IRB ADVISOR

Your Practical Guide To Institutional Review Board Management

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Conflict of interest in all its many forms requires institutional guidance

Policies must address myriad issues

The editors of the prestigious British medical journal *Lancet* recently issued a public statement acknowledging a failure to disclose conflict-of-interest concerns about a 1998 study they published connecting autism to childhood vaccines.

On Feb. 20, *Lancet* editors announced the results of their investigation into allegations of research misconduct against the authors of a paper detailing possible links between the combination measles-mumps-rubella (MMR) vaccine and autism and inflammatory bowel disease in children.[1] Publication of the study, and the resulting publicity, has been cited as a major factor in declining vaccination rates in the United Kingdom.

Now, journal editors have learned that the lead investigator, British researcher Andrew Wakefield, was conducting a related research endeavor at the same time the autism project was under way. The second project, about which editors claim both they and Wakefield's co-authors were unaware, involved Wakefield collecting information to determine whether there was clinical evidence to support a legal action by parents claiming the MMR shot had harmed their children.

"We regret that aspects of funding for parallel and related work and the existence of ongoing litigation that had been known during clinical evaluation of the children reported in the 1998 *Lancet* paper were not disclosed to editors," the statement by editor **Richard Horton** said. "We judge that this information would have been material to our decision making about the paper's suitability, credibility, and validity for publication."

The paper's key authors also responded in writing to the journal's statement, with Wakefield denying that his participation in the second project compromised the integrity of the initial research or the journal publication.

"The clinical and pathological findings in these children stand as reported," Wakefield states. "They have now been confirmed independently by reputable physicians and pathologists. . . . My colleagues and I have acted at all times in the best medical interests of these children

and will continue to do so."

The *Lancet* debate highlights the difficulty that many research institutions — universities, medical journals, and medical centers — have in managing potential conflicts of interest.

In the United States, there are no clear, universal standards for what constitutes a conflict of interest for a researcher, research sponsor, or institution, says **Robert S. Bienkowski**, PhD, executive director of research at Iowa Health – Des Moines, a three-hospital health system.

"There is not much language in the federal regulations beyond that stating that conflicts of interest must be disclosed and managed," he says. "And there is no simple way to say that something is a conflict or it is not. What might be a serious issue at one institution might never come up at another one."

Research institutions must develop their own policies and procedures about research conflict of interest (COI), including what it deems to constitute a potential conflict, policies and procedures for discerning and disclosing potential conflicts to participants, and what institutional processes will be involved in managing potential conflicts so that they do not impact the ongoing research.

Institutions might want to start by modeling their own policies after that of another institution, but the development of a policy should be seen as a process, he cautions.

Some larger universities may see types of conflicts that another institution might not deal with, and detailed procedures dealing with that type of conflict would be unnecessary.

For example, some research institutions have developed separate, for-profit corporations to market commercial uses of the results of some of its sponsored research. A researcher might have a dual role, doing work both as an investigator and in developing markets for the separate corporation.

That institution would need policies about what types of research the investigator could and could not participate in, and how the dual relationships would be disclosed to subjects in projects the investigator would be involved in.

At the same time, as a smaller institution gains experience in research, it may discern areas of potential conflict unique to that setting.

"It's important that this be a process that can continue to evolve," Bienkowski says. "And it's important that it not be just the IRB that is involved in developing conflict of interest policies."

Representatives from the institution's administrative and executive offices should, if not directly participate in policy development, be at least very aware and supportive of the ongoing development of institutional policies on COI, he notes.

At many institutions, a separate committee or task force is charged with developing and institutional policy.

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Although the stereotypical COI scenario involves an investigator with a monetary interest in an entity sponsoring research — for example, a clinician who holds stock in a company that later wants to sponsor research in the clinician's practice area at his or her institution — it is important to realize that not all COIs are financial.

"Money is a frequent issue, but you have to look at other potential conflicts as well, that might not be as obvious," Bienkowski says.

The potential of certain research findings to be published in a prestigious journal, for example, or a particular clinician's strong interest in a particular disease or condition, could influence his or her conduct in a research protocol.

And potential conflicts exist at the institutional as well as the individual level, he adds.

An institution's mission to treat a particular illness or disease, for example, could produce an institutional bias in favor of pushing the envelope in clinical research.

For example, a noted cancer hospital would be an ideal setting for oncology research, but how would the institution ensure that appropriate protections existed to balance research progress with protections against coercion and undue influence on patients to participate?

When is a COI too much to manage?

IRBs will usually be the entity deciding whether a potential conflict of interest can be addressed by implementing certain safeguards, or whether a particular investigator should not be allowed to participate in or conduct certain trials.

Again, different institutions may make vastly different decisions with regard to what kinds of COI they feel they can comfortably manage, says Bienkowski.

Where one institution may simply prohibit an investigator from conducting a particular project, another institution — possibly with more experience in that particular area — will feel comfortable implementing certain procedures to ensure the conflict does not influence research conduct.

For example, a clinician who is an expert in a particular treatment area and has conducted groundbreaking research of that particular type, may also have business ties the company seeking to sponsor a trial.

An institution may decide that if they prohibit this person from involvement in subject recruitment — and restrict him to only the study design and interpretation of data — that the integrity of the data could be protected.

Another IRB, faced with a perceived institutional conflict, might decide that a particular study would best be conducted elsewhere. Different IRBs will be of different minds.

At some institutions, such as Vanderbilt University in Nashville, TN, a separate committee has the responsibility for evaluating COI, says **Gerald S. Gotterer**, MD, PhD, senior associate dean for faculty and academic administrative affairs at Vanderbilt University School of Medicine.

The university's faculty COI committee assesses the potential impact of a conflict of interest on the design and implementation of a research project, but then the IRB decides on appropriate measures of disclosure to the patients/subjects.

"Both committees have a role in relationship to COIs," Gotterer says.

The more research conducted at an institution, the more need there is for such "separation of powers" in terms of evaluating the potential impact of COIs and making decisions about how COIs will be managed, Bienkowski notes.

Such extra safeguards help prevent institutional complacency and acceptance COIs, he says.

Screening for conflict

Above all, it is important for institutions to have some way of evaluating investigators for conflicts of interest that is not largely dependent on self-reporting, Bienkowski says.

If the institution has set out definitions of what it considers to be areas of potential conflict, it should still not be left up to investigators to report this to the IRB up front.

"Even those of us with the best of intentions often believe we are incapable of being unduly influenced," Bienkowski notes. "We can feel absolutely certain that we would be able to disregard certain influences in favor of the integrity of the research."

It is up to the IRBs to develop procedures for questioning potential investigators about any potential COIs in such a way that they will feel inclined to report clearly and completely.

"You have a questionnaire that goes over each potential area thoroughly," Bienkowski explains. "For example, 'Do you have a financial relationship with any of the sponsors of this trial?' not, 'Can you report any potential financial conflicts of interest related to the sponsor?'"

Few researchers believe themselves vulnerable to COI, but all are, he continues.

Money, though many will deny it, can be a difficult inducement to resist.

Several years ago, during the course of a clinical trial that had run vastly over budget, Bienkowski and colleagues received an unexpected bonus check for subject recruitment — a practice strictly prohibited by institutional policy.

"We didn't agree to it or apply for it or anything — it wasn't mentioned in any contracts," he says. "The check just showed up."

Bienkowski says he is almost embarrassed by how much he wanted to rationalize keeping the money.

"We were way over budget, and the check just appeared. It's amazing the lengths that your mind will go, thinking up ways that you might be able to cash that check," he notes. "But it clearly said 'recruitment bonus' right on it, so we sent it back."

Since then, the experience has served as a lesson that institutions cannot be too careful when considering COI.

"No one wants to admit it, but we are all vulnerable," Bienkowski states.

Reference

1. Horton R. A statement by the editors of *Lancet*. *Lancet* 2004; 363:820-824. ■

Lay members often leave when they feel excluded

Empower and keep community members

Attend any major IRB conference and one common complaint is that IRBs are having difficulty recruiting and retaining community members.

Usually, when they do find someone to serve on the board as a community representative, it's done informally as an ask-somebody-to-ask-somebody process, notes **Priscilla Craig**, health science specialist with the Department of Veterans Affairs (VA) Office of Research Oversight in Washington, DC.

"It's a word-of-mouth search for someone who fits the criteria, and a lot of times they tried to combine the functions by having a member who is both an unaffiliated member and nonscientific member," Craig says. "That's not always a good idea."

It's difficult for one IRB member to fulfill two roles in a professional capacity, Craig adds.

To prevent this type of shortcut in recruiting IRB members, the VA created new avenues for finding and empowering community members, including emphasizing the possibilities of recruiting from advocacy and community groups, Craig reports.

Convincing IRB members that these types of groups are good potential sources of community members is a bit challenging because of existing stereotypes, Craig says.

"They hear word 'activist' and think they might get someone on the IRB who is difficult to work with," Craig says. "But that's not the case with most professional organizations that exist."

IRB members should think about the community member as someone who adds an essential perspective to the protocol review process, and, as such, they should make an effort to find community members who have personal experience in areas that are commonly being studied at a particular institution, says **Susan Rose**, executive director of the Office for Protection of Research Subjects at the University of Southern California in Los Angeles.

"One of the IRBs for which I had oversight responsibility had lots of drug addiction studies, and when we reviewed the IRB, we found they had no community members or even consultants who had been a drug addict," she recalls. "The IRB said it wasn't possible to find someone with that experience, but it took me four hours to find a group that was willing to find someone [who was a former addict] who could be a consultant or community member."

Obviously, IRBs can't have community members for every topic the IRB might review, but if there are significant number of protocols in one area of research, then it's a good idea to find someone who could represent that community, Rose notes.

Likewise, IRBs should attempt to recruit community members who are representative of a particular community's ethnic, socioeconomic, or cultural diversity, suggests **David Bernhardt**, IRB chair of Public-Private Ventures in Philadelphia and San Francisco, and the interim chair of the University of Pennsylvania IRB. He also is a member of Networking IRB at Albert Einstein Healthcare Network, Albert Einstein Medical Center in Philadelphia.

Finding such people could be as simple a

matter as asking staff at an institution to recommend someone who might be interested in serving on the IRB, he says. **(See story, at right, on novel ways to recruit and educate community members.)**

Make community members feel welcome

Retaining community members can be as simple as showing them respect through actions and policies, but this ideal sometimes is not met. Too often, IRBs treat the community member as a guest or second-class member of the board, the experts say.

There is the hierarchy created by the use of titles and assigning the scientific members protocols to read, but not having the community member be a primary reviewer, Rose says.

At one IRB where the institution has deliberately worked to make certain each member feels as though he or she is on equal footing, everyone is called by his or her first name at the meetings, she notes.

Likewise, community members should be made primary reviewers, and their concerns about a protocol at a board meeting should be respected, Rose adds.

When a community member attends a first meeting, the board should introduce him or her with a presentation about this person's background, rather than just a perfunctory "we're so happy to have this member" statement, Bernhardt says.

Also, the IRB should provide the new member with a detailed list of the members of the IRB, including their telephone numbers in case the person has questions, Bernhardt says.

There is even an on-line source of information for community IRB members at this web site: www.orau.gov/communityirb/.

During IRB meetings, it's important for the other board members to listen respectfully to the community member's concerns and not through physical or verbal attitude make this person feel that he or she is a hindrance to the process or wasting people's time, Craig notes.

"The community member's role is to bring everybody back to reality and to point out that certain things may or may not be a good idea," she says. "The dynamics are that the community members should be equal and assertive and be listened to when they present objections to certain procedures or tests that cause them discomfort — that's their role." ■

Recruiting lay members? Think outside the box

Consider professional and special interest groups

Too often, an IRB doesn't take the time or make it a priority to recruit and educate community members who can offer value to the IRB and its mission of improving human subjects research protection.

Or perhaps an IRB has a high turnover of community members and finds it difficult to retain committed board members for the nonscientific role.

In any event, the recruitment and education of community members can be successful if IRBs take a closer look at novel ways to find and train people who will contribute through their affiliation with the community in which a researcher finds study subjects.

Experts offer these suggestions on how to recruit and retain community IRB members:

1. Think outside the box when looking for community representatives. Besides recruiting IRB members from groups that represent a particular research population, IRBs also might find members in some organizations that are off the beaten path.

For example, at one IRB, there is a member who meets weekly with various community groups, developing a long-term relationship that sometimes results in recommendations for community members, says **David Bernhardt**, IRB chair of Public-Private Ventures in Philadelphia and San Francisco and the interim chair of the University of Pennsylvania IRB. He also is a member of Networking IRB at Albert Einstein Healthcare Network, Albert Einstein Medical Center in Philadelphia.

Also, a Women's Hadassah organization, local chapters of the AARP, veterans groups, and equal employment opportunity offices might be able to provide the names of potential IRB members, suggests **Priscilla Craig**, health science specialist with the Department of Veterans Affairs Office of Research Oversight in Washington, DC.

Naturally, veterans' organizations are a big resource for IRBs at the Department of Veterans Affairs, but there are other good possibilities, too, she notes.

Some IRBs might have local Native American groups and minority groups from which they can

recruit members. Others may look to professional societies, including groups representing lawyers, teachers, or journalists.

"One of the things I have done is go to the local bar association to find an up-and-coming attorney who will serve," Bernhardt says. "The important thing is to start by developing a job description that lays out clearly the responsibilities and the commitment; and in order to do that, one of the things you need to do is produce a list of hoped-for qualifications."

Some of the qualities that are most desirable in an IRB's community representative are having an inner strength, which would mean that someone is not intimidated by doctorate degrees; willingness to display ignorance and to ask questions; displaying the ability to articulate and analyze; and having the time to prepare for meetings, Bernhardt says.

Although finding members who represent particular communities may pose some challenges, it's a good idea, Bernhardt and Craig say.

"If you have a particular focus in your research — like Alzheimer's research, for example — then you will want a community member, but it also would be a good idea to have someone who has a grasp of the science involved," Craig says.

Such people could be found in the local Alzheimer's support group, perhaps, she adds.

Similar resources can be found in local multiple sclerosis societies and other organizations that exist to help people affected by a particular disease.

"All you have to do is go to the phone book sometimes, but there is a fear of finding someone who is too vocal and who would obstruct the process of the IRB," Craig says. "That's like a hidden fear, but it's worth mentioning. And when people find out that it's not the case and people are motivated by the greater good, then they're much less reticent to contact them."

Other sources of community IRB members include the following:

- churches;
- North American Treatment Advocacy Forum;
- Women Alive;
- Coalitions of volunteer groups;
- local community business groups.

Prepare members through education

2. Provide better-than-minimal education and training. "IRBs don't always provide the indoctrination or orientation that community members need," Craig says. "They don't have the education they need to function as an equal member of the IRB."

Community members need education, partnering, and mentoring, says **Susan Rose**, executive director of the Office for Protection of Research Subjects at the University of Southern California in Los Angeles.

One area that especially is lacking is a continuing education program for IRB members and particularly for community members, Bernhardt says.

A small number of enlightened IRBs will send their community members to IRB and human subjects research conferences and meetings, Rose says.

For example, the University of Southern California pays for its community members to attend the annual Public Responsibility In Medicine and Research conference, she notes.

During a new member's orientation period, it is a good idea to have someone affiliated with the IRB sit down with the community member and describe the job description of serving on an IRB, Bernhardt suggests.

"Make sure there's a real understanding of the responsibilities and obligations attached to the appointment," she advises. "As far as I'm concerned, continuing education starts with the initial get-together of the candidate."

Other education sessions might include an all-day training session that covers the three R's — roles, responsibilities, and relationships — of IRBs, she says.

The continuing education training should be formally developed and include funding for sending members to outside training workshops, such as ARENA's IRB 101, Bernhardt suggests.

"Another thing would be to use the films that were developed by the Office for Protection from Research Risks, the predecessor of OHRP," says Bernhardt.

Also, someone on the IRB staff should ask the new member what he or she has experienced and whether they feel prepared to do their assignment.

"This is very rarely done," Bernhardt notes. "And yet it could be a source of improvement."

Some IRBs provide free e-mail services to community members who don't have personal computers, and still others provide laptop computers to IRB members, Craig notes.

"If you have the money to do that, then that's fine; but there are a lot of ways to facilitate their education," she says. "Mentoring is one way."

Mentoring also isn't done enough, and this is a

very good way to introduce members to the IRB culture, Bernhardt adds.

For instance, another member of the IRB can work with new community members to review the informed consent process and show them what to look for in informed consent documents, Craig suggests.

Community members also might need to be taught how to decipher medical language in the more technical informed consent documents used in biomedical research involving cancer, for instance, she says.

Simpler education ideas include providing community members with an IRB orientation folder or package, giving them access to on-line web sites and education programs, including the Office for Human Research Protection training, Craig says. ■

VHA to begin audits of research affiliates

These will impact all IRBs affiliated with VAs

This spring, the Veterans Health Administration (VHA) will begin to conduct routine not-for-cause audits of institutions and IRBs that are affiliated with Veterans Affairs (VA) research.

"This is a prospective, on-site visit that reviews compliance with regulations for humans, animals, and research safety," says **David Miller**, PhD, director of the Southern Region Office of Research Oversight for the VHA in Decatur, GA.

These audits will not be the result of a known compliance problem or due to a whistle-blower or federal agency referral, as is the case with the standard for-cause audits, he notes.

"It's a routine review that takes the tack that we'd like to make the medical center aware of any minor, as well as major compliance issues, before they escalate or get out of hand," Miller explains.

All institutions and IRBs, including those based at universities, that are used as the IRB of record by a VA or that review protocols from VA researchers are eligible for the audit.

"We will have a team of three to four individuals go out to each VA facility," Miller reports. "The team will spend the better part of a week and look at standard operating procedures [SOPs], IRB minutes, and will do a random review of actual source documentation and study folders."

The review team will interview institutional officials, including administrative officers, and will help the facility take a closer look at its human research protection program, he notes.

"We'll only look at those records that specifically pertain to VA protocols," Miller adds.

Study coordinators will be asked to provide everything they're required to maintain on site, including serious adverse events, he says.

"The assumption is that everything is fine, and we just take a look at what they have, and we'll review pharmacy logs," Miller explains. "If we find something questionable, we may need to go to the clinical record to review progress notes."

Reviewers will look at individual files and informed consent documents as well.

Institutions and IRBs will be given a couple of months notice before the audits are scheduled, so there will be no surprises, Miller says.

"We may ask for documents to review even before we go out to the site so we can look at them here and not have to spend hours in an office, and we'll give facilities a list of people we want to interview," he reports.

To prepare for one of these audits, institutions and IRBs should review the regulations and make certain they are complaint with the letter and spirit of the law, Miller recommends.

Both the VA and the Food and Drug Administration (FDA) have checklists they could follow, and the Office for Human Research Protections (OHRP) has a list of common findings that might be helpful to review, he says.

"Our findings are very similar to OHRP's," Miller says. "We find that policies are out of date, there's a lack of continuing review, and people are missing parts of their informed consent documents, or have had the inappropriate use of expedited or exempt reviews."

IRBs need to make certain their membership rosters are up to date and that they have the appropriate mix of people on the IRB, he notes.

Also, one area that sometimes poses problems for VA-affiliated IRBs is that there's an additional committee called the research and development committee (R&D) committee that needs to be sent the IRB's minutes in a timely fashion, Miller says.

"Universities don't have R&D committees, but VAs do, and they need to send the minutes to the R&D committee for review," Miller explains. "IRBs know they need to do this, but the issue is getting them the minutes in a timely way."

Another problem area is that investigators are not permitted to start a study until they have

received approval from both the IRB and the R&D committee, and IRBs need to make sure investigators know this rule, Miller says.

"We want to get the word out so that investigators and institutions don't make unforced errors, like in tennis where someone serves you a ball and you just look at it," he explains.

Once an audit is complete, the reviewers will note any regulatory issues that need to be addressed and ask the facility to create an action plan to correct the deficiencies, and then the VHA office will track these corrections until they are complete, Miller says.

"If we find best practices and things a facility is doing very well, then we'll certainly note that," he adds. ■

Analyst clarifies use of the exempt category

It's not exempt if it's not human research

New IRBs and new IRB members, as well as those who have been working in the field of human research protection for years, often have questions regarding the use of the exempt category when research protocols are reviewed.

The first three things to consider is whether a protocol meets the definition of research, involves human subjects, and who will make the decision of whether it is exempt from IRB review.

While IRBs may find that they are never shown exempt research, the official position of the U.S. Department of Health and Human Services Office for Human Research Protections (OHRP) is that someone other than the researcher should make this determination, says **Glen Drew**, MS, JD, a health policy analyst for Rockville, MD-based OHRP.

"This could be the IRB chair or an administrator," he says. "A number of institutions have a form to fill out if you are doing a project that you think is qualified for exemption, and this form could be reviewed by someone on the IRB or another group that is designated by the institution."

But the important thing is that the researcher does not make this decision on his or her own, Drew adds.

Another initial question is whether a particular protocol actually meets regulatory definitions for human subjects research, he notes.

"So when IRBs get a proposal, the first thing for them to look at is whether it does in fact involve the requirements for it being research," Drew says. "Is it organized activity intended to generate or produce or lead to generalizable knowledge, and if that is true then it is."

Once it's determined that it is research, then the next question is whether it involves human subjects. For instance, research that involves only deceased people would not qualify as human subjects research, he notes.

Also, if a researcher is using a repository or source of data that has information about people, but this information is not identifiable and it's information that is expected to be shared publicly, then it is not considered human subjects research, Drew says.

Once it has been determined that a protocol does involve human subjects research that may qualify for an exemption from IRB review must fall into one of six categories:

• **Category one.** This is research conducted in an established or commonly accepted educational setting.

"It includes schools and universities and anywhere teaching activities are undertaken, including medical residencies and teaching hospitals, etc.," Drew says. "You don't have to find that there is no or low risk for the exemption to apply, but exemptions are designed to cover things that are considered low risk."

He offers this example of what would qualify for a category one exemption: "If a teacher were teaching how to do research and describing the process, the research procedure would be the content of the education rather than research on education," Drew says.

For instance, a far-fetched example would be one in which a professor divided a class in half and had one half watch a movie based on a book and the other read the book, and then tested the students to see which technique was more effective, Drew says.

• **Category two.** This category applies to research involving educational tests, survey procedures, interview procedures, or observation of public behavior.

"It's probably the most confusing to work through," Drew says. "This exemption is available to use unless information is recorded in a way that the human subjects can be identified or if identifiers are linked with subjects."

So if an investigator recorded John Smith and gave a code number of A02 to John Smith, and all of the information related to A02 is available to

the investigator who has access to a list that says who A02 is, then that research would not qualify for an exemption, he explains.

Alternatively, if a researcher is conducting a survey of passersby in a shopping mall and is not asking them for their names or recording them in an identifiable way, then this study would qualify for exemption, Drew says.

Category two research also requires that if a disclosure were made outside of the research study then it would not reasonably place subjects at risk of criminal or civil liability or be damaging to their employment, financial standing, or reputation, he adds.

"So if an investigator is asking subjects in a mall whether they use marijuana or other controlled substances, and if the investigator is just recording this information by male or female, then that could qualify for an exemption," Drew says. "But if the investigator is recording identifiable information, then the answer could be related to a particular individual and it would not qualify for an exemption."

The use of Internet surveys is a controversial area under category two exemptions, he reports. "If you're obtaining identifiable information and it's of a sensitive nature, then I think it would not be qualified for the exemption."

For example, an anonymous survey completed on-line and then sent to a designated e-mail address would be potentially identifiable because even with safeguards the person's e-mail address could be traced back to that subject, and so that would not qualify for an exemption, Drew says.

• **Category three.** Category three mirrors category two, except that it applies only to elected officials or candidates for political office, he notes.

"Federal statutes require that confidentiality of identifiable information will be maintained throughout the research or thereafter," Drew says. "So if someone is running for a political office, you can identify information about them and still qualify for exemption."

This definition of elected officials or candidates does not apply to the staff who work for the elected officials, he adds.

"It would be the mayor rather than the mayor's secretary, or the head of the school board rather than a teacher," Drew explains.

An example of a study that might qualify for category three is one that involves asking elected officials or candidates whether they have ever smoked marijuana, he says.

• **Category four.** This category applies to research involving the collection or study of existing data, pathological specimens, records, documents, or diagnostic specimens if the information is recorded in such a way that it cannot be identified or if it's publicly available and de-identified, Drew says.

"The researcher can have access to it, but just can't record the names or identifiers with information he or she records. The wrinkle here is the data or information has to be existing at the time the research is proposed," he explains. "You can't just propose the research and have an ongoing collection of data and qualify for the exemption."

An example might be a study of X-rays or medical records to see if some diagnostic characteristic is related to a particular disease or conditions, such as if a review is made of X-rays of the head to look for an anomaly in people who have developed Alzheimer's disease, Drew says.

• **Category five.** This is a limited category that is available for the use by the Social Security Administration (SSA) and the Centers for Medicare & Medicaid Services.

"These are research and demonstration projects conducted by or subject to approval by department heads to study the benefit of service programs, people receiving benefits under programs, alternatives or changes to the programs, or possible changes to the methods of levels of benefits paid under those programs," Drew says.

For example, the SSA may wish to study whether it saves the government money and/or provides greater client satisfaction to make direct deposits to a client's checking or savings account rather than sending the patient a check by mail.

• **Category six.** Drew says he has never heard of this category being used, although it has a specific purpose. This category is for taste and food quality evaluation and consumer acceptance studies.

It has to meet one of two conditions: It has to involve wholesome food without additives being consumed or, if food is consumed with additives, it has to have levels of chemicals that are found to be safe by the Food and Drug Administration, the Environmental Protection Agency, and the Department of Agriculture, Drew explains.

"So if may be that someone in the supermarket asks whether you would prefer turkey sausage or pork sausage as part of a survey," he says.

Although these six categories are available for exempting research for IRB review, some institutions have separate policies that require all research to be reviewed by the IRB, and that also is acceptable by OHRP, Drew notes. ■

Is centralizing IRB duties the wave of the future?

There are different models for centralization

As IRB staff and members find their workload increasing more quickly than their resources, some may consider using a centralized IRB model as a way to allow them to spend their time and energy where it is most needed.

The idea is that when protocols are submitted for research that will be conducted at multiple sites across a region or the country, then the best way to handle these could be to cooperate with one IRB who will review the initial protocol and all continuing reviews. The other IRBs that are involved could reserve the right to disagree with a review or make changes to suit their community.

"Central IRBs usually operate in an environment in which there are no local IRBs, and the model here is we are involving all of these institutions that have local IRBs," says **Jacquelyn Goldberg**, JD, project officer on the Central IRB Initiative of the National Cancer Institute (NCI) in Bethesda, MD. The initiative is a pilot project sponsored by NCI in consultation with the Office of Human Research Protections (OHRP). "People are looking for new ways to protect the rights of research participants, and I think this model is one of several that will be out there."

For some large multisite trials, there could be hundreds of IRBs reviewing the same protocol, and there is no evidence that this provides better human subject protection than if the same protocol were reviewed by a central IRB that works with all of the local IRBs, Goldberg adds.

Also, a centralized IRB review reduces both IRBs' and investigators' administrative burdens and frees time for IRBs so that they may concentrate on actual conduct of research at their institutions and staff education.

"We have created a model where we have a central IRB and local IRBs that share regulatory responsibility," Goldberg explains. "The central IRB handles initial and continuing review protocols, and the local IRB's function is primarily a consideration of the local context and oversight of the local performance."

In another model for centralizing the IRB process, an IRB could have a cooperative arrangement with other IRBs in the geographical area so that, for certain multisite protocols, several different IRBs could rely upon one IRB for the main review process, says **Karen Hansen**, director of the Institutional Review Office of Fred Hutchinson Cancer Research Center in Seattle. Goldberg and Hansen describe how these two centralized IRB models work and what might be gained from becoming part of a centralized IRB process:

1. One IRB reviews a protocol before it is distributed nationally. In the case of the Central IRB Initiative, the central IRB reviews a protocol and makes its decision and all protocol materials available on-line to local IRBs, Goldberg explains.

"The local IRB sees everything the central IRB utilizes in making a decision," she says. "So when the local IRB has all that stuff, they don't have to do a full board review."

For instance, the local IRB could assign the chair or a committee to review the central IRB's documents for local concerns and to decide whether it will accept the central IRB's decision. If the local IRB accepts this facilitated review, then IRB staff notify the central IRB via e-mail, and the central IRB becomes the IRB for life of the protocol, conducting all continuing reviews, amendments, etc, Goldberg says. "The local IRB remains in the information loop when the central IRB makes decisions."

However, if the local IRB decides not to accept the central IRB's review, then the local IRB can conduct a full board review of that protocol, she notes.

2. A group of IRBs cooperate and more efficiently handle multisite research protocols. "I support a centralized IRB review provided that all parties involved are truly engaged in the spirit of the process," Hansen says.

For example, the IRB at the Fred Hutchinson Cancer Research Center has developed a cooperative arrangement with other IRBs so that in cases of certain multisite research protocols, one IRB could be the IRB of record, she explains.

"You can avoid duplicate reviews by permitting another IRB to be the one of record," Hansen says. "These types of arrangements are documented in an assurance if you receive federal funding."

Then the IRBs that have allowed another IRB to be the IRB of record will provide an administrative review of the protocol that will be fully reviewed by the selected IRB. This is not the same as a full review or expedited review, and is listed only as an administrative review that either approves or does not approve of the full review done by the IRB of record, she explains.

"Typically, your agreement with the other IRB states that we always reserve the right to conduct our own full review," Hansen adds.

3. Work toward developing trust between central IRB and other IRBs. For the model in which a group of IRBs share responsibilities for reviewing multisite protocols and also share opportunities to be the IRB of record, it's important that IRB members know how each of their partner IRBs operate, Hansen notes.

For example, the Fred Hutchinson Cancer Research Center IRB has exchanged IRB members with a partner IRB. Members can sit in on this other organization's IRB meetings and gain first-hand knowledge of their processes and procedures, she adds. "It's a good way to get a sense of the review process, and seeing how the IRB is conducting its review helps to promote understanding. We would send two visiting IRB members a packet, and they were welcome to come and share in deliberation with the rest of our IRB reviewers."

This trust-building process continued for six months, and the Fred Hutchinson Cancer Research Center IRB members also would receive their packets from the other IRBs and, likewise, attend their meetings, she reports.

"That was one step to lead us toward coming into an arrangement of IRB acceptance," Hansen says. "I went to these meetings also, and I can only say that both IRBs gained from it."

NCI's central IRB now has about 150 local IRBs involved in the initiative, and there is potential for the initiative to include 1,500 IRBs, Goldberg notes.

All of the IRBs involved in the Central IRB Initiative review adult, Phase III, NCI-cooperative group trials, which are the only kind that the central IRB reviews, she says.

So far, the anecdotal evidence suggests that the IRBs who have used the central IRB's facilitated review have been satisfied with the process, Goldberg adds. "Investigators appreciate the ease of use, and the local IRBs think the quality of the review is really high," she reports. "Now, we're beginning an evaluation plan to measure this more formally, so we'll have objective qualitative data."

4. IRBs can focus on their strengths. When a group of IRBs work together to share reviewing responsibilities, there is potential for improved quality and a streamlined process, saving resources, Hansen says.

For example, one IRB would be the lead IRB and conduct the review of a protocol because that IRB's institution would be the main site for actual intervention with human subjects, she explains.

Then another IRB could oversee the laboratory and research analysis of the same study because that site has greater expertise in these areas and its site is where lab work and analysis will take place, Hansen adds.

Since the IRBs involved in a cooperative arrangement have developed trust and understanding, it's easy to keep communication lines open.

"Because of the dialogue and communication we have with other IRBs, if there is anything we notice that might need more attention, then we can just give the IRB office a call and share that information," Hansen says.

5. Improve technology and infrastructure to facilitate central IRB processes. NCI's Central IRB Initiative includes experts from across the country, so some IRB members have to travel long distances to attend IRB meetings, Goldberg says.

To make the board meetings more efficient and convenient for IRB members, the initiative plans to make better use of electronic technology, including having board meetings conducted through the Internet, teleconferences, and hybrids of both, she adds.

For instance, IRB members would access a specific web site at the appointed meeting time, and while they are on the telephone in a conference call with the other board members, they could scroll to places in the web site where protocol information is available, Goldberg explains.

For IRBs involved in a cooperative agreement, the process might be slower than desired if some of them don't have access to the Internet.

"We use all hard copy at this point," Hansen notes. "However, we do meet fairly regularly with two other academic IRBs because we're all part of a consortium, and as time goes on there could be more blending of processes electronically."

Some IRBs have been using enhancement grant money to update their electronic capability, and when all of the participants have made this technological progress, there will be potential for coordinating electronic submissions, she adds. ■

COMING IN FUTURE MONTHS

- Informed consent best practices and improvement
- Expedited reviews causing problems?
- Are IRBs overlooking areas of risk to human subjects?
- Are IRBs doing too much?

CE/CME objectives

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.

13. Research institutions should develop their own policies and procedures about research conflict of interest, including what it deems to constitute a potential conflict, policies and procedures for discerning and disclosing potential conflicts to participants, and what institutional processes will be involved in managing potential conflicts so that they do not impact the ongoing research.

A. True B. False

14. The VHA began a not-for-cause audit program for research institutions. Whom will this program impact?

A. All institutions that receive federal research grants.
B. Only VA hospitals.
C. All institutions and IRBs, including those based at universities, that are used as the IRB of record by a VA or that review protocols from VA researchers.
D. All institutions that employ or provide subsidies to VA researchers.

15. Which is not a category that qualifies for exemption from an IRB review under federal regulations?

A. The study of wholesome food without additives being consumed or, if food is consumed with additives, it has to have levels of chemicals that are found to be safe by the Food and Drug Administration, the Environmental Protection Agency, and the Department of Agriculture.
B. Research involving the collection or study of existing data, pathological specimens, records, documents, or diagnostic specimens if the information is recorded in such a way that it cannot be identified or if it's publicly available and de-identified.
C. One that only applies to the Social Security Administration and the Centers for Medicare & Medicaid Services and involves research and demonstration projects conducted by or subject to approval by department heads to study the benefit of service programs, people receiving benefits under programs, alternatives or changes to the programs, or possible changes to the methods of levels of benefits paid under those programs.
D. All of the above

16. Which of the following would not be an advantage for creating a central IRB to review certain types of multisite research protocols?

A. It could free time and resources at other IRBs, who otherwise would duplicate the protocol review that has been conducted thoroughly at one institution.
B. It could easily handle local and community issues by sending an IRB member to the particular trial site.
C. It could review protocols for which it has special expertise, and this would help to improve quality.
D. All of the above

Answers: 13-A; 14-C; 15-D; 16-B.