IRB ADVISOR

Your Practical Guide To Institutional Review Board Management

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IN THIS ISSUE

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IRB refusal of behavioral study garners attention

Individual vs. institutional behavior

A California IRB that had turned down a proposed study of cigarette sales in two San Francisco neighborhoods, instead found itself to be the object of scrutiny — in the form of a journal article about its decision.

The author of the article, **Ruth E. Malone**, RN, PhD, FAAN, a professor of health policy at the University of California, San Francisco, School of Nursing, says she was trying to make the best of a disappointing decision by the IRB not to let her pursue the study, which would have looked at the illegal sale of single cigarettes in African-American neighborhoods.

"Writing this paper was really our effort to sort of make some lemonade out of the huge effort that we made to try to gain their approval," she says.

Malone says her experience pointed to an area of research that needs greater IRB understanding — the behavior of institutions, as opposed to individuals, in affecting the health of a community.

"I think there is a message, in terms of considering whether there is activity worth studying that does not constitute individual behavior," she says.

But **Victor Reus**, MD, a psychiatry professor and chairman of the board that turned down Malone's proposal, says the IRB was concerned that the investigators' plans to send volunteers into liquor stores to attempt to illegally purchase single cigarettes constituted entrapment of clerks, who had not consented to participate in the study.

"I still stand by the reviews and the feedback [Malone] got," Reus says. "Sometimes you second-guess decisions and say this could have been done better, but I really don't see it in this case."

Reus says he was surprised to see the article in print in the November issue of the *American Journal of Public Health*, since no one from the journal had contacted him to get the IRB's response to Malone's complaints.

He was particularly offended by the article's title: "'It's Like Tuskegee in Reverse': A Case Study of Ethical Tensions in Institutional Review Board Review of Community-Based Participatory Research."

"To basically connect you with one of the worst violations of medical ethics in the last century. . .a lot of people will just read the title and think, 'What is UCSF doing?'" Reus says.

He says he asked for an opportunity to write an article in rebuttal, and was offered a chance to submit a letter to the editor instead. Attempts to interview editorial staff from the journal regarding their decision were unsuccessful.

PHAT project

The study in question grew out of a project called Protecting the 'Hood Against Tobacco (PHAT), which looked at tobacco use in two predominately African-American neighborhoods in San Francisco.

As part of the PHAT project, Malone and others created community focus groups to discuss strategies for addressing tobacco problems in the community.

Among those involved in the PHAT project was **Carol McGruder**, BA, director of the San Francisco African American Tobacco Free Project and the community co-principal investigator on Malone's study.

McGruder says her experience on an IRB at the research consulting company where she works was helpful in navigating the problems with the UCSF IRB for the PHAT project.

"If I had been someone from the community who hadn't had this broader experience, I probably would have been just rolled over by the whole thing." McGruder says.

When focus groups for the PHAT project discussed factors that they saw as problems in controlling tobacco use, they focused on the sale of single cigarettes, Malone and McGruder say. Although it is illegal in California to sell single cigarettes or "loosies" from an open pack, they say the practice is widespread at small stores in poor neighborhoods.

McGruder says the sale of "loosies" is particularly harmful to the neighborhoods because it allows people who can't afford a full pack of cigarettes, including minors, to maintain a smoking habit, as well as giving storekeepers an enormous markup on a pack.

"I think they sell them for 25 cents apiece," she says. "It's so exploitive, because you're making three times as much off of a pack of cigarettes."

In addressing the issue, the community members wanted to see how widespread the practice was.

The original proposal was for volunteers to monitor the small liquor stores in the neighborhoods to record the sale of loosies. But after the IRB had approved the observational study, the community members rethought the plan, Malone says.

McGruder says it became clear that an observational study wasn't feasible in this case and could, in fact, endanger the volunteers.

"You can't just hang around these stores and observe, watching what's going on" she says. "Stores get robbed. Someone would think they were casing the place. It could make trouble."

Malone and her team returned to the IRB with a revised plan, this time calling for volunteers to enter the stores and attempt to buy the cigarettes themselves, recording how often they were successful.

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The IRB denied the amended proposal, citing a number of concerns. Reus says the most important consideration was the lack of informed consent for store clerks and storekeepers whose businesses would have been targeted.

And while he says deception is sometimes a legitimate tool of research, in this case, the IRB did not find that it outweighed the risks, especially when other designs could gain the needed information.

"We would have approved an observational design," he says. "If [single-cigarette sales] were really as common a practice as they were describing, they should have been able to get some pretty good data. And it would have been real data. It wouldn't have been an artificial situation as constructed by them."

Malone, however, thinks the concern about the informed consent of the storekeepers misses the point about the subject of the research. She says the group was not planning to record any information about the individuals selling the cigarettes, but wanted aggregate data about the institutional practice of selling them.

She says the investigators' difficulty in making their case to the IRB is a reflection of an American culture that focuses on individuality.

"We often don't see collective activity and institutional activity except as a collection of individual activities, but I think that's one of the distinctions we realized was really important here," she says.

Malone worries that a focus solely on individual behavior could make it difficult for researchers to conduct important research into public health matters.

"There's an increasing interest in studying the corporate contribution to health and health disparities and health problems," she says. "I think there could be a lot of very useful research in terms of institutional practices within communities that have effects on health that would be precluded if every IRB took this stance."

Third denial

After the UCSF IRB first denied the amended request, Malone and McGruder resubmitted it twice more, attempting to answer the IRB's concerns. They obtained assurance from the district attorney that no one would be prosecuted as a result of the study. Malone and McGruder themselves appeared before the board to argue their case.

Finally, after a third denial, the community partners decided to do the study independent of the PHAT project. Ironically, McGruder says, that meant that all of the safeguards they had promised, including the agreement with the district attorney, were no longer binding on the volunteers.

"We did actually give some of the information to the city," she says. "If we had done it under PHAT, we wouldn't have because it was one of the conditions we had agreed to."

She says the group found that about 30% to 40% of the liquor stores in the area they studied were illegally selling single cigarettes.

McGruder says that even given her previous IRB experience, she found the IRB review of the PHAT project frustrating. In particular, she disagreed with the board's emphasis on protecting the stores that sold the cigarettes illegally.

"They were looking to defend the people who were preying on my community," she says. "They were worried about what their rights were. I was worried about the effect that it has on my community."

McGruder says she was the source of the "Tuskegee" quote used in the journal article and its headline.

"Many of these boards have come about because of [researchers] preying on us," she says. "So we're harmed by Tuskegee, and then we're harmed by the process that was put in place to protect us from these kinds of things. I found it to be very ironic."

Since the article was published, Malone has heard from other researchers who have had difficulties with IRB review.

"I was actually somewhat surprised at how many people seem to be having problems with IRBs, particularly people doing more social science or policy-related research," she says.

But Reus says he doesn't believe this was a case of an IRB failing to understand behavioral or community participatory research. He says his IRB has worked with other community groups, including AIDS awareness groups, monitoring unsafe sexual activity in sex clubs.

"The article suggested that our IRB isn't appreciative of, or sensitive to, community participation or psychosocial design, and while that may be true at some institutions and on certain IRBs, it is certainly not true on this IRB," he says.

"We have ample representation of individuals who are appreciative of behavioral design, understand it very well, and who have sympathy for the intent of acquisition of this type of data. This was not a biomedical review that didn't appreciate this type of research." ■

Factors cited in IRB's decision to deny study

Who was the subject? Investigator, IRB disagree

When the University of California, San Francisco's IRB denied a plan to have volunteers attempt to buy single cigarettes illegally at neighborhood stores, they cited the following concerns:

• **Legal issues** - The study's principal investigator, **Ruth E. Malone**, RN, PhD, FAAN, a professor of health policy at the UCSF School of Nursing, says volunteers in the program faced no legal risk since the state penal code makes it only illegal to sell the cigarettes, not to buy them.

In dealing with the potential legal risk to the store clerks, she says the group consulted with the local district attorney, explaining what they wanted to do, and gained his assurance that he would not prosecute store owners or clerks who sold cigarettes to volunteers as part of the study.

But IRB Chairman **Victor Reus**, MD, says the district attorney in question has since left office, and the IRB was concerned at the time that his assurance wouldn't be binding on his successors.

• **Confidentiality** - Malone proposed to report findings from the study only in the aggregate, without naming either individuals or stores at which single cigarettes were sold.

Carol McGruder, BA, co-principal investigator on the study, says it would have been possible to collect useful information while protecting the identities of the stores and store clerks.

"We could have done it. We would have done it," she says. "All research is an agreement. It's about being ethical and respecting whatever you're saying your guidelines are. We would have done that."

But Reus is less convinced that the investigators could achieve the confidentiality they promised.

"If you're talking about a very small community and a small number of stores as institutions, I would suggest that those are readily identifiable," he says. "If you have a document that says six out of eight grocery stores within this region committed this act, it's not going to be a big problem for people to figure out which ones these are."

Reus says he also was concerned that community volunteers participating in the study might not keep the information confidential.

• **Potential risk and liability** - While investigators believed that an observational study represented a potential risk to the volunteers, Reus says that the modified study could have posed risks as well.

"The committee expressed the concern that if, in fact, this subterfuge were detected, there might be some altercation that might result," he says. "The storekeeper might try to evict the person doing it or some unpleasant activity could occur."

Malone says she was surprised when, in one of its responses, the IRB referred her group to the university's risk management department, which eventually referred them back to the IRB.

"We were just dumbfounded," she says. "I think they just thought it was too much: 'We can't deal with this. Go talk to somebody else.' I think it was just a sort of avoidance thing."

Reus says the proposal was never actually referred to risk management, although the IRB did raise issues of the university's liability in case something went wrong.

"If a shopkeeper discovers that he has been an unwilling participant in this research project and that, in turn, results in a boycott of his store by the community at large, does he have a cause of action against the university?" he says. "If an altercation results, what is the role of the university?

"These are questions that somebody needs to think about," Reus says.

• **'Entrapment' and informed consent** - Reus says this represented the heart of the problem with the proposal. Store clerks and storekeepers who had not been told they were part of a study could be led into committing an illegal act.

"The IRB was obviously concerned about protecting all the individuals who are involved," he says. "From the IRB's point of view, the community included the people who were the shop owners and the people who worked in the shops in question."

Malone argues that the individuals selling the cigarettes, and even the owners of the stores, were not the subjects of the study. The group instead was looking at the institutional practice of single-cigarette sales.

"Normally, on a research subject, you collect data like age, demographic data, whatever," she says. "We didn't care if they were blue, fat, old, young — we didn't care about any of that. We were only assessing whether when we went to that store, we could buy a cigarette." ■

Reference:

Malone RE, et al. "It's Like Tuskegee in Reverse": A Case Study of Ethical Tensions in Institutional Review Board Review of Community-Based Participatory Research. *Am J Public Health*. 2006;96:1914-1919.

Program educates parents about pediatric research

Award for best practice in human subjects protection

A web site designed by Boston's Children's Hospital to better educate parents about pediatric research has won the top award for best practice in human subjects protection by the Health Improvement Institute.

The institute, which annually recognizes exemplary efforts in protection of research subjects, announced its awards in December.

Susan Kornetsky, MHP, CIP, director of clinical research compliance at Children's Hospital, says the development of the site was among improvements at the hospital funded by a human subjects research enhancement grant from the National Institutes of Health.

She says the project was spurred by a fruitless search for existing unbiased information about research that was tailored toward parents of patients.

"We noticed that there was some information — web sites, books — geared toward participating in clinical research, and the things we found seemed very pro-clinical research," Kornetsky says. "We also didn't find anything that was geared specifically toward pediatrics. It's a different decision when you're deciding for yourself to participate in research, versus deciding for your child.

"So we decided there was a need for something that was very unbiased, that would give parents the opportunity to think about the questions they should be asking before they allow their child to participate in research," she says. "Our hope would be that after someone reviewed the materials or parts of it, some [parents] would decide yes, and some would decide no — that it was really unbiased."

Worked with consultant

The team at Children's that worked on the project was led by James Mandell, MD, the president and chief executive officer of the hospital. Kornetsky says the content was developed on-site, but for video and graphics to help convey the information, the team turned to a company which had previously worked on a similar web site for the hospital's informed consent process.

"The content, the actual script, was developed here at the hospital," Kornetsky says. "We had a consultant who worked with us and developed the content, and we had that reviewed by several ethics advisory people here at the hospital. Then the content was turned over to [the company], who actually put it together — they hired the actors and did all the graphics."

The finished project includes basic information about clinical research, along with deeper discussions about the issues involved in making decisions about participating. The text is sprinkled with links to glossary entries for such terms as "clinical trial," "principal investigator," and "placebo."

Parents get practical information, such as what would be required of them if their child were enrolled in a study, as well as questions they can ask to evaluate whether a study is a good choice for their child.

Video clips feature actors portraying parents speaking with research staff in order to explain research concepts. Another feature on the site helps parents create a list of questions they can print out and take with them to a meeting with the research team.

The site also includes a "family journal," with comments by families who have gone through the decision whether to enroll a child in research.

"We wanted to include people who had made the decision and what went into that decision," Kornetsky says. "Another area that we had not seen any site deal with was a little section on conflict of interest, since we thought that was important for people to be aware of so they can ask the right questions."

Input from families

In addition to having the content reviewed by an ethics board, the hospital also enlisted the help of a committee at Children's Hospital made up of families whose children have been treated at the hospital. While that step didn't lead to major changes in the content, Kornetsky says, "it helped us make sure that it was on target and that it was understandable and used appropriate lay language."

The site took about 18 months to develop and was launched in 2004. Kornetsky says she's noticed that the site is being linked to by other research organizations, including government sites and research subjects advocacy groups.

"We tried to make it so it would not be specifically about research at Children's," Kornetsky says. "You will see the Children's Hospital logo in

the back, but we tried very hard to make it about research with children and pediatrics in general. And I think we succeeded."

She notes that the site focuses on biomedical research, even though Children's does conduct social-behavioral studies. "We had to make a decision really early on to put some parameters around it," Kornetsky says.

But the site is set up so modules can be added later, if time and funding permit.

"We could add a section: 'If you're being asked to participate in educational research or behavioral research,'" she says. "Those are the types of things we hope to someday do — that and get it translated into Spanish."

Kornetsky says institutions considering a similar project should focus on presenting the information as simply as possible.

"You don't want to make it seem as if people are stupid, but you also don't want to make it so that it's technically very difficult to understand," she says. "And you want to try to make it as engaging as you can. We tried to make it interactive and multimedia — there are words and phrases that come up, but also people and graphics and areas where you can stop and ask questions."

She warns that the process takes a serious commitment of resources.

"By resources, I'm not just talking about dollars," Kornetsky says. "I think that's the easy part. But it's the time and manpower. You write it, you review it, then you see the video of it, and it comes out differently than you thought it would. So we learned how to work with that."

Kornetsky is happy that the web site appears to be useful to others outside the Children's Hospital research community.

"When we submitted the grant [to the NIH], we saw that a lot of people were using it for infrastructure and databases," she says. "It was funded, but I remember getting a comment back that they thought we were a little off the mark on what we intended to do with it."

"But I think we've had much more impact than we would have buying computers and building a database," Kornetsky says.

The Health Improvement Institute, based in Bethesda, MD, is a nonprofit organization dedicated to improving the quality of America's health care. It began giving awards for excellence in human research protection in 2002. ■

To view Children's Hospital's parent education Web site, go to www.researchchildren.org.

Placebo use in pregnant herpes patients critiqued

Active control vs. alternative drug not proven safe

The debate about the appropriateness of placebos in clinical trials recently spilled over into the pages of the journal *Obstetrics and Gynecology*, where two obstetricians and a representative of the national public-interest watchdog group Public Citizen wrote to complain about a published study of an antiviral drug used to prevent herpes outbreaks in pregnant women.

The original study, published in the July 2006 issue of the journal, measured the efficacy of an antiviral drug, valacyclovir, against a placebo in preventing herpes outbreaks that would have required the pregnant subjects to have a cesarean section at delivery.

The study by researchers at the University of Texas Southwestern in Dallas found that valacyclovir treatment, after 36 weeks of gestation, led to a significant reduction in recurrent herpes outbreaks requiring cesarean deliveries. Thirteen percent of the women in the placebo group had a herpes outbreak that required a cesarean, compared to 4% of the valacyclovir group.

Adam Urato, MD, an assistant professor of maternal-fetal medicine at the University of South Florida, Tampa, FL, was one of the authors of a letter published in the December 2006 issue of *Obstetrics and Gynecology*, criticizing the use of a placebo in the study. Urato says he was struck by the timing of the valacyclovir study, when compared to two events:

- The 1999 recommendation by the American College of Obstetricians and Gynecologists (ACOG) that another antiviral drug, acyclovir, be considered for women who suffer a first episode of herpes during their pregnancy. Women with first episodes during pregnancy are at increased risk for additional outbreaks, including those that might make a cesarean section necessary.

While the ACOG guidelines for those women recommend only that acyclovir be "considered," Urato says that advice was given a Level B recommendation, which carries great weight with obstetricians.

"Level B is almost [ACOG's] strongest recommendation," he says. "There are not a lot of things in our field that are supported to that extent. So that's a significant recommendation that they made back in 1999."

- A 2003 meta-analysis, by many of the same

authors of the valacyclovir study, concluded that acyclovir reduced rates of cesarean section for women with recurrent herpes outbreaks.

Given those two findings, Urato says, the researchers were ethically bound not to give placebos to women in the study after those dates — 1999 for women with their first herpes episodes, 2003 for those with recurrent outbreaks.

"[The valacyclovir authors] say that in 2003, if a woman with herpes outbreaks is given acyclovir instead of placebo, it will decrease her rate of C-section, as well as decrease her rate of viral shedding," he says. "That's their conclusion, it's pretty unambiguous.

"They said that in 2003, but then they continued giving women placebo through 2004. So you have to ask the question, as we did, were these investigators knowingly placing their patients at increased risk?"

Authors defend study

The main authors of the study, along with the IRB at UT Southwestern, did not respond to requests for interviews regarding the study. Public relations officials at the university's medical center referred inquiries to the published response by the study's authors in the December 2006 issue of *Obstetrics and Gynecology*.

In that response, the authors argue that when their IRB approved the study in 1997, the effectiveness of acyclovir was unclear, and that clinical equipoise, or genuine uncertainty about the effectiveness of the two arms in their study, existed throughout the time that they enrolled subjects.

They write that previous studies of acyclovir didn't provide "sufficient power" to address whether the use of acyclovir reduced the risk of neonatal herpes, and that the safety of the drug to the fetus hadn't been established.

"Even in 2003, when there existed evidence of some maternal benefit, the risk of exposure to the fetus remained," the authors write. "In our opinion, the balance of risks and benefits to both the fetus and pregnant woman justified continuation of the placebo-controlled trial."

Urato calls that response disingenuous, pointing out that women and fetuses in the active arm of the study were being exposed to valacyclovir.

"I don't think their lengthy justification regarding fetal safety addresses the principal issue — they were placing their patients at known higher risk for cesarean," he says. "They knew it because they published it in 2003."

He says that at the very least, patients would have to be informed during the consent process that if they were randomized into the placebo arm of the study, they could be at increased risk for cesarean delivery.

Group monitors placebo use

Peter Lurie, MD, MPH, deputy director of Public Citizen's Health Research Group in Washington, DC, co-authored the letter with Urato and lead author **Aaron Caughey**, MD, PhD, an obstetrician at the University of California, San Francisco.

Lurie says Public Citizen has spoken out for years against what it sees as the inappropriate use of placebo controls in clinical trials. The group criticized clinical trials in Africa during the 1990s that used placebos with HIV-positive pregnant women instead of a drug known to be effective in preventing mother-to-child transmission of HIV.

He says inappropriate use of placebos is "widespread," in part because the FDA tends to favor them over active-control trials.

Lurie says his group doesn't entirely rule out the use of placebos in clinical research.

"We do think it's acceptable to give a placebo for let's say, a treatment [for a serious condition], which barely works and which has adverse effects," he says. "We think it's acceptable to give a placebo for seasonal allergy, for headache, we think that's fine, because it's less serious when assigned to a placebo group.

"But the moment that it involves life or death, a serious outcome, I don't think it's reasonable to randomize people anymore," Lurie says. "When more women will end up with cesarean sections, I think that's a serious outcome." ■

References:

Sheffield JS, et al. Valacyclovir prophylaxis to prevent recurrent herpes at delivery: a randomized clinical trial. *Obstet Gynecol*. 2006;108:141-147.

Caughey AB, et al. Valacyclovir prophylaxis to prevent recurrent herpes at delivery: a randomized clinical trial. *Obstet Gynecol*. 2006;108:1550; author reply 1550-1552.

Follow lessons from the trenches to improve your IRB

Complaints fell, response time rose

When faculty and researchers' anger and complaints rose heavily against a university's IRB, a new vice chancellor of health sciences took charge,

hiring someone to answer the criticism through policy and personnel changes.

The IRB's overhaul has resulted in a paper published in *Academic Medicine* in January 2007, and it produced some best practices, including two-day turnarounds on investigator submissions that do not require a full committee review.[1]

The IRB at East Carolina University of Greenville, NC, was founded about three decades ago, but in recent years it had not kept up with increasing demands, says **Kenneth De Ville**, JD, PhD, a professor at the Brody School of Medicine in Greenville.

"There are regulatory goal posts moving all the time, and I don't think the IRB kept up with it in terms of the amount of staff and scrutiny needed," De Ville says.

When the university's administration first noted the large volume of staff, they reacted by making mechanical changes, such as increasing its full-time staff from one person to five, De Ville notes.

But the problem was that the full-time equivalent (FTE) employees they hired were all clerical workers who were largely unskilled in research and IRB work, he adds.

"My view of this is that even though IRBs have and are suffocating under paperwork, virtually none of the work is clerical in the traditional sense," De Ville explains. "So the institution did the right thing by providing more FTEs, but they were the wrong kind."

When the complaints continued, the vice chancellor responded by appointing De Ville to overhaul the IRB in June 2003. He reorganized the IRB over a 14-month period and remained involved, monitoring improvements, for a long period after that.

Since then, the IRB has been visited by the Office of Human Research Protections (OHRP) as part of its quality improvement outreach, and the result of the voluntary QI audit was very useful and positive, De Ville says.

"They said it was the most engaged IRB they had ever seen," De Ville says.

Also, the complaints have been greatly reduced, and investigators have developed collaborative relationships with the IRB staff.

"Investigators began to trust the IRB office and the advice they received," he says. "It really helped the relationship between investigators and the office once investigators began to believe in the capacity and credibility of the office staff."

Here's what institution officials learned from the experience of rejuvenating the IRB:

• **Hire the right staff.**

"When they brought me in, I said, 'There are enough people, but the wrong kind,'" De Ville says.

De Ville listened to the faculty/investigator complaints about the IRB, and he concluded that the existing IRB staff did not understand the research environment and the dynamics of a clinical trial.

"So I tried to figure out how to remedy that," he says.

The solution was to replace existing IRB employees with staff who had clinical trial experience, including an associate director who had extensive clinical trial experience, De Ville says.

"Then I hired another research coordinator who had run trials for five years for outpatient drug trials, and the third person I hired was somebody who had worked in the industry at a big pharmaceutical company," he says. "So these people would know research better than I did, and they knew how research worked."

The IRB's remaining employee was the person who had five years of experience working on the same IRB.

"So the highest qualified person in the office turned into the lowest qualified person in the office," De Ville says.

The new IRB staff could talk with investigators, understand their material, know the institutional context of studies, and propose policy changes, he notes. **(See story on IRB's new policy and procedure changes, p. 45.)**

"I'm really convinced that personnel quality is where this really matters because even with a less than ideal system, you can run an office and work to make the system more perfect," De Ville explains. "In research, regulations are so fact-intensive, and there are judgments that need to be made, so you really need high quality people."

• **Change the way the IRB is structured.**

The IRB had been operated for years with one employee and a board chairman who was in charge of both the committee and the office, in addition to his clinical duties, De Ville says.

"The chair's duties were too much of an overload," De Ville says.

Under the new format, the IRB was divided into two committees, with one handling behavioral/social science research and the other handling biomedical research.

The existing chairman, who is a professor in pediatric oncology, became the chairman of the biomedical IRB, and the chair for the new behavioral/social science IRB is a full professor in psychology, De Ville says.

"They are both researchers," he adds.

Also, De Ville recruited anthropologists, sociolo-

gists, and social science researchers to fill the new IRB's membership. There are some members who serve on both committees, including the chair of the behavioral/social science IRB.

Having a separate biomedical IRB stopped the complaints about the board having English majors review biomedical studies, De Ville notes.

De Ville found it easy to attract new board members: "I'd invite the people who had the most concerns about the committee to become members, and they could have input, and that helped a lot," he said.

The IRB meetings were streamlined, and a wider range of specialties were represented on the new boards, De Ville says.

Also, for some specialties, adjunct board members were recruited. For instance, a trauma surgeon is an adjunct board member who is called to a meeting when emergency research is being reviewed.

"For areas where we didn't have a specialist, such as an endocrinologist, we would sometimes use an in-house consultant," De Ville says.

• Better educate IRB members and make processes more efficient.

The IRB has always used Internet education, but among the changes enacted was providing human subjects research textbooks to all IRB members and having a little education at each board meeting, De Ville says.

"The education piece is decided according to what's on the agenda," he explains. "So if there was an issue related to children on the agenda, then we'd do an education piece about that topic."

For example, De Ville noticed that IRB members had fallen into a habit of dissecting certain wording and phrases, often when these were not important issues.

"What I think happened was the committee members learned from the IRB, so as new members started on the board, they would take up the same habits," De Ville says.

"So the associate director and I would attend every meeting and encourage them to look at the more important issues and not focus so much on capitalizations and upper and lower case styles," he says. "This freed members to look at the real issues instead of style issues."

Also, whenever members review a protocol involving vulnerable populations, the IRB staff puts special templates into the minutes, and these templates follow all of the regulatory requirements. This ensures that nothing of importance is omitted from the review, De Ville says.

"So instead of someone saying, 'Yeah, that looks good for kids,' you can see how the board considered each point in the regulations," De Ville adds. ■

Reference:

1. De Ville K, et al. Rejuvenating a foundering institutional review board: one institution's story. *Acad Med*. 2007;82:11-17.

Reduce complaints with new policies and procedures

Make IRB office responses professional

The IRB at East Carolina University of Greenville, NC, was able to satisfy investigators' complaints and improve response times, partly through an overhaul of its policies and procedures.

"We put a lot of effort into turning paper around and providing service to investigators, and we tightened down on the regulatory items to make certain it was done right," says **Kenneth De Ville**, JD, PhD, a professor at the Brody School of Medicine in Greenville.

De Ville was hired by the university's vice chancellor to reorganize the IRB into a biomedical IRB and a behavioral/social science IRB. He started by hiring research professionals who could understand investigators' issues and regulatory requirements and put new policies and procedures in place.

As a result of the reorganization, the IRB's workload rose from 434 protocol submissions in 2003, to 662 in 2005, after the changes took place.[1]

Once investigators saw how the IRB office was run more efficiently, they stopped complaining when more was asked of them, De Ville notes.

"We'd send protocols back to have them redo items, and we would have them reshape the study or send more documents," De Ville says. "Previously, I think they resented the time loss, and they resented legitimate regulatory requests too."

One of the efficiencies enacted was an announced turnaround time of three to five days on queries and items that didn't need a full board review. But the IRB office has even improved on the committed turnaround time.

"I've done a number of audits, and they're always under two days," De Ville says.

The IRB office made the full committee review time more efficient by starting some new practices.

For example, the biomedical IRB, which meets every two weeks, would assign reviewers for a full committee review to a protocol, and the reviewers could write their comments in a secure

Web site, 48 hours prior to the committee meeting, De Ville says.

"Our office staff would download those comments into a template for the minutes, and that would be projected during the meeting," he adds. "The discussions would be typed at the same time the meeting was going on."

This way, the IRB staff could return to the office and immediately generate letters based on the committee's decisions.

"So if there were queries, comments, or revisions, those could be out within 48 hours," De Ville says.

One of the benefits of this process is that the IRB has complete documentation by the time the meeting is complete, De Ville adds.

There was another benefit to having the IRB reviewers type in their comments two days before the IRB meeting.

"The skilled office staff could call investigators before the meeting and ask them to send in any missing information or make any changes," De Ville explains. "Then their changes would be taken to the committee and the investigator wouldn't need to wait until the subsequent meeting to have a response." ■

Reference:

1. De Ville K, et al. Rejuvenating a foundering institutional review board: one institution's story. *Acad Med*. 2007;82:11-17.

Online IRB expert offers examples of ethical issues

Privacy, security top list

Many of the same ethical issues need to be considered for on-line research as with any other type of research, but there are a few differences, an expert says.

It's working out the details of these differences that can be challenging.

For instance, privacy issues, security, and qualifying participants can be trickier with Internet studies, says **Robert Kraut**, PhD, a professor at the Human Computer Interaction Institute, Carnegie Mellon University in Pittsburgh, PA. Kraut was the lead author of an article published in *American Psychologist*, in the February/March 2004 issue, that offers recommendations to researchers and IRBs on how to deal with on-line research.

At the same time, Internet research creates many new opportunities, and IRBs sometimes are too cautious, Kraut says.

"I'm on our institution's IRB, and I got on it because I thought they were erring too much on the side of caution," Kraut says. "They didn't know enough about what life is like on-line."

Since Kraut joined the IRB and has educated members about Internet research, their review approach has improved, he notes.

Some of the reasons why researchers are attracted to Internet research, include the following:

- the Internet decreases the cost of recruiting survey subjects and others;[1]
- social behavioral scientists can observe a wide variety of communication archives;[1]
- other archived data about human behavior can be observed on-line;[1]
- computers provide automation and experimental controls that otherwise are difficult or unavailable;[1]
- the Internet itself is a social phenomenon that raises research questions.[1]

However, IRBs and researchers need to be sensitive to how Internet research may impact ethical debate and resolutions.

Here are Kraut's suggestions of ethical areas to consider in on-line research:

- **Recruitment criteria:** One of the major issues with on-line research is that it's difficult to exclude children from participation, Kraut says.

"You can put a statement on the study saying a participant has to be 18 years of age to enter, but there's no guarantee that any kid who's interested wouldn't still participate in your research anyway," he says. "And you have no way of excluding kids."

So if the research involves greater than minimal risk and it's likely to appeal to children, then it probably shouldn't be conducted on-line, Kraut says.

Here's one example: One researcher has done experiments on-line, looking at the issue of ostracism. Participants play a small game in groups of three. After they have played for a little while, two of the people in the game ignore the third person, who is the real research participant, Kraut describes.

"There's evidence that ostracism makes you feel bad, makes you feel excluded, and if that's greater than minimal risk, then that might not be research you want to do if you think you can't exclude underage participants," he says.

In the example above, the IRB debated the ethics of the research and finally decided that it was of minimal risk, and so they allowed the investigator

to conduct it on-line, Kraut adds.

• **Knowing when harm has occurred:** In a laboratory, researchers can observe how participants react, and they will typically know whether someone is upset by a psychological or social experiment, Kraut says.

"On-line you can't see that," he says. "So you might want to build in probes that give you more insight because you're missing this other thing that's happening to them."

For instance, the Internet survey might include intermediate questionnaires that ask about the person's mode, and those can be used to terminate a study for a particular participant, Kraut suggests.

"The flip side is when somebody comes into the laboratory, the experience of being there places them in a quite compelling social situation," Kraut says. "It's hard for someone to extract themselves without feeling stupid or feeling they've violated a set of norms or promises they've made."

For this reason, participants are more likely to sit through events they might find distasteful or potentially harmful because it's hard for them to exit the laboratory setting, Kraut explains.

So IRBs have to balance the risk with the flip side in on-line research.

"It's harder to tell whether someone is being adversely affected by the experience when they're on-line, but there's less necessity for researchers to do that because the research participant has more control over his or her behavior," Kraut says. "There's a trade-off there."

• **Privacy poses the biggest risk:** "Probably the biggest risk of on-line research is not the psychological risk of participation itself, but the risk that the data that's collected is going to be exposed and cause harm outside of the research context," Kraut says.

However, that risk exists with any research project in which data is put on a computer, he notes.

"Although many people worry about the ability of outsiders to get the data when it's on-line, it's a risk that's common to any network computer application system," Kraut says. "If you use data analysis software, it's the same risk of privacy violations whether it's on-line or off-line and collected and stored on a computer."

The answer is the same: "Separate personally-identifying information from information that's harmful, if exposed outside of the research context, and try to do that as soon as possible when you collect the data on computer," Kraut explains.

Although many Internet surveys are conducted anonymously, not all are, he notes.

For example, for a gay men's health study, one researcher is conducting the survey on-line, and as part of the inducement is giving participants a payment, Kraut says.

"So you need some way to crack their identities so they don't receive multiple rewards for participating in the research," he says.

The key is to separate the identifiers from the potentially revealing health and behaviorial information, Kraut adds.

• **Is Internet behavior public or private?** "A number of people have started to do research that looks at the many on-line groups and communities," Kraut says. "One issue that's unique to on-line research is how to figure out the extent to which the behavior you are observing is public behavior where people have the expectation that strangers are able to see what it is that they do."

For example, suppose a participant is in a user group that talks about testicular cancer.

"This is an intimate topic," Kraut says. "You're revealing intimate things about yourself, and you're doing it in a public forum that anybody in the world can see."

In another example, users may belong to a registration-only usernet in which the information shared is not entirely private, but can only be viewed by others who have gone through the effort of registering with the Internet site, he says.

This example might involve a cancer support group on-line that requires registration, and an investigator also registers to be able to view the messages that are exchanged, Kraut says.

"That's a borderline case of whether it's public behavior that's exempt from the IRB regulations or whether it's considered private behavior that requires informed consent," he explains.

Unlike the real world, where it's very clear that

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observing people playing with their kids in a park is public, and observing them play with their children in a living room is private, the Internet provides various shades of gray on the public versus private continuum, he notes.

"People are more likely to think they are behaving privately when they have to log in when posting these messages," Kraut says.

"IRBs have to be sensitive to that issue of where in this continuum of private versus public a particular circumstance is," he says. "You have to evaluate that based on each circumstance."

• **Consider harm to the group:** "The other thing that's quite distinct, and we're still talking about the study of on-line groups, is to think about the group and it's potential harm," Kraut says.

"The IRB regulations focus on potential harm to research participants, but people who are doing research in on-line settings also have to think about the potential harm to bystanders who are not participants," Kraut explains.

"You need to take group-level harms into account, and not just the people about whom you are collecting data," he adds. "You need to consider the bystanders, as well." ■

Reference:

1. Kraut R, Olson J, Banaji M, et al. Psychological research online. Am Psych. 2004;59(2):105-117.

CE/CME *questions*

12. What was not one of the concerns of the University of California, San Francisco's IRB regarding a study in which volunteers would attempt to purchase single cigarettes at neighborhood stores?
A. That the study could entrap store clerks into an illegal act.
B. That volunteers could be at risk if their real purpose was detected.
C. That volunteers could be at risk for exposure to second-hand smoke.
D. That storekeepers could be at risk of a community boycott if they were identified from the study.

13. In a clinical trial of the antiviral drug valacyclovir, what percentage of pregnant women using placebo had a herpes outbreak that required a cesarean delivery?
A. 2 percent
B. 4 percent
C. 13 percent
D. 15 percent

14. In a case study of how a troubled IRB was rejuvenated, which of the following changes helped to reduce investigator complaints and improve IRB response time?
A. The IRB was divided into two IRBs, with one handling biomedical research and the other one looking at behavioral/social science research.
B. The institution replaced existing clerical-level staff with professionals who had extensive backgrounds in clinical trials and research.
C. The IRB began to send protocols to IRB members prior to full committee meetings, asking for their comments on a secure Web site 48 hours prior, so the comments could be included in the committee meeting agend and so they could be used to request more investigator information prior to the committee meeting.
D. All of the above

Answers: 12. (c); 13. (c); 14. (d)