IRB ADVISOR

YOUR PRACTICAL GUIDE TO INSTITUTIONAL REVIEW BOARD MANAGEMENT

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INSIDE

U. of Minnesota Fights Bill Giving State Oversight of Psych Research

Fallout from patient suicide in 2004 continues

By Gary Evans, Senior Staff Writer

Reeling from a decade-long series of investigations and allegations after the suicide of a psychiatric research patient, the University of Minnesota (UM) in Minneapolis is now facing a proposed state law that would assign oversight for its psychiatric drug research program to an independent ombudsman's office.

The action is just the latest in a tumultuous series of events that began with the 2004 suicide of Dan Markingson, who was enrolled in a psychiatric drug trial at the university at the time he took his life. *(For more information, see related story on page 64.)*

Markingson's suicide resulted in lawsuits and a series of independent and state investigations, opening a national dialogue on the recruitment of mentally ill patients into clinical trials. The university has not been able to escape the long shadow of the incident, which has morphed into an indictment of leadership and accountability at UM and the state Board of Regents.

> "INVESTIGATIONS AND REVIEWS INDICATE SERIOUS ONGOING PROBLEMS WITH RESEARCH COMPLIANCE IN THE DEPARTMENT OF PSYCHIATRY."

In that regard, the proposed oversight law comes on the heels of a recent announcement by state legislative auditor **James Nobles** that he would investigate the university for a third time. In a scathing report issued last year, Nobles made the recommendation for the state ombudsman oversight after concluding that, "a primary problem uncovered by our review is past and current university leadership that is defensive, insular, and unwilling to accept criticism about the Markingson case either from within or outside the university."[1]

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EDITOR: Melinda Young.
MANAGING EDITOR: Jill Drachenberg, (404) 262-5508 (Jill.Drachenberg@ahcmedia.com).
ASSOCIATE MANAGING EDITOR: Dana Spector
DIRECTOR OF CONTINUING EDUCATION AND EDITORIAL: Lee Landenberger.

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EDITORIAL QUESTIONS
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While stating that directly linking the suicide to the drug study was impossible given Markingson's mental illness, the state report said that the case "raises serious ethical issues and numerous conflicts of interest, which university leaders have been consistently unwilling to acknowledge. They have repeatedly claimed that clinical research at the university meets the highest ethical standards and dismissed the need for further consideration of the Markingson case by making misleading statements about past reviews. This insular and inaccurate response has seriously harmed the University of Minnesota's credibility and reputation."

IRB member testifies

The university is opposing the ombudsman oversight bill, arguing that sufficient oversight and ongoing improvements are now in place to protect human subjects research. However, a current member of the university's IRB spoke in favor of the bill at an April 5, 2016, hearing of the state House of Representatives Committee on Higher Education Policy and Finance.

"Investigations and reviews indicate serious ongoing problems with research compliance in the department of psychiatry," said **Niki A. Gjere**, RN, a clinical nurse specialist at the university and IRB member. "A lack of meaningful oversight has contributed to these ongoing problems. We hear from university leaders that everything is better now. We're spending money to improve research processes, we have oversight boards and a compliance office. … Even though [Markingson] died in 2004, reports continue to identify a pervasive pattern of serious noncompliance with regulations for protecting human subjects. These serious problems are sustained and firmly embedded. This bill would give the ombudsman office the needed authority for oversight now, without waiting for years to see improvement in the psychiatry department. We need a formalized advocacy process for people participating in department of psychiatry drug studies."

The sponsor of the bill, state Rep. **Cindy Pugh**, said she wanted to believe that the university was taking all appropriate actions, but couldn't "un-hear" concerns being expressed by faculty members like Gjere. As proposed, the bill would charge the state Office of Ombudsman for Mental Health and Developmental Disabilities to monitor the treatment of individuals participating in drug trials at the university's department of psychiatry.

"I responded with this bill not only to ensure that we the legislature are doing our part at holding the university accountable, but that we are providing Minnesotans with the highest level of assurance of patient protections within human drug studies conducted at the [psychiatric] department," Pugh said.

A panel of legal and ethical experts commissioned by the university after a faculty vote for an independent investigation of psych research programs concluded last year that, "there are significant problems with core functions of the human research protections program, including IRB review, investigator education, practices related to consent to research, and the effective coordination of administrative oversight, clinical care, and research."[2]

The report observed that some university personnel described

considerable "fatigue" of what they considered unrelenting and unjustified criticism of the university's human subjects protection program. "In contrast, others expressed bewilderment and frustration that, in their view, the university has failed to understand and remedy problems stemming from and related to 'Markingson,'" the panel reported. "Most striking was the commonly conveyed sense of doubt in leadership's commitment to human subjects protection."

UM lists positive steps

In testimony[3] at a state senate hearing last year after both Nobles' findings and the independent report, university President **Eric W. Kaler** emphasized several actions being taken to correct the problems. He conceded the university IRB should have done a more extensive review of the original study in which Markingson was enrolled and is now committed to improvement.

"While the IRB carried out a minimal review, in hindsight the IRB should have investigated more thoroughly at the time," Kaler stated. "To the extent the [university's] descriptions of what the IRB did has been misleading, I apologize. While we disagree with some of Mr. Nobles' findings, we must get better in caring for our most vulnerable patients."

According to Kaler, the university's corrective actions in response to both the independent panel and the state investigation include the following:

• Suspended enrollment in all department of psychiatry interventional drug studies — those that are active or awaiting approval — until they are reviewed by an independent IRB.

• Created a task force to plan the implementation of the external review panel recommendations.

• Engaged an independent IRB to work with the university's post-approval monitoring process to examine other clinical studies that target vulnerable populations, and to ensure they are meeting best practices.

• Appointed a Community Oversight Board of external experts in human subjects research and research ethics to ensure best practices are used.

Reiterating some of these efforts at the hearing on the proposed ombudsman bill, **Brian Herman**, PhD, vice president of research at the university, argued that the additional level of oversight is not needed.

"We recognize the value of working with the ombudsman office when issues arise under its purview," Herman told the legislative committee. "We sought their involvement in the past and recently we asked for [their] assistance in filling openings in the institutional review board. Today the University of Minnesota research participants — including the department of psychiatry — are subject to oversight from a number of organizations. I think it's important that you hear that, despite what you may think, the university's oversight of its human subject research protections is actually reviewed by a number of different outside entities."

The university is accredited by the Association for the Accreditation of Human Research Protection Programs (AAHRPP), has an internal department conducting regularly scheduled audits, and has established a community oversight board to advise the university on best practices on research participants, Herman said.

"A large number of those individuals on the oversight board [have] expertise in interacting with individuals with impaired decision-making capacity," he said. "Lastly, as you know, the office of the legislative auditor is now conducting a follow-up review to their review last year. So our position is we believe that these avenues of oversight combined with our current professional relationship with the ombudsman [office] represents sufficient monitoring of the university's research work that utilizes human participants."

Herman also reminded the committee that IRBs are accountable to federal law under the Common Rule and any state action would have to be consistent with those overriding regulations.

Simmering tension

In a seemingly minor matter that revealed some of the acrimony beneath the surface, one member of the House committee questioned whether the university administration made sufficient efforts to allow concerned faculty members to meet recently with a visiting consultant on psychiatric research. An outspoken critic of the university's handling of the fallout from the Markingson case, **Carl Elliott**, MD, PhD, associate professor in the university's Center for Bioethics, said he was told there was not time for him to meet in person with the consultant, but he could talk to him by phone — which he did.

"This is very concerning to me," responded state Rep. **Connie Bernardy**. "We hear testimony and commitments and promises from the University of Minnesota and they don't get followed through. I'll speak for myself: I expect those commitments to be followed through and it raises issues to me — what are the other things that we are being

told that are actually being followed through on?"

"The lack of honesty and truthfulness by the university administration has been a big issue from the beginning and it was identified in last year's legislative auditor's report," Elliott testified.

Having been at the university since 1997, Elliott has seen the entire saga unfold and called the university to account in addressing research problems that he now fears may go beyond the psychiatry department.

"I was on the IRB myself when I first arrived here," he tells *IRB Advisor*. "Part of what disturbs me about the entire affair — and I actually think some things have improved with our research oversight program — is that the criticisms of our research oversight program and the gaps [reported in the investigations] were so serious and so severe that you are left wondering, can you actually trust our research and oversight program to flag issues if they are occurring in other departments?"

Elliott was skeptical that the measures taken by the university have sufficiently addressed the research protection issues, saying the ombudsman oversight bill should be enacted to fulfill the recommendation for action in the state's investigation.

"The reason the university is opposing it — and the reason I think it is a good idea — is that it would be external monitoring," he says. "If you go back and look at the legislative auditor's report they say the disturbing part of the entire affair is the continued series of misleading statements by the university administration, their defensive attitude, and their unwillingness to consider any kind of external criticism. [They have been] attempting desperately to deflect criticism for 11 years. Those very people are not going to admit their own actions [are] at the root of the problems."

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Who was Dan Markingson?

A violent suicide still haunts the University of Minnesota

On May 8, 2004, Dan Markingson killed himself while participating in a University of Minnesota Department of Psychiatry drug study. The violent nature of Markingson's suicide — he slashed open his neck and abdomen with a box cutter — is cited by some as evidence of his continued psychotic condition despite having been in the university drug study for approximately five months, according to a report by Legislative Auditor James Nobles.[1]

The following are some of the key points in the auditor's report:

• In 2003, Markingson was a 26-year-old aspiring screenwriter living in Los Angeles after having earned a BA in English from the University of Michigan. When his mother visited in July, she noticed disturbing changes in her son's behavior. For example, Markingson had set up wooden posts around his bed to create an "astral field," and he thought an alien had burned a spot on his carpet.

• While back in Minnesota on November 12, 2003, Markingson talked about participating in a satanic ritual in which he might be required to kill people, including his mother. In response, Markingson's mother called police, who took him to Regions Medical Center in St. Paul. Medical staff determined that Markingson was mentally ill and posed a danger to himself or others. They placed Markingson under a 72-hour hold.

• Due to a lack of available beds, Markingson was transferred that same day to Fairview University Medical Center (FUMC) hospital and placed under the care of a psychiatrist, an associate professor at the University of Minnesota Department of Psychiatry.

• A judge put Markingson's slated commitment to a state psychiatric facility on hold for six months

on the condition that he agree to comply with FUMC's treatment plan. Markingson's treating physician at FUMC was also participating in a clinical drug study funded by AstraZeneca Inc., a pharmaceutical firm headquartered in London. The University of Minnesota was one of 26 sites in the U.S. and Canada conducting the three-year "CAFÉ" drug study. The study compared an AstraZeneca antipsychotic drug with two other similar drugs on individuals experiencing their first psychosis.

• The FDA had already approved the three drugs as "safe and effective" treatments for schizophrenia, so the study did not involve a new experimental treatment. The double-blind study randomly assigned one of the three medications to the patients. The study coordinator took Markingson's psychiatric and medical history and obtained his informed consent to participate.

• Markingson was extremely vulnerable when recruited into the study, according to the report. He was mentally ill and faced commitment to a state psychiatric hospital if he did not cooperate with the FUMC treatment plan and the treatment team's aftercare recommendations following discharge.

• Markingson's mother, Mary Weiss, expressed strong concerns about her son's participation in the drug study and continually warned that he was not improving. There is little evidence that the study team adequately followed up with her about her concerns, according to the report.

• His subsequent suicide occurred in the bathroom of a state-licensed group home for people with mental illness.

• In 2009, the Minnesota legislature passed a law restricting the enrollment into drug trials of persons under a stay of commitment.

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What You Don't Know About NIH RAC Review Changes Could Hurt

Experts will be necessary

IRBs might not have asked for it, but the National Institutes of Health (NIH) and the FDA have handed them a new responsibility when it comes to oversight of clinical trials involving human gene transfer.

NIH has transferred the responsibility for the initial assessment of the risk-benefit of human gene transfer applications from the NIH Recombinant DNA Advisory Committee (RAC) to the local IRBs and institutional biosafety committees (IBCs), says **Joan Robbins**, PhD, senior vice president of biosafety and gene therapy for WIRB-Copernicus Group in Princeton, NJ.

RAC is a federal advisory committee that gives the NIH director recommendations about basic and clinical research involving recombinant or synthetic nucleic acid molecules.

"What that means is IRBs and IBCs will now need to look at the gene therapy protocol and determine if it requires RAC review," she explains. "They might say, 'This is something we're not concerned about and we've seen it before,' and then the IRB will recommend that it is not given a full RAC review."

Or if the IRB or IBC are concerned about the protocol, they can recommend that it is reviewed by the RAC, she adds.

The problem is that human gene transfer research is not an area that many IRBs have considerable experience in reviewing, Robbins says. So if they are presented with this type of study and are not accustomed to doing an evaluation of it, will they feel comfortable saying that it doesn't require RAC review?

"Will a lot of less experienced IRBs say, 'We don't know a lot about this, so should we just recommend a RAC review?'" she says. "If they do that and it's not appropriate, the NIH director can overrule them."

IRBs and IBCs that review for the initial study site for gene therapy research will need to have a number of processes in place, Robbins says.

"They'll have to have already implemented new processes to do what is essentially a pre-review," she says. "NIH recommends that IRBs and IBCs augment their

memberships with ad hoc experts. They may need expertise in everything from DNA plasmids to CAR T-cell, modified T-cells."

The NIH Office of Science Policy published a *Federal Register* notice on March 22, 2016, about the revised procedures for reviewing gene transfer trials. The changes were effective as of April 27, 2016.

When the changes first were proposed there were not a lot of comments, Robbins notes.

"We reviewed the guidelines very carefully when they came out," Robbins says. "We asked NIH to clarify some of the points that were not well defined, and we hope that further clarification will help us to steer through the process."

The revised review process was intended to streamline the process for the RAC, but it does require that the IRB and IBC at the first trial site assess each protocol to determine whether it meets one or more of three criteria, according to the NIH's RAC revisions fact sheet. The criteria are the following:

• "The protocol uses a new vector, genetic material, or delivery methodology that represents a first-in-human experience, thus presenting an unknown risk; or

• "The protocol relies on preclinical safety data that were obtained using a new preclinical model system of unknown and unconfirmed value; or

• "The proposed vector, gene construct, or method of delivery is associated with possible toxicities that are not widely known and that may render it difficult for oversight bodies involved to evaluate the protocol rigorously."

IRBs may find it difficult determining any of the three criteria, Robbins suggests.

For example, while it appears to be a simple matter to determine whether the research will be using a new vector or genetic material, this can land in a gray area: "Even defining if it's new material is not that easy because there could be a complex hybrid," Robbins says.

Also, it might be challenging to determine which preclinical model system has value.

"It's very difficult to get model systems that actually do predict everything you would want them to predict in people," Robbins says.

"There have been instances where preclinical studies have shown good safety profiles with nothing to worry about, and still when it comes to human testing some really serious adverse events occur," she says.

Examples include Jesse Gelsinger's death during a gene therapy study and the recent French drug study in which one volunteer died and several were injured.

"So I think it will be a little challenging for IRBs to necessarily know whether that criterion is met," Robbins says.

"Another point is that the proposed vector or gene construct — if it's associated with toxicity, which is not widely known — that it needs to be sent for RAC review," she says. "But it's really challenging to interpret what is widely known."

As IRBs begin to absorb and handle this new responsibility, the key might be to prepare for the change and identify a broad range of experts who can help them assess each of the different kinds of gene transfer studies, Robbins suggests.

"They'll need to have their process in place in order to do the pre-review," she says. ■

Transparency About Participation Incentives Could Benefit IRBs, Researchers, and Patients

Dearth of data on incentives, compensation to research subjects

Compensating research subjects is a thorny issue. Some marginalized populations may need financial support to participate and have access to potential therapeutic benefits, but researchers are warned against "undue influence" of payments in federal regulations.

While the issue of incentives raises a host of ethical issues for discussion, the problem is the dearth of data on what study participants have been compensated for all manner of studies and clinical trials.

Researchers, IRBs, and even study participants could benefit by more transparency on the issue, says **Brandon Brown**, PhD, MPH, a health services researcher and assistant professor in the Center for Healthy Communities at the University of California, Riverside School of Medicine. With a research focus on HIV and human papillomavirus, Brown says even outwardly transparent platforms like ClinicalTrials.gov provide little information to inform discussions on compensating research subjects.

"So the one place where everything

is transparent, at least at the onset of a study, you can't find the incentives," he says. "If I am going to start a study in a certain population in a certain place, how do I know what to provide participants? What I have found is there is really no guidance in terms of incentives — not in the IRB handbooks and not in the U.S. Code of Federal Regulations. Some of what I have found in the literature has really shown kind of a haphazard allocation of incentives in different contexts."

The incentives or compensation should be in the study protocols submitted to IRBs, but the information is not posted in a central database, he notes.

"Probably the biggest concern about the lack of having this incentive information is in high-risk studies," Brown says. "We don't really have a good working definition of what coercion is — it has to be an excessive offer, poor judgment, and risks of harm. But it's very difficult to agree on what is an excessive offer. People don't really know what is being provided. There could be the same study at different sites in the U.S. and people are paid different amounts. And we don't really know how those decisions are made on how to pay people. It could be — what I and some others think — primarily budget-driven. It could be what investigators think is fair or market forces where previous [experience suggests], 'If we don't pay x amount of dollars, we are not going to be able to recruit people.'"

A study[1] looking at participant compensation in 207 published research articles found that only 13.5% mentioned financial compensation in any way, and only 11.1% listed amounts. Though the study was published in 2007, the lead author says that transparency about research participant compensation is still very much a current issue.

"I think that fees to study participants should definitely be transparent and available, since it can also help in understanding the study and potentially in interpreting and determining how to apply to the results to other situations," says **Robert Klitzman**, MD, professor of clinical psychiatry and director of the Master of Science in Bioethics program at Columbia University in New York City.

> "PROBABLY THE BIGGEST CONCERN ABOUT THE LACK OF HAVING THIS INCENTIVE INFORMATION IS IN HIGH-RISK STUDIES."

There is a risk that payment may bias results, undermining the generalizability of a study's findings to broader populations, Klitzman and colleagues warned in the study. In addition, offering compensation may attract subjects with less concern of the study risk.

"This information is important, since fees can affect how participants respond in studies," Klitzman tells *IRB Advisor*. "I think journal articles should thus also report not only whether they have compensated participants, but how much."

Klitzman's study looked at compensation and incentives in research on HIV, substance abuse, depression, hypertension, and cardiac surgery. Studies on substance abusers were more likely than other studies to mention payment, suggesting that the researchers may be more sensitive to ethical concerns when working with vulnerable populations. However, overall, even studies that entailed "more than minimal risk" had low rates of reporting compensation and did not differ significantly from other studies, the researchers found.

Echoing Klitzman's calls for research transparency, Brown advocates the establishment of an accessible database or website where incentives for various types of studies are available.

"I definitely like the idea of it being transparent, and if it is, then other people who have skills different than mine could kind of look at this as 'Big Data' and analyze the impact of incentives in terms of recruitment and retention and look at the mean and range of incentives in different contexts for different kinds of studies," he says.

As a starting point, Brown is mapping out a research proposal in the area of HIV that would include the man-hours to go through records and find out what was provided in study protocols as an incentive.

"We could ask different groups who might be considered stakeholders in terms of incentive decision-making: IRBs, investigators, study coordinators, and participants themselves," he says. "They could probably tell us a lot about what [incentive] they would need to be recruited into a study and what they would want to adhere to a protocol — to make sure that the science that was being conducted is hopefully successful."

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Some Spit, Polish, and Creativity Can Solve IRBs' Education Efforts

Interactive, evidence-based practices work

Human research protection education has evolved into a practice that is both easier and more challenging than it was decades ago. On the one hand, IRBs and research institutions have online tools and best practices available at the click of a button. On the other, they now know through evidence-based practices that the easiest ways to educate IRB staff and researchers often do not work as well as innovative educational methods.

So where do you begin?

"The biggest message is clear and consistent communication," says **Pamela Johnson**, MPH, research education and quality improvement specialist at Hartford HealthCare in Hartford, CT.

Hartford HealthCare needed an effective and efficient educational process prior to launching a new electronic submission system.

"We started with live computer classroom-style education and held a dozen live classes," Johnson says. "But after we went live and did all of this training, we started noticing problems: IRB administrators and investigators alike were all complaining that they didn't know how to do this, and the same mistakes kept happening."

This led to Johnson putting together a common pitfalls document to supplement the education and share with all users of the new electronic system. *(For more information on Hartford's educational effort, see story on page 69.)*

IRB leaders at Christiana Care Health System in Newark, DE, revamped their research education sessions in response to dwindling attendance numbers, says **Janet Leary-Prowse**, MSEd, CIP, IRB research education specialist and IRB member.

"People would leave partway through the sessions because they were tired of hearing only IRB staff talk about rules and regulations," Leary-Prowse says.

Melanie Chichester, BSN, RNC-OB, CPLC, an IRB member and labor and delivery nurse, suggested they make the sessions interactive so attendees still would learn about rules and regulations, but also hear examples of implementing these rules from research nurses.

> "I EDUCATE PEERS IN THE INSTITUTION I WORK IN AND I SPEAK AT A NATIONAL LEVEL, AND MOST ADULT LEARNERS DON'T LIKE HEARING, 'HERE'S THE BACKGROUND AND HERE'S WHAT YOU DO.'"

"I educate peers in the institution I work in and I speak at a national level, and most adult learners don't like hearing, 'Here's the background and here's what you do,'" Chichester says. "They want evidence-based practice information about what the current literature says they should be doing, and they want examples of how they should do it."

The idea was to polish up the decades-old research sessions by asking research clinicians to talk briefly about their challenges and best practices, Chichester says.

"We said to research nurses, 'All you have to do is talk for five minutes, but tell us of a challenge in your practice,'" she says. *(See story on revamped educational sessions, page 71.)*

The IRB at the University of Miami has found that holding IRB grand rounds is an effective way to educate researchers and others involved in human research protection, says **Kenia Viamonte**, MA, senior manager of IRB affairs.

Previously, the IRB's educational sessions were poorly attended and cumbersome, with sessions occurring at 20 different places. Topics did not appear to interest much of the research community, Viamonte notes.

"We were moving things along and getting things done, but it wasn't fluid, harmonious, or collaborative," she says.

Dr. Dushyantha Jayaweera, interim executive dean for research and research education and former associate vice provost for human subject research, was concerned about the low attendance of regularly scheduled training, Viamonte says.

"He wanted to ensure regular attendance, but also greater cohesion and harmonization of educational opportunities," she explains. "There

was an increasing need to have our research enterprise work less in each respective silo and more like a high-performing team for the greater good of the institution and our human research enterprise."

Jayaweera suggested they try a different style of education. "He said, 'Why don't we do grand rounds? People have to be there, and they carve out this hour in their schedule, and they know they'll get continuing education credits,'" Viamonte recalls. "We reached out to different speakers to see when they were available, and we reached out to the logical stakeholders in HRPP, plus leadership."

Everyone — including senior leadership — liked the idea, so Viamonte worked to develop the content and communication strategy.

The idea was to hold educational sessions on topics that were of particular interest to researchers and to vary them between biomedical and socio-behavioral, Viamonte says.

Instead of having IRB educators and lecturers move from department to department, the attendees move to them.

"They get all the information in one place that's relevant," Viamonte says.

The grand round sessions are held the second Tuesday of each month, from 2-3 p.m. "That's the time that makes the most sense," Viamonte says. "It's not too late in the day, and it's not in the busy morning rush of the clinics; it's right after lunch when things dwindle down somewhat, and it's easy if they want to take a late lunch."

The IRB grand rounds are not mandatory, but attendees can earn continuing education credits toward CIP renewal or for licensing purposes.

Once the new process was underway, educational session attendance increased from 20-30 to as many as 100 attendees, including principal investigators, study teams, compliance professionals, IRB members, staff, and chairs, she says.

The grand round sessions cover a variety of topics, including the following:

- applying the approval criteria and the inner workings of an IRB,
- trusted governance and biobank research,
- ethics, translational science, and the IRB,
- social and behavioral research,
- consenting study participants in the 21st century, and
- IRB library and policies: What you need to know.

Viamonte identifies people at the university who have expertise in an educational topic area and reaches out to them via email. The email tells them about how the IRB designed the Grand Round Series to include best practices, quality improvement initiatives, and other topics. Then it includes a direct ask: "We are reaching out to you because of your compliance charge and how your scope includes a topic of great interest for our community," according to one email.

The speakers are encouraged to open up their sessions to questions and discussions and to use visual aids, Viamonte says.

"These sessions provide our research community with real-time information of what they need to know about our HRPP and how we can better serve them," she says. ■

Smart Training Can Prevent Problems with New Technology

Common Pitfalls tool created

Adopting new electronic submission technology across a research enterprise organization can prove to be challenging for IRBs, which have a long list of stakeholders to train and educate. But as one research health organization discovered, mistakes made along the way can be as instructive as any of the successes.

"It started at a meeting of IRB staff, where we brought to the table similar complaints," says **Pamela Johnson**, MPH, research education and quality improvement specialist at Hartford HealthCare in Hartford, CT.

"We asked every IRB staff member to send me their top problems, mistakes people make consistently," Johnson says. "Each administrator sent me a list and I noticed some themes, so I sent the same request to all [electronic submission system] super users and asked for their top complaints."

Johnson learned that the biggest complaint had to do with documents not being attached properly or in the right place.

"People were attaching the wrong documents to the informed consent tab, or they were naming things in strange ways, maybe using the name the sponsor had on it, and we didn't know whether it was the informed consent," she explains. "Then we'd have to find the document and put it in the right section, which was a hassle."

There also was confusion about how to modify a document that was already in the system, Johnson says.

The program has a check-in/check-out feature that stamps documents approved by the IRB. But many investigators were accessing earlier versions of the consent document, thinking it had been approved when it was the version prior to approval, Johnson explains.

"The problem was the coordinator wasn't using the check-in/check-out procedure, so they were making changes to the wrong version and it was really hard for IRB administrators to track," she says.

The educational solution was to address each of these common mistakes in a "Common Pitfalls" tool that was sent to super users for vetting and refinement. Then the IRB created a supplemental user's manual with step-by-step guidance on how to identify and prevent each pitfall. The following are some examples of the common pitfalls:

• **Incorrect response to stipulations.** IRB administrators sent all requests for clarification to investigators with stipulations, Johnson says.

For example, if an investigator wanted to add a person to the study, IRB coordinators would check to see if the person had completed all CITI training. If the additional research staff person had not completed the CITI coursework, the IRB would send a notice to the investigator, asking him or her to please resubmit after the CITI coursework was completed, she explains.

The investigator would see that the person completed the coursework and then return the request without having made any changes. This showed an incomplete answer.

"When investigators had trouble doing this, we'd send them this document and highlight the common pitfalls with stipulations, and we'd say, 'The reason we can't process this is because you didn't complete the stipulation,'" Johnson says.

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The investigator would have to show on the document that the training had been completed, and then it could be accepted.

Having the common pitfalls tool ready to cut and paste into communications via the electronic system with researchers made it a consistent and simple way to educate and train them on how to use the new electronic system correctly, she says.

Johnson notes that the IRB did not want the back-and-forth communication to be handled through email because it needed to be tracked in the electronic system. "The system has tracking so you know when a stipulation was sent and when it was received, and we can log in to see when they are working on it," she says. "In the electronic system it shows up as a task they have to do."

• **Attaching revised documents without noting a modification.** "People were attaching consents and ads and documents to their continuation report, which was good," Johnson says.

But sometimes researchers would revise the forms and check "no" when asked about any modifications in the electronic system. "If they said 'no' because they didn't understand the question, we'd approve it without knowing there were changes," Johnson says. "I think they thought that anything they submitted would be reviewed and approved by the IRB, which is true, but they have to tell us if they are making changes and what those change are."

This pitfall was sent to researchers, telling them they cannot attach any reviewed documents without telling the IRB that they're requesting modifications, she adds.

The common pitfalls educational strategy worked, Johnson says.

"Submissions improved," she says. "The best use for the tool was to help IRB administrators give the research community a consistent message." ■

IRB Continuing Education Series Turns Students into Teachers

Having diversity in speakers helps

Newark, DE-based Christiana Care Health System's long-time educational program was set up to keep research nurses up to date, but over time it lost its luster.

The sessions were becoming boring, and attendance records backed up that sentiment, says **Janet Leary-Prowse**, MSEd, CIP, IRB research education specialist and IRB member.

"People would leave partway through the sessions because they were tired of hearing only the IRB staff talk about rules and regulations," she says.

The sessions needed to be more interactive, says **Melanie Chichester**, BSN, RNC-OB, CPLC, an IRB member and labor and delivery nurse at Christiana Care.

"The enticement was continuing education hours," Chichester says. "Every clinical research nurse has to have a certain number of education hours each year."

The following is how they changed the educational program and nearly doubled the number of attendees:

• **Encourage interactivity.** "The sessions have very, very lively discussions," Chichester says. "I hear from nurse researchers how much they enjoy this kind of setup where they talk to each other."

It gives participants a professional opportunity in a low-stress situation, she adds. "It's comfortable and not as intimidating, so they enjoy this education time working with their peers and collaborating."

• **Find diverse speakers.** "We encourage speakers to come from other departments, so it's not just the IRB talking," Leary-Prowse says. "We've had clinical research nurses talk, and last month one of the physicians talked about big data."

Investigators who work in translational research have talked about tissue procurement and tissue engineering, and a former IRB member spoke about health literacy, she adds.

"Occasionally someone from the IRB office will do the presentation, but not as frequently as in the past," Leary-Prowse says.

• **Include non-regulatory topics.** "One of our most popular topics was the teach-back method," says Leary-Prowse. "It was taught by a research nurse who also is a professor at a local university, teaching nursing students."

There was one session in the fall that was based on a project related to caring for the caregiver. The presenter was an emergency medicine physician, she recalls.

"She talked about a support program for staff members who have gone through a traumatic or upsetting situation," Leary-Prowse says. "She related a few instances of how she needed help, and she opened up the floor to comments."

Two nurses spoke about patients they had cared for who died. "There was not a dry eye in the room because so many people could relate to what they were talking about," she adds.

• **Have IRB staff and director on hand for questions.** "There almost always is one question for the IRB," Chichester notes.

"Consistently there's a higher-level question that only the IRB director can respond to, so it's helpful to have the director at those sessions," Leary-Prowse says. "This way, multiple people have the benefit of receiving the response, rather than one person who makes a phone call later."

• **Broaden marketing efforts.** "Previously, I'd send out a blast email to research nurses," Leary-Prowse says. "Now I have an announcement for the session posted on the internal website so any employee logging into the hospital website will see that this presentation is happening."

The educational sessions originally were designed to give IRB staff a way to connect with and answer questions for research nurses on a routine basis, but it's evolved, Leary-Prowse says.

"We are branching out into topics they wouldn't normally have thought about," she adds. ■

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CME/CE QUESTIONS

1. A panel of legal and ethical experts commissioned by the University of Minnesota to investigate human research oversight found significant problems with:

A. IRB review
B. investigator education
C. practices related to informed consent
D. All of the above

2. The National Institutes of Health's Recombinant DNA Advisory Committee (RAC) provides all but which of the following criteria for protocols that are referred by IRBs and IBCs to RAC?

A. The protocol uses a new vector, genetic material, or delivery methodology that represents a first-in-human experience, thus presenting an unknown risk.
B. The proposed vector was not studied in primate research prior to human subject clinical trials.
C. The protocol relies on preclinical safety data that were obtained using a new preclinical model system of unknown and unconfirmed value.
D. The proposed vector, gene construct, or method of delivery is associated with possible toxicities that are not widely known and that may render it difficult for oversight bodies involved to evaluate the protocol rigorously.

3. A study looking at participant incentives in 207 published research articles found what percentage actually listed amounts of financial compensation?

A. 0%
B. 5%
C. 11.1%
D. 22.5%

4. According to Melanie Chichester of Christiana Care Health System of Newark, DE, what is one word that might describe the type of IRB education that engages research staff and leads to better attendance at sessions?

A. Interactivity
B. Didactic
C. PowerPoint
D. Lunch