IRB ADVISOR

Your Practical Guide To Institutional Review Board Management

AHC Media LLC

IN THIS ISSUE

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You say UP, I say UE: What's the new government guidance all about?

OHRP and FDA offer new language, definitions

Now that IRBs have both the final guidance on unanticipated problems and adverse events from the Office for Human Research Protections (OHRP) of Rockville, MD, and the draft guidance from the Food and Drug Administration (FDA), their duties in handling these issues should be clear, right?

Well it's not so, say government research experts, who also have to abide by these guidelines.

"There is a tremendous struggle right now, especially with multi-site trials, regarding IRB approvals and subsequent IRB communications when it comes to adverse events (AEs) and serious adverse events (SAEs)," says **Stephanie J. Zafonte**, BSN, RN, CCRP, CQA, RAC, senior extramural regulatory analyst (quality assurance) with the Office of Clinical Research, National Heart, Lung, and Blood Institute (NHLBI) in Bethesda, MD.

OHRP prefers to use the term "unanticipated problems" (UP), and defines these separately from the more commonly used term "adverse events." The FDA's draft guidance uses both of those terms plus the additional term for device studies for "unanticipated adverse device effect" (UADE). And NHLBI uses the term "unexpected events" (UE).

"We revised out serious adverse event policy and call it 'reportable events,'" Zafonte says.

After OHRP issued its final guidance, Zafonte's office did a significant revision of its reportable events policy to incorporate the concept of unanticipated problems into reportable events, she says.

"I made the decision that we did not want to separate into policies the two types of events: unanticipated problems and adverse events, so we made one policy that speaks for both of them," she adds.

"The staff I work with have had a tough time wrapping their heads around adverse events versus unanticipated problems," Zafonte says.

"The FDA and OHRP guidance are steps in the right direction, but in my personal opinion I think everyone needs to sit down, at the

same table, and get this all hashed out," says **Patricia Sweet**, RN, MSN, CCRP, CIP, a nurse consultant in the Office of Clinical Affairs for NHLBI.

"I think it's harder for [IRBs] when you have all of these different institutions developing policy, and they don't use the same terminology," Sweet says.

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Until the FDA guidance is finalized, Sweet's office will continue to follow its institutional policy, which more closely follows the FDA's current regulations than OHRP's guidance, she notes.

"OHRP's guidance is confusing to people," Sweet says. "It would be nice if it would have simple definitions."

As it is, IRBs are the filter for all gray-area decisions, she notes.

"The IRB sometimes is the filter for a lot of things, and people will think, 'Oh send it back to the IRB and let them make the decision,'" Sweet adds.

"Part of the problem is that historically a lot of events that should be classified as unanticipated problems are reported as protocol violations or AEs, for lack of a better way to report them," Zafonte adds.

"IRBs are struggling and insisting on over-reporting of research teams because they're afraid that something is going to be missed," Zafonte says. "So it's a very difficult environment, and, unfortunately, OHRP and FDA are not helping."

While OHRP and FDA made some effort to use the same terms in their guidance, what would have been most helpful to IRBs and researchers is if they had produced a single statement, co-endorsed to the research community, Zafonte says.

"Instead of going together as a united front, we're taking two steps backwards," she adds. "It creates more confusion for the research community and IRBs, and it leads to over-reporting."

Despite the FDA's attempt to incorporate unanticipated problems in its draft guidance, it appears that the agency still is more interested in adverse events, while with OHRP, the opposite is true, Zafonte says.

"IRBs will have to read the FDA's guidance and then look at OHRP's guidance — both side by side — to see if they've covered all bases," Zafonte suggests.

In general, it's helpful to think of unanticipated problems as encompassing a broader picture than adverse events, Zafonte says.

"An adverse event is a particular event related to a product, device, biologic in a study," she explains. "The unanticipated problem is looking at a much broader picture, and it's looking at something that impacts someone's participation in research."

OHRP's final guidance states that unanticipated problems must meet three criteria, including

being unexpected in nature, severity, or frequency, possibly related to participation in research, and places, subjects, or others at greater risk than was previously known. **(See *IRB Advisor's* March 2007, issue for the cover story about OHRP's new guidelines.)**

For instance, an unanticipated problem could breach a study's security, such as a laptop being stolen or broken, Zafonte says.

"It's something that's directly related to someone's participation, as opposed to an event related to a product," Zafonte says. "That's where the two are different."

If a research participant accidentally is given an inaccurate dose of the study drug, but has no adverse effect from the incident, then that would be classified as an unanticipated problem, Zafonte says.

"The incident does impact the person's participation and risk, but it's different from an adverse event, and it requires a different view of the problem," she adds.

As it stands, IRBs and institutions will continue to be cautious, and this creates volumes of paperwork, which was one of the problems the OHRP guidance noted when it was released in January 2007.

"There was a goal to try to alleviate some of the burden IRBs are experiencing in over-reporting, but I don't think that was successful," Zafonte says.

"OHRP guidance is leaning toward reporting only those things that are unexpected, which is certainly understandable," Sweet says.

"OHRP, with the word 'unanticipated,' absolutely does muddy the waters," Sweet says. "We have 'expected' and 'unexpected.'"

IRBs will continue to require reporting of most AEs out of concern that the one they miss would not pass the *Washington Post* test, Sweet says.

In other words, does a particular institution/IRB want to be the one that let's an adverse event slide that later might end up making headlines and resulting in bad publicity for the research program?

The NHLBI IRB that Sweet works with meets every two weeks. Several years ago, the IRB handled about two AE reports per meeting, Sweet says.

"Now we get 12 to 15 per meeting," she adds. "Our IRB is much more conservative than most."

The increase is due to better investigator and research/IRB staff education, she says.

"We've really made an effort in the past two to three years to educate and say, 'You need to make sure that if something like that occurs, you let the IRB know," Sweet explains. "On a rare occasion, it happens that something is reported that doesn't need to be."

The IRB looks closely for trends, Sweet notes.

"Some of our studies are bone marrow transplant studies, dealing with graft-host disease, and there are certain IND studies with new treatments for fighting infection and aplastic anemia," Sweet explains. "Someone with severe aplastic anemia is prone to opportunistic infection, so you're giving them a compound that will for a while lower their immune system and compromise them."

While the compound is expected to help the person in the long run, it's a dilemma for IRBs when there's an adverse event because they have to determine whether it was caused by the treatment or the underlying disease, she adds.

Sweet's office is involved with research that is funded and conducted by NHLBI staff and investigators. Zafonte's work at NHLBI is with outside research institutions that have received federal funding for research of interest to NHLBI.

"NHLBI has just revised our policy on reportable events, and we only want to see what's unexpected and definitely related," Zafonte says. "Expected events can be reviewed by a monitoring committee or research team, and they can be reported in an aggregated format."

Another issue IRBs will need to deal with involves standard operating procedures (SOPs), Zafonte says.

OHRP's new guidance requires IRBs to review their SOPs and continuing review behaviors, and this could have a ripple effect on IRBs, she says.

"IRBs have to go back and make sure they have processes in place so that unanticipated problems are adequately thought about, reviewed, and handled," Zafonte says. "And now they have to review the FDA guidance and make sure there isn't anything they've missed."

The OHRP and the FDA had to write their guidance documents as broadly as possible to cover a wide range of studies, Zafonte says.

"And so a lot of times they lack the specificity that's needed to implement them," he says. "That's where you end up with people individually having to interpret the guidelines and be comfortable with what they have developed for their own policies and procedures."

One solution is for institutions to better utilize data safety monitoring (DSM) plans within the

IRB-approved protocols, Zafonte suggests.

The DSM plan will handle the expected events, whether they are serious or not, and this will leave for the IRB the unexpected events and trends, which will significantly cut down on what is reported to the IRB, she explains.

"If an institution empowers the data safety monitoring entity to look at the aggregate data and the expected events on a regular basis, then that entity can report back to the IRB, and it will provide a more meaningful review for IRBs," Zafonte says.

"Every protocol has a data safety monitoring plan to it, and in that plan you delineate who will monitor what and how," Zafonte says. "And if we hold those entities and research teams accountable for that monitoring, then that's where the ongoing safety monitoring should happen, instead of at the IRB." ■

FDA's guidance addresses adverse reporting of items

Here's FDA advice in nutshell

In April, 2007, the Food and Drug Administration (FDA) issued its draft "Guidance for Clinical Investigators, Sponsors, and IRBs; Adverse Event Reporting — Improving Human Subject Protection."

The guidance addresses IRB concerns about how investigators and sponsors interpret regulatory requirements about reporting unanticipated problems.

"IRBs note that they receive increasingly large volumes of individual adverse event reports — often lacking in context and detail — that are inhibiting their ability to assure the protection of human subjects," the draft guidance states.

"IRBs reported difficulties in reviewing and interpreting the significance of information when large volumes of individual adverse event reports are received in isolation (neither aggregated nor analyzed) at sporadic intervals during the course of a study," the guidance says.

The FDA recommendations in the draft guidance are as follows:

- Investigators must notify IRBs of unanticipated problems, which are not the same as adverse events. "FDA believes that an individual adverse event report cannot be readily concluded to represent an unanticipated problem, even if the event is not addressed in the investigator's brochure, protocol, or informed consent documents," the guidance says.
- In multi-center studies, investigators must rely on the sponsor to provide them with information about adverse experiences occurring at other study sites. "We recognize that for multicenter studies, the sponsor is in a better position to process and analyze adverse event information for the entire study, and to assess whether an occurrence is both 'unanticipated' and a 'problem' for the study," the guidance states.
- Investigators studying devices must submit a report of a UADE to the sponsor and the reviewing IRB as soon as possible and not any later than 10 working days after the investigator first learns of the event, the guidance says.

The FDA draft guidance offers these examples of when adverse experiences should be reported to the IRB as unanticipated problems:

- "Any adverse experience that, even without detailed analysis, represents a serious unexpected adverse event that is rare in the absence of drug exposure (such as agranulocytosis, hepatic necrosis, Stevens-Johnson syndrome)."
- "A series of adverse events that, on analysis,

is both unanticipated and a problem for the study. There would be a determination that the series of adverse events represents a signal that the adverse events were not just isolated occurrences and were significant to the rights and welfare of subjects. We recommend that a summary and analyses supporting the conclusion accompany the report."

• "An adverse event that is described or addressed in the investigator's brochure, protocol, or informed consent documents, or expected to occur in study subjects at an anticipated rate (e.g., expected progression of disease, occurrence of events consistent with background rate in subject population), but that occurs at a greater frequency or at greater severity than expected. We recommend that a discussion of the divergence from expected rates accompany the report." ■

Risks/benefits of a cancer trial from patient's view

IRBs should keep this difference in mind

When IRB members weigh risks and benefits of an oncology clinical trial, they need to put risks and benefits in perspective for this particular population, or else they'll err by being too cautious, an expert suggests.

"Cancer patients may be more willing to put up with risks in trials that have less to offer because there may be no good alternative for them," says **Scott H. Kurtzman**, MD, FACS, director of surgery and director of the surgical residency program at Waterbury Hospital in Waterbury, CT. Kurtzman also is a professor of surgery at the University of Connecticut School of Medicine in Farmington, CT.

"An informed adult is entitled to take risks in clinical trials," Kurtzman notes. "Often in cancer, neither of the alternatives are good, so informed people could make a decision to take a drug that might be toxic to them or likely will be toxic to them if it would give them a chance at a benefit."

IRB members should keep in mind that cancer patients typically have different characteristics than other people who have life-threatening illnesses, he says.

"For one thing, these are generally healthy patients to begin with," Kurtzman says. "This is as opposed to someone who has had diabetes or heart disease for many years and is in a debilitative state and couldn't tolerate drug toxicities."

Also, the general public perceives cancer differently than other diseases, he says.

"It's perceived as life or death — 'Either fix the cancer or I die,'" Kurtzman says.

This is a more urgent viewpoint than that of the diabetic or heart patient's perspective that they might live with their disease for a long time, he adds.

"Believe it or not, cancer patients are willing to accept chemotherapy that is very toxic even if there's only a one percent chance of survival," Kurtzman says. "Studies have shown that cancer patients are much more motivated to take risks because they see this disease as an imminent threat to their lives, with no good alternative, so they can handle discomfort and disability more than other patients."

So when IRB members review the risks and benefits in a cancer trial, they need to place themselves in the cancer patient's mindset, which is that a person is willing to make an investment in being miserable for a short period of time in exchange for the potential of a long-term survival, Kurtzman says.

The key to assessing a cancer trial's risks and benefits is to have an oncologist on the board and to look carefully at the study design, Kurtzman advises.

Look at the study design and ask these questions, he advises:

• Are these reasonable drugs to try in a patient population?

• Is this a reasonable operation to try in this patient population?

• Is there a less toxic alternative with a high likelihood of success?

Another factor to consider is that cancer drugs do not have the same expected effect on everyone who takes them, Kurtzman says.

For instance, if 10 people have pneumonia, and the treatment is penicillin, then all 10 will get better if put on penicillin. But if 10 cancer patients are put on the same medication, two won't get better, and eight might, but doctors don't know from the outset which two won't get better, he explains.

"Since there's more variability in response, cancer is a more variable disease and there's more reason to do clinical trials," Kurtzman adds. "In the area of cancer, it's more reasonable

and ethical for patients to participate in clinical trials because there is no regimen or treatment with absolute guaranteed success."

Another difference about cancer trials that IRBs often fail to consider is how the consent form is worded.

"We're usually asked to put into the consent form all of the complications from chemotherapy, while it's typical in other drug studies to not list all of the side effect, but only to list the more common ones," Kurtzman says.

Cancer patients know about the risks of chemotherapy and understand that in a clinical trial they're being randomized to one or two arms of a chemotherapy regimen, he explains.

"So when they read every detail in the consent form, they're just seeing it rehashed," Kurtzman says.

While it's not unreasonable to put in every detail of each side effect, it isn't necessary because the cancer patient is not going to learn about the toxic effects from the informed consent document, he adds.

It's also common for cancer patients to have some therapeutic misconception during these trials, and this should not worry IRB members, Kurtzman says.

"Every patient is sure he's going to be the survivor," Kurtzman says. "How much you feel obliged to take that away from him/her is a matter of personal choice and style."

Patients will need to be told that this is not a guarantee that they'll live, but to take away the person's hope that he will not be the one who will survive would be unkind, he says.

"I don't think you have to do that," Kurtzman says. "You don't want to misrepresent the trial or give the patient false hope, but you don't need to take away the fantasy that he's going
to be a survivor."

On the positive side, cancer patients tend to be very motivated to follow their physician's instructions precisely, and are highly adherent, he says.

"People say, 'Oncology — isn't that a terrible field to be in?'" Kurtzman says. "I say, 'What if you're a cardiologist and you have a patient who is 400 pounds, smokes cigarettes, and lives on the couch all day? You tell him to stop smoking and lose weight and he says he doesn't know if he can do that.'"

A cancer patient will react to doctor's advice very differently, doing everything the doctor suggests even if it means putting up with toxic side effects, he adds. ■

Does your IRB need some help? Expert offers tips

Individuals are rarely the only problem

For IRB offices to run smoothly, employees need to work well together and count on each other when the work overflows.

So what should an IRB administrator do when the team is not in synch, deadlines aren't met, and morale suffers?

"The flow of work in IRB offices these days is so intense and there's so much paperwork and detail because federal funding agencies have increased the reporting requirements," says **Laura Freebairn-Smith**, MBA, a research associate in pediatrics, a doctoral candidate, and an instructor at the Drama School in Theater Management Program at Yale University in New Haven, CT. Freebairn-Smith also is the president of Organizational Design and Development Associates in Hamden, CT, and she has spoken in the field and has been published on the topic of building teams.

"IRB offices have to deal with the fact that they're under a lot of pressure and deadlines and in a high-risk situation for their universities because they're the legal oversight for these research experiments," Freebairn-Smith adds. "So there's intensity to their work that other units don't feel."

Also, much of the IRB office's paperwork is detail-oriented, and the stress of day-to-day production work can be difficult for a team to handle, she says.

"The other interesting thing about IRBs is that they're paid by the university, but they're also the policemen of the university's research," Freebairn-Smith says. "This creates an internal psychological tension that's not discussed a lot: how do you police the person who writes your paycheck?"

Due to all of these special factors, it's very important that IRB administrators pay special attention to their team's norms, guidelines, and psychological dynamics, she advises.

"The leader has to understand people's behav-

ior and be more articulate about the psychological dynamics of the team," Freebairn-Smith says.

And it's crucial that an IRB office have an adequate number of employees, she notes.

"One IRB team I worked with was understaffed, and the stress was very high because they can't adjust the flow of work," Freebairn-Smith recalls.

The danger is that once an IRB becomes understaffed, employees stop taking vacations, and then the team runs the risk of real trouble and stress, she says.

To avoid this problem, the IRB administrator needs to convince higher-ups that the staffing should be increased in order to reduce the institution's financial and legal risks, she says.

Freebairn-Smith also offers these pointers on how to improve team work and management skills:

1. Remember that teams are organic entities onto themselves.

Teams are separate from any individual on the team, Freebairn-Smith says.

"They have their own developmental phases that are relatively predictable and observable if you're trained in how to do that," she explains.

"So my core premise when I teach team building is that you have to be an observer of your team's behavior," she says. "What you're doing is helping your team move through a phase at an appropriate moment, recognizing that it's an issue and working through it."

Standing back from one's own involvement in the team and looking at the team through an outsider's eyes is one way to be freed from the notion that a particular team is fantastic or horrible, Freebairn-Smith says.

"All teams have certain kinds of behaviors under certain conditions and are knowable or predictable," she says.

"If we only operate from one instance to the next, we don't understand what an aberration is and what's not," she says.

So it's important to look objectively at the team in terms of financial flow, leadership, and skills building, and then do an analysis and suggest a plan to make changes where needed, Freebairn-Smith says.

2. Pay persistent attention to the team.

"Be sure people take vacations and are not always operating under crunch deadlines," Freebairn-Smith says.

Too often an IRB office will work under emergency conditions, and employees are either explicitly or subtly discouraged from taking vacation or holiday time off, she says.

"This can go on for years," she adds.

"So an IRB office needs to structure the team and staff in a way that people can take breaks for holidays and vacations," Freebairn-Smith says.

This can be done through making sure there is adequate staffing, as well as cross-training staff and having people rotate their work on a regular basis, she explains.

"Don't let workers become numb to what they're looking at," Freebairn-Smith says. "When you have production lines that are rote, but require attention to detail, it's a good idea to have people rotate off that production line."

The person who is trained to review each protocol should be asked to do something else for a portion of the day, so he or she won't become zoned out and miss something important, she adds.

Also, keep in mind that the IRB office team will never reach nirvana, where everything runs blissfully well.

"There is no ideal end state that a team reaches," Freebairn-Smith says.

"We often have people say, 'Fix my team, and then I'm done,'" she says. "But a team is like a garden and always needs feeding and care."

To manage a team, one needs to pay attention to the team's regular activities and observe checkpoints throughout the year, she says.

Checkpoints are like performance reviews, working with staff to make career decisions annually to see where their careers are going, Freebairn-Smith says.

Every few years, it's time to ask for feedback from team members by conducting a customer survey, she says.

Ask these questions of individuals and the team as a whole:

- Do you have a strategic plan with a mission statement and goals?
- Are you revisiting the plan annually and overhauling it every five years?
- Do you have staff meetings on a regular basis?
- Does your team go to off-site retreats and do strategic planning and team-building stuff?
- Do you have regular activities to honor transitions, such as team members having babies, getting married, etc.?
- Is there a good orientation program?

"A good team-building consultant will help an

organization construct an ongoing program and activities to make sure the team stays healthy," Freebairn-Smith says.

3. Problems on a team usually are not because of one individual.

"We tend in America to pick out an individual and say, 'If that person wasn't here the team would be fine,'" Freebairn-Smith says. "And 99 times out of 100, that's not true."

However, when a team has problems, usually the first step management takes is to get rid of one problem individual.

In an IRB office, this solution is tempting because one tardy employee or one person who is unable to keep up with the workload can have a profound impact on the team, but this person's problems likely are only a symptom of a bigger team issue.

"You always want to see if you can work it out with the person and try to figure out what the problem is," Freebairn-Smith says.

But it becomes a judgment call on the manager's part: is the employee's underlying problem due to a lack of individual skills or due to burnout caused by a team that is asked to do too much for its current staffing level?

"You need a manager to ask this question more often: Are these employees' competency skills and aptitudes a good fit for this work?" Freebairn-Smith says.

If the employees have adequate skills, then the underlying problem relates to the team and overall structure of the workplace.

Putting a team's problems into a greater context also is a more compassionate way to handle problems, Freebairn-Smith notes.

4. Learn techniques and model a team leader's impact.

"Leaders often underestimate the amount of power they have over people on their team," Freebairn-Smith says. "They underestimate the effect of their own behavior, words, and decisions, so I encourage them to slow down and be careful."

Also, some leaders follow a scarcity paradigm where they starve people for compliments, she says.

"There's more room in people's carts than they realize for giving out compliments and compassion to others," she says. "It's one of the few sources of energy on the planet that are unlimited."

Team leaders shouldn't scoop out undeserved praise, but they should be lavish with it when it's earned.

"We use role-playing and modeling to show people how they impact others on the team," Freebairn-Smith says.

"I watch team leaders in action, and then I mimic their actions in private, and they are blown away," she says.

There are simple body language mistakes that people make, such as nodding their heads too much, which sends the message that you're not really listening, she adds. ■

Sex abuse surveys don't harm participants

Abused subjects aren't more likely to be angered

A new study adds to the growing body of evidence that surveying people about past trauma doesn't put them at increased risk for harm.

The study, published in the May-June 2007 issue of the *Journal of Sex and Marital Therapy*, takes on what could be an IRB's most worrisome trauma survey subject — childhood sexual abuse.

Co-author **Bill N. Kinder**, PhD, a psychology professor at the University of South Florida, Tampa, FL, says that the study, along with a previous study on the same subject, showed that college students who reported having been abused sexually as children were not more likely than other students to show signs of anxiety, depression, or anger after being surveyed about abuse.

He says these findings should help IRBs feel more confident that sexuality research won't put sexual abuse victims at greater than minimal risk, and that such studies can be expedited, rather than requiring a full board review.

Measuring 'State,' 'trait'

Kinder notes that when he first began doing these type of studies, his own IRB required them to have full board review. His research has focused on survivors who have adapted well, in order to help account for what causes their resilience in the face of abuse.

"Anytime the words 'sexual abuse' came up, it had to go to the IRB," he says. "If we were asking about that, they were worried that it would be above minimum risk. My argument was that it should not be full board but expedited. Each time I would go in, I would argue that there's nothing

in the literature that suggested more risk."

When he served on the IRB himself, he wrestled with the question.

"It's a tough issue," he says. "There were no data out there."

Finally Kinder says, he decided to confront the question head-on. His team surveyed 207 women, measuring "state and trait" levels of anxiety, anger and depression. The subject's "state" would measure how they were feeling at the time they took the survey; "trait" was a measure of their general inclinations.

Then, the women were exposed to a battery of sexually-charged surveys. One specifically screened for childhood sexual abuse, while the other surveys asked them about their orgasm frequency, use of condoms, and genital self-image.

The additional surveys were employed only to expose the subjects to sexually explicit content, and that data was not analyzed.

Afterward, the researchers again measured the women's levels of anxiety, anger and depression.

"The researchers found no significant differences between pre- and post-testing on the measures of state anxiety, depression, anger, and curiosity, as well as no significant differences when compared to the non-abused participants," the authors wrote.

Including men

Kinder says the more recent study expanded the survey to include males, a group he says has not been studied as extensively in sexual abuse research.

"Females are much more likely to be abused, although lots of people have pointed out that there's probably more abuse going on with men than we know about," he says. "Also, women, if they were abused, are much more likely to go into treatment (where much of the sexual abuse research is conducted)."

Kinder says the second study was conducted in exactly the same way as the first, except that the participants included 125 male and 125 female university students.

They were subjected to the same questionnaires and state-and-trait measurements.

In the second study, 32 percent of participants reported having a sexual abuse history, with 17 percent of them classed as severely abused.

Kinder says no significant differences were found between pre- and post-testing for anxiety, anger and depression among the non-abused, abused and severely abused subjects.

Males were not found to suffer any greater effects than females.

As part of their debriefing, all of the subjects were given a contact sheet they could use to seek help if they were upset by the test.

"We listed 15 places locally in Tampa that you could go if you have a problem, including the counseling center on campus and our training clinic in clinical psychology on campus," Kinder says. "It included mental health centers, crisis hotlines, that sort of thing."

The study's authors do note that they did not attempt to assess whether these resources were tapped by the participants afterward. And Kinder says the question of whether such studies cause long-term problems in participants hasn't been definitively answered.

"My hunch is if there's no real short-term effects, then there are no long-term effects, but nobody's looked at that," he says. "It's tough to look at, particularly in the group we're looking at — adult survivors — because they're basically college students. Finding them a year from now might be tough."

Convincing IRBs

Kinder says the results from his studies have helped convince his own IRB to allow more recent studies to be expedited. He's heard from other researchers who hope to use his data to convince their IRBs to make similar decisions.

Kinder says the collection of studies pointing to little or no risk from asking these types of questions may finally convince more IRBs to consider them minimal risk surveys.

"I would tell IRBs, 'look at the data.' We've published several studies, and there are lots of other researchers across the country who are publishing these studies," he says. "And if you look at them, usually somewhere in there it's going to say there were no adverse reactions reported."

Kinder says IRBs may still find it necessary to require full board review for new questionnaires that might ask much more intrusive or potentially upsetting questions.

"Although I can't imagine something more intrusive than asking about sexual abuse or what your orgasms are like," he notes. "If somebody were to come up with a scale like that, it would be important I think to go before a full board. But then again, it's a Catch 22 — I have to convince you that there's no data out there to say these people are going to be at no risk, other than just to say that's the fact."

He says researchers would have to provide the usual extra protections for vulnerable populations being surveyed, such as children or prisoners.

And all surveys of this type, he says, must include contacts for subjects who may need counseling or some other help after the fact.

"That's absolutely vital," he says. "Whether it's expedited or full board, not just for sex research, for any kind of research that may cause any kind of discomfort to people. You have to provide them with some sort of referral source. It would be even more important with people who are at risk, such as patients." ■

References

1. Savell JK, et al. Effects of administering sexually explicit questionnaires on anger, anxiety and depression in sexually abused and non-abused females: implications for risk assessment. *J Sex Marital Ther*. 2006 Mar-Apr;32(2):161-72.

2. Rojas A, Kinder BN. Effects of completing sexual questionnaires in males and females with histories of childhood sexual abuse: implications for institutional review boards. *J Sex Marital Ther*. 2007 May-Jun;33(3):193-201.

Networks help physicians research practice-based care

Group has research network, IRB devoted to studies

Primary care practice-based research networks (PBRNs) bring together physicians and clinicians in practices across the country to research how patients are treated in a primary care setting.

Although many of the studies conducted in these networks are of relatively low risk, PBRNs have reported difficulties working with IRBs, particularly on large, multisite studies.

IRBs in different locations can require changes to applications and consent forms, and different IRBs can categorize the same protocol as exempt, expedited or requiring full board review.

Deborah G. Graham, MSPH, associate research director for the American Association of Family Physicians (AAFP), based in Leawood, KS, says that, often, IRBs simply don't understand the type of research they're dealing with.

"Generally, it's multisite research that's conducted in family physicians' offices," she says. "It could be survey-type research, or it could be the implementation of a new type of care. It's a very low-risk type research, on a different scale from what most academic IRBs are used to."

Instead of acting as principal investigators, participating physicians send their data along to the network.

In order to help those individual physicians navigate the IRB system, the AAFP has created its own National Research Network, a PBRN that collaborates with investigators and practices to help conduct research.

The AAFP National Research Network includes about 350 clinicians and study coordinators from 180 practices across the U.S. and Canada.

Graham reports that that about 40 percent of the active members are not required to report to a local IRB, as well as use the AAFP's own IRB, created last year. The AAFP IRB is composed of members who understand practice-based research and its specific needs, she says.

AAFP IRB oversight

Physicians who want to use the AAFP's IRB sign an agreement to allow oversight by the board. The IRB also has an arrangement with the Collaborative Institutional Training Initiative (CITI) to provide online courses in required human subjects protection for those physicians and their staff.

The AAFP IRB also serves as a HIPAA privacy board for the research network's studies.

Unaffiliated members who use the AAFP IRB need not fill out any additional IRB applications or HIPAA forms.

But for physicians who are attached to a medical center, or other institution that requires local IRB review, the process is more cumbersome, Graham says.

Individual practices, which may not have staff dedicated to research activities, must cope with local forms, as well as turn in the submissions themselves, although they are not principal investigators.

To help these physicians, the AAFP research network has taken on much of the burden of dealing with individual IRB forms.

Individual IRBs' demands can vary, Graham says.

"Sometimes they want more protection for a low-risk study than it really calls for," she says. "Sometimes it's just that each local IRB wants their say in it — they want a change in the consent form, either because they have their own templates or their own information they want.

"If you're dealing with 20 different IRBs, and they all want to change it just a little bit, that's a lot of bureaucracy and a lot of problems," Graham says. "At these practices, many of whom don't have a research coordinator, either the central (AAFP research network) office needs to complete all the IRB forms, or the practice just isn't able to participate."

Even with the AAFP research network's help, the bureaucracy involved in getting a number of IRBs to approve a study can delay its implementation.

"For most of our studies, because of that, we have to kind of roll things out as IRBs approve it," she says. "It's very difficult to roll out a study across the board at the same time. You kind of do it in one location as you get approval."

She says the AAFP research network has asked individual IRBs if they would be willing to accept a centralized application from the network, or the AAFP IRB's approval, but few have agreed.

"I don't think they're equipped to go outside of their system for now," Graham says. "I think a lot of them feel the responsibility that they need to review everything and they're not set up to accept the approval of another IRB."

IRBs: Open to education?

Graham says the research network encourages local physicians to educate their IRBs about the specifics of practice-based research. She recommends that IRBs be open to this education.

"There's definitely different types of research with different types of challenges, and they need to be open to working with the needs of different types of groups," she says.

For example, Graham notes that physicians and their staff, at their individual practices, often are required by their IRBs to go through hours of human subjects protection training, much of which is irrelevant to the studies they do.

The AAFP IRB requires completion of only four CITI modules, which have been geared specifically toward practice-based research.

"They are not principal investigators, they are not co-investigators — they're just the local staff," she says. "The AAFP IRB understood that, so they set up a special section just for them."

She says many investigators who report to local IRBs now are trying to convince those boards to accept a similar training program.

CE/CME Objectives

The CE/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 medical education program by reading the issue, 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 letter of credit. When your evaluation is received, a letter of credit will be mailed to you.

COMING IN FUTURE MONTHS

- Should there be an IRB appeals court?
- Here's how IRBs can assist investigators with ethical problems
- Lessons from Katrina: What have we learned about disasters and research?
- Preventive misconception: What it is, how to avoid it

Graham says she also would encourage IRBs to be willing to work with groups such as the AAFP NRN and its IRB. She says she's optimistic that more IRBs will be open to this type of arrangement, particularly considering OHRP's recent interest in alternate models of IRB review.

"They've had a couple of conferences now on alternate models of review, so it does seem that different places are investigating different options," she says. "I would hope so."

She says the AAFP and its IRB plan to bring together stakeholders in the research process to discuss various possibilities for streamlining review of multisite practice-based research.

Those options could include IRBs allowing review by another institution's IRB or by a centralized IRB such as the AAFP IRB. Sites also could form a consortium and elect one IRB to serve as the reviewing body.

"A goal down the road would certainly be to have a kind of centralized process that local IRBs would accept," she says. ■

CE/CME *questions*

1. In the Food and Drug Administration's draft guidance on reporting adverse events, which of the following term is used by the FDA, but not by the Office for Human Research Protections (OHRP) in its own guidance issued in January, 2007?
A. Unanticipated problems
B. Unexpected event
C. Unanticipated adverse device effect
D. Serious adverse event

2. When IRBs review cancer trials, which of the following questions is not considered a reasonable one to ask regarding the study's design?
A. Are these reasonable drugs to try in a patient population?
B. Is this a reasonable operation to try in this patient population?
C. Is there a less toxic alternative with a high likelihood of success?
D. Will the study drug work similarly in all subjects in whom it's administered?

3. *True or False*: A study of university students showed that male students who have been sexually abused are more likely to be upset by sexually explicit surveys.

4. What percentage of the American Academy of Family Physicians' active members report that they do not have to have research reviewed by a local IRB?
A. 10 percent
B. 40 percent
C. 75 percent
D. 95 percent

Answers: 1(c); 2. (d); 3. (False); 4. (b)