've written about the Lean Process point out that it takes years to learn how to do this," he says.

Even as a research organization begins to use the process, it can gain some valuable tools and make efficiency changes. For instance, Emory Healthcare came up with 30 just-do-it items, and one of these proved to be a valuable clinical trial readiness checklist. *(See an article about the checklist in the November, 2011, issue of* IRB Advisor*).*

Another rapid improvement event was related to a feasibility assessment of the protocol prior to it going through the IRB submission process, he notes.

It was a waste of time to have investigators submit protocols that had not been well thought out. For instance, the planned trial might not have a large enough subject population to complete enrollment or might be competing with a similar study for the same patient population, Bornstein says.

"That's a classic example of waste," he says. "People start going through the pipeline with the protocol and are a good ways through it with the IRB's approval, but then they never accrue any patients."

The rapid improvement event created a process for making sure early on in the protocol development that the study was feasible, and it involved the IRB director and a medical director. This particular project is ongoing, Bornstein says.

"Rapid improvement events are when you redesign a process for improvement over several days, as opposed to making changes over the course of months or years," he adds. ■

IC experts advocate improvements to process

But proposals in ANPRM may not entirely solve readability problems

In the proposed revision of the Common Rule, the Department of Health and Human Services (HHS) responds to years of complaints about informed consent documents – that they're too long, too complicated, too full of boilerplate and risk management language.

The improvements proposed in the revision of the Common Rule address all of those points:

— mandating that certain content be included in consent forms, with more detail than is currently required and that other content be removed;

— limiting the length of certain parts of the forms;

—providing more detail about how information should be presented (what information belongs at the beginning of the form, for example, or what belongs in an appendix);

— reducing locally required content that doesn't protect subjects and primarily is intended to shield the institution;

— proposing creation of consent form templates, giving institutions a format that they can be confident will pass regulatory muster.

Those who have studied the challenges of providing appropriate consent say these proposals aren't new.

Michael Paasche-Orlow, MD, MPH, associate professor of medicine at Boston University School of Medicine and a nationally recognized expert in health literacy, says he assisted in an initiative by the National Cancer Institute that is taking on many of the same goals, including creating templates for consent documents.

Furthermore, he says it's not even the first attempt by NCI.

"I'm friends with people who were involved with the NCI informed consent effort that happened about 15 years ago," Paasche-Orlow says. "And they had some of the same recommendations back then that they did this last time.

"The issue is how come no one followed their recommendations?"

Complicated studies

One obstacle is the sheer complexity of modern clinical trials, says **Mark Hochhauser**, PhD, a readability consultant who serves on an IRB at North Memorial Medical Center in Robbinsdale, MN.

"It used to be that you would see a study that involved, say, an experimental drug vs. a placebo," Hochhauser says. "And you have a clinical trial now that has maybe three or four research parts to it. That's complicated and hard to understand even for IRB members."

He says it's hard to limit the length of documents when there are so many required elements that have to be communicated.

"You've got somewhere around 20 topics that have to be covered in the consent form. You can't ignore 15 of them and just do five. You have to do all of them."

He says that removing some of those elements to focus on what patients truly need to know would be an improvement.

Adding to the murk of an informed consent document is that many groups involved in its development often have goals in addition to informing subjects, Paasche-Orlow says.

"The organizational goals have to do with risk management," he says. "Until there's a much stronger hand from the regulators, the risk managers for the organizations are going to fear changing what they're currently doing. Because what they're currently doing is considered acceptable, appropriate and defendable."

Paasche-Orlow says previous efforts at simplifying informed consent had input from regulators, but the agencies were reluctant to give templates their official "approval." He says he's happy that the ANPRM provides for the creation of templates.

But he and Hochhauser say templates won't by themselves solve readability problems.

Hochhauser notes that a template can only provide a general outline of the information in a specific study.

"The problem is that the template will start off

with some sample language and it's to be filled in by the researcher," he says. "That's where it all falls apart. It's the to-be-filled-in part that winds up being written in incomprehensible legal and regulatory language."

Paasche-Orlow notes that even when forms actually are written plainly, it may be hard to get certain concepts across to subjects.

As an example, he points to language he was testing to be included in an informed consent toolkit developed by the Agency for Healthcare Research and Quality. He was trying to find the simplest way to tell subjects they would not be compensated for injuries they might suffer in a study.

"It turned out that actually it was very common for people to assume that we were saying the opposite," Paasche-Orlow says. "Because, in fact, the assumption is, 'Of course, if I'm injured in your study, you would pay for that. How could you not pay for that?'"

Flexibility, evaluation

Hochhauser and Paasche-Orlow say there are steps HHS could take that could improve the informed consent process.

"The form itself is just a piece of the puzzle. There are a lot of things that even with best language in your documents will need to be supported by a process," Paasche-Orlow says.

Their suggestions:

• **Use real forms:** Instead of templates, Hochhauser would like to see HHS take existing drug and device trial consent forms and simplify them, to give researchers a better jumping-off point for their own forms.

"I don't think a template is going to do it," he says. "People need to see real consent forms from real projects. Change any of the proprietary language, and show it in 'before' and 'after' versions — the before version, which is long and complicated and hard to understand, and the simplified version.

"And say, 'Feel free, if you're a researcher, to take this simplified form and adapt it so that it fits your needs.'"

• **Allow for flexibility:** Giving developers of consent forms flexibility to get their information across in different ways may not necessarily shorten documents, but can make them clearer. For example, Hochhauser argues for a table of contents in consent documents. Since participants rarely read the whole form, he says, it makes sense to direct them easily to the most important parts.

Paasche-Orlow promotes the use of tables and figures and images to help explain difficult concepts. But he's found opposition to adding such tools, because incorporating them would require further IRB approvals.

He notes that on the NCI project, he suggested creating simple software that would illustrate rates and percentages by generating a field of, say, five out of 100 dots to signify five percent.

"They said: 'Oh, that's way too complicated -- we'd have to have all the IRBs approve the software.'"

"When you're dealing with complicated concepts like percents and rates, which are broadly misunderstood, the adult education literature shows that there are ways to improve how we talk to people about these things," Paasche-Orlow says. "Really, the whole system has to be much more flexible and amenable to the use of various kinds of teaching aids."

• **Evaluate understanding:** The ANPRM asks whether, in certain types of studies, investigators should assess how well potential subjects comprehend the information before allowing them to enroll.

Paasche-Orlow says this would be an appropriate requirement, particularly in concert with a shorter form that focuses only on the most important information.

"This is not like some sort of memory test where you say, 'How long is the third study visit?' That's not the crucial component here," he says. "The crucial components are things like understanding that this is voluntary. That this will not impact their relationship with their doctor. These are the critical things.

"Having a shorter template can substantively help the process, by focusing on the ethically relevant ideas. And that would put us in a good position to say, 'And yeah, confirm comprehension of those things.'" ■

AAHRPP says regulators need more information

Before proceeding with revisions to Common Rule

In assessing the recent revisions to the Common Rule proposed by the Department of Health

and Human Services (HHS), the accrediting agency for human subjects protection programs suggests that HHS may lack the necessary information to move forward with a final rule.

While the Association for the Accreditation of Human Research Protection Programs (AAHRPP) supports the need for revising the regulations, its comments express concern over the many questions asked in the document.

Marjorie Speers, PhD, president and chief executive officer of the independent, non-profit accrediting body, says that given the reach of the new recommendations, it's important for HHS to be as informed as possible in order to go forward.

"Based on what they are asking for in this advance notice, it appears to us that they don't have the very basic information that they need in order to proceed with rule-making," Speers says.

"I think that if they get a lot of comments that are similar to AAHRPP's comments or they get comments where there's no clear consensus, then I would look for them to make a decision to start over," she says. "There's nothing that says that this advance notice has to move to a notice of proposed rule-making and then to a final rule. They can stop it and start afresh."

Focus on burden or protection?

AAHRPP's response to the advance notice of proposed rule-making (ANPRM) details its concerns with the revisions — concerns that are echoed in many cases by other organizations (see accompanying story).

One complaint addressed by the ANPRM is that oversight of research often doesn't match actual risk level of studies, resulting in both excessive restrictions on low-risk studies and too little attention to higher-risk studies.

While AAHRPP shares that concern, the organization says there is not enough emphasis in the ANPRM on strengthening human subjects protections.

"The apparent primary purpose of the proposed rule-making seems to be to reduce burden on researchers," Speers writes in AAHRPP's official comments. "We are disappointed that it is not clearly stated in the ANPRM, and not observed in many of the proposed revisions, that reducing the burden on IRBs is an additional intention — not the principal objective."

AAHRPP also opposes the planned expansion of the Common Rule to all research conducted at an institution that receives funding from a Common Rule agency, saying it lessens IRBs' flexibility in handling different types of protocols.

And the organization does not favor the ANPRM's proposal to strengthen data protection standards by applying the HIPAA criteria to all covered research. Speers says that she believes there is strong opposition to this provision, and notes this is a good example of an issue where OHRP needs to gather more information.

"The HIPAA data security requirements are not appropriate, but to go back and say 'What is appropriate, do we need something?'" Speers says. "They can gather some information on that and come out with a better idea."

Suggesting new changes

In addition to critiquing the various provisions of the ANPRM, AAHRPP's response suggests a number of changes that the organization would like to see in a future version of the federal regulations.

For example, Speers says the revisions do not address the growing importance of community-engaged research.

"One of the major funding initiatives, for example at the NIH, are the clinical and translational science projects, where they all have a community engagement component," Speers says. "The Centers for Disease Control and Prevention, just by the nature of their mission in public health, are constantly engaged in community-based research.

There is plenty of community-based participatory research occurring, and our regulations are not sensitive to it."

She says that on this subject, along with others, OHRP could benefit from looking at regulations in other countries.

"In a number of areas, other countries have moved beyond the basic regulations that the U.S. has," Speers says.

"Canada addresses research in communities. The European Union, for Phase 1 clinical trials, has one deadline on review time; for Phase 3 trials they have a different deadline. In Mexico, for example, they have some very good regulations that relate to protecting vulnerable populations.

"There are other countries that have really moved beyond us and it's time for us to learn from them." ■

Groups finding common ground on Common Rule

From researcher responsibilities to training, consensus seen in several areas

In the waning days of the comment period for the advance notice of proposed rule-making (ANPRM) for human subjects protection regulation, some of the IRB community's heavy hitters have weighed in.

In addition to a submission by the Association for the Accreditation of Human Research Protection Programs (AAHRPP), detailed comments also were filed by the Secretary's Advisory Committee on Human Research Protections (SACHRP), the Association of American Medical Colleges (AAMC) and Public Responsibility in Medicine and Research (PRIM&R).

While each organization has its own specific take on the proposed revision of the Common Rule, there were many areas of agreement in their comments:

• Minimal risk definition

AAHRPP, SACHRP and the AAMC all propose that HHS should develop a better definition of "minimal risk" as it applies to research oversight.

SACHRP states that the definition should compare potential harms and discomforts in a study to those that an average person in the general population would ordinarily encounter. As an example, AAMC offers the case of a study of cancer patients. In that case, the risks and discomforts of the study intervention should be compared to those a healthy individual would encounter in a routine medical examination.

• Researcher/Sponsor responsibilities

SACHRP and AAHRPP both call for the regulations to more clearly spell out the responsibilities of researchers and sponsors in protecting subjects.

Those responsibilities would include knowing when to seek IRB oversight, disclosing financial interests, employing sound study design that minimizes risks, ensuring there are necessary resources to protect subjects, recruiting subjects in a fair manner, using appropriate informed consent and ensuring that subjects understand it.

"The Common Rule is written such that it applies to the institutions and the IRBs," says **Marjorie Speers**, AAHRPP's president and chief executive officer. "It is silent on the role of the researcher, who deals with the research subject every single day."

Other than requiring the investigator to obtain consent, the rule "does not spell out the responsibilities," she says. "They're just inferred. All of these regulations should address the roles and responsibilities of the major players."

• Informed consent

All of the organizations believe that the revisions to the Common Rule focus too much on documentation of informed consent and not enough on the process of obtaining consent.

"This focus may have the effect over time of preventing IRBs from allowing the implementation of novel, effective methods of communicating critical study information to research subjects," **Ann Bonham**, PhD, chief scientific officer for the AAMC, writes in that organization's comments.

The groups did not support the ANPRM's proposal to set length limits on various parts of consent documents, but supported the idea of moving some topics to appendices rather than the main document.

Proposed new consent templates could be useful, if they demonstrate to researchers how to craft a shorter document with an addendum that gives more detail, SACHRP proposes.

• Researchers self-exempting

AAHRPP, SACHRP and the AAMC all raise concerns about the proposal to allow researchers to determine for themselves that their studies qualify for the new "excused" (currently exempt) determination.

"Anecdotal evidence from some accredited organizations suggests that between one-quarter and one-third of researchers misclassify research as exempt when it is not exempt," Speers writes in AAHRPP's comments.

She says that while the process of exempting or excusing research could be much simpler, someone needs to review it – whether it's an IRB member or staffer or even a departmental board.

• Central IRB for multisite research

While the organizations agree that the regulations should encourage more use of a single IRB for multi-site studies, some balk at making that mandatory.

SACHRP calls such a requirement "premature," recommending instead a more deliberative process of encouraging single-IRB use.

In situations where one IRB is designated, organizations say that IRB must be chosen carefully, must have the necessary expertise to handle the

study and to communicate and interact with local sites. They note that the costs incurred by IRBs handling different levels of oversight need to be compensated fairly.

• **Training requirements**

All of the organizations ask that HHS make education of IRBs and researchers a requirement in the regulations.

"This system that we have now, and any system we have in the future, is based on people being knowledgeable and competent to conduct research," Speers says. "And if you don't have any education requirement, if you don't have any way to measure competency, then we're going to continue to have incompetent IRBs and researchers involved."

In all, more than 1,000 comments were filed with HHS during the extended comment period that ended Oct. 26.

OHRP spokeswoman **Ann Bradley** says the government will be considering all of the comments before deciding how to move forward. ■

Dispatching CARs to inform the public

Community liaisons get the word out about emergency research

When investigators seek an exception from informed consent (EFIC) for emergency research, they must show that they have engaged in community consultation and public disclosure, informing the public that they may encounter an experimental intervention while being treated in an emergency setting.

It can be difficult for researchers and IRBs to know that the consultation has been truly effective, reaching the population most likely to be affected by the study and giving the public an opportunity to ask questions and make suggestions.

At Virginia Commonwealth University in Richmond, the community engagement staff at the university's Center for Clinical and Translational Science Research has launched a program to build capacity for engaging the community in these EFIC consultations.

The approach relies on community liaisons who are already involved in local social services and community advocacy in the Richmond area. They were tapped for their knowledge of how to reach different populations and inform them about studies.

Cornelia Ramsey, PhD, MSPH, a community research liaison with the center, says the involvement of the liaisons, called community advocates for research (CARs), has extended her institution's reach in the community. She says VCU's Clinical and Translational Science Award helps maintain the network of CARs and makes them available as a resource to other investigators going forward.

Ramsey says the idea was developed while developing a community consultation plan for VCU's participation in the national Rapid Anticonvulsant Medications Prior to Arrival Trial (RAMPART). RAMPART studied whether it was more effective to give seizure patients anti-seizure medication in the field via an IV or an intramuscular injection.

Because it would be impracticable to gain informed consent from seizure patients being treated by paramedics, the investigators sought an EFIC, which includes a requirement for community consultation and public disclosure.

At first, Ramsey says, the local group conducted this consultation process through traditional means, including advertising in newspapers, television and radio.

"We connected with those particular community groups that might be in the target population for the study — epilepsy groups, head trauma groups, people who were likely to have a seizure," she says. "The principal investigator went to those groups, presented the study and opened it up for questions."

Extending the conversation

In listening to those exchanges, Ramsey says she was impressed by the conversation that took place between the investigator and the public.

"It's really the bi-directional communication that is the intent of community consultation/public disclosure," she says. "Having that experience made me see that unless we figured out other ways to support that conversation, we would never hear all of their questions."

Drawing on several models of community engagement in public health, her group developed the concept of the CARs, people active in the communities affected by the study. Some were with epilepsy groups, others worked with community organizations serving populations such as homeless people and some were associated with churches in the area.

After training the group in research integrity and

human subjects protection principles, the CARs were sent out to survey people about their knowledge of research at VCU and more specifically the RAMPART study. In an effort to measure exactly where the message was spreading, the CARs asked those they surveyed for the nearest intersection to their home. Ramsey's group mapped the results, showing which areas were reached by the education efforts.

After gathering this information, the CARs helped develop a plan to take the disclosure further. They called their own community meetings, and brought in the study coordinator to explain the study and answer questions. They handed out fliers and posted information on their bulletin boards and in their newsletters.

Ramsey says that because of the CARs' knowledge of their communities, the meetings they held were better attended than the university-initiated ones had been.

"It was the community advocates who opened the door a little bit more into the communities, particularly the harder-to-reach communities such as the homeless population," she says.

That increased access could be measured in survey responses.

The initial surveys about the RAMPART study, conducted in fall 2009 before the CARs began their own outreach, showed that 8.4 percent of the respondents had heard about the study, Ramsey says.

A separate but similar EFIC study was launched the following year. This time, the CARs were involved from the outset, and helped the investigator create his community consultation/public disclosure plan, using the same strategies they had piloted in the RAMPART study.

A survey conducted in fall 2010 showed that 21.5 percent of respondents now had heard of RAMPART, and 24 percent had heard about the second EFIC trial.

Building capacity

Because of the CTSA funding, Ramsey says VCU can maintain this network of CARs, activating it when needed to help with a study. A second generation of CARs is being recruited and trained, using materials the earlier CARs helped develop.

And the CARs themselves have gained from the experience. After spending so much time brainstorming together about community engagement strategies, Ramsey says the liaisons have begun to work on projects together outside the university.

"That's truly building that community's capacity for research," she says.

Ramsey, who also serves on VCU's social-behavioral IRB, says IRBs have an important role to play as they review community consultation and public disclosure plans, to help ensure that the plans include strategies that are likely to reach the intended people in the community.

"It's asking the important questions," she says. "Who is at high risk for being in this study? How are they represented in our community? Has every effort been made to reach into those communities and have that bi-directional communication? How is that represented in the plan? And how are we taking the information back to the community, once we have study findings?"

CNE/CME OBJECTIVES & INSTRUCTIONS

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 continuing education program and earn credit for this activity by following these instructions.

1. Read and study the activity, using the provided references for further research.
2. Log on to www.cmecity.com to take a post-test; tests can be taken after each issue or collectively at the end of the semester. First-time users will have to register on the site using the 8-digit subscriber number printed on their mailing label, invoice or renewal notice.
3. Pass the online tests with a score of 100%; you will be allowed to answer the questions as many times as needed to achieve a score of 100%.
4. After successfully completing the last test of the semester, your browser will be automatically directed to the activity evaluation form, which you will submit online.
5. Once the completed evaluation is received, a credit letter will be e-mailed to you instantly. ■

COMING IN FUTURE MONTHS

- ■ Educate IRB, researchers on health literacy
- ■ Best practices in giving results to communities
- ■ Anthrax vaccination research raises ethical issues
- ■ Institution, tribe create innovative research agreement
- ■ Video improves patients' understanding of clinical trials

To reproduce any part of this newsletter for promotional purposes, please contact: *Stephen Vance*
Phone: (800) 688-2421, ext. 5511
Fax: (800) 284-3291
Email: stephen.vance@ahcmedia.com

To obtain information and pricing on group discounts, multiple copies, site-licenses, or electronic distribution please contact: *Tria Kreutzer*
Phone: (800) 688-2421, ext. 5482
Fax: (800) 284-3291
Email: tria.kreutzer@ahcmedia.com
Address: AHC Media
3525 Piedmont Road, Bldg. 6, Ste. 400
Atlanta, GA 30305 USA

To reproduce any part of AHC newsletters for educational purposes, please contact:
The Copyright Clearance Center for permission
Email: info@copyright.com
Website: www.copyright.com
Phone: (978) 750-8400
Fax: (978) 646-8600
Address: Copyright Clearance Center
222 Rosewood Drive
Danvers, MA 01923 USA

While not every institution has access to a CTSA grant, she says IRBs can direct investigators to institutional resources that can help them craft a more effective plan.

"Most universities have a service learning component or community outreach; if it's connected with a health system they have a health system outreach education person," Ramsey says. "There's usually somebody within the university structure who is connecting with the community and could help figure out how to start this." ■

CNE/CME QUESTIONS

1. Which of the following is a way that an IRB could be involved in improving clinical research organizations' efforts to include more minorities?
   A. IRBs could assess data from study submissions to identify recruitment trends and find the sites that are most successful at including minorities
   B. IRBs can lead educational efforts that focus on inclusion of minorities in research
   C. IRBs could withhold continuing review approval from sites that fail to make an adequate effort to recruit minorities
   D. Both A and B

2. Which of the following is not one of the six steps to writing an effective corrective action plan?
   A. State the problem or weakness succinctly, including the root cause
   B. Break the solution into discrete, measurable actions that address the root cause
   C. Identify the penalties for repeated violations or mistakes
   D. Set achievable deadlines

3. True or False: The use of templates for informed consent documents has limitations, because it can only provide a general outline of the information needed for a specific study.

4. Which of the following was NOT an area of agreement in major human subjects protection organizations' review of the ANPRM?
   A. That the regulations should require training for both IRBs and researchers.
   B. That investigators should be allowed to determine for themselves whether their project qualifies for the new "excused" category.
   C. That there needs to be an improved definition of "minimal risk" in research.

IRB ADVISOR
Your Practical Guide To Institutional Review Board Management

2011 Index