IRB ADVISOR

Your Practical Guide To Institutional Review Board Management

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AAHRPP: Human protections programs have made great strides

Bioethics, genetic research also addressed at annual conference

Once deemed "a mess," IRBs have shown huge improvement in the last decade, says Association for the Accreditation of Human Research Protection Programs (AAHRPP) CEO **Marjorie Speers**, PhD.

Bioethics, global expansion, and the state of the organization were also big topics at AAHRPP's conference in Miami, April 3rd-5th.

Outgoing AAHRPP CEO Speers took time to reflect on changes to the IRB system and to AAHRPP itself. Around the time of AAHRPP's formation in 2001, IRBs were "a mess," Speers says, dealing with a host of noncompliance issues. "In the past, IRBs did everything they could to stay under the radar," she says. "IRBs had a negative image and did not want to make it worse by dealing with noncompliance."

The organization formed as a way to advise organizations and government on human research protections. Today, Speers says, human research protection programs are the norm, and the number of governmental noncompliance warnings has plummeted.

"We have accomplished three things: knowledge, communication and confidence," Speers says. "There has been a tremendous growth in confidence in research organizations and the research community in general."

Communication among research organizations is growing. "University systems are accredited and can form partnerships and work together in ways they could not previously," Speers says.

IRBs have been more willing to take risks and try new things to promote human subject protections, including the growth of IRB collaborations and consortia. "We can push the systems in ways we couldn't before," Speers says.

The current IRB system is outdated and doesn't meet the needs of IRBs today, Speers says. "That is what will be the challenge in the next decade or so," she says. There have been "dramatic changes"

in larger, independent IRBs in the last several years, including mergers and acquisitions. "[Independent IRBs] will be sustainable for a long time — they are owned by companies, which guarantees sustainability," Speers says. "There will be fewer [independent IRBs] in the next three years, but they will be larger and capable of reviewing a wide range of research."

"We have only just dabbled" in collaborations, Speers says. "Collaborations will grow and become stronger."

AAHRPP is also seeing international growth and is expanding into Europe, Asia, and the Middle East. China and India are seeing major growth in research — in fact, Speers says, China is expected to surpass the U.S. in the number of scientific, peer-reviewed papers published. "We are seeing growth in other countries because they are making financial investments in their scientists," she says.

The gap between research and bioethics

Trying to define how to bridge the gap between bioethics and research is not simple, says **Sergio Litewka**, MD, MPH, international director, University of Miami Ethics Programs and CITI Program. "Sometimes this bridge is very frail and is over more than just a gap," he says.

Sometimes, Litewka says, the gap is related to differences in personality between researchers and bioethicists. Ethicists, he says, look at the means in which results are found, while researchers may simply want results. "Bioethicists are thinkers, others are doers," Litewka says.

Bioethical concerns include justice, cultural sensitivity, and standard of care:

- **Justice:** This is a very complex issue, according to Litewka. "Who will benefit, and who will be responsible for delivering the benefit? Who will be entitled to receive it, and when? Most international guidance confuses the issue and tries to be too politically correct," he says. Other justice considerations include finding an acceptable definition of exploitation, and determining who should decide what post-trial benefits should be shared with whom in the community.
- **Cultural sensitivity:** "This is also a very delicate issue," Litewka says. "Doing research multilaterally means different ways to communicate same idea. Is it ethical to accept moral values exclusively related to cultural norms or habits from a particular society, even when these habits might harm minorities or ethnic groups?" One size of care does not fit all, he says.
- **Standard of care:** What is the best established method of caring for research

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subjects? Should the standard of care be tailored to a community's established ideas?

Standard of care is also related to what Litewka refers to as "ethical imperialism." Is it, he asks, ethical to accept moral values exclusively related to cultural norms or habits, even when it might harm other groups? Which cultural values should be followed? "The danger is when we accept blindly situations that could harm other people," Litewka says. "We do not harm and do not kill."

Challenges for researchers and subjects in developing countries include:

— weak regulations and enforcement of current regulations;

— research ethics committees that may be inadequately funded or with very little expertise in some particular areas;

— economic disparities and access to the healthcare system;

— insufficient or absent policies for research ethics education;

— ideological tensions;

— lack of agreement in critical issues.

Findings of the International Panel of the Presidential Commission for the Study of Bioethical Issues 2011 suggest the following areas for improvement:

— Increasing accountability: Improve through public access.

— Helping those who are harmed as a result of research participation.

— Respecting equivalent protections of international partners.

— Promoting a culture of responsibility.

— Evaluating site selection and the justification for chose study design.

— Engaging communities at all levels of research.

"Research with humans is a multinational enterprise in need of interdependent solutions," he says. "Site accreditation throughout a set of accepted global standards is a considerable step towards the protection of subjects and the integrity of research."

Following the Common Rule

A study presented by **Paul S. Appelbaum**, MD, Dollaro Professor of psychiatry, medicine, and law at Columbia University in New York City, suggests that IRBs may not be discussing Common Rule requirements as they should.

To get to the bottom of things, Appelbaum and colleagues observed 10 IRBs around the country by recording meetings and performing interviews with 263 IRB members. In 20 different meetings the researchers attended, 114 protocols were reviewed. After poring over hours of transcribed interviews and meetings, the researchers found that IRBs frequently failed to discuss many of the human subjects protection criteria mandated by the Common Rule:

- Equitable recruitment of research subjects was not discussed 80% of the time, and most discussions involved exclusion of pregnant women.
- Vulnerable populations were not discussed 50% of the time.
- Safety monitoring was not discussed 73% of the time.
- Risk minimization left out 37% of the time.

Appelbaum conceded that the study data do not capture the work that is done in preparation for meetings. "But what these data do capture are aspects of what goes on inside the room and how it might differ from the regulatory or administrative vision of what should be going on," he said.

Appelbaum also reported high numbers of members among the interviewed IRBs — usually around 15, with one study reporting a high of 44. Federal regulations only require five. "IRBs are filling the rooms of meetings with many more people than are required. This may be a good thing, it may not be a good thing … There may be too many people around the table."

(For more details on this study, see the related article on page 56.)

Paternalism vs. partnership in genetic research

Research subjects want greater involvement in the study process — and in what may later happen to any tissue or other biological samples they may give. "Leaving patients out of the process misses out on a lot of good information," says **Rebecca Dresser**, JD, professor of law and ethics in medicine at Washington University in St. Louis.

For the most part, researchers lack experience in being research subjects and tend to only see things from one perspective. "We all have our professional glasses on and see things through a different lens than subjects do," Dresser says.

There is no particular role for a layperson in research, she says. More and more, members

of the public are becoming interested in moving research forward and getting help for themselves and others — and represent subjects' interests, feelings, and issues in the course of research. "The traditional [research] model is under pressure, and nowhere more than in the genetics field," Dresser says. "There is a push to look at subjects for ethical guidelines and see them as true partners in research."

Research subjects, Dresser says, want to be respected as partners in research and seen as more than just patients or passive providers of tissue samples. "Participants view themselves as having an ongoing stake in research and want to be informed of further use of their samples," Dresser says.

In a University of Washington focus group, 90% of participants said it is important to be asked for permission for further use of samples and for permission to share de-identified data with other investigators.

A vast majority, Dresser said, wanted to know about individual results, including health risks "even if there was nothing they could do about them." Participants also wanted to know information relevant to family risk, reproductive decisions, environmental risks, life and financial planning, and potential future research. "People just want to know what could be wrong with any tissue samples," Dresser says.

There is also the question of whether participants are adequately informed of the risks and benefits of a study in order to be a partner in research. "Some will overestimate benefits of genetic research. Some will fail to realize potential harms, such as the stress of finding out genetic issues, and the effects it could have on insurance," Dresser says. These are issues that can be addressed through counseling and education, she says, rather than just withholding the information. Many people may be unwilling to participate in research if they don't have control over what may happen to their samples later, and could result in a decrease in participants. And there is some justified paternalism, Dresser says. "We don't want it [research] driven by overhype and blind consumerism."

"Researchers can benefit from listening to input from subjects who have been through the process and have that perspective researchers may not have," she says. ■

SWAT! project provides support to investigators

IRB's best practice is popular with PIs

IRBs searching for highly effective ways to improve protocol submissions and enhance education and training efforts might check out the SWAT! program at Washington University in St. Louis.

SWAT! — Staff With Answers Today! — provides just-in-time education and an ongoing training program for IRB and research staff. Seven members of the IRB's 28-member staff are trained to provide expedited reviews, and they also serve on the IRB.

They spend two days a week in the university's psychology building and at the biomedical campus, meeting with investigators who have questions or studies that might need expedited reviews, says **Martha Jones**, MA, CIP, executive director of the human research protection office. SWAT! received a 2012 Award of Excellence in Human Research Protection from the Health Improvement Institute.

"We wanted to be of service," Jones says. "We have expedited reviewers on staff, and they have authority to do approvals through the expedited review process."

Since opening the onsite office hours more than 18 months ago, the program has been well received. Every month, between 10 and 20 investigators visit each satellite office, she notes.

"We provide a more efficient way for studies to get approval through the expedited review process," Jones says.

The program also has a dedicated staff position for answering researchers' phone calls or responding quickly to online chat questions as they complete the protocol submission form electronically. These, as well as the staffed satellite offices, are available during weekday office hours, she adds.

SWAT! has grown to 300 to 450 monthly phone calls and its visits from biomedical researchers has increased by nearly 40% from a year ago, says **Mike Leary**, MA, CIP, education and compliance specialist in the human research protection office of WUSL.

How it works

Here are some details about how the SWAT! program works:

• **Offer in-person consultation:** The HRPO SWAT! team offers in-person consultation on myIRB submissions to any researchers who ask for help. The team staffs offices at the biomedical campus and behavioral science campus, each for several hours twice a week.

"The IRB office sits three to four blocks from the main medial campus," Jones says. "So we identified a computer center directly on the medical campus where we could hold in-person office hours twice a week."

Investigators can meet with the IRB experts and work on their IRB submissions at a computer in the offices.

"We keep a combination of expertise available, depending on what kind of questions come through the door," Jones says.

IRB experts staffing the offices also are trained to serve on the IRBs and provide expedited reviews, providing a more efficient expedited review process, she notes.

"Typically, these are people who have research experience, and we train them in regulatory criteria for expedited review, which is what they do on a full-time basis," she explains. "They attend board meetings with other IRB members, and we take the approach that their job is to reflect what the full board would be doing."

• **Provide on-call service:** HRPO professionals take turns staffing the on-call lines between 8 a.m. and 4 p.m. weekdays.

"Researchers can call the staff person to ask any questions and get help with their applications by phone," Jones says. "This is available weekdays so they can get the same kind of help they would in person."

The IRB office has one staff member dedicated to the on-call service and chat service in the mornings and a different person dedicated to them in the afternoons, she says.

The idea is to offer different areas of expertise during the day.

"One person might have expertise in full board reviews, so if an investigator has a full-board question, there is someone available to consult with," Jones says.

If the on-call expert doesn't have an answer, the expert will research the question and get back to the caller within the four-hour shift window whenever possible, she adds.

• **Make online chat service available:** The same HRPO employee who is staffing the on-call service also will answer investigators' questions through the live support chat service. Investigators can access the chat service through myIRB where a chat icon appears on the top right side of the screen. They can click on the link and then click on the "join chat" button.

The goal of having an online chat service is to provide more flexibility in the online application process with real-time answers to investigators' questions as they are completing electronic forms, Jones says.

The live chat service is not available at night or on weekends, Jones says.

• **Collect metrics on what kind of questions and issues arise:** "We're looking at metrics on whether SWAT! decreases time to approval," Leary says.

The IRB also has collected information about investigators' questions and trends that might point to educational needs.

"We record names, role at the university, what kind of questions they ask us, and we keep data on how long it takes us to get a response," Leary says. "We're able to demonstrate that if you come to SWAT! the approval time is less than if you went through the usual process."

The IRB can check data in each department to see how many visits they've had with SWAT! and what kinds of questions they're asking IRB staff. This helps Leary and the IRB determine what each department's educational needs are.

For example, in recent years the university has had a rapid increase in biobanking, and data collected through SWAT! suggest this was a frequent topic of discussion and questions, Leary says.

"We didn't have standardized advice for investigators, and it's a complex issue," he explains. "We found that a lot of people at the medical school would have pre-submission questions about biobanking and want to sit down and talk with us about their studies and ideas," he says. "We can help them set up their study and application on the spot, since they do that in collaboration with us, and this reduces their approval time considerably."

Leary reviews data regularly and looks for trends that might require additional educational materials or sessions.

"We have developed a lot of educational materials just for SWAT! that we didn't

previously have," he says. "We can sit down with the research community and say, 'Here is the beating pulse of your questions.'"

The SWAT! program has changed the IRB's culture and interactions with stakeholders, Leary notes.

"This is a way to create more transparency for the IRB process," he says. "In many institutions, the IRB is a black box, and people don't know how it works; with SWAT! you can walk people through the process over the phone or in person."

SWAT! increases the IRB's mission of protecting human subjects, and it fosters collaboration with IRB staff, researchers, and faculty members. Plus, it's an affordable model that IRBs small and large could employ, he adds.

"It fosters a sense that we're in this together," Leary says. ■

No-tech solution to compliance wins award

Placemats: Simple, effective, easy

In the age of smart phones, iPads, electronic checklists, text message reminders, and other tools, it would be easy to forget that sometimes the best solution is the simplest: no-tech. At least that's what one research and human subjects protection expert discovered when trying to find a way to improve IRB meeting and review quality.

The solution uses old-fashioned materials with a novel twist: laminated, 11-by-17-inch placemats containing research guidelines and rules. IRB members each have an IRB "cheat sheet" placemat in front of them at every meeting.

"You have to find something that works. I like using a placemat because it addresses the issue at hand and provides continuing education in a nonintrusive manner," says **David Vulcano**, LCSW, MBA, CIP, RAC, AVP & responsible executive, clinical research, clinical research group, Hospital Corporation of America (HCA) in Nashville, TN. HCA's IRB placemats received the 2012 Best Practices Award for Excellence in Human Research Protection from the Health Improvement Institute.

The educational placemats have been well received by IRB staff and members, and there is anecdotal evidence that they are used as references during IRB review meetings, Vulcano says.

"Sure, we could have developed an iPad app to come up with this sort of thing, but then there are people who don't have iPads, or taking it out increases the temptation to play games or check emails," Vulcano explains. "Sometimes technology for technology's sake is not a solution."

Vulcano came up with the idea for the placemats after trying to find a way to keep IRB meetings on track and well-informed about research regulations, particularly decisions that have regulated criteria.

"Training is expensive and time-limited, and you start to forget a lot of the training you have," he notes. "Part of my job is to make sure the IRBs are educated in the regulations."

Policy books are useful, but all too often these remain unopened while they're having discussions. Likewise, rules and regulations can easily be put on an iPad or laptop computer, but these have other purposes, as well, and can be distracting, he adds.

"The challenge was getting this information in front of IRB members while they're having a meeting so they could make sure all IRB meeting criteria are addressed," Vulcano says.

Vulcano liked the idea of putting a poster on the wall, as he had seen one commercial IRB have "The 8 Criteria To Approve Research" poster, but that would be a little challenging in most healthcare delivery settings when IRBs meet in rooms used for multiple purposes. Also, at every meeting the IRB with the poster held, no one got up to look at the poster, he notes.

"How can we achieve getting this information in front of everyone's eyes during the meeting, yet do so in the most pleasant, unobtrusive and non-threatening manner?" he says. "Then the idea hit me — put the information on a placemat. Many meetings have food, and they put placemats out."

The placemat idea proved very easy to implement. They were cheap, costing $20 to $25 for a set of 14 different placemats. Each of HCA's 32 IRBs has one set of the placemats. The placemats are rotated so members see different ones at each meeting. IRB coordinators collect the placemats after each

meeting and distribute them again at the next one.

The biggest challenge was deciding which regulatory information to put on the placemats so there wouldn't be 50 different ones.

"We did this based on the most common criteria-based IRB decisions we are faced with," Vulcano says. "For example, we don't do a lot of reviews of prisoner studies, so we don't have a placemat for that."

After implementation companywide, the reports were mostly positive. When IRB members were asked whether they thought the placemats enhanced IRB discussions, 85% of IRB members said "yes."[1]

Also, Vulcano decided to not put all of the necessary information on a single placemat because it would result in very small fonts and be unreadable. Instead, the placemats contain simple, clear content with one or two themes per mat. *(See sample from an IRB placemat, this page.)*

The placemat topics include:

- establishment of a quorum and checklist for meeting minutes;
- eight criteria required to approve research;
- required elements of informed consent part 1, including 12 items;
- required elements of informed consent part 2, including 14 items;
- waiver of some or all of the elements of informed consent, waiver of documentation of informed consent, and waiver of HIPAA authorization;
- requirements of a HIPAA authorization;
- special documentation for device studies;
- humanitarian use devices (HUDs)/ humanitarian device exemption (HDE);
- de-identified data;
- "limited data-set" requirements;
- exemption from IRB review;
- expedited review (for studies of no greater than minimal risk);
- expedited review and eligibility criteria for expedited review of request for reapproval (continuing review);
- special documentation for pediatric studies.

"One day an IRB member will see the requirements of HIPAA in front of them," Vulcano says. "At the next meeting there might be a placemat with special documentation for device studies in front of them. This provides for constant reminders without the humdrum of formal and traditional didactic training, which is expensive and often not welcome."

IRB coordinators can make certain the placemats are rotated so members do not see the same placemat at consecutive meetings.

Both IRB members and staff have responded positively to the placemats, Vulcano notes.

"The only two complaints we've gotten were from one IRB coordinator who said the members spill jelly and butter on them and she has to wipe them off, and an IRB chair said members were just reading the placemat instead of paying attention during the meeting," he says. "If they're bored during meetings, I'd rather have them read the placemat than check their iPhone for messages."

REFERENCE

1. Vulcano DM. The development and acceptance of a simple tool to aid IRB compliance. Poster presented at the 2012 PRIM&R Conference, Dec. 4, 2012. ■

IRB placemats give quick look at federal rules

HCA shares its tool with others

IRB "cheat sheet" placemats provide IRB members with clear regulatory information for reference during IRB review meetings.

The idea is to give board members a simple tool that defines human subjects protection rules and terms. Since the printed material is right at their place at the table, they are more likely to refer to it than they might if it was in a book or in an electronic application, says **David Vulcano**, LCSW, MBA, CIP, RAC, AVP & responsible executive, clinical research, clinical research group, Hospital Corporation of America (HCA) in Nashville.

HCA printed 14 different placemats for each IRB. The topics refer to regulatory material that is most relevant to the institution's research mission, as well as some general research regulatory material that often poses problems during IRB discussions.

For instance, IRB members sometimes confuse the various waivers, so one placemat lists three different waivers and their criteria: the waiver of elements of informed consent, the waiver of

documentation of informed consent, and the waiver of HIPAA authorization.

"I wanted to lump those three categories together because a lot of IRBs don't appreciate the difference between the waiver of consent and the waiver of documentation of consent," Vulcano explains. "I put the waiver of HIPAA authorization on there, too, because when an investigator comes in and says he wants to waive consent, the subsequent question in the IRB's mind would be that they also have this HIPAA authorization and will the investigator want to waive that as well?"

Vulcano has shared the placemats with other IRBs upon request and offers this sample of the waiver placemat as an example of their content:

• Waiver of some or all of elements of informed consent

1. No more than minimal risk* to the subjects;

2. The waiver or alteration will not adversely affect the rights and welfare of the subjects;

3. The research could not practicably be carried out without the waiver or alteration; and

4. Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

• Waiver of documentation of informed consent

1. The only record linking the subject and the research would be the consent document, and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern; or

2. The research presents no more than minimal risk* of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.

• Waiver of HIPAA authorization

1. The use or disclosure of the PHI involves no more than minimal risk* to the privacy of individuals based on, at least, the presence of the following elements:

i. An adequate plan to protect health information identifiers from improper use and disclosure.

ii. An adequate plan to destroy identifiers at the earliest opportunity consistent with conduct of the research (absent a health or research justification for retaining them or a legal requirement to do so) and

iii. Adequate written assurances that the PHI will not be reused or disclosed to (shared with) any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of the PHI would be permitted under the Privacy Rule.

2. The research could not practicably be conducted without the waiver or alteration.

3. The research could not practicably be conducted without access to and use of the PHI.

4. Required documentation of IRB approval of waiver: The IRB must provide the principal investigator specific documentation of its approval of a HIPAA waiver. The documentation must include:

i. The name of the IRB or privacy board (not the names of individual members of the board);

ii. The date on which the waiver was approved;

iii. The signature of the IRB or privacy board chair, or other member designated by the chair;

iv. A statement that the IRB or privacy board has determined that the waiver satisfies the required criteria;

v. A brief description of the PHI that the IRB or privacy board has determined is necessary for research purposes; and

v. A statement that the waiver has been reviewed and approved under either normal or expedited review procedures and that all applicable procedures were followed.

** "Minimal risk" means the probability and magnitude of harm or discomforts anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests of healthy individuals.* ■

Do IRB meetings follow the Common Rule?

Subjective rules part of problem

Too often, IRBs spend precious meeting time debating the merits of a study's scientific

and other subjective fine points, overlooking issues that have a greater impact on human subject safety, experts say.

A recent study found that of the chief Common Rule criteria regarding items that IRBs should address, only informed consent was universally discussed at each IRB meeting. Others, including risk minimization, risk-benefit comparison, equitable subject selection, data monitoring, privacy protection, and protection of vulnerable subjects were far less consistently addressed during IRB meetings.[1]

While all IRBs talk about informed consent, the risks-benefits issue is often overlooked, says **Charles Lidz**, PhD, a research professor and sociologist in the department of psychiatry at the University of Massachusetts Medical School in Worcester.

Lidz was the lead author of a study of IRB meeting discussions at 10 academic medical centers receiving the most federal funding from the National Institutes of Health (NIH). The study found that many IRBs failed to discuss most of the Common Rule criteria.[1]

For instance, 21% of IRB reviews failed to address risk minimization, 57% made no mention of a risk-benefit comparison, and 60% did not discuss equitable subject selection.[1]

"These are institutions with enough resources that they should be able to do this well," Lidz notes.

"The broad pattern is pretty clear," Lidz says. "If you have a committee making a decision, then at least the sorts of things identified as critical should be acknowledged at the IRB meeting."

Researchers often find the IRB review process frustrating precisely because of the subjective focus of many ethics boards, says **Robert Klitzman**, MD, professor of clinical psychiatry and director of the masters and certificates in bioethics program at Columbia University in New York City.

"The IRB's mandate in the Common Rule is to make sure risks are minimized and risks are commensurate with benefits," Klitzman says.

A study's risks and benefits often are not what IRB meetings focus on, he adds.

Instead, IRBs are over-focusing on certain subjective issues at the expense of others, and this creates problems, Klitzman says.

The larger issue is that the regulations are subjective rules, and IRBs might think they are interpreting the regulations the one and only way, but they're not, he says.

"IRBs say, 'We represent our community values, so that is the way it will be interpreted,' but in fact that's not the case," Klitzman says. "You have five or six IRBs at one institution, and they'll review the same study at the same institution differently."

For example, how can an IRB say when a stipend paid to a research participant is too much and unduly influencing subjects?

"Is $100 okay, but $150 is not?" he says. "There's no hard and fast rule."

The concept of undue influence is only one of the subjective philosophical concepts IRBs encounter. There are other areas in which an IRB's misinterpretation of the regulations can lead to problems, Klitzman says.

"One area would be the quality of science," he explains. "Researchers often say IRBs are getting involved in redesigning the science of a study when they should not do that."

IRBs also could be spending an unnecessary amount of time on the details involving the informed consent document, Lidz suggests.

One IRB member who heard of the IRB meeting study's results commented, "That's exactly what we see — we spend all of our time fussing about the wording of the consent form."

While the wording is important, it also is beside the point, which should be the protection of human subjects, Lidz says.

"Whether or not the wording of the consent form follows an IRB's wording in describing what sorts of health care benefits a person might get if they are harmed is all very nice, but people don't read 18-page consent forms," he says. "I'm not sure an 18-page consent form protects anybody."

Lidz and Klitzman suggest IRBs improve their study review meetings by making these changes:

• **Use checklists to enhance and focus discussions:** Some IRBs use checklists at meetings, and some research sites have checklists built into their application forms.

An IRB coordinator and/or chair could keep a checklist on hand with the list of Common Rule criteria and help direct discussions to these areas, making sure all are at least addressed.

But in some cases, checklists are used less than optimally, Lidz notes.

In researching the study, Lidz noticed that some IRBs have checklists regarding vulnerable populations, but there would be no discussion about why some vulnerable populations were

excluded from a study, he says.

"There is a lot of discussion about various medications we study in adults, but we never know whether they work the same way for children or any other vulnerable populations, so why do we exclude them?" Lidz says.

• **Invite more specialists and experts to serve on boards:** "If I'm a cardiologist and I'm reviewing a kidney protocol, I probably don't know enough by myself to tell what the risks of the protocol were," Lidz says. "I know more than a sociologist, but these are tremendously complicated things when testing a new medical intervention."

This is why it's important for boards to have members who are experts in the areas of studies that come before the IRB.

"It would be helpful if we had a system of having reviews outsourced to highly specialized people, much like you would with a journal review," Lidz suggests. "IRBs have good people on their committees, but I still wonder if that is enough."

Small ethics boards, especially, have limited substantive expertise to handle questions of risks, he adds.

• **Recognize the subjectivity of IRBs' decisions:** "IRBs need to become more aware that what they're doing is subjective," Klitzman says. "They need to be open to the fact that others might see what an IRB decides differently than what they see, and other views might be legitimate."

Just as a literature student might interpret the novel *War and Peace* differently from another literature student, one IRB's interpretation of undue influence might not match another board's interpretation, he adds.

• **Create industry-accepted guidelines for interpretation of regulations:** The Office of Human Research Protections (OHRP) or a professional human subjects research organization need to create a set of guidelines for interpretation of the regulations, Klitzman suggests.

If IRBs had guidelines as a reference, they could make less subjective decisions about whether a particular protocol's informed consent is adequate, and this would help create a more consistent and fair study review process, he explains.

"We know there are huge problems with how IRB reviews vary, and that holds up multisite studies," Klitzman says. "There should be a consensus."

REFERENCE

1. Lidz CW, Appelbaum PS, Arnold R, et al. How closely do institutional review boards follow the Common Rule? *Acad Med*. 2012;87:1-5. ■

Handling incidental findings in genomic research

Biobanks face particular challenges

An issue that can frequently arise in the area of genomic research is what to do with incidental findings (IFs) — discoveries concerning a research subject that are beyond the scope of the study, but could have potential health importance for the subject. The findings can arise during the collection or analysis of research data, such as unexpected discoveries in neuroimaging (such as a mass or aneurysm) or genetic studies (unexpected genetic variation).

The debate, says **Jeffrey Kahn**, PhD, MPH, lies in whether to disclose the incidental findings, and which are appropriate to disclose. "The key question is whether the results are clinically meaningful," says Kahn, Levi Professor of Bioethics and Public Policy, Johns Hopkins Berman Institute of Bioethics in Baltimore.

Reports state that incidental findings occur in 13-40% of research MRI subjects and up to 84% of scans, Kahn says.

Questions that researchers will encounter with incidental findings include: What should researchers do when they encounter IFs? With whom should researchers consult? What, if anything, should be disclosed? What should the researcher tell that subject? "There is almost no way to do this in a way that won't worry them [the subjects] a lot," Kahn says. As far as disclosing IFs that are not life-threatening or clinically significant, "you may be creating more morbidity than you help treat," he says. For example, a study subject could end up undergoing unnecessary surgery due to an incidental finding, and would have to then deal with associated risks and recovery of the surgery.

There is a proposed duty of reciprocity to subjects, that "they put themselves in harm's

way for science, so we give them a little bit to compensate for it," Kahn says. "Some would argue that we owe them [subjects] more than that and if something is incidental, we would tell them and do something about it."

Biobank challenges

Biobanks face particular challenges with incidental findings, Kahn says. "Advancing technologies will increase incidental findings — stronger magnets in imaging and longer DNA strands will make things worse," he says. "Researchers and biobanks should establish a pathway for handling suspected IFs. IRBs and biobanks should oversee compliance with IF-related obligations. Guidance should be developed by funders as part of research guidance."

The four key responsibilities of biobanks are referred to as CARR:

— **Clarify** the criteria to determine what kinds of findings are returnable, and the roster of returnable IFs and individual research results.

— **Analyze** the finding to decide whether it should be offered to the individual contributor.

— **Re-identify** the contributor.

— **Re-contact** the contributor and offer the finding along with genetic counseling or other appropriate counseling.

Researchers should establish a pathway for handling suspected incidental findings, and IRBs should oversee compliance with the guidelines, Kahn suggests. Consent forms and study protocols should include a section on IFs and what researchers intend to do if any are discovered. "Whatever the answer is, tell them [the IRB] what you're going to do, and tell the subjects as well." There should also be language detailing how IFs will be handled if discovered in reanalysis of archived patient samples. ■

CNE/CME OBJECTIVES & INSTRUCTIONS

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

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

Physicians and nurses participate in this continuing education program and earn credit for this activity by following these instructions.

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

COMING IN FUTURE MONTHS

■ The lowdown on FDA's new draft guidance

■ Community engagement's role is evolving in HRP

■ Collaboration is new buzzword among institutional IRBs

■ Finding flexibility in regulations

CNE/CME QUESTIONS

1. According to Sergio Litewka, MD, MPH, international director, University of Miami Ethics Programs and CITI Program, an issue with "ethical imperialism" is whether it is ethical to accept moral values exclusively related to cultural norms or habits, even when it might harm other groups.
   A. True
   B. False

2. Which of the following is a potential benefit to having a satellite IRB office staffed to meet individually with investigators to answer questions?
   A. The trained IRB specialists could handle expedited reviews.
   B. Trained IRB staff could help investigators complete applications correctly.
   C. Having available in-person helps foster collaboration and transparency.
   D. All of the above

3. Which item below is related to waiver of documentation of informed consent?
   A. No more than minimal risk to the subjects
   B. The waiver or alteration will not adversely affect the rights and welfare of the subjects.
   C. The research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.
   D. The research could not practicably be carried out without the waiver or alteration.

4. In a recent study of IRB meetings and how often they discussed the criteria listed in the Common Rule, which of the following was the item that IRBs most often failed to discuss?
   A. Risk minimization
   B. Risk-benefit comparison
   C. Equitable subject selection
   D. Informed consent