IRB ADVISOR

IRB Salary Survey included in this issue.

Your Practical Guide To Institutional Review Board Management

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IN THIS ISSUE

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AHC Media

Proposed Common Rule changes have pros and cons for institutions

Harmonization: thumbs up; Exempt policy: thumbs down

When human subjects research directors finish sifting through the proposed Common Rule changes, they likely will find some things they can live with and plenty of others they'd like to modify.

For one thing, IRB and researcher directors might object to the proposed requirement that they register exempt studies with the IRB even though the proposal also states that an IRB review is not required.

"I disagree with requiring a form to be filed and not reviewed, both in principle and as a practical matter," says **Paul W. Goebel**, Jr., CIP, president of Paul W. Goebel Consulting Inc. of Monrovia, MD. Goebel is a member of the Chesapeake IRB in Columbia, MD, and previously was chair of the Food and Drug Administration IRB and a member of the Dana Farber Cancer Institute IRB in Boston, MA.

"In general, you shouldn't have someone submit something that won't be reviewed," he says.

The risk is that regulators will have new leadership, leading to regulatory creep. Federal auditors might note in findings that the forms were not reviewed, and this could have negative consequences on research organizations.

"Also, how do you enforce having investigators submit this form if nobody looks at it?" Goebel says.

Exempt studies should be reviewed at least by IRB staff, he suggests.

"It doesn't have to be reviewed in a convened meeting or even by IRB members," Goebel adds. "If it's exempt that document can be sent back to the investigator, stating the IRB agrees it's exempt."

This affirmation is a good thing for investigators to keep on hand in case regulators second-guess their decision. And it's an incentive for investigators to file their studies with the IRB, he says.

The U.S. Department of Health and Human Services (HHS) published the advance notice of proposed rulemaking (ANPRM) in the July 26, 2011, issue of the Federal Register. The 20-page notice includes an explanation about why HHS is proposing changes to 45 CFR 46, 150, and 164, as well

as to Food and Drug Administration's (FDA's) 21 CFR Parts 50 and 56. The proposed changes answer critics' charge that IRBs spend too much time reviewing minimal risk research and that some IRBs overestimate these studies' risks.

Critics also note IRB review inefficiencies, including overlapping reviews for a single study and bureaucratic complexity, the notice states.

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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.

One the changes proposed in the ANPRM directly relates to the fundamental goal of enhancing research oversight while reducing burdens, delays, and ambiguity. The notice seeks to improve harmonization of regulations and related agency guidance.

This isn't a new goal, but the changes will help focus more attention on this objective, says **Jerry Menikoff**, MD, JD, director of the Office for Human Research Protections (OHRP).

"Over the years, OHRP has worked with FDA and other entities to ensure — to the degree possible — harmonization on related rules, regulations, and guidance," Menikoff says.

"The Common Rule departments and agencies have procedures in place for sharing proposed guidance before they are adopted," he adds. "OHRP will continue to work with these entities in the future to attempt to maximize harmonization of any future rules, regulations, and guidance."

One area that should be harmonized involves confidentiality rules in the existing Common Rule versus the HIPAA privacy rule, Goebel notes.

"The rules and definition in the HIPAA privacy rule and the Common Rule regarding de-identification, anonymization, authorization, and informed consent should be made absolutely identical," he says. "There is no reason why IRBs and investigators must make multiple decisions in this area and why the informed consent document and the HIPAA authorization form are separate documents."

The way it works currently, IRBs and investigators have to ask separate questions of studies: "Does this meet HIPAA, yes or not? Does this meet the Common Rule, yes or no?" Goebel says.

Harmonization also would eliminate the Common Rule add-ons that various agencies, such as the Department of Education and the Department of Justice, have, he adds.

"The DOJ has its own separate rules for the research of prisoners," he says. "How is that different, and should they be harmonized? Why are their rules not good enough for everybody? I think that's worth pursuing."

Wholesale harmonization could be impractical, Menikoff notes.

"As the name 'Common Rule' suggests, there is a compelling case for consistency across federal departments and agencies regarding protections of human subjects," Menikoff says. "Nevertheless, there are arguments in favor of some departments or agencies imposing specific requirements, apart from the Common Rule, that are tailored to certain types of research."

The proposed changes focus on data security and

information protection standards, strengthening consent protections related to reuse or additional analysis of existing data and biospecimens, as well as expanding HIPAA privacy protections. HHS proposes having all research involving the collection and use of identifiable data adhere to data security standards modeled on HIPAA. Since these mandatory protections would apply to all research studies, IRBs would not need to review studies posing only informational risks, the ANPRM states.

Current technology already provides bulletproof protection in how private data are de-identified, but the proposed changes could call for a specific recipe for de-identification, and that might require clinical trial sites and technology vendors to make significant changes, notes **Dan Kerpelman**, chief executive officer of Bio-Optronics Inc. of Rochester, NY. Bio-Optronics develops software products and information technology solutions for the health care and clinical trial industries.

"It's an unfolding rule change, so we'll have to see how deeply it will go," Kerpelman says.

From an IRB's perspective, the proposed revisions in data security and information protection standards are positive, Goebel says.

"Setting uniform specific standards assures appropriate privacy and confidentiality protections to all subjects, without administrative burden of needing a specific committee review of each study," Goebel says.

"If there were uniform rules for confidentiality then I don't think this type of research needs to come before an IRB," he adds. "The only risk is disclosure of protected health information, and the IRBs are not very good at assessing that anyway."

The ANPRM addresses the criticism that IRBs are overburdened and attempts to alleviate some of that burden through proposals to change the review process for multisite studies and standardizing informed consent and adverse event reporting.

"Specific changes that are expected to reduce the burden to IRBs include the proposed single IRB of record for multi-site studies; streamlined forms for informed consent; a standardized system for reporting adverse events; and clearly delineated categories of risk," Menikoff says.

In principle, the change to allow a single IRB review multi-site studies is a good one, Goebel says.

"Much depends on how it is implemented," he says.

If HHS uses the National Cancer Institute's (NCI's) central IRB process as a model, then this change likely will not work, Goebel says.

"The CIRB model utilized for NCI-sponsored studies is fatally flawed," he adds. "Their process is more trouble than it's worth: the central IRB reviews it; then the local IRB still has to review it, and then the question is, 'Who reviews the adverse events?'"

HHS has asked for extensive comments on the ANPRM, which was designed to improve human research subject protections while answering critics' charges that the process has become too burdensome, Menikoff says. *(See info box on submitting comments to HHS, below.)*

Here's how to give HHS your opinion on Common Rule changes

The U.S. Department of Health and Human Services (HHS) has given IRBs, researchers, and others in the human subjects research industry until 5 p.m. on Sept. 26, 2011, to comment on the advanced notice of proposed rulemaking for changes to the research Common Rule.

HHS seeks a thorough discussion process and has included dozens of questions seeking input throughout the 20-page ANPRM, published in the Federal Register, on July 26, 2011.

Throughout the 20-page document, there are sections stating, "Comments and recommendations are requested on the following."

Here are a few examples:

- Question 30: What are the advantages and disadvantages of mandating, as opposed to simply encouraging, one IRB of record for domestic multi-site research studies?
- Question 35: What factors contribute to the excessive length and complexity of informed consent forms, and how might they be addressed?
- Question 48: What, if any, are the circumstances in which it would be appropriate to waive the requirement to obtain consent for additional analysis of biospecimens?

To answer these and any other questions, send comments to HHS through the Federal eRulemaking Portal at http://www.regulations.gov, or mail/hand deliver/courier comments to Jerry Menikoff, MD, JD, OHRP, 1101 Wootton Parkway, Suite 200, Rockville, MD 20852. ■

"The goal of the proposed changes is to enhance the effectiveness of the Common Rule in protecting human research subjects while facilitating research and reducing burden, delay, and ambiguity," Menikoff says. "These and other changes under consideration are intended to enable IRBs to focus their energies on higher risk studies." ■

Reporting incidental findings: ethical & vital

Pros outweigh the cons

The way investigators, research institutions, and IRBs handle incidental findings has evolved in recent years, with a consensus now forming around the belief that research sites have an ethical responsibility when it comes to reporting certain incidental findings to research subjects.

"Things are changing in clinical medicine as well as in research," says **John P. Phillips**, MD, medical director of the Mind Research Network in Albuquerque, NM.

Researchers sometimes encounter incidental findings during neuroimaging research for which it would be unethical to not give the information to research subjects, he notes.

The problem involves the logistics and equity of these reports: how do you report these in a systematic, feasible, and equitable way?

The Mind Research Network recently has developed and implemented a process that so far has worked well for both investigators and research participants. It involves a template for reporting the incidental findings. It also includes having Phillips handle cases in which findings are abnormal and require a telephone call to a subject before the letter is mailed.

One ethical consideration is deciding what to do if there is an incidental finding that has unclear implications, Phillips says.

For example, a scan finding might indicate that a person has white matter disease, but the implication is nebulous, he notes.

"We don't know if it harbors multiple sclerosis or if it won't go anywhere," Phillips says. "The research subject who hears these findings has his own understanding, and it's always different from what the researcher understands."

Investigators might not know whether to downplay such findings or push for an evaluation, he adds.

As MRN developed this reporting process, ethical implications involving referrals proved to be a hurdle that needed to be overcome, says **Jody M. Shoemaker**, MS, CIP, CCRP, director of research at the Mind Research Network.

If a participant's letter said that a referral was recommended, although it didn't indicate the referral was urgent, then this could fall into a gray area. The participant might experience additional stress or face financial implications if he or she visited a community provider or had another neurological scan as part of a clinical examination. Then it could be the findings indicated nothing more serious than a sinus infection, she explains.

"So we put extensive language in the consent form to address this issue," Shoemaker says.

Another risk is that an incidental finding might indicate a serious problem, but the research participant lacks medical insurance that would cover a referral or treatment, Phillips says.

"We do everything we can to help them out," he adds. "I have subjects with some follow-up and no financial resources at all, and there are physicians who will treat them for free or they have to negotiate with the university system for a sliding fee scale."

Even with these types of risks from the reporting of incidental findings, there is support in the literature for making these routine, Phillips says.

"Secondly, even if an informed consent form says the person won't get the results, the subject expects to be told if there's anything found at all," he adds.

Sometimes an incidental finding that appears to be a great example of why these need to be reported to subjects can prove to be problematic.

For instance, Phillips recalls a case in which an incidental finding noted a potential brain tumor. It was clear to Phillips that the research participant needed to see a neurosurgeon and have another brain scan.

However, when he spoke with the participant to relay this news, the person's reaction was unpredictable.

"The person said, 'Thank you very much, but I'm going to go on with my life,'" Phillips says. "I felt the person could die from this."

The research participant's sister got involved in the case and had Phillips meet with her and the research participant to discuss it and make certain there was some follow-up.

This extra step seemed ethically warranted because the participant's family member provided information that put doubt on the participant's ability to make a fully informed medical decision. But the entire situation highlights how even seemingly black-and-white cases of reporting incidental findings can pose an ethical dilemma.

The Mind Research Network reached the decision that the benefits of providing incidental finding reports outweighed the risks, and that consensus in the research world is starting to form around the idea that incidental findings in neuroimaging research must be addressed in some fashion, Phillips says.

"My feeling is we owe something to our research subjects," he explains. "They give a lot of themselves to be a part of the study."

From an ethical point of view, compassion should be a part of the equation, he adds.

"Researchers have an obligation, just like in clinical medicine, to recognize the power differential between themselves and subjects," Phillips says. ■

Common Rule makeover denotes research reform

Proposals include streamlining process, expanding federal oversight to more studies

In its proposed revision of the Common Rule, the U.S. Department of Health and Human Services is considering the most extensive changes to human subjects protection regulations in decades.

If approved, the new regulations would affect nearly every aspect of research review, including data collection and security, biobanking, informed consent and the assessment of research risk levels.

The changes had been long rumored, and in many quarters, long hoped for, because of concerns that the original Common Rule, written in 1991, is ill-suited to the changing research landscape of genomics, Internet research, multisite trials and increased social and behavioral studies.

Social and behavioral researchers in particular had complained that the current regulations force a biomedical template onto their work, subjecting it to informed consent requirements and risk assessments intended for clinical trials, rather than the minimal risk research that they typically conduct.

They argued that the regulations lead IRBs to spend too much time and energy on these low-risk studies, rather than higher-risk biomedical research that could benefit from more IRB attention.

The revisions under consideration, included in an advance notice of proposed rulemaking (ANPRM) released in late July, address many of those concerns:

• Revising existing review categories to better match the risk levels of different types of research. These changes, detailed in Section II of the ANPRM, have potentially the most significant effect on social and behavioral researchers and IRBs. *(see accompanying story, page 91)*

• Establishing mandatory data collection and protection standards for all studies that involve potentially identifiable information. At the same time, IRBs would no longer be required to review the risk of possible harms that could come from the inappropriate disclosure of study information.

• Extension of federal regulatory protections to all research, regardless of whether it is federally funded, at any institution that receives funding for human subjects research from a Common Rule agency.

• Improvement of consent forms and the consent process to make forms shorter and clearer, to remove boilerplate language that doesn't protect subjects and to clarify rules for waiving consent and consent documentation.

• Requiring a mechanism for allowing researchers to appeal an IRB's decisions.

Other provisions of the revised federal regulations include requiring a single IRB review of record for domestic multisite trials; improving the collection and analysis of data about unanticipated problems and adverse events; clarifying rules for use of biospecimens and identifiable data; and improving harmonization of regulations and guidance across federal agencies. *(For details, see accompanying story, cover)*

'Very positive in tone'

C.K. Gunsalus, JD, director of the National Center for Professional and Research Ethics at the University of Illinois at Urbana-Champaign, has for years been advocating changes to IRB oversight of social and behavioral research.

Gunsalus says she is pleased with the proposed changes to the handling of social and behavioral studies in the ANPRM.

"There are many proposals that I'm pleased and excited to see," she says. "The presumptions about what shouldn't be included, talking about appeal, talking about removing IRB duties, talking about why it's important to streamline and to focus on things. I think it's very positive in its tone, its direction and its contents."

And Gunsalus says she's happy to see an emphasis on improving informed consent documents. "It takes into account a lot of the research that shows that regular human beings simply don't read 15- or 30- or 100-page consent forms."

Simon Craddock Lee, PhD, MPH, a medical anthropologist at the University of Texas Southwestern Medical Center in Dallas, also serves on the institu-

tion's IRB. While he personally has not had problems getting his research approved by the IRB, he thinks the idea of an appeals process is a good one, especially for investigators in disciplines unfamiliar to their IRBs.

"If, for example, an anthropologist has tried to do their due diligence with an IRB and there continues to be resistance, than you can go to the vice president for researcher services and have a conversation," Lee says. "And maybe what that requires is that they make phone calls to their peers at other institutions of repute and say, 'How does your institution handle this? Is there a learning process that needs to happen here?' And maybe that needs to come from above."

One question in the ANPRM asks whether certain types of activities, including history, languages, literature and journalism, should be covered by the Common Rule at all. This issue has long been a sore point between IRBs and researchers in those disciplines.

Zachary M. Schrag, PhD, an associate professor of history at George Mason University in Fairfax, VA, who blogs about IRB issues at www.institutionalreviewblog.com, says this change is long overdue.

"Congress has never said we want you to regulate journalism or oral history or folklore," he says. "No one sat down and said, 'That kind of research should be covered by the Common Rule,' and it's only sloppy drafting and a failure of regulatory interpretation that ever got it covered in the first place."

Concerns about extension

One provision in the ANPRM that Gunsalus and Schrag do have concerns about is the proposed extension of the Common Rule to all research at an institution that conducts any human subjects research funded by a Common Rule agency.

They're worried that the extension will jeopardize some universities' attempts to streamline review by following a limited assurance, rather than an institution-wide federal assurance.

"It could impact some of the more innovative research institutions, where people have thought more carefully about alternative systems of oversight," Schrag says. "I'm concerned that it could stifle some innovation."

The proposed expansion could have an impact on audits of institutions as well, says **Paul Reitemeier**, PhD, who chairs the Human Research Review Committee at Grand Valley State University in Grand Rapids, MI.

Currently, he says, when an institution is audited by the Office for Human Research Protections (OHRP) or the Office of Research Integrity, the agency can only look at files of federally funded research — unless the institution has checked the box on its FWA form agreeing to apply HHS regulations to all research regardless of funding.

He says studies themselves are reviewed in the same way, regardless of funding source.

"It's just a question of which research files do you open to the feds — the ones they pay for, or everything? And if they didn't pay for the research, then where does their authorization to snoop around in those files come from?

"I think there's going to be strong resistance to that one."

Her concerns aside, Gunsalus says she's happy with the ANPRM, particularly its emphasis on seeking comment from those affected by the rule.

"The intent of the ANPRM is to put these changes out for public comment, and let investigators and others speak out about whether these changes are good," says OHRP director **Jerry Menikoff**, MD, JD. *(See information on submitting comments, p. 87.)*

Menikoff says feedback will be analyzed at the conclusion of the comment period.

"You couldn't ask for a more open, clear, inviting, collaborative approach," Gunsalus says. "There is invitation for a lot of response and I think we need to sharpen our pencils and start putting together considered responses that show as much effort and thought as has gone into this document."

Those interested in commenting on the plan have until 5 p.m. Sept. 26 to do so. It's a fast turnaround, particularly at a time of year when many academics are out of the office, Gunsalus says.

"But we've been talking and thinking about this for so long," she says. "I think those of us who have spent a long time thinking about this out to be able to pull things together."

View the advance notice of proposed rulemaking at www.gpo.gov/fdsys/pkg/FR-2011-07-26/pdf/2011-18792.pdf ■

Exempt, expedited studies face ANPRM changes

'Excused' would be the new exempt; list of expedited activities would grow

The Advance Notice of Proposed Rulemaking (ANPRM) proposes extensive changes to the way that exempt and expedited studies are currently han-

dled, with an emphasis on streamlining the process for researchers who conduct minimal risk activities, particularly in the social sciences.

The proposed changes would substitute an "excused" level of review for exempt, expanding the current exemption categories to include research with adults that might include identifiable information, as long as data protection standards mandated by the new rule are in place. The excused category also would take in some new minimal risk social and behavioral research activities — for example asking subjects to watch videos, solve puzzles or read a paragraph, then asking them questions.

If a study fell into one of the excused categories, the investigator would file a one-page form registering the study, and shortly afterward begin collecting data. The ANPRM states that routine review of excused studies would be "neither required, nor even recommended," although there would be a requirement to audit a small number of these studies to ensure that they qualify.

In addition, the proposal would expand the list of minimal risk activities that qualify for expedited review and would ensure regular updates of the expedited activities list. There would be no continuing review of expedited studies, unless a reviewer deemed it necessary.

Under this proposal, the process of full board review would remain largely unchanged, except for continuing review, which would not be required in cases where the only activities remaining in a study are data analysis or assessing follow-up clinical data from routine medical procedures that patients would undergo as standard care.

The changes will benefit IRBs, who can be freed up from minimal risk activities to concentrate on protocols with real potential for risk to subjects, says **C.K. Gunsalus**, JD, director of the National Center for Professional and Research Ethics at the University of Illinois at Urbana-Champaign.

"I think the time of IRB members is a really valuable resource," she says. "Making sure that we use their time for things that are really important strikes me as all the way around a terrifically valuable contribution for improving things."

SBER institutions affected

But **Paul Reitemeier**, PhD, who chairs the Human Research Review Committee at Grand Valley State University in Grand Rapids, MI, says the proposed changes to the exempt and expedited categories may pose problems for institutions such as his own, which handle almost entirely social, behavioral and educational research (SBER).

"One way our institution has adapted to these (existing) regulations is by relying on the IRB and research protections office to do both a compliance review and a quality review over the design and the construct and the qualifications of the investigators," Reitemeier says. "Even though probably 45 to 50 percent of our total volume is currently eligible for exemption, we still find many opportunities to make suggested revisions, and improvements and strengthenings of those protocol submissions back to the researchers, whether they're students or faculty.

"And that's generally pretty well appreciated. It's not overly burdensome, it sharpens the focus, increases the scientific validity and merit."

Reitemeier says that if these studies fall into the new "excused" category — subject to only a one-page form filed with the institution and never necessarily reviewed by anyone — they lose that opportunity for improvement and for ethical assessment by someone other than the investigators themselves.

"Even though it might be consistent with the federal regulations' desire to minimize regulatory oversight, if you don't have a robust research infrastructure at your institution where everybody knows what's required and everybody's familiar with the regulations, you won't have any oversight (on research proposals that currently are exempt)."

Reitemeier also has concerns about eliminating continuing review of expedited studies, saying that while these studies may have been only minimal risk when they began, things can change over time.

"The first thing you ask in a continuing review is, 'Have you made any changes to this since the last time we saw it?'" Reitemeier says. "(Investigators) are supposed to have filed changes in protocol, but a lot of times they don't. They forget, or they thought somebody else did it, or they weren't aware that they were supposed to."

He says those changes can nudge what was a minimal risk study into something more risky.

If the ANPRM's proposed changes to the exempt and expedited categories become a part of the final regulation, Reitemeier says SBER institutions may find themselves needing to revamp their policies to fill in the gaps in oversight created by the revisions.

"There's nothing in the proposed new rule-making to prohibit them from instituting their own ethics review and their own standards and requirements, if they think the proposed new rulemaking goes too far," he says. "By taking away the IRB role in the big way that it has been there, we're inviting the institutions to either take the lazy low road of no oversight or, on their own authority, to institute the same type of review and protections consideration that the IRB formerly had provided."

The researcher/IRB relationship

Simon Craddock Lee, PhD, MPH, a medical anthropologist at the University of Texas Southwestern Medical Center in Dallas, sees the tension between social-behavioral researchers and IRBs from both sides, since he also serves on the UT Southwestern IRB.

He says many of the proposals in the ANPRM have the potential to ease those tensions. But Lee says there still is a need for researchers to explain their proposed work to an impartial outsider to ensure that the system they've set up to protect subjects is sufficient to do that.

"Most of the travesties of human subjects violations in our past, in any discipline, have come from people who at the time thought they were doing the right thing," he says. "The way that we ensure that we're doing the right thing is to have transparency."

He favors the idea of periodic audits of studies submitted as excused, to make sure that the studies actually meet the criteria.

Lee says that even if the changes outlined in the ANRPM are implemented, it doesn't eliminate the need for social behavioral researchers or IRBs to reach out to each other in order to achieve more effective reviews.

Researchers, he says, need to educate IRB members and staff about their work.

"Go meet your staff person at the IRB and talk to them about what you do," he says. "Stop thinking of the IRB as some black box that you submit a proposal to and then just cross your fingers and hope it comes back."

IRBs, on the other hand, must have the humility to know that they need to seek help when presented with proposals in disciplines that may be unfamiliar to them, Lee says.

"Our job is to educate ourselves, which means you should have staff able to find other specialists to consult if you have a protocol you don't understand. There should be inservice educations routinely, where people who look largely at clinical protocols learn about methods from other groups that we may occasionally need to look at." ■

OHRP cites lack of safety reporting in hip study

IRBs told to create plans to report back to subjects, improve reporting on future studies

Researchers studying whether specially padded underwear protected elderly wearers from hip fractures came up with a one-sided garment design that allowed them to compare the results of a padded hip and an unprotected hip on the same person.

However, when the study unexpectedly revealed more falls and fractures on participants' protected sides, the investigators failed to notify IRBs of the development and did not inform continuing and new participants about the potential risks of the study, according to a determination letter released by the Office for Human Research Protections (OHRP).

The June 23 OHRP letter (http://www.hs.gov/ohrp/detrm_letrs/YR11/june11a.pdf) cited letters and emails among the investigators to show that they had identified a problem with increased falls and fractures, but "failed to report unanticipated problems, i.e., increased falling to the pocketed (protected) side and the associated risk of possible fractures, to their respective IRBs, institutional officials, the funding agencies and OHRP, in contravention of the requirements of HHS regulations…"

In addition, emails quoted in the OHRP letter suggest that the data safety monitoring board (DSMB) that was monitoring the study was not told of the significance of the data involving falls.

The letter notes that had the new risk associated with the study been disclosed to subjects, "it is reasonable to conclude that such information might have significantly affected their willingness to continue to participate."

Plans for contacting subjects

The three institutions involved in the study – Hebrew Rehabilitation Center for Aged in Roslindale, MA; the University of Maryland Baltimore School of Medicine; and Washington University School of Medicine in St. Louis — all have been instructed by OHRP to provide plans for contacting subjects enrolled in this study to provide them with the previously undisclosed risk information.

The institutions also have been required to come up with corrective plans to ensure that researchers:

— disclose "reasonably foreseeable risks to the subjects;"

—whenever appropriate, give the IRB and subjects new information developed during the study that may affect subjects' willingness to continue participating;

—and report unanticipated problems to IRBs, institutional officials, funding agencies and OHRP.

How can an institution make such assurances if researchers do not give them the necessary information? Representatives from the three institutions

involved in the study all declined to comment to IRB Advisor about the matter, citing continuing efforts to evaluate the situation and formulate their responses to OHRP.

'Creating a culture'

But **Mark S. Schreiner**, MD, chairman of the Committee for the Protection of Human Subjects at The Children's Hospital of Philadelphia and a member of the editorial advisory board for IRB Advisor, says IRBs' options are limited in this type of situation.

"This is exactly the sort of information that IRBs should get," Schreiner says. "This was an important safety signal that affected the likely willingness of subjects to enroll and of subjects already enrolled to continue with the study.

"If people don't report this type of thing, there's nothing the IRB can do."

He does note that the larger institution has the obligation to educate investigators about what information they need to report to IRBs and about the importance of doing so.

"This is a matter of creating a culture where investigators understand their responsibility," Schreiner says.

Dale E. Hammerschmidt, MD, an associate professor of medicine at the University of Minnesota in Minneapolis who served on IRBs for 25 years, agrees that there is little IRBs can do to uncover safety problems that occur within a study, particularly in cases where the DSMB is not getting the proper information, either.

However, he says the IRB can examine at the outset of a study how the safety reporting is supposed to be handled. It can require that safety monitoring reports from the DSMB or other oversight body be provided on a regular basis.

"The IRB can look at the DSMB charter for a study and can look at the monitoring plan," he says. "They usually cannot serve a police function at a remote site. What they can do is examine the infrastructure, and make a judgment as to whether it would suffice if conscientiously implemented." ■

New AAHRPP metrics show less IRB funding

The most recent statistics gathered from the Association for the Accreditation of Human Research Protection Programs' (AAHRPP) client institutions don't look all that different from the baseline metrics released last year.

But in one key area, the numbers changed quite a bit — IRB operating budgets tumbled, as organizations coped with the loss of federal stimulus money, says **Marjorie Speers**, PhD, president and chief executive officer of the Washington, D.C.-based organization.

"Many of our accredited organizations are universities," Speers says. "Universities had benefited from the stimulus funds and those stimulus funds started to run out. So universities are doing as much or more with less dollars."

The numbers for 2010 were released this summer, based on responses to surveys of AAHRPP's clients. Compared with the 2009 numbers released last summer, nearly every size of human research protection program reported declines in operating budgets. The sharpest drop was reported by institutions handling 101-500 protocols a year — down nearly 65 percent, from $921,903 in 2009, to $325,404 in 2010.

In only one category, relatively large organizations handling 2001-4,000 protocols per year, did the annual budget increase, from nearly $1.3 million in 2009 to $1.6 million last year.

At the same time, AAHRPP organizations reported increases in the number of protocols they handle. The median number of total active protocols in 2010 was 525, up from 306.5 in 2009. Those increases were seen in every category of protocol — exempt, expedited and full convened board.

Workloads up

With only two years of data, it's hard to discern trends at this point, Speers says. In many areas where there were minor changes from 2009 to 2010 it's unclear whether the cause is changes in the organizations themselves or the inclusion of data from newly accredited institutions.

But Speers does see the increase in IRB workloads as a real phenomenon.

"Organizations are growing their research programs and as they grow their research programs, they have to make sure they've got the infrastructure to review and oversee those studies," she says.

One result of this, she says, is the change in the number of IRBs reported by organizations. Fewer reported having only one IRB in 2010, while more reported having two.

Organizations are closely following review times as an indicator of IRB efficiency. The 2010 AAHRPP numbers show slight declines in review times across all categories of research:

— For studies reviewed by a convened IRB, the

mean time from submission to approval was 45.7 days, down from 48.8 in 2009.

— For expedited studies, the mean time from submission to approval was 27.9 days, down from 29.8 days the year before.

—For exempt studies, the mean time from submission to exempt determination was 16.9 days in 2010, down from 18.1 in 2009.

"As we said, we only have two years of data, and we don't know exactly whether we have a pattern or a trend," Speers says. "But review times are on everybody's radar screen. Many institutions are using IRB review times, particularly the metric we've put out, as a benchmark. It's very possible because of the sensitivity around IRB review times (that this decline reflects a trend)."

Benchmarking plans

Speers says that to get a real picture of changing trends in human research protection, it probably will take about five years of metrics data. In the meantime, she says, AAHRPP will work with its client institutions to compare their own organization's data with the AAHRPP group as a whole.

"The service we want to provide for our organizations is to provide this information and then do a screenshot of their own information, so they would have the benchmarks," she says. "It's a project that we hope to get started on this year and then put that on the Web." ■

COMPLIANCE CORNER

QA assessments render positive review changes

Experts perform QA assessment

Many research institutions now have quality assurance/improvement projects that include research site audits or quality checks. But how many have thought about performing such a quality check on the IRB's work?

The institutional review board at New York University (NYU) Langone Medical Center in New York, NY, pilot-tested a project that assesses the quality of its IRB's reviews of exempt and expedited study submissions with the goal of finding problems and correcting them.

"We traditionally have been focused on our IRB's turnaround time, but what about the quality of the IRB review?" says **Helen Panageas**, CIP, associate director of the human research protection program at the IRB at NYU Langone Medical Center.

The IRB has five people, including Panageas who are trained to act as expedited reviewers. The other reviewers include physicians, nurses, and scientists.

"We review minimal risk research and decided it was time to look at the quality of our reviews," she says. "We wanted to see if the quality assurance findings were useful and whether these were something we could employ as part of a day-to-day process in our office."

So the IRB had experts who were not involved in the expedited and exempt reviews perform the quality assurance assessment.

"Our quality assurance manager would do external audits and actual protocols that the IRB has approved, and we decided to see if this could be part of his responsibility," Panageas says.

The IRB's education analyst also was involved.

The office developed standard operating procedures (SOPs) for the quality assurance reviews. They include the following:

1. Identify an issue: "We looked at exempt and expedited first, using the 111 criteria as our benchmark," Panageas says. "We looked at 70 projects over a six month period, assessing 50% of our volume and 50% of exempt and 50% of expedited reviews."

2. Analyze compliance: For exempt reviews, the team looked at whether or not research really met the categories, she says.

For example, an institution's research might include retrospective chart reviews where identifiers are not recorded. A project to review educational practices would not need identifiers, Panageas says.

The quality assurance reviewers would read through these and make sure they're assigned to the right category.

3. Check minimal risk: For expedited reviews, which have to meet 111 findings, the QA team could make sure these meet the clearly defined federal regulations of what minimal risk is.

"We need to make sure the expedited review fits into one of seven categories allowed for initial expedited review," Panageas says. "And those are things like surveys and focus groups with identifiers are allowed if it's minimal risk research."

4. Create a checklist: "First, we decided what to look at, and then we created a one-page checklist," Panageas says. "It's very straightforward."

They created the checklist with Excel software.

"We found when looking at the categories assigned to an expedited review that we wanted to make sure they were put in all of the right categories," Panageas says. "There could be a blood draw in the survey, and we were assigning it to the blood draw category, but not recognizing that it was also a survey."

IRBs sometimes overlook this point.

"You should check all that apply," she says. "The regulations don't spell out that, but our process involves making sure we check all of these appropriate categories."

5. Assess performance: "Once we gathered all of the information we looked at our findings and started to evaluate the percentages of what our findings essentially were," Panageas says. "We had a very high rate of making those 111 findings and being correct about minimal risk."

There typically are some areas identified that need improvement, and IRBs should focus on making changes that target their weaknesses, she adds.

6. Share results: "We've brought our findings to the attention of the reviewers and highlighted why it's important to make sure they include all of the categories for the projects," Panageas says. "What we were thinking about doing when we started the pilot project was to apply the same checklist to the full board review, measure the quality of the board's actual committee reviews."

Instead, the team came up with standards for each of the 111 criteria.

"If we say the risks to subjects are minimized, how in fact does the protocol substantiate the fact that the risk to subjects were minimized?" Panageas says. "We want benchmarks and indicators that say, 'Yes, the risk to subjects are minimized because of the following things.'"

7. Incorporate reviewer's checklist: "For the next phase of the project, we're incorporating the checklist they have into our project and seeing if we can add to that," Panageas says.

The IRB has addressed protocol language about minimal risk through staff education. IRB reviewers go back to investigators and say, 'I think you need to do a better job with this in this section,' if they didn't document the informed consent process, she adds.

"They're now able to go out on a case-by-case basis and say to the principal investigator, 'This is what we need from you to meet our criteria and approve this project,'" Panageas says. "Our purpose was to identify whether we were missing anything in our reviews and then help improve our analysts' reviews, helping them identify the weaknesses."

These types of quality assurance reviews could be held every three or four months. Eventually they should help improve the consistency of IRB reviews, Panageas says.

Once IRBs have conducted such a checks-and-balance of their protocol reviews, it's a good idea to meet with the full IRB to give members additional education and to share the results, she adds.

"We could target information where they are weakest," she says. "So if we find that maybe there's always a paragraph addressing subject selection, but it's not strong, then that could be an area where we target education and training for our members so they can better understand what the standards are and what to look for." ■

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

- ■ Prevent persistent IC problems
- ■ What do IRBs say to HHS about Common Rule changes
- ■ Prevent common IRB-PI conflicts
- ■ Studying blogs: the fine line between public and private
- ■ CA IRB uses technology to help investigators properly report external AEs

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CNE/CME QUESTIONS

33. Which of the following should be included in standard operating procedures (SOPs) for the quality assurance reviews, according to a site that established best practices for this process?
    A. Analyze compliance
    B. Check minimal risk
    C. Create a checklist
    D. All of the above

34. True or False: Even with the risks from the reporting of incidental findings to study subjects, there is support in the literature for making these routine.
    A. True
    B. False

35. True or False: The proposed revision of the Common Rule would extend its authority to all research institutions in the United States, regardless of whether they receive federal funds for human subjects research.
    A. True
    B. False

36. Which of the following changes is proposed for the exempt category (called 'excused' in the ANPRM
    A. Waiving any need for submission to the IRB
    B. Requiring submission of a 1-page form registering the study, with a requirement that some of the forms be audited to ensure that they meet the criteria.
    C. Requiring submission of a 1-page form registering the study, with IRBs required to review all forms to ensure that they meet the criteria.