IRB ADVISOR

Your Practical Guide To Institutional Review Board Management

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Full review vs. a primary reviewer system: IRBs discuss pros and cons

Best solution not always easy to decide

Whether an IRB's protocol volume is small, medium, or large, it's not easy to decide whether to have the entire board read every page in a protocol submission or have a primary and/or secondary reviewer system in which point people take on the bulk of the work.

"All too often, the whole reason for a full board review is I need seven different pairs of eyes and seven different sets of experiences to look at the protocol," says **Sally Mateja**, CIP, IRB coordinator at the IRB for Murray (KY) State University.

"From my experience, I know that I get a much more in-depth review when I have seven people looking at something than when I have two," she says. "So in my opinion, all seven members need all materials because I don't know how someone can make an informed judgment based on someone else's opinion."

The Murray State IRB does have a subcommittee of two members who review the protocols that qualify for expedited review, Mateja notes.

"The decision is made in subcommittee and reported back to the board at the monthly meeting," she says. "The subcommittee is not allowed to decline a protocol, but can send it back to the full board to review."

Also, the selected reviewers of an expedited review case are not permitted to be someone from the same department as the principal investigator, Mateja says.

When IRB members meet, they are prepared with questions and concerns, and the IRB chair manages and directs the meeting, she explains.

Investigators are strongly encouraged to attend and answer the board's questions, and the entire process is handled collegially, Mateja says.

"We have only 10-12 full board protocols a year," she notes. "We have around 100 reviews a year, but most are expedited reviews."

The expedited reviews include survey research, while the full board reviews tend to be sociobehavioral studies, including prisoner studies and psychological studies that deal with sensitive materials, Mateja says.

Studies with more than minimum risk involving children must go before the full board also, she adds.

The IRB's board includes a biologist, psychologist, organizational communications specialist, a lawyer and past judge, an education specialist, a speech therapist, and a zoologist, Mateja says.

"There is a wide range of talent and specialties, and each one of these people brings something different to the table," she says.

So by requiring each board member to read all the materials submitted with each protocol, the IRB is ensured a wide variety of opinion, Mateja notes.

"That makes a big difference in what you bring to the forum; and for us, that is the best way to do things," she says.

A different point of view

On the other hand, the ethics review board (ERB) at St. Thomas Hospital in Nashville, TN, has a primary reviewer system for new protocols, and it works very well, reports **Martha Green**, CIM, ERB coordinator.

The ERB averages about two to four full-board reviews per month and has a caseload of 10-15 continuing reviews, she says.

"They are always biomedical studies, but some are chart reviews and data collection," Green adds. "Over the course of the year, we do have some studies that are exempt, and we use expedited review on some that are minimal risk, such as chart reviews, so long as they're compliant with privacy regulations."

"We assign a primary scientific reviewer and a community member for new studies," Green says. "That doesn't mean the rest of the IRB is excused from reading through the material, but the people who are assigned know it's their responsibility to lead the questions and answer with the principal investigator."

The ERB also uses primary reviewers for amendments, revisions, and continuing review. If there's a reason something needs to go the full board, it will be sent there, and the primary reviewers will lead the board in discussing the item, she adds.

St. Thomas ERB administrator **Penny Clark**, RN, CIM, previously has worked with an ERB that didn't use the primary reviewer process, and she found that it resulted in less focus on safety.

"Everyone was responsible for the materials in the packet, and people took less of a leadership role in directing the discussion and conversation," she says.

The primary reviewer system works well and can be used to encourage primary reviewers to call principal investigators prior to meetings to clarify issues, Clark adds.

"I'd like to see them go that route more," she says. "I see a lot more consistency of reviews of

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all studies with better discussion of risks."

The ERB's primary review system extends to continuing reviews in which one reviewer ensures that all qualifications are met and then makes a recommendation to the board, Clark says.

The IRB at the University of Maryland, Baltimore County, also uses primary reviewers in the case of expedited review protocols, but does have a primary and secondary review system for full board reviews, as well, says **Timothy Sparklin**, MSW, CIM, administrator of the human and animal research protections at the school.

"The whole board gets the packet, and the primary reviewer will lead the discussion," he says. "The primary reviewer talks about the issues, concerns, questions; and once that occurs, the board discusses the whole protocol."

The 12-member board has a small workload, a handful of full board reviews per year, Sparklin notes. Although there is a primary reviewer, it's apparent that the entire board will review the protocols and raise their own questions and concerns, he says.

"I believe the process works very well," Sparklin says. "Having this primary review system provides timely information and comments."

For example, if a particular expedited review protocol is not being handled as quickly as it should be handled, then he can call the reviewer assigned to the protocol and find out what's going on.

"We usually have about 150-160 total reviews and renewals per year," Sparklin reports.

Thomas E. Ball, MDiv, CIM, program director for the National Association of IRB Managers Inc. in Atlanta, has served on IRBs that use the primary reviewer system, as well as on a board that uses the full review system.

"I would probably support the primary reviewer system based on my IRB management job at Northside Hospital in Atlanta vs. my 10 years of Kaiser IRB membership here," he says. "At Northside, I had a primary reviewer system and two primary reviewers for each protocol, and they would be systematically selected rather than randomly selected."

The reviewers would include one scientific IRB member and one lay reader, Ball notes.

"The opposite system is to send all board members every packet and overload everybody," he says. "If you overload everybody, then no one is likely to be well prepared; but if you balance the work out, you are more likely to get a good reviewer."

Under the primary review system, the other board members would receive a copy of the consent form and a summary, Ball says.

"They know what is going on and what investigators are telling subjects and what is asked of subjects," he says. "So they're really not lost, and they can skip the other stuff."

In Ball's experience, the primary reviewer system results in some IRB members becoming experts on a particular protocol, and both the reviewers and full board liked the responsibility being divided in that way, he says. Since every member of the IRB would serve as a primary reviewer on some protocols, the workload was evenly divided.

St. Thomas Hospital's ERB meets twice a month, and all members are trained and experienced, says Green. "We take maybe seven or eight ERB members and staff to the PRIM&R [Public Responsibility In Medicine & Research] conference, including board community members.

"We went to a Food and Drug Administration-sponsored seminar in Florida early this year, and there again we had four community members attending," Green reports.

ERB members also receive training through a human research subjects handbook, a three-part video, and a notebook that lists specific policies, procedures, and forms, she reports.

Potential members also are asked to observe two or three ERB meetings to make certain they'll be comfortable taking part in discussions and voting, Green adds. ■

IRB splits to improve quality and efficiency

Research advisory council reviews study design

The IRB at Oakwood Healthcare System in Dearborn, MI, reviews protocols for four hospitals, including protocols written by master's level, doctoral level, nursing students, and the 150-plus residents.

The caseload is challenging. The institution recently decided that the IRB cannot do all of this alone in as effective a manner as desired, so officials came up with an innovative solution: "We created another body called the research advisory council [RAC] that basically derives authority through the IRB, although its function is different," says **Mary Barnhart**, CIM, CIP, manager of IRB programs.

"We're finding that because of the amount of paperwork and protocols, it's too easy to rubber-stamp protocols, and people don't have time to go through 900 pages of paper," she explains. "We're hoping the process will alleviate the amount of time both boards have to meet and work."

The idea for splitting the IRB into two groups that worked jointly came from the Institute of Medicine's suggestion for institutions to form ethics boards, Barnhart notes.

"We took our cue from this to divide the workload of the IRB, and we took it a step further and said, 'We don't need an ethics review so much as study validity and study design,'" she reports. "So that's how we split it, which makes sense to us because we have ethics people on the IRB, and that to us is part of human protections."

The RAC will look at the scientific review, while the IRB focuses on human subjects protection, Barnhart says.

The new program will work this way: When investigators, students, and residents submit protocols, the application process begins with the RAC, whose members study the protocol's validity, design, study analysis, budget, financial issues, and conflict of interest, she explains.

"The RAC's make-up is more technical than the IRB's," Barnhart says. "Their function is to look at those areas of the protocol and report to the IRB so the IRB can then be free to focus on human subjects protection."

The IRB's 18 members are divided between the IRB and the RAC. The RAC will have more physician members, and the IRB will have all of the community members.

Also there will be some membership changes, she adds. For example, the RAC with its 10 members will have a grants expert to address budget, grants, and financial issues, Barnhart says.

"We never had a grants person on the IRB before, so we revised who we have admitted to each board," she says. "We haven't added members so much as adjusted memberships, letting some board members go and putting others in."

When the RAC needs additional expertise, it can call on additional experts.

"We have an ad hoc committee we can pull from that would be suggested by chairs of departments when we have a protocol in a particular area where we may have a little expertise," Barnhart says.

For example, for a dermatological study, the RAC might ask for consultation with a dermatologist. Once satisfied with the science and study design of a protocol, the RAC will sign off on it and hand it to the IRB, which will look more closely at the informed consent process, study population, level of risk, and subject recruitment, Barnhart notes. "This is our innovative way to deal with not having enough time and too much to review," she says. "We hope this will streamline the process."

The institution has plans to begin educating staff and board members about the new program this month, Barnhart reports.

After the education process is complete, the IRB will be divided, and the new process will begin, she notes.

"Then we'll do our own study and review the process to see if it is indeed helpful," Barnhart says. "Our biggest challenge has been duplication and getting this program rolling without duplicating processes."

With one submission process and close interaction between the RAC and IRB, it hopefully will roll out smoothly without adding to the time it takes for a protocol to receive full IRB approval, she adds.

"We're still trying to do this within a four- to six-week approval time, but we won't know if we can do this until it's up and running," Barnhart explains.

Since the IRB will be a much smaller board that can focus on the human subjects aspect of research, it likely will have shorter meetings than it has, she says. "Our meetings now are two to 3½ hours, and it's too much of a burden on our IRB."

Another benefit is that with a smaller board it will be easier to obtain quorum, Barnhart adds. ■

SPOTLIGHT ON COMPLIANCE

Is data collection research? It depends

OHRP clarifies use of data in research

By **J. Mark Waxman**, JD
General Counsel
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One of the challenges faced by clinicians and investigations in accumulating data that might be used for research, is to determine the rules that

apply to ensure its availability if and when the research moves forward. The challenge that arises stems from the need to protect patients' privacy, as well as meeting other requirements of HIPAA and the IRB process. Meeting this challenge requires an understanding of a series of issues:

- What is research?
- What is human subjects research?
- Under what circumstances can the accumulation of data be considered the creation of a data repository?
- What rules apply to research involving coded private information?

OHRP has addressed these issues on several occasions in the past, most notably though its guidelines published in November 1997, and the HHS guidance on research repository databases published in January 2004. Notwithstanding these publications, many questions remained. The publication in August of its *Guidance on Research Involving Coded Private Information or Biological Specimens* helps to clarify OHRP's views on a number of the key issues.

The definitions

What Is Human Subjects Research? *Research* is defined by regulation [45 CFR § 46.102(d)] to be "a systematic investigation, including research development, testing, and evaluation designed to develop or contribute to generalizable knowledge." The definition is flexible and, at the same time, leaves a number of open questions. For example:

- Are all quality reviews designed to develop best practices research?
- If risk management activities are reported to carriers, are they research?
- Is simply collecting data in the hopes that it could be used at some point in the future for an as yet undefined research activity, classified as research?

The regulations also defines "human subject" [45 CFR § 46.102(f)] and delineates parameters of human subjects research which would be subject to IRB oversight:

Human subject means a living individual about whom an investigator (whether professional or student) conducting research obtains:

1. data through intervention or interaction with the individual;
2. identifiable private information.

Intervention would include direct physical activity — gathering blood — or environmental changes for research purposes. Interactions would expand the reach to the communication process, such as when an investigator takes a history.

Information, which for these purposes, is private, is the product of the reasonable expectations of the subject. If information is gathered in a setting or from a record in which the subject would not expect an observation to occur or to be made public (e.g., the patient's chart), then, under the regulations, it is private. The definition is designed to be flexible and protect the privacy expectations of the patient/subject. It is not, however, a black-and-white test. (Are photographs of people sunbathing in a private club private information? At the beach?)

To actually constitute human subjects research, the private information must be individually identifiable. This means that the subject's identity is or can be readily ascertained by the investigator or associated with the information.

For purposes of this guidance, *coded* also is defined as: identifying information (such as name or Social Security number) that would enable the investigator to readily ascertain the identity of the individual to whom the private information or specimens pertain has been replaced with a number, letter, symbol, or combination thereof (i.e., the code); and a key to decipher the code exists, enabling linkage of the identifying information to the private information or specimens.

Finally, the scope of coverage of the guidance, and, in turn, the rules, is important. Those covered by the applicable research structures would include not just the principal investigator or those investigators specifically responsible for the conduct of the study, but anyone actually involved in conducting the research. Hence, those who study, interpret, or analyze data; author research reports; or participate in presentations related to the research would also be bound to adhere to the rules governing human subjects research.

OHRP notes, however, that the conduct of research does not occur solely by providing coded private information or specimens. This may mean that simply gathering data for some unspecified future use is neither research nor is the individual performing such a function engaging in research. On the other hand, if the same person who provided coded information collaborates on other activities, they would, of course, be a part of the research team.

OHRP's guidance presents a concerted effort to let the research community know where the boundaries will be. From OHRP's perspective,

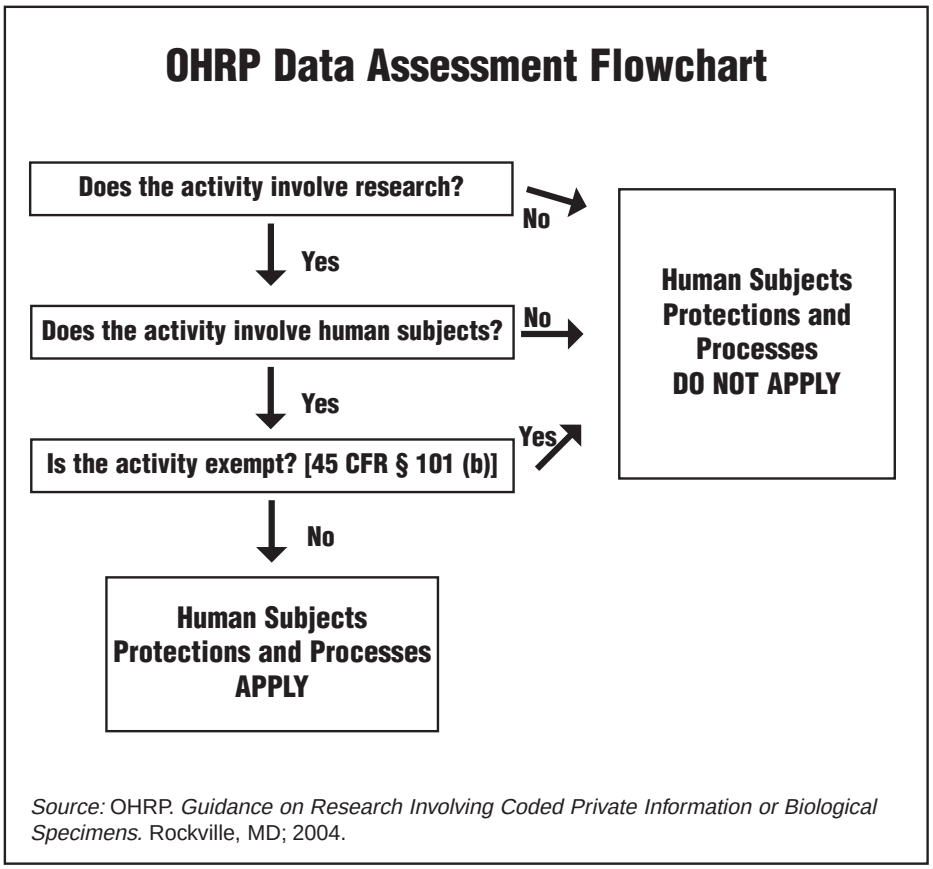
in interpreting the regulatory requirements [45 CFR § 46.102(f)], the key is to understand what it means to "obtain" the information or specimens in question. For OHRP, *obtaining* means:

• receiving or assessing them for research purposes;

• an investigator's use, study, or analysis for research purposes.

Private for these purposes means that the information or specimens can be linked to specific individuals — directly or indirectly (such as through coding system). Where that linkage does not exist, or cannot be made, human subjects research subject to the applicable rules is not occurring.

Importantly, this means that if the information (or specimens) is not collected specifically for a currently proposed research project through an interaction with living individuals, and the identities of those providing the information or specimens is not readily ascertained by the research team, human research is not involved. This formulation is at the core of any analysis.



Source: OHRP. *Guidance on Research Involving Coded Private Information or Biological Specimens.* Rockville, MD; 2004.

OHRP points out, it means that human subjects research is not occurring if:

• the ability to decipher the code is destroyed before the initiation of research;

• the investigators and those creating or holding the keys to deciphering the code enter into an agreement prohibiting their release under any circumstances, provided any of the individuals involved remain alive (an agreement that OHRP says need not receive IRB approval);

• the IRB itself adopts formal policies and procedures for a repository or data management that prevent release of the code key while patients remain alive;

• there are some other legal requirements which accomplish the same goals.

Applying these parameters to daily experiences mean that, at least, routine hospital or physician information or specimen gathering, observations and analysis would not be human subjects research — absent a specific gathering of such for currently proposed research. In this group of activities, there would be ordinary creation and maintenance of medical records or the ongoing collection of a tissue repository.

To implement the guidance requires education of those who will be affected. The approval that may be useful is through a Q&A type of communication to the academic and research community within the institution. That communication could also provide examples of the application of the underlying principles. For example: What happens if an appropriate agreement exists not to release or share the material necessary to decipher coded information, but the identity of one of the individuals is unexpectedly or accidentally disclosed?

In other words, the investigator now knows, or could readily discern, the identity of a participating patient, and the information related to that subject no longer meets the definition of private. The guidance tells us that human subjects research now is being conducted, and absent the application of some exemption [see 42 CFR § 101(b)], the IRB processes must be involved including, where appropriate, informal consent.

Or what happens if information unexpectedly comes to light where it is necessary to identify one of the participants, and it is possible to do so? Again, to proceed, the information would no longer be private, and human subjects research processes would be required.

To address the myriad situations that may arise,

the OHRP also recommends that there be an individual nested with decision-making authority. That individual should be someone other than an investigator to ensure an independent determination.

To assist the decision-making process itself, the OHRP Guidance provides a helpful sequential assessment process. **(See chart, p. 114.)**

To apply the outlined process, the focus must be on what actually is being obtained by the investigators. If it is limited to information or specimens where the investigator — as opposed to the patient's own physician — is not able to readily ascertain the patient's identity, then the investigation is not engaged in human subjects research. Neither, of course, is the physician.

Where the patient's physician also is the investigator, the opposite conclusion is the case.

A closer question exists when, for example, a physician begins collecting data without a current research project in mind. Later, the physician decides that the data bear investigation for research purposes and asks a third party to mask the data to prevent identity discovery. To be safe, this should be considered human subjects research, even though technically arrangements could be made to ensure privacy requirements were met.

If the information was coded from the inception, however, although human subjects research was being conducted, the research study could potentially still qualify for an exemption under 45 CFR 46.101(b)(4) as that data could be adequately masked.

Finally, OHRP cautions that the Privacy Rule, which is the product of HIPAA legislation, has its own rules and requirements. Thus, in contrast to the HIPAA privacy requirements, information that is linked with a code derived from identifying information is not considered to be individually identifiable under the research rules [45 CFR § 46.102(f)] provided the investigations cannot readily ascertain subject identities.

The guidance can be accessed at www.hhs.gov/ohrp/humansubjects/guidance/cdebiol.pdf. ■

Medical research lacks female participants

Women should be recruited for clinical trials

Patients who participate in clinical trials not only have access to newer, experimental treatments, they also have access to more routine medical checkups and state-of-the-art technologies.

For people with serious illnesses, and those without access to routine medical care, participation can make a significant difference in their care.

Yet for many women, participation in medical research studies is still not an option. More than a decade after the NIH issued guidelines encouraging the inclusion of women as subjects in clinical research, they still are not fully represented in clinical trials that determine which drugs and treatments get marketed in this country.

Although progress is being made, advocates say, women still have a lot of catching up to do after decades of historical, cultural, and legal barriers that excluded them from both the benefits and risks of participation in medical research.

Many women still are reluctant to participate in clinical trials. And many clinical investigators are reluctant to recruit them, fearing additional complications if a female subject becomes pregnant during the course of treatment or experiences reproductive complications later.

In fact, until 1993, regulations by the FDA prohibited the inclusion of women of childbearing age as subjects in early clinical trials. Those regulations have since been changed and the restriction removed, thus allowing more women to be included in clinical trials, but the results are only now being felt.

"Even though the guidelines changed in 1993, it's been like turning a battleship," says **Sherry Marts**, PhD, vice president for scientific affairs for the Society for Women's Health Research, a Washington, DC-based nonprofit organization that encourages the inclusion of women as research participants and research into gender-linked differences in health and medicine.

"You have to consider trial design and finding ways to recruit and retain women into studies — that took a few years. It is really only in the last few years that some of the data are starting to emerge. That shows you how long it takes to change the system. Data that you collect today will be in front of the FDA in 10 years."

Though more women are being recruited and are participating in clinical trials, there is little evidence that researchers are examining the data to look for any differences in response that might be linked to gender, Marts says.

"That is sort of the follow-up issue to inclusion," she notes. "What's the point if you are not going to at least look to see if there is a difference?"

Historically, women were excluded from participation as research subjects because of the risk untested agents posed to their future children, says **Georgia Sadler**, MBA, PhD, clinical professor of surgery in the Cancer Prevention and Control Program at the University of California-San Diego, and director of the center's community outreach program. Even today, investigators must take painstaking steps to ensure that participants are not pregnant when a trial starts and they understand the importance of not becoming pregnant during the course of the trial.

"There is always the concern about doing harm. You want to weigh the risks and benefits," Sadler says. "You want more benefit than risk — that is the goal, especially when there could be another person involved, namely the child."

Prior to the change in regulation, women of "childbearing potential" (i.e., those who had not yet reached menopause or not undergone a sterilization procedure) were excluded from early trials of drugs that had not been tested for the potential to cause birth defects.

Exceptions were made in instances in which a patient had a life-threatening condition and no other source of treatment was available, Marts adds. "It meant that there were some women in cancer clinical trials, but it did keep them out of trials of most drugs, and it certainly kept them out of the early phase trials," she says.

For many years, the medical community assumed that what worked in men would work — and work in the same way — for women, and vice versa. Drugs not proven effective in male subjects were assumed to have no value for women either.

"For a long time in medicine, we had this thing called the 'male norm,'" Marts continues. "I say this in my talks and it always gets a laugh, but it is true. It was just assumed that the male was 'normal' and women were just small men with different plumbing and a hormone problem. Come to find out, we are not. Our biologies are very different, and that has an impact on our health."

Recent experience has borne this out. For example, the only two drugs currently marketed specifically to treat irritable bowel syndrome seem to be more effective in women. And there are drugs that metabolize differently in men and women.

"There are some drugs that women break down faster than men, so they may need a higher dose or more frequent dosing, and there are some where it is the other way around," Marts says. "It is very challenging to kind of break the data out and figure out exactly what is going on."

Pharmaceutical manufacturers have an understandable disincentive to discover the need for different doses for different populations, she adds. It is great if one dose works for everyone, but that's not always the case.

And although more women are being included in clinical trials, there is some residual perception that trials are easier with men as subjects.

"We understand perfectly that manufacturers have a profit disincentive to doing this because if they look for a difference, and they find one, then they are going to have to label the drug to say, 'These people should take it,' or, 'These people should not,'" Marts says. "When Drug Company X is looking for the next blockbuster 'everybody's-gonna-take-this' drug, then some advocacy group comes along and says, 'But does this work differently in women than in men?' The reaction we get is, 'We don't want to know.'"

Pregnancy always a concern

There also is the risk of pregnancy. What happens if a subject is in the early stages of pregnancy and doesn't know it? Equally dangerous is the potential of a subject becoming pregnant during the course of the trial.

However, both Sadler and Marts say this potential complication is overblown in the minds of some researchers.

"You can ask a woman, 'Is there any chance you might become pregnant?' By definition, that means, 'Have you missed your period?" says Sadler. "Once you have determined that she is not pregnant right now, the next question would be, 'Are you trying to get pregnant, or do you have any plans to get pregnant? If you have someone who says they are, then you could exclude them because of the potential to do more harm than good."

The riskier the product being tested, the more solid assurance the investigators will want that subjects are not going to become pregnant, she continues. "If you are doing things that are relatively safe, you might say, 'Well, being on birth control is probably adequate; but if you are testing a new drug for the first time in humans, and [the drug] was highly toxic in animal models, you might say that, unless the person has had her tubes tied or some other procedure, you might not want to take the chance."

During the informed consent process, it also is important to emphasize this risk, the importance of not becoming pregnant, and — should an unplanned pregnancy occur — stress that the investigators need to be notified immediately.

Even with the change in the guidelines and attempts by many investigators to recruit female participants, women are not exactly knocking down clinic doors to get into trials.

Almost any conference involving research professionals will feature a session on recruiting women and minorities — and usually, it's a single session titled "Recruiting Women and Minorities," as if they were one population, Marts notes.

"You still tend to hear investigators say, 'Oh, but it is so hard to recruit and retain women," she says. "I always ask them, first of all, 'Are you listening to your site staff?' Maybe they have some ideas about how to do this better."

There are some recent examples of large-scale clinical trials involving women and other populations who were thought difficult to recruit that can provide helpful lessons about how to recruit and retain study subjects.

The first, says Marts, is the Women's Health Initiative, which recruited many older women and followed them for several years. "People said it could never be done. You could never recruit that many older women and keep them in the trial," she points out. "But, as we know, they did."

Other examples can be found in the HIV prevention trials that involve women who are either drug users, partners of drug users, or are professional sex workers.

There are some study sites that have had 98% retention rates over two-year periods with these populations, she says. The sites developed unique ways of maintaining contact with these women, even though the subjects may have been moving frequently, sometimes in and out of homeless shelters, or work in dangerous and illegal conditions — not exactly conducive to regular follow-up visits.

"What they are finding is that it takes more than just herding people into the clinic, performing the visit, writing the next appointment on a note card, patting them on the head, and sending them out," Marts says.

Because women typically shoulder the lion's share of responsibility for child care and household maintenance, clinics that offer weekend and evening hours, and those that combine multiple services (blood draws, X-rays, other monitoring) at a single visit are often more amenable to female participants, she adds.

They also may be concerned about the safety of the clinic's location, and whether security is provided.

Obviously, this is not a sole concern for female participants, Marts adds, and researchers may find that concessions they make to attract female participants may recruit more participants overall as well.

Working on a contract with one of the HIV vaccine trials, Marts helped produce a video featuring the subjects talking about the benefits of participating in the study. "There was one interview with a drug addict — who, in this instance, happened to be a man — and the interviewer asked, 'Why are

you doing this? Why agree to be in the trial?'" she relates. "The guy looked at her and said, 'Lady, I'm a junkie. No one has ever asked me for nothing. These people came, and they asked me to do something for other people. How could I say no?'"

Because clinical trials have, in the past, focused exclusively on men, it's possible that many women simply don't recognize this as something that is possible for them — they don't realize they are able to contribute, Marts notes.

"It is sort of a truism in the not-for-profit world that people don't volunteer unless they are asked. One of the things that occurred to us early on after they changed the guidelines was that half the population had been reading about medical research and seeing reports in the news, and it was always about men," she says. "Heart disease in men; men should take aspirin, etc. We imagined that women simply don't feel asked. They don't feel welcome to participate in these studies."

To help remedy that problem, the society initiated its "Some Things Only a Woman Can Do" campaign, which included a web site, brochures, and other educational materials that encourage women to consider participating in clinical trials.

"It emphasizes that you don't necessarily have to have a disease or condition to participate, and women are really intrigued to find this out," Marts says.

Conducting clinical research on essentially one population — white men — has handicapped medical research in a number of ways. Studies that include diverse groups of people can yield better information, faster, notes Sadler, whose research focuses on improving recruitment of both women and minorities. "It is important, for example, to have women of childbearing age represented in clinical trials. Let's say you are looking at blood pressure medication for hypertension. You would not want to exclude women between the ages of 18 and 50 [because] that is a large segment of the population that will eventually take this medication," she says. "Would you want them to take it without it ever having been tested in that population? That is essentially what happens now. If you have a study, and you don't have a large enough representation of African Americans, Hispanics, or Asians, it is the same thing."

The issues go beyond just genetics and gender, she continues. For example, say a particular drug does really well in subjects who are Asian women, but none of the other participants. Researchers would then look to see why. Perhaps it is something in the diet that these women all had that enhances the drug's efficacy? Once that is determined, that information could be included in the drug's labeling.

Conversely, say a certain group does poorly in a trial. For example, all of the Hispanic men don't respond. Perhaps there is a reason there. Once the likely cause is found, then researchers can recommend a possible solution.

However, if these people are never represented in clinical trials, this information is likely to never be found. For example, say the drug that worked so well for Asian women only is tested in groups of Caucasian men, is found to not work well, and is dropped. Researchers would never know its true potential.

Or suppose a drug that has significant complications for people with certain dietary habits or genetic differences makes it to market. Patients who do not respond to the drug, or worse, experience a poor reaction, are rarely noted.

Outside a clinical trial, Sadler says, individual complications or adverse events occur too far apart for their significance to be noted.

Sadler and her colleagues at the University of California-San Diego have initiated several projects attempting to improve the recruitment of women as clinical research participants.

First, they have written articles in several different professional journals advocating the benefits to patients who participate.

"The media has given clinical trials a bad public reputation," Sadler says. "There are a lot of good things you can say about clinical trials, but you don't hear about it in the media. You only hear about the bad cases, where someone is injured or a participant dies."

The public, at large, has no idea that development of new drugs and treatments would not

happen if patients did not sometimes agree to be subjects. "You may read an article about a new exciting drug that has now been found to reduce cancer mortality by 10%, but you never hear about the clinical trial that yielded this information," she continues. "It looks like it just appeared out of the clear blue sky — someone figured it out, and it worked. No, it was actually 10 different studies and 895 people took part in those various studies. They were Phase 1, Phase 2, and Phase 3 studies; and now, eight years later, here are the results [that] they are very excited to bring that to you. You never see that information in a newspaper article or TV report."

Sadler has written articles for nurses, physical therapists, chaplains, and even nurse-midwives.

"We wanted to reach people, in addition to physicians — who may not have enough time to talk with patients at length about clinical trials in general — [and whom] patients might seek advice from," Sadler says. "We want those professionals to know about clinical trials so that they can pass on reliable information."

Sadler's group also works to enroll women in small research studies that are very low risk, such as opinion surveys, to acquaint them with the informed consent process. At a later time, some of these people may have a chance to be a trial subject, and will hopefully find the process less intimidating.

"One of the reasons we spend so much time educating health professionals and the public is to try to help communities understand that 'no participation' is really 'no voice,'" Sadler says. "Someone has to step up to the plate. Obviously, we are not saying everyone should do everything, but keep your eyes and ears open, and don't have a knee-jerk negative response." ■

Correction: In the article "Is investigator certification the wave of the future?" in the August issue of *IRB Advisor*, the IRB administrator for Maricopa Integrated Health System in Phoenix was identified as Robert Reed, PhD. She should have been identified as Roberta Reed, PhD.

Swedish team looks at human proteome

While the mapping of the human genome provided scientists with a blueprint for understanding disease, Swedish researchers are trying to take the knowledge one step further, with the human proteome.

Mathias Uhlen, a professor at the Royal Institute of Technology in Stockholm, is leading a 75-person research team on the project, which is funded mostly through a $30 million grant from the Knut and Alice Wallenberg Foundation. Funding from the Wallenberg foundation will take the project through four years of research.

Sweden is not the only country turning to proteins to understand disease. China is working with proteins to find the cause of hepatocellular carcinoma, a form of liver cancer in which half of the people inflicted worldwide are Chinese. Researchers in the UK, Germany, and Denmark also are studying protein array technology.

Uhlen's team already has completed its work on chromosome 21 through a pilot project. It now is focusing on chromosomes 14, 22, X, and Y.

A human body has more than 50 million antibodies, and there are tens of thousands of variations to proteins. Uhlen has pared down his project to focus only on the 24,000 nonredundant proteins.

Like the human genome, the human proteome would become public property on a global basis, Uhlen said. But even those who mapped the human genome retained some value for themselves. The sequence is available, but not the clones that produced it. Uhlen would welcome the sharing of human proteome knowledge, but intends to use the antibodies to generate value in some way through various research collaborations. ■

COMING IN FUTURE MONTHS

- Here's how one institution set up its IRB monitoring program
- Improve education and training with these tips
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- The benefits of self-assessment

CE/CME objectives

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

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

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

CE/CME *questions*

Physicians, nurses, and others participate in this continuing education program by reading the article, using the provided references for further research, and studying the questions at the end of the issue.

Participants should select what they believe to be the correct answers, then refer to the list of correct answers to test their knowledge. To clarify confusion surrounding any questions answered incorrectly, please consult the source material. After completing this activity at the end of each semester, you must complete the evaluation form provided and return it in the reply envelope provided to receive a certificate of completion. When your evaluation is received, a certificate will be mailed to you.

13. A Dearborn, MI, IRB recently was split into two bodies, including a research advisory council (RAC) that takes the first look at the protocol, reviewing it from a scientific perspective. Which of the following is a major advantage to dividing IRB duties in this way?
A. It can give an institution the opportunity to hire professionals to serve on the RAC while keeping the IRB as an unpaid volunteer group.
B. This leaves the IRB more time to discuss human subjects protection issues, including the informed consent process.
C. It can reduce the protocol review time by 50%.
D. All of the above.

14. According to OHRP guidance on coded private information or biological specimens, if information (or specimens) is not collected specifically for a currently proposed research project through an interaction with living individuals, and the identities of those providing the information or specimens is not readily ascertained by the research team, human research is not involved.
A. True
B. False

15. For OHRP, *obtaining* information means:
A. Receiving or assessing information or specimens for research purposes
B. An investigator's use, study, or analysis of information or specimens for research purposes
C. Both A and B
D. None of the above

16. In what year was the FDA regulation prohibiting the inclusion of women of childbearing age as subjects in early clinical trials changed?
A. 1976
B. 1982
C. 1993
D. 2001

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