IRB ADVISOR

Your Practical Guide To Institutional Review Board Management

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IRBs may be less effective if policies fail to address psychological dynamics

Credentials and personality should be weighed

IRBs are no different from other boards in how their psychological structure could lead to personality clashes and conflicts. However, unlike many organizations, when IRBs ignore such conflicts, the outcome might be a less-effective human subjects protection program or regulatory problems.

"I think, traditionally, IRBs have power differentials that we need to pay attention to," says **Mary Faith Marshall**, PhD, director of the Institute for Bioethics Law and Policy at Kansas University Medical Center in Kansas City.

"One thing that happens quite frequently is that there may be people who dominate the conversation at the table and/or jump in and interrupt other people while they're speaking," she says. "And the chair and their colleagues need to meet that issue head-on and stop that person."

While IRBs primarily function as highly organized and structured organizations with clear agendas, there also is a psychological aspect that comes into play. IRBs primarily comprise members who have worked together and with investigators in a variety of ways and are from the same types of backgrounds and experiences, says **Gerald Mozdzierz**, PhD, who is retired as the chief senior manager of psychology service at Hines (IL) VA Hospital and professor of psychiatry and behavioral neurosciences at Loyola University Stritch School of Medicine in Maywood, IL.

This dynamic that exists between IRB members and investigators can lead to psychological conflicts that impact IRB deliberation on protocols, he says.

Subtle influences

"It's a low probability, but potentially high impact when psychodynamics influence in subtle ways the outcomes of IRB proceedings," Mozdzierz says. "That is where IRB chairs can play a more active part in being sensitive to and monitoring the group for the kinds of comments

that are made."

Take, as an example, this psychological dynamic that he observed: An IRB was discussing a protocol submitted by a professor/investigator who had proposed using students as research subjects. One member of the IRB said if the investigator recruited subjects from among the professor's own students, then this would be a potential conflict of interest. Another IRB member, who knew the investigator personally, made an off-the-cuff remark that called the other IRB member's motivations into question and sullied that member's character in an attempt to verbally bully the IRB into deciding in favor of the investigator's recruitment tactics.

The IRB chair did not react to the verbal exchange, even when the same derisive comment was repeated, and the IRB discussion was chilled by the shock other members experienced from the bullying remarks, Mozdzierz notes.

In a subsequent meeting, the IRB member who had questioned the potential conflict of interest returned to the subject, and eventually it was decided that the investigator would have to change recruitment tactics and closely follow the principles of research ethics, he says.

However, the psychological damage to the group dynamics had already occurred. Even if the individual who had been singled out for the verbal bullying chose to continue to make comments in the future, there likely would be less free exchange among other members who would be inhibited by the prospect of being criticized and singled out during IRB discussions, Mozdzierz notes.

Attitude adjustment

"There are other dynamics where people raise their voices or pound the table, and these all are power tactics that can be employed," he says. "Physicians in hospital settings are accustomed to getting their way — they need to write orders and have those orders followed — which is in most cases the appropriate thing to do."

When that same attitude is transferred to an IRB setting, problems may occur because the IRB is supposed to be composed of individuals who share an equal responsibility in the protection of human subjects, and one member's status or experience should not trump another member's concerns or opinion, Mozdzierz says.

Community members, who already may feel intimidated by the professional stature of other IRB members, could be vulnerable to being silenced by power tactics.

Marshall also has witnessed verbal bullying at IRB meetings.

"It's quite often from medical-science folks who have a very narrow perspective of the research itself or of the scientific questions, and

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Editorial Questions

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they aren't open to hearing other things or other questions," Marshall says. "Comments are made like it's the final word."

For this reason, Marshall recommends that IRBs have a minimum of 25% of their membership composed of community members.

"There needs to be more than one community member, and ideally a minimum — if not more — of 25%," Marshall says. "I'd like to see a co-chair who is one of the community members, and we need to train IRB chairs to be more cognizant in bringing out the community member's voice."

Chairs set the course

The IRB chair also has a responsibility in making certain an IRB meeting is conducted with respect for all members and their comments, Marshall notes.

"I think there should be some education through PRIM&R [Public Responsibility in Medicine & Research] or guidelines by OHRP that speak to the training of IRB chairs in the dynamics of committee leadership," she says.

"The chair needs to focus on bringing out the community members' voice to make certain these members are called upon and their contributions aren't minimized by other people at the table and that they're taken seriously," Marshall says. "The community representatives bring important perspectives to the table that no one else has, and this perspective too often is marginalized or not paid attention to in a serious way."

IRB chairs have a responsibility to make certain discussions do not turn into power plays, and one way to do this is for the chair to call a person out of order when a personal and derisive comment is made, Mozdzierz suggests.

"IRB chairs need some training in the subtle overuse of power, and they need more familiarity with the Robert's Rules of Order, as well as exposure to cultural diversity," he says. "As society becomes more culturally diverse, it makes sense for people to know that people who come from different cultures may express themselves in different ways."

At the beginning of each IRB meeting, the chair could remind members about privacy rules and remind them that the public funds most research and because the research ultimately will affect everyone, then the public voice is very important, Marshall suggests.

"The chair could remind members to be respectful of the beliefs of everyone else at the table and that they need to be respectful of each other as colleagues, as far as not interrupting, and to be respectful in how they couch their remarks," she adds. "People can and should disagree — that's the whole idea, but they need to be respectful in how they put their ideas forward."

For instance, when one member cuts off the remarks of another member, then the chair could intercede by saying, "So and so is speaking, and let's not interrupt," Marshall says.

Or another way to handle the situation is for the chair to say, "I'm really interested in what Jane Community Member has to say," she adds. "Part of this may be gender related because we know from research that men tend to dominate conversations and interrupt, and women let them do that."

The key is to address the situation immediately and stop the interruption at once, Marshall says. "Let them know these sorts of dynamics can't or shouldn't happen."

If an IRB member consistently violates these norms, then the chair should take an active role in telling the member that the behavior needs to be corrected and in offering the person help in doing so, or the chair should ask the person to leave because the behavior cannot be tolerated, Marshall says. ■

Special Report: Regulations and Rules — Are We Heading in the Right Direction?

Improving consent form should be top priority

Think outside the box and go beyond regs

(Editor's note: IRB Advisor *asked IRB and human subjects protection experts from across the nation to discuss the state of human subjects protection regulations and how IRBs are interpreting federal requirements. In this issue, we discuss how IRBs and institutions can improve the informed consent process.)*

If someone wants to show how IRBs and research programs have become burdened with documentation and requirements that provide no additional quality to the process of protecting subjects, then the informed consent document is Exhibit A,

experts suggest.

"Informed consent documents used to be in the range of two or three pages," says **Bernard Schwetz**, DVM, PhD, director of the Office for Human Research Protections (OHRP).

"Now the documents are up to 10 pages or more," he says. "There are informed consent documents over 100 pages and, as people have commented, the reason you have an additional 90 pages more than what it used to be is for protecting institutions — not subjects."

While it'd be nice to return to the two-page consent forms, it might not be possible under the current regulations, says **Robert M. Nelson**, MD, PhD, associate professor of anesthesia and pediatrics at the Children's Hospital of Philadelphia.

"I would challenge [Bernard Schwetz] to take the elements in the federal regulations and put them on two pages," he says.

There is no easy answer to reducing unnecessary burdens, including the lengthy informed consent forms, Schwetz notes.

"That's one of the reasons I'm trying to bring more people to the table to talk about the function of the enterprise," he says.

Such discussions in the past usually involved IRB members, but now it's important to bring many different parties to the table, including investigators, lawyers, research executives, and others, Schwetz says.

"I'm trying to bring a broader range of people to the table so that when we're talking about burdens we don't just point fingers at the people who are not at the table," he says. "I've sought these people out, group by group, and have talked with them about my concern for the future success of the research enterprise."

Slowly, this communication process is building bridges that may lead to better human subjects protection within an environment that is less burdensome with regard to rules and regulations, Schwetz says.

Getting a new box

In some ways, perhaps the entire informed consent process needs a radical change, Nelson proposes.

"I agree that consent forms are too long and impossible to understand, and many studies have documented that," he says. "But the more fundamental question is: What do we hope to achieve by the consent process?"

Thinking outside the box, perhaps a solution would be to create a different sort of measure showing the adequacy of the informed consent process, Nelson suggests.

"Would we be willing to tell investigators, 'We won't look at your consent form, but we will check with your participants, and let's see how much they understand of what's going on?'" he says. "We could look at the outcomes and not spend as much time on the informed consent document."

This type of outcomes-based monitoring would be similar to what has happened in other fields, including the health care industry, Nelson notes.

"Third-party payers will relieve institutions from regulations if they meet certain guidelines, such as relieving someone of having to obtain prior authorization if they are able to discharge a patient within a certain period of time," he explains. "So are we willing to move toward that system where we relieve people of the upfront paperwork and instead use outcomes measures?"

For example, IRBs could conduct random audits and interviews of research subjects to ascertain how well they understand the research and their own participation in it.

"If the audit is random then you're replacing an upfront review process with a back-end, random auditing process," Nelson says.

Since IRBs would have to spend less time on the upfront review process, they might have more time for a critical analysis of a protocol's risks, he adds.

Form and process separate

If IRB members want to monitor a study's consent process in addition to reviewing the informed consent document, then they may do so under the current regulations, says **Steven Peckman**, associate director for human subjects research at the Office for Protection of Research Subjects at the University of California-Los Angeles.

Peckman says he agrees with Nelson that IRBs should spend more time looking at the process of the informed consent communication because that is more important than the actual informed consent document.

"There is a place to monitor the consent document to make sure it all works, but the document is not the process," Peckman says. "And we're going down a dangerous road if we think the document is the process when in my mind the document should serve as a summary or outline of what needs to be discussed with the subject."

True informed consent occurs during the process

of an investigator and subject discussing the study, while the informed consent document explains what is discussed in a specific way, Peckman adds.

"The key word is 'process,'" says **Mark Hochhauser**, PhD, readability consultant and an IRB member at the IRB at North Memorial Healthcare in Robbinsdale, MN.

"Many IRBs focus way too much time on consent forms as a piece of paper, and there's not enough time devoted to the consent process of the research staff," he says. "IRBs can't be the consent process police; they don't have the money or staff to sit in and observe what's going on and make suggestions during the process."

Instead, the question is "Why can't multibillion-dollar drug companies write a consent form that's understandable?" Hochhauser asks. "It would be nice that instead of having a panel of us folks at the IRBs and those who are interested in language rewrite consent forms to have a representative from the drug company write consent forms that could be understood," Hochhauser adds. **(See story on improving lengthy, complex consent forms, p. 78.)**

Who will pay?

While it's a good idea to have IRBs monitor the informed consent process, this is a costly addition to the IRB's duties, and who would pay for it? asks **Felix A. Khin-Maung-Gyi**, PharmD, MBA, CIP, chief executive officer of Chesapeake Research Review Inc. of Columbia, MD, and senior policy fellow with the Center for Drugs and Public Policy at the University of Maryland in Baltimore.

"The ability of the IRB to interact with subjects in the informed consent process would be tremendously valuable, but at the present time I don't know of any IRB that has the resources to do those things," he says.

"Informed consent and decision making are things that require time and effort, and that has to be factored into the cost of doing business," Khin-Maung-Gyi adds.

Both industry-sponsored research and federally funded research fail to provide adequate funding for this level of quality in IRB oversight, and so there are not enough resources to address these issues, he says.

The most important part of the informed consent process is not readily accessible to an audit, notes **Dale Hammerschmidt**, MD, FACP, associate professor of medicine at the University of Minnesota Medical School in Minneapolis.

For instance, the IRB has no control over the actual consent encounter between the principal investigator and the subject, he says.

"The other thing is the consent he may be the only retrospective document the person has to look at a month later when trying to recall something, so it remains important that it be a good document, even if it is a small part of the process," he says.

"It's a unique quality to human life that you devote a lot of energy to tasks you can accomplish rather than to the ones you wish you could accomplish," Hammerschmidt notes.

Focus on the document

Improving the informed consent process is an issue that also concerns the Secretary's Advisory Committee on Human Research Protection (SACHRP) for the U.S. Department of Health and Human Services, says **Ernest Prentice**, PhD, chair of SACHRP and an associate vice chancellor for academic affairs at the University of Nebraska Medical Center in Omaha.

"Many IRBs are requiring some kind of description of the process of consent in forms, but they don't pay as much attention to the process as they should," he says. "What they do is concentrate on the consent document, dotting all i's, crossing all t's and simplifying the language."

SACHRP members have discussed alternatives, including educating investigators about how to obtain valid and informed consent and then doing quality outcome assessments, Prentice says.

But to change federal regulations to permit IRBs to forgo review of informed consent documents in exchange for providing random audits of the informed consent process, as Nelson proposes, would not be feasible, he adds.

Changing regulations is an onerous process, Prentice notes.

"In 1991, you had 17 agencies sign on to the Common Rule, and to change the Common Rule you have to get all of these agencies to agree," he explains. "The fact that we got 17 agencies to agree is remarkable — it will never happen again."

The solution is not in revising the Common Rule and regulations, but in making OHRP and the Food and Drug Administration give IRBs clear guidance as to what their expectations are, Prentice says. ■

What can be done about the unwieldy consent form?

First step: Revise sponsors' documents

Ask most critics of the modern informed consent document what the biggest problem is, and they'll say investigators rely too heavily on the sponsor's cumbersome informed consent form.

"When informed consent comes from the sponsor, it isn't all that readable," says **Steve Joffe**, MD, an attending physician at the Dana-Farber Cancer Institute and the Children's Hospital, both located in Boston.

Then the IRB is put into the position of negotiating how phrases will be changed, he says.

"The consent form is the IRB's document, but the sponsor may say, 'If you're not willing to include this language, this disclaimer, then we won't open the trial at your institution,'" Joffe explains. "Then the IRB can think of creative ways to put it in there without distracting from the message they want to convey in the consent form."

Since drug and device companies want to avoid lawsuits, they take the easy route of lifting language from the *Federal Register* and putting it into the consent form, says **Mark Hochhauser**, PhD, a readability consultant and a member of the IRB at North Memorial Healthcare in Robbinsdale, MN.

"They want to be compliant even if it means no one can understand what they are writing," he explains. "Everyone wants to protect themselves from being sued, and they don't really care whether someone understood them or not, and yet when they are sued it's often because the language is ambiguous, and people didn't understand what they meant."

At most academic health science centers, the investigator takes the sponsor's model consent document and converts it into a format that the IRB has adopted, says **Ernest Prentice**, PhD, associate vice chancellor for academic affairs at the University of Nebraska Medical Center in Omaha. He also is the chair of the Secretary's Advisory Committee on Human Research Protection for the U.S. Department of Health and Human Services.

It's important to make certain the IRB's format is as clear and readable as possible, Prentice and the other experts say.

Here are some of their tips on improving the informed consent document:

- **The key is to simplify the language and design the format.** This is not as easy a process as running the consent document through a software program that is scaled for a particular reading level, Hochhauser says.

"People assume that if you write something at a statistical eighth-grade level that anyone with an eighth-grade education will be able to understand it," he says. "People who assume this don't understand readability and reading skills and how they develop."

Studies have shown that when a document written at college level is rewritten to a lower grade level, there is some improvement in comprehension, but it's only a small improvement, Hochhauser notes.

"It's maybe a 10%-15% improvement in understanding," he says. "So it's not a panacea to get it down to an eighth-grade reading level."

One strategy IRBs might employ is having a junior high school English teacher on the committee that writes the consent document, Hochhauser suggests.

"I'd like to see a private accrediting agency give awards for a particularly good consent form," he adds. "I'd like to see the whole simplified consent form on-line so people could see what it looks like."

Equally important is the consent form's design. It should be designed with the same sort of eye-catching features used in marketing materials, Hochhauser suggests.

Documents could use bold-faced words and italics, along with different font styles and sizes to emphasize key points, he says.

Consent forms also could feature a glossary and graphics, and they could include blank space for subjects to write notes or questions.

"There is no reason why a consent form couldn't look more like a newsletter," Hochhauser says. "There are all kinds of document design features that could make the consent form a much more appealing form that someone might actually want to read."

- **Create a template for use by investigators.** IRBs could create a template that uses standardized subheadings that identify the consent elements and are placed in a standard sequence, Prentice suggests.

"For example, don't talk about benefits before discussing risks; don't allow first-person narrative, don't allow a mixture of elements, and don't throw in procedures with the risks," he explains.

Sponsor-written consent documents have boilerplate language on confidentiality and compensation

Checklist for Easy-to-Read Informed Consent Documents Text

- ☐ Words are familiar to the reader. Any scientific, medical, or legal words are defined clearly.
- ☐ Words and terminology are consistent throughout the document.
- ☐ Sentences are short, simple, and direct.
- ☐ Line length is limited to 30-50 characters and spaces.
- ☐ Paragraphs are short. Convey one idea per paragraph.
- ☐ Verbs are in active voice (i.e., the subject is the doer of the act).
- ☐ Personal pronouns are used to increase personal identification.
- ☐ Each idea is clear and logically sequenced (according to audience logic).
- ☐ Important points are highlighted.
- ☐ Study purpose is presented early in the text.
- ☐ Titles, subtitles, and other headers help to clarify organization of text.
- ☐ Headers are simple and close to text.
- ☐ Underline, bold, or boxes (rather than all caps or italics) give emphasis.
- ☐ Layout balances white space with words and graphics.
- ☐ Left margins are justified. Right margins are ragged.
- ☐ Upper and lower case letters are used.
- ☐ Style of print is easy to read.
- ☐ Type size is at least 12 point.
- ☐ Readability analysis is done to determine reading level (should be eighth grade or lower).
- ☐ Avoid:
  - — Abbreviations and acronyms.
  - — Large blocks of print.
  - — Words containing more than three syllables (where possible).

Graphics

- ☐ Helpful in explaining the text.
- ☐ Easy to understand.
- ☐ Meaningful to the audience.
- ☐ Appropriately located; text and graphics go together.
- ☐ Simple and uncluttered.
- ☐ Images reflect cultural context.
- ☐ Visuals have captions.
- ☐ Each visual is directly related to one message.
- ☐ Cues, such as circles or arrows, point out key information.
- ☐ Colors, when used, are appealing to the audience.
- ☐ Avoid graphics that won't reproduce well.

Source: National Cancer Institute, Bethesda, MD.

for injury, so the investigator's job is to take this unwieldy consent form and revise it to fit the IRB's template, Prentice says.

"Don't use the sponsor's language," he adds. "Sponsors occasionally will discuss with us the inclusion of certain language, and sometimes we agree, and sometimes we don't agree."

A well-written consent form can make a difference in how well subjects understand the research process, Joffe says.

The National Cancer Institute (NCI) recently updated its booklet on consent documents. It addressed clarity, readability, and the use of standard language. **(See table, above.)**

"What happened was our hospital was going along using the old consent form with its one- or two-word titles, dense paragraphs, and then the NCI recommendations came out, and we flipped over to using a new template with all new consent forms," Joffe recalls. "We had studies with the older consent forms and studies with newer consent forms, and we compared those subjects."

Evidence showed that subjects who were given the new consent forms demonstrated better understanding of the clinical trials, he says.[1]

• **Give subjects time to think about the study and consent process.** "It makes a difference to delay the consent decision and to give people

time to think about the decisions they're making, particularly for more complicated studies," Joffe says. "If you ask them right then to make a decision, they won't understand as well as if you told them to go home and return to talk about it in a few days."

This extra time to consider and think is crucial to a person's comprehension, he says.

"In our study, we asked people, 'Did you sign the consent form right then, or did it take a day or two to think about it?'" Joffe says. "One quarter of the people signed right then and there, and those who signed in the moment didn't understand as well as those who took time to think about it."

Reference

1. Joffe S, Cook EF, Cleary PD, et al. Quality of informed consent in cancer clinical trials: A cross-sectional survey. *Lancet* 2001; 358:1,772-1,777. ■

Expedited reviews call for same due diligence

OHRP official offers guidance on process

IRB members and others in the research community sometimes have misconceptions about the use of the expedited review process, including the idea that an expedited review is different from a review by the full IRB.

"The standards of review are unchanged," says **Glen Drew**, MS, JD, health policy analyst with the Office for Human Research Protections (OHRP) in Rockville, MD.

The expedited review process is not intended to be seen as IRB-light, he says.

"The study needs to have risks minimized and risks balanced with potential benefits and informed consent," Drew explains. "The only difference is that the review can be conducted by one or more members of the IRB without the requirement for there to be a convened meeting of the IRB."

An expedited review only can occur with a study that presents with no more than minimum risk to subjects and which involves only the procedures included in the list of categories that are qualified for the expedited review, he states.

Studies do not qualify for expedited review if the study could result in the identification of subjects whose participation would place that at risk for criminal or civil liability. Likewise, studies cannot be stigmatizing or damaging to the reputation, and the expedited review process may not be used for classified research involving human subjects. Such research would require a full board review, Drew says.

The first seven expedited review categories apply to both initial reviews and continuing reviews. Then there are two more categories that apply only for continuing review of research previously approved.

The nine categories are as follows:

• **Category 1 - Clinical studies of drugs and medical devices only when two conditions are met.** Condition A pertains to research on drugs for which an investigational new drug (IND) application is not required, Drew says.

"Research on marketed drugs that increases risk or decreases the acceptability of risk is not eligible for expedited review," he explains.

For example, if a study involves a drug that does not require an IND, but which will be investigated with a different route of administration, such as being administered orally instead of intravenously, would not be eligible for Category 1 because it would alter the risks or change the balance of risks, Drew says.

Condition B is for medical devices for which an investigational device exemption is not required or for medical devices that have been approved for marketing and are used in accordance with their approved labeling.

• **Category 2 - Blood samples, heel stick, venipuncture, hand stick of health adults.** With this expedited review category, subjects can have up to 550 mL drawn in an eight-week period, but they cannot have blood collected more than twice a week, even if these are small amounts. For other adults, as well as for pregnant women and children, investigators have to work in consideration of their age, height, health, and weight. The method of blood collecting and frequency will have an upper limit of not exceeding the lesser of 50 mL or 3 mL/kg in an eight-week period and not have these collected more than twice a week, Drew says.

"So if you're doing a study that includes collecting blood from an infant three times a week, the study can be done, but it has to be reviewed by the convened IRB," he explains. "There is a 110-pound minimum for healthy, nonpregnant adults."

Also, if a study includes one of the categories of collection of blood samples, but also includes an X-ray of some part of the body, it would not qualify for exemption because it would include

procedures that quality and some that do not qualify, Drew says.

• **Category 3 - Prospective collection of biological specimens for research purposes by noninvasive means.** These specimens may include hair, nail clippings, deciduous teeth at the time of exfoliation and if patient care indicates need for extraction, and external secretions including sweat, he says.

Amniotic fluid could be obtained at the time of the rupture of the membrane, during labor, but at any other time it would require full board review, Drew adds.

The collection of hair and nail clippings must be done in a nondisfiguring manner. For example, if the study included the cut of a fingernail past the section that has grown out, then it would not be eligible for Category 3, he says.

• **Category 4 - Collection of data through noninvasive procedures, not including anesthesia.** This category specifically excludes X-rays and microwaves, as well as excluding medical devices that have not been approved for marketing and studies that involve studying safety and efficacy of devices, Drew says.

The category does apply to physical sensors applied to the surface of the body or at a distance, and it does not involve the input of energy into the body or invading a person's privacy, he says.

"Weighing a subject or testing for sensory acuity, doing a vision examination, and looking down the room at a classic eye chart would qualify for expedited review," Drew says.

Other tests that would qualify include electrocardiography and electroencephalography, ultrasound, diagnostic infrared imaging, thermography, detection of naturally occurring radioactivity, and electroretinography, he notes.

Also included are moderate exercise and muscular strength testing, body composition assessment, and flexibility testing.

"I would think that moderate exercise in patients with congestive heart failure would require a full review if they're done for research purposes and not to assess the individual's need for medical care," Drew says.

• **Category 5 - Research involving materials, data, records, documents, or specimens that will or have been collected for nonresearch purposes, such as medical treatment or diagnosis.** "This refers only to research that is not exempt," he says.

An example for this category would be if patients were given X-rays for diagnostic purposes and a research proposal would look at those X-rays, Drew says.

"You can do an expedited review procedure on a study of X-rays taken for treatment or diagnostic purposes," he adds.

• **Category 6 - A collection of data from voice, video, or imaging recordings made for research purposes.** "In essence, if these are made for nonresearch purposes, you could do an expedited review under Category 5 or have it considered exempt," Drew explains. "If it's just for research, like a study on accents in the United States or some stress analysis of voices of people in mock job interviews, then it's a Category 6."

• **Category 7 - Research on individual or group characteristics or behavior.** This includes, but is not limited to, research on perception, motivation, identity, language, communication, cultural beliefs or practices, and social behavior.

This also could include research employing survey interviews, oral history, focus groups, human factors, or quality assurance methodologies, Drew says.

"Some of this research may be exempt from Health and Human Services regulations, and this research list only applies to research that is not exempt," he says.

An example of a Category 7 expedited review study would be death rituals of a subculture, Drew says.

Category 7 might not be used as much as it should be, he notes.

"Certainly there are institutions that don't utilize expedited review procedures at all for any research, whether it would qualify or not," Drew says. "They made an institutional decision."

• **Category 8 - Research previously approved by a convened IRB.** This category applies to research that was not reviewed by expedited procedures at initial or continuing reviews, he says.

The first part is for research that is permanently closed to enrollment of new subjects and all subjects have completed research interventions, Drew says.

"Research remains active only for long-term follow-up of subjects," he says. "That's one type that would qualify for expedited continuing review, even if reviewed by a convened IRB previously."

Category 8 is the only expedited review category where research that is of greater than minimal risk can be reviewed under expedited review procedures, Drew says.

And the second part applies to studies in which no subjects have been enrolled and no additional risks have been identified, he says.

"These are studies in which you have a study

open, but no subject presents for over a year, and there is no one exposed to risk and no new risk has been identified," Drew says.

The third part applies to research activities that are limited to data analysis, he adds.

• **Category 9 - Research of relevance to the Food and Drug Administration.** This category applies to the continuing review of research that is not the investigation of a new drug or device, but which does not apply to the other categories, Drew says.

"This is a study where for some reason it did not fall within the prior categories and had been required to be reviewed by the convened IRB, but in that review the IRB found that the research was of no greater than minimal risk, and there's been no change in risk profile," he explains. "This can occur only after there has been a convened meeting at a previous review." ■

SPOTLIGHT ON COMPLIANCE

Who pays when trial subjects are injured?

Institutions need to develop own policy

By **J. Mark Waxman**, JD
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A basic tenet of research involving human subjects is those who agree to be participate must give their informed consent after being informed about the known and *unknown* risks inherent in their participation. One category of risk is the possibility of injury. The scope of potential injuries is broad, ranging from injury while en route to the hospital for a follow-up interview or test to a reaction to the study drug. Additionally, an adverse result from an unforeseen psychological trauma could occur.

In each example, there would likely be no fault that might be assessed against the institution or principle investigator (PI) conducting the trial. Yet, the question arises, who should bear the risks of those injuries and, in turn, the resultant costs?

On this issue, the rules regarding informed consent are nonexistent. Other than mandating that the risks and benefits of treatment be assessed, there is little guidance for IRBs and institutions grappling with this problem. Other source documents offer some additional guidance in framing the issue, but little help in resolving it. The Belmont Report, for example, does reference the notion of "distributive justice" in the sense of avoiding unjust distribution of the burdens and benefits of research. It also notes that in making a risk/benefit assessment, "economic harm" should be addressed. There is not, however, a specific reference to research related injuries, or how their costs might be borne as a result of the devised consideration.

How then can an IRB and an institution approach this problem? First, we can simply list the potentially involved parties — the patient; the institution; the PI; the sponsor; any other trial funder; the potential commercial beneficiary of the research; or, where otherwise qualifying, the taxpayer through Medicare or Medicaid program support; or the private insurers.

Second, we might consider who within this group could, would, or should have insurance to help spread the risk among a larger group. In the ordinary course, an institution would not have insurance to cover the costs of a research-related injury that required care and treatment — for example, for an unanticipated adverse side effect. On the other hand, in some cases Medicare may help. Under its National Coverage Determination (NCD), Medicare will cover "reasonable and necessary" items and services used to diagnose and treat "complications" arising from participation in clinical trials. Whether commercial carriers will offer similar coverage will require a careful review of the specific terms and conditions of coverage.

In this regard, some state laws specifically mandate coverage in a variety of instances. For example, in Massachusetts, the law provides that defined patient care services provided as a part of a "qualified clinical trial" (e.g., one intended to treat a diagnosed cancer) must be covered and reimbursed.[1]

Different institutions will address these issues differently, and there is a range of possible outcomes. Some have adopted rules that require, without exception, that commercial sponsors to indemnify the institution and the patients against the costs. On the other hand, the institution itself will bear the costs of governmentally or institutionally sponsored trials. The theory for this

result is twofold — the commercial sponsor likely has (or should have) the necessary insurance as a cost of doing business, and that the commercial sponsor has the most to gain directly in a commercial sense from the conduct of the trial. At the extreme, a number of institutions have chosen to simply state that the trial participant is on their own — e.g., "there is no commitment to provide monetary compensation or free medical care to you in the event of a study-related injury." Or stronger, "The institution assumes no obligation to pay any money or provide free medical care in case this project results in any harm to me . . . . The costs may include medical treatments, laboratory test, and a possible stay in the hospital. I understand that the exact cost cannot be determined at this time since any harm to me would be unforeseen. My insurance company may not pay for such treatments, in which case payment of costs will be my responsibility . . ."

Other approaches might distinguish between the various injuries that might occur. For example, in South Africa, the policy in the area provides, among other things, that "compensation should only be paid in the more serious injury of an enduring or disabling character (including exacerbation of an existing condition) and not for temporary pain or discomfort or less serious or curable complaints."[2]

One choice to be made is whether billing of available third-party insurance will be required. If this occurs, in a macro sense, the cost of injury are borne by the patients. In the more specific case, it means that the deductible and copayments are borne by the patient. Indeed, were there amounts to be forgiven, there is a risk that the insurance would not be extended to cover the injury costs at all.

In the end, each institution must reach its own conclusions on the issues presented in this area. That should involve a review of its own policies, its view of the ethics of each presented situation, the likelihood of serious injury and other relevant factors. Whatever the result of that process, the conclusion should be explained to the participant to ensure the informed consent process includes this important element.

References

1. Mass Gen. Laws, Ch.175 §110L.
2. Guidelines for Medical Experiments In Non-Patient Human Volunteers, Association of British Pharmaceutical Industry. Web site: www.sahealthinfo.org/ethics/book1appen4.htm; March 1988, as amended May 1990. ■

House subcommittee probes consulting fees

Drug and biotech companies that have paid government scientists for consulting services soon will receive a request from a House subcommittee to voluntarily release financial details of such agreements.

Since scientists at the National Institutes of Health (NIH) have been reluctant to disclose details of their financial contracts with the private industry, the House Energy and Commerce Subcommittee on Oversight and Investigations will go directly to the industry for the information, Rep. **James Greenwood** (R-PA), subcommittee chairman, said during a recent hearing.

Under current policies established in 1995 by former NIH director Harold Varmus, there is no limit on the amount of compensation or the number of hours that NIH scientists can be paid for outside consulting with drug or biotechnology companies. Furthermore, the government does not require scientists to disclose what they are paid. (Other government departments operate under similar rules. The subcommittee will investigate those departments as well.)

Lawmakers on both sides of the aisle are looking to tighten those rules for the sake of the NIH's integrity. Rep. Joe Barton (R-TX), chairman of the House Energy and Commerce Committee, said the American public needs to be assured that NIH research grants are awarded based on merit and not because a scientist received a monetary award.

According to figures released in May, 117 NIH scientists (out of 17,000 NIH employees) are under consulting contracts with private firms. ■

COMING IN FUTURE MONTHS

- Experts suggest a certification process for investigators
- Providing conditional IRB approval can be sticky issue
- International research and IRBs
- Web-based IRB education

CE/CME objectives

For more information on this program, contact customer service at (800) 688-2421; e-mail: customerservice@ahcpub.com.

The CE/CME objectives for *IRB Advisor* are to help physicians, nurses, and other participants be able to:

- **establish** clinical trial programs using accepted ethical principles for human subject protection;
- **describe** the regulatory qualifications regarding human subject research;
- **comply** with the necessary educational requirements regarding informed consent and human subject research;
- **apply** the necessary safeguards for patient recruitment, follow-up, and reporting of findings for human subject research;
- **explain** the potential for conflict of financial interests involving human subject research;
- **discuss** reporting adverse events during research. ■

CE/CME *questions*

Physicians, nurses, and others participate in this continuing education program by reading the article, using the provided references for further research, and studying the questions at the end of the issue. Participants should select what they believe to be the correct answers, then refer to the list of correct answers to test their knowledge. To clarify confusion surrounding any questions answered incorrectly, please consult the source material. After completing this activity at the end of each semester, you must complete the evaluation form provided and return it in the reply envelope provided to receive a certificate of completion. When your evaluation is received, a certificate will be mailed to you.

1. Some experts say that IRBs have a responsibility to understand group psychological dynamics to prevent verbal power tactics, such as bullying and intimidation. Why are understanding and some training in this important for IRB members and chairs?

A. An academic or medical member of an IRB could use his/her professional authority to inhibit the expression of opinions by nonaffiliated members, such as community IRB members, and this would in turn lead to a less comprehensive and effective debate over the ethical issue involving human subjects protection.
B. Personal criticisms should not be tolerated at an IRB meeting, and so it may require chairs to be trained in methods for preventing verbal power tactics that would minimize the opinion or contribution made by another member of the IRB.
C. Both A and B
D. None of the above

2. What is one of the major challenges IRBs face when they review a lengthy and difficult to understand consent form?

A. It's difficult to get investigators to make major changes to their consent documents.
B. The consent form often was written for legal protection by a sponsor, who may insist that certain aspects of the form remain or else the study would be held elsewhere.
C. The federal government requires consent documents to be thorough and scientifically precise, so it's impossible to shorten them beyond the typical 10-plus pages.
D. None of the above.

3. Graphics in an informed consent document do which of the following?

A. They are helpful in explaining the text.
B. They can provide visual cues and point out key information.
C. They can create a cultural context for the information being presented.
D. All of the above

4. Category 8 is the only expedited review category where research that is of greater than minimal risk can be reviewed under expedited review procedures.

A. True
B. False

Answers: 1-C; 2-B; 3-D; 4-A.