CLINICAL TRIALS
ADMINISTRATOR
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Services help clinical trial sites and sponsors locate "lost" participants

Concerted efforts find many of the missing

The reality of clinical trial enrollment is well known to all in the clinical trial industry: it's increasingly difficult to recruit study participants. This means that the people who are recruited are exceedingly valuable, and it is particularly frustrating to lose any of them at follow-up.

"Some of CenterWatch's surveys have reported there's an average of about 25 to 30 percent of patients who drop out of a trial, and some percentage of those become lost to follow-up," says **Helen E. West**, director of client relations for MMG of Rockville, MD. MMG is a patient recruitment and retention firm. West has spoken at national research conferences about how to find lost research subjects.

Lost to follow-up is a coined term which means there have been repeated attempts to re-engage a patient in a clinical trial, and the site has exhausted its resources trying to bring them back in for a study visit or follow-up, West says.

The good news is that about 80 percent of the participants contacted will re-engage in the trial, West says.

As a best practice, sites should send no-show participants a certified letter that is kept on file, showing the site had due diligence in trying to engage the client in the trial, West says.

From a sponsor's perspective, there is a significant investment made in each subject, in terms of the cost of study products and the collection of data. Also, the loss of patients means there might be problems in demonstrating a product's efficacy, so additional patients have to be enrolled to make up for the loss, West notes.

Clinical research organizations increasingly are shifting focus on retention programs, but that's only part of the picture.

"What do you do when the retention program is unsuccessful and the patient disappears?" West says. "Some might engage the efforts of missing person locators, and some Internet services can be used, but that process in and of itself is not ideal."

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These types of services typically are not experienced in locating research patients, and their approach might be wrong, West says.

This is where MMG and Patient Locator of Mansfield, TX, fill a void.

MMG focuses on clinical research, and is skilled at handling confidentiality and other issues pertinent to this industry, West says.

Patient Locator, which is a spin-off of Worldwide Tracers, was begun in 1999, when a major pharmaceutical corporation asked the company to consider finding patients who are lost to follow-up, says **Kirk Rutherford**, director of Patient Locator. Rutherford also has spoken about this topic at national research conferences.

"It was a program no one had ever entered into, and I suppose it was because of our recognition and reputation that they chose us," Rutherford says. "We went through the contracts and areas of confidentiality they wanted us to uphold, and we pretty much knew how to go through a clinical trial search without violating a patient's confidentiality, which is the most important part of our involvement."

Rutherford and West describe how they are able to locate lost participants:

1. Use a model that ensures confidentiality.

Licensed investigators who contract to search for clinical research subjects need to have a confidentiality agreement with the sponsor or CR organization, Rutherford says.

"Part of our licensing qualifications command we maintain the confidentiality of our clients, and that puts us in a better position to actually go along with what HIPAA compliance is," Rutherford explains.

When Rutherford speaks with clinical research professionals, the first question he typically is asked involves HIPAA compliance.

"Every sponsor interprets our participation in a different way," he says. "If we're a third party contractor they allow us to make the contact — others do not."

Another model is to hire a company such as MMG to serve as a conduit that passes information to the site and to the search firm, like Patient Locator, in a way that is secure and protects patient confidentiality, West says.

For example, MMG will work with sites during the enrollment process to make certain they include information on the informed consent document that has patients agreeing to be contacted by the third party if they fail to show up for visits, West explains.

"It also sets the expectation with patients that they are agreeing to make themselves available," she says. "So it can be preventative in nature."

"We work with the site and sponsor to ensure appropriate permission is gained through the informed consent process," West says. "If the site is not able to get in touch with the patient to perform the follow-up visit, then the site gives permission to a third party to assist in that effort."

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When MMG receives information from the site, they pass that on to Patient Locator.

"We act as a conduit to track and manage and make sure status reports are available to the sponsor, without the patient information being disclosed to the sponsor," West says.

"We provide forms the trial site fills out and submits to us," West explains. "It's logged in and sent to Patient Locator, who performs the search."

Then MMG manages the process to make sure they know how many lost subjects remain outstanding, West adds.

2. Verify information only as permitted.

Sites provide the retention or search company, the participant's last known contact information, but they omit information about what trial the person is in and what the person's condition is, West says.

"All of this is to protect patient confidentiality and to be in compliance with HIPAA," West says.

Depending on which model a company uses, either MMG, Patient Locator, or the CR site will verify the information they've found regarding the patient's new contact information.

"MMG has the credentials that, in some cases, allow them to make contact with the patient," Rutherford says. "This process is a new thing, and some clinical trial sites and sponsors are afraid to go forward with this type of situation of locating lost-to-follow-up patients out of fear of using licensed private investigators."

When the information is found, verification involves having someone call to make certain that the correct person was located, West says.

"If we confirm the current contact information, we'll pass that information back to the site," West says. "Then the site can make attempts to re-contact the patient, or MMG can do that on behalf of the site."

When MMG is contracted to provide this follow-up contact, it can save time, as MMG can act on the updated information very quickly, West notes.

"The advantage there is that our patient contact center staff deal with patients every day and have information on how to approach them about engaging in the trial," West says.

3. Use caution when making contact with participant.

The patient contact is either by telephone or email, West says.

"First and foremost, you want to communicate to the person that the reason they're being pursued is out of concern for their health," West explains. "And you tell them that the investigator is obligated to do everything within his ability to safely follow-up with the patient as part of the person's participation in the clinical trial."

It's important to convey that the visit isn't about pestering or hounding a participant, West notes.

The person who calls the patient also explains that he or she is acting on behalf of the physician or study center, and their responsibility is to make certain the person is okay, West adds.

"We ask them to return to the trial, and if they have any issues about doing that, then we're engaging them in a discussion about the details of that situation," West says.

"We would record the response if the patient has concerns about continuing in the trial and what those reasons are, and then we notify the site so they can close out the patient's participation in the trial," West adds.

Also, MMG would not engage in any Patient Locator search for a research participant who has indicated that he or she wanted to withdraw from participating in a trial, she says.

Sometimes patients have decided to withdraw from the study, but did not feel comfortable telling CR professionals their intention, West says.

"They're more comfortable telling us that they are not able to fulfill it, and we communicate that back to the site," West says. "We tell the patient, 'I'm sure that's not a problem; would you be able to come in for a last visit so we could get your safety information.'"

Other reasons why patients become lost to follow-up include crises in their families, including illnesses, job loss, etc., West says.

"Some patients feel like there's a lack of efficacy with the study treatment, either because they suspect they're on placebo, or if they think it's not working as well as the previous treatment," West explains. "And there are folks who move and just forget to provide forwarding information, so they become disconnected with the trial."

4. Employ tools used by licensed investigators to find people.

Licensed investigators have more tools available in finding people than does the average Internet user, Rutherford says.

There are federally-approved databases like Choice Point, which has credit bureau information, such as addresses, that are available to licensed investigators and law enforcement officials, he says.

"They don't allow us to get into individuals' credit reports because that would be a violation of many laws," Rutherford notes.

But the information a licensed investigator can find includes the latest recorded contact data.

"There are a number of different things contained in databases that help us discover the most recent address and phone numbers for the patients," Rutherford says.

Finding patients lost-to-follow-up is a program Rutherford personally believes in.

There is a future for this kind of work in clinical trials, Rutherford says.

"The more patients sites can find, the better off everyone is," he adds.

Clinical trial sites that go to this degree of trouble to find lost-to-follow-up patients will benefit both from finding some of the lost trial subjects, but also from being able to show regulatory agencies how they did everything they could to find participants who had not returned for study visits and follow-up, Rutherford says. ■

Coordinator advice on how to improve minority recruiting

Site is # 1 in recruiting African American women

Clinical trial professionals who wish to increase minority participation in their studies might learn a few tips from the research outreach coordinator whose enrollment efforts resulted in her becoming the number one accruer of African American women in the national Study of Tamoxifen and Raloxifene (STAR).

"I had to do some very out-of-the-box thinking," says **Melinda D. Hudson**, RN, CCRC, CCRP, clinical outreach coordinator with Spartanburg Regional Medical Center in Spartanburg, SC.

Hudson enrolled 39 African-American women, who were 15 percent of the total women enrolled in the breast cancer prevention trial, which enrolled about 19,000 women nationally at more than 100 sites.

The five-year STAR trial was one of a number of studies conducted by Upstate Carolina Community Clinical Oncology Program (UC-CCOP) of the Spartanburg Regional Healthcare System, Hudson says.

UC-CCOP was the fourth highest minority recruiter in the SELECT trial, having randomized 197 African-American men from the site, Hudson says.

The STAR trial posed a variety of challenges to sites focusing on minority recruitment, Hudson notes.

"This trial's inclusion criteria was very stringent," Hudson says. "It was based on a woman's risk of developing breast cancer over a five-year period."

The way the risk calculation model worked made it more difficult to find African-American women who met the inclusion criteria because research has shown that African-American women have a lower incidence rate of breast cancer than Caucasian women, although they have a higher mortality rate from it, Hudson explains.

Also, Hudson lives 40 miles away from the Spartanburg community, and so she had to start from scratch in getting to know African-American groups there, she says.

"We definitely wanted to look at this community and population because of research showing that Spartanburg County has one of the highest rates of breast cancer incidence in the state," Hudson says.

"So one thing I did here as a minority outreach coordinator is get to know my community and its history," she says. "I wanted to know what kind of research was done here in the past, what was the community's response, what were the barriers, were the criteria difficult to enroll?"

One key to building trust in a minority community is to show that you'll be there to provide support and answers after the study is complete, Hudson notes.

"So many times the African-American community has seen people come in and recruit for studies and get what they want," Hudson says. "Then when the study is over, there is no lasting commitment."

The STAR trials included this level of commitment to participants, Hudson says. **(See story on how to continue building trust after trial ends, p. 139.)**

Here is how Hudson and UC-CCOP achieved success in minority recruitment:

- **Meet key people in the community.**

Hudson met with key leaders of the African-American women community in Spartanburg, as well as with local pastors, nurses, professional nursing organizations, and other groups.

"I met with leadership councils in this community to find out what kind of health education was being done: what kind of programs worked

and what didn't," Hudson says. "I went to churches and spoke, holding health education sessions from the pulpit."

She expanded her recruitment area to beyond Spartanburg and into neighboring counties.

Basically, Hudson let local African-American women know who she was and what she was working on, and she started the outreach as soon as she began to work on the STAR trial, she says.

"Being African American really helped in that sense," Hudson says. "That helped me get to know the African-American community and gave me access to closed and private sessions, as well as access and connections with local leaders."

Hudson also served as a mentor to several other community outreach coordinators who worked on the study.

"Those who were not African American did express some complications as far as building trust and conducting outreach in African-American communities," Hudson notes. "It's not that it can't be done, and I had colleagues who definitely have been able to do this and did it very effectively."

But when clinical trial professionals are trying to gain trust and break through barriers to reach women in the African-American community, it's definitely helpful to be both a woman and of African American descent, Hudson says.

• Stress your health background more than the research.

One of Hudson's strategies when meeting potential study participants was to stress her health care background and her intention to help women in the community improve their own health.

"Being a nurse and also being a clinical research coordinator, I know it's extremely important for minorities to be included in clinical trials," Hudson says. "I don't go into the community pushing clinical trials; I go in educating African-American women about breast cancer."

She would tell women, "I'm here to help increase breast cancer screenings in this area, and I'm here to help you live and not just participate in the study."

UC-CCOP conducted free breast clinics in the community as a strategy to create awareness of the clinical trials and offer health services to identify eligible women, Hudson says.

"We did this monthly so that women would have access to breast services," she says. "The clinic provided clinical breast exams, blood pressure checks, and breast risk assessment counseling."

Women began to see Hudson as their community breast health representative, and so if they found a lump in their breast, they'd call her, or if they needed a mammogram they'd call her, she says.

• Educate the community and doctors about research.

The Spartanburg community needed some basic education about clinical trials, including what is involved in research studies, and how eligibility is determined, Hudson notes.

"So I did educational sessions and forums on clinical trials," she says. "We held informational sessions and seminars to create awareness about clinical trials and breast cancer prevention trials."

Hudson spoke at women's conferences and lunches, and she attended many of these where she was not a featured speaker.

"Sometimes I would be there just to have a presence there," Hudson says. "You need to respect the group's agenda and not push for clinical trials; sometimes you have to be patient and attend a function just to have a presence there that will speak louder than words."

At every function she attended, if she were given permission, she would hand out the STAR trial's risk assessment form. These listed demographic risk factors for breast cancer, and women could fill them out and mail them in to find out if they were at high risk, Hudson says.

Hudson could use the form's information to see which women might meet the study's criteria as being at high risk, and then she could contact the women, thank them for filling out the form, and let them know that they were at high risk.

"I'd invite the woman to come in and have a one-on-one session with me to discuss what the results mean," Hudson says. "I did this with every woman identified as being at high risk with breast cancer."

Once she met with the woman, she'd tell her more about the STAR trial and suggest that she speak with her husband, family, friends, and doctor about it.

"I enrolled about 50 percent of the women doing it that way, taking the personal approach," Hudson recalls.

Hudson also met with OB/GYNs, internists, oncology doctors, community health center staff, family practitioners and other physicians, nurses, and their staffs, educating them about the STAR trial.

These clinicians would then know enough to discuss the trial with their patients should

their patients approach them about the study, Hudson says.

"We also met with professional nursing organizations because a lot of community people call their nurses for advice," Hudson says. "We had lunch with them, discussed the trial and gave them opportunities to contact us if there was something we could do for them."

Clinical research coordinators may help improve enrollment if they combine the skills of coordinating, collaboration, and partnering, Hudson says.

For example, for the STAR trial, Hudson coordinated educational efforts with the minority outreach manager of the American Cancer Society, who was conducting seminars throughout the area.

"So we decided that wherever she went I'd tag along, and after she was done she'd give me five to 10 minutes of time so I could speak about clinical trials," Hudson says.

"Additionally, we recruited several women through a partnership with the Best Chance Network — an organization that provides breast and cervical services to low-income women," Hudson says. ■

Study seeks reasons for drop in female investigators

New physicians not engaging in research

For the past five years, the proportion of women physicians conducting clinical research has declined, despite increasing numbers of women graduating from medical school, according to a researcher who has studied trends in clinical research for two decades.

"We're looking at gender disparities among principal investigators, and our intent is to get a better handle on why we're seeing this rate of low involvement among women physicians in clinical research," says **Ken Getz**, MBA, MS, a senior research fellow at the Tufts Center for the Study of Drug Development at Tufts University in Boston, MA.

Some possible explanations for the decline include the following:

- In general, the turnover among clinical investigators is at an all-time high, Getz says;
- Regulatory and financial burdens in conducting research are onerous;
- Financial rewards in clinical research are not nearly what they were five years ago, Getz adds;
- It's becoming more difficult to recruit and retain subjects.

"There are many ways that investigators are finding their involvement in clinical research to be a challenge," Getz says.

"For quite some time, a lot of physicians who went into clinical research were physicians who wanted more stimulating ways to supplement their income and, in those days, it was a word of mouth kind of experience," Getz explains. "Back then, if you spoke with enough pharmaceutical companies, you'd land a grant."

Today's research environment is much more competitive, making it difficult for new investigators to succeed, he adds.

"A lot of the investigators who stuck with this business are those who got in many years ago," Getz says. "The average age of the principal investigator (PI) is rising."

Although more women now are entering medical school than in decades past, young physicians are less likely to go into clinical research than they were five years ago, he says.

"Clinical research is very competitive, especially for younger physicians," Getz says. "Unless they have a good handle on their financial operations and have an established practice and can introduce clinical research activity into that practice, they may be more reluctant to get into this new line of business."

One reason why the Tufts Center for the Study of Drug Development is closely following PI trends is related to a growing body of evidence suggesting that the types of patients attracted to clinical research are tied to the gender and ethnicity of the clinician, Getz says.

"As more clinical research targets specific ethnic-based and gender-based communities, the NIH and industry research sponsors need to have a good workforce with a diverse mix of investigators," Getz says.

Getz and his colleagues are collecting surveys from physicians around the country, aiming for more than 1,000 responses as part of a study that is looking for answers to why there is a lack of diversity among investigators.

"There is very little data, surprisingly, to give us even a general sense of the proportion of investigators who are African American, Hispanic, or Asian," Getz says. "The study we're con-

Minority community wants long-term commitment from clinical researchers

This includes sending them the results

A coordinator who was the most successful nationally in recruiting African Americans for a clinical trial involving the study of drugs to prevent breast cancer, says that long-term trust can only be achieved with a long-term commitment.

The key to recruiting minorities, especially when there will be additional studies over time is to build relationships, partnerships, and trust, says Melinda D. Hudson, RN, CCRC, CCRP, clinical outreach coordinator with Spartanburg Regional Medical Center in Spartanburg, SC. Hudson received accolades for her success at the Upstate Carolina Community Clinical Oncology Program (UCCCOP) in recruiting African American women to the Study of Tamoxifen and Raloxifene (STAR), which was a national, multisite trial.

"Say I was to pull out of the community after the study and have no more representation in the community, then the mistrust starts all over again," Hudson explains. "You don't want to exploit the African American community through research trials and then take representation away."

This long-term commitment includes letting participants know the results of a study after it's completed.

When the STAR trial's results were available, the site let participants know the results by sending each woman a letter that explained the results, Hudson says.

The letter explained whether the woman was taking a drug or placebo in the trial, as well.

Although the STAR enrollment stopped last year, Hudson remains available to women as a health care outreach worker and educator.

Soon there will be another study involving breast cancer, but it will not be open to the same participants, so Hudson's work will continue both with follow-up involving STAR participants and with recruiting for the new study.

Time and funding are crucial to successful enrollment of clinical trials, but it's equally important that clinical research coordinators be committed to the cause, Hudson says.

"I tell people I ate and slept STAR the entire time it was enrolling," Hudson says. "I totally committed myself to the community for this trial: they could reach me at home at night, and on weekends I'd do community sessions, going to churches to speak."

Hudson's dedication was grounded in both personal and professional inspiration. She had witnessed her family's grief and devastation when her brother-in-law died of colon cancer at age 28, and she wanted to contribute to medical knowledge so that such tragedies could be prevented.

"I saw in the STAR trial a population of African American women who didn't have a high incidence of breast cancer, but had a death rate that was high," Hudson says. "So these women needed not just clinical trials, but also education empowerment against this disease, and that was my driving force."

Hudson says her commitment to the work was reinforced as she met with women participants and heard their stories.

For example, she recruited four sisters from one family, and they each expressed their fear of breast cancer because of having a family history in which virtually every female member developed breast cancer, Hudson recalls.

"We recruited all four women, and that was a personal commitment for me," she says.

"Because of the work I did for the first two to three years here in our community, I now have women calling me to ask, 'When is the next breast cancer study going to be ready?'" Hudson says. "There's a higher educational level in our community about clinical trials, and the fear is not as extreme as it was." ■

ducting is designed to provide some descriptive and basic information to help us get a handle on the current landscape."

The study also will look at existing barriers to clinical research involvement and how that impacts women and minorities, he adds.

"The survey has been specifically designed to gather representative responses from a variety of ethnic communities and from female physicians," Getz says.

Globalization in clinical research is a trend that's increased partly in response to the prob-

lems of finding investigators and research participants in the United States, Getz notes.

Current clinical research forces have made subject recruitment more difficult in recent years, and these forces include stricter eligibility requirements, increasing protocol complexity, and competing studies in the same geographical area and even in the same research clinic, Getz explains.

"There has also been tremendous negative publicity about clinical research, and that has made the lay-public more leery of the clinical research community," he adds. "All of these factors have created challenges in patient recruitment and enrollment."

There are very large populations of patients in developing regions around the world. While American patients are increasingly skeptical of their physicians and medical care, patients in India and other parts of the world continue to place greater trust in their health care providers, Getz says.

And often, for patients in these developing regions, investigational drugs are the first treatment that they can access, so there is high motivation to participate in clinical research, he adds.

"As a result, it is easier to enroll patients from these regions into clinical research studies," Getz says.

When the survey of physicians and research is published early in 2007, it's possible the information could be used to facilitate the development of solutions to the problems of decreasing involvement by women physicians and increasing subject recruitment obstacles, Getz says.

"We are hoping this data will be used to raise awareness of the disparities that exist today, to inform discussion and debate around new policies that will improve the research landscape," Getz says.

The study may help to identify ways to improve physician education about clinical research, and it might influence policies and practices that make getting involved in clinical research more attractive to physicians serving ethnic communities, he adds.

"There's a lot of criticism today that patients from many of these ethnic communities don't have access to investigational treatments because their physicians don't have an interest in conducting the studies," Getz says. "The results from our research might ultimately facilitate greater access to patients who will benefit by these life-enhancing and life-saving treatments." ■

Compliance Corner

Compliance course teaches ethics and best practices

Investigators improve submissions after course

A successful compliance program begins with education, which is why a research compliance director at the University of Texas at Arlington has created a comprehensive compliance educational program that has been exported to research institutions around the country.

"We have a very large compliance focus because the University of Texas is a large institution, and there is much responsibility and accountability with all that," says **Patricia W. Myrick**, BS, CCRP, CIP, director of research compliance at the University of Texas at Arlington.

"There are institutional compliance offices on each of the campuses," Myrick says.

Myrick has created a 3.5 hour compliance education training program called, "Responsibility in Human Subject Research."

Using videos, a PowerPoint presentation and case study review, the program provides a three-year certification for all who score at least 85 points out of 100 on the exam, she says.

The course is open to all IRB members, investigators, and key research personnel, and she has taught it to about 4,000 research professionals and IRB members, including people at institutions across the country.

The course has contributed to a dramatic change in the way that protocols come into the IRB office, Myrick says.

"They are written better, are more complete, and investigators understand the process in the ways we'd expect," Myrick says. "Their protocol is presented to the IRB in a straightforward and streamlined way, making the whole process of review a better place."

Myrick's idea was to give research professionals a broad overview of human subject research, compliance, regulations, and ethics.

"I teach people how to understand the regulations," she says. "They learn that if they are doing this, they will need to know where they need to go

and how to find help because sometimes the hardest task is finding the right [regulatory] person to call."

Here is an overview of the compliance education:

1. Historical background and research design:

"We review guidance documents, the Belmont Principles, the Nuremberg Code and Declaration of Helsinki, research ethics, and conflicts of interest," Myrick says.

Before research volunteer Jesse Gelsinger died in 1999, the clinical trial community wasn't talking much about conflict of interest, Myrick notes.

Gelsinger's death during a gene transfer trial resulted in a mantle of change in the industry, leading to closer looks at how money might influence research decisions, Myrick says.

Myrick discusses statistics in research design because this is an area that causes consternation for investigators when they are working through the IRB review process, she says.

"Investigators don't like anyone to look at the scientific merit of their research," Myrick says. "But when you look at section 111 of the regulations, research design is first on the list that an IRB is responsible for reviewing because if the design is off, then the hypothesis is not the best."

This means a study could put participants at increased risk because of a poor design, she adds.

2. Regulations — both application and audit:

"Our technology is changing very quickly, so regulations have to evolve more rapidly to keep up with the changing environment," Myrick says.

The training course covers Federalwide Assurance, the Common Rule, for-cause and no-cause audits by the Office of Human Research Protection (OHRP) and sponsor or cooperative group monitoring.

The University of Texas has its own monitoring program, and Myrick has given presentations in which she lists monitoring as part of the model for success in compliance.

Her model of success in compliance is as follows:

- Conduct a risk assessment;
- Review internal policies and standard operating procedures;
- Audit/monitor research sites and records for both internal and external entities;
- Provide continuing education opportunities;
- Implement internal quality improvement programs;
- Make bi-directional recommendations for improvements;
- Establish an IRB advisory committee;
- Put in place review and reporting mechanisms;
- Provide an annual research forum for investigators and human subject research participants.

3. Research definitions:

"Imagine the number of discussions that take place in regards to what research actually is," Myrick says. "We clarify that issue and say only the activities included in 45CFR46.102(d), which is where you find the definition for research or systematic investigation, are included."

Crossing the line can be tricky, particularly for academic institutions that are always involved in systematic investigations, including Internet searches, Myrick notes.

So it has to be added that the investigation contributes to generalizable knowledge, she says.

"Suppose a faculty member asks the class to survey a block in the community to see if people know about available health services, and the goal of the assignment is to have the students write a paper that is presented in class and graded," Myrick says. "That's simply homework."

However, if the same scenario is slightly tweaked to have a different end goal in which the students will write a paper that is presented at a meeting or is submitted to a professional journal, then the activity has crossed the line and is now contributing to generalizable knowledge, she explains.

"You are now putting out findings so that others can contribute to research, and that study will need to be brought to the IRB," Myrick says.

4. IRB committee's authority, requirements, reports, and other considerations:

The course covers who IRB members are and why these ethics boards were established, including a look at the approval process, modifications, suspensions, how they vote, and what the quorum is, Myrick says.

Typically, the class discussion centers around how the committee is not a typical committee but is independent of the institution and has a higher level of commitment and responsibility, Myrick says.

"We talk about the federal regulations for membership, reporting, and what our office does for them in terms of administrative support," Myrick says. "We talk about institutional considerations, since any successful compliance program starts from the top down."

Also, research professionals are told that IRBs have the responsibility for reviewing grant proposals when they are attached to human subjects protocols, Myrick says.

"In years past, investigators would give one scenario to a granting agency to ensure funding, and then they'd give a slightly different scenario to the IRB to gain approval for research," Myrick says.

"Many times those didn't match, and that was a problem, so the IRBs were asked to review grant proposals as well."

When OHRP issues a compliance report on its significant findings and noncompliance concerns, that is number two on their list — the failure of the IRB to review Department of Health and Human Services (HHS) grant applications, Myrick notes.

"OHRP found numerous discrepancies between the title and relevant documentation in IRB records," she adds.

5. The IRB office's function and IRB reviews:

The IRB staff are involved in pre-screening submissions, research monitoring, and handling a variety of regulatory details.

The course helps research professionals understand what is meant by minimum risk and the IRB's criteria for approving a protocol, Myrick says.

Other issues covered are subject recruitment, the required elements of informed consent, and the levels of review, including exempt, expedited review, and full review.

Even if an informed consent signature is waived, it's important for investigators to maintain the spirit of consent by explaining to subjects what's going on, including the purpose of the research, Myrick says.

"We talk about the waiver because it has to be clarified and carefully documented in study records and minutes to be sure the research does qualify with the provisions of the waiver," Myrick explains.

"We talk about required documentation of the informed consent process, and we talk about the process in terms of it beginning even before research starts," Myrick says.

The class includes information about how investigators submit a proposal for review and what pieces of information are required, Myrick says.

The training goes into the details of how files are maintained and archived for both safety and security considerations.

Then, at the end of the course, attendees are divided into two groups, in which they represent IRB members of a clinical and a non-clinical board. Each are given a case study in which they discuss the study, determine the level of risk, and discuss the subject population's vulnerability, Myrick says.

"They present their cases and use all of the information we had just presented in that activity," Myrick says.

"Personally, I hate skits, but this is one activity that I have found to be worthwhile because they actually get to pretend to be an IRB member and face the same questions they would in that role," Myrick says.

6. The exam's opportunities for teaching:

Once the case studies are complete, students are handed a written exam, which they can complete while in the classroom, or they can take it with them and return it within 30 days, Myrick says.

"We also allow them to take it with a buddy," Myrick says. "I strongly believe the way the exam is written that if they take it with a buddy there will be a dialogue, and they'll talk about safety issues and ethical issues, which means the learning is still going on."

The idea is that research professionals should talk about the course and exam as another means to help them retain the knowledge, Myrick says.

"We see a change in the research work coming in here," Myrick says. "It's a big change, and I'd like to say the class is part of the reason why." ■

[Editor's note: Patricia W. Myrick, is available to provide the research compliance education course to other institutions at a fee of $500 to $800 plus travel costs. For more information, contact Myrick at (817) 272-0834 or pwmyrick@uta.edu.]

Clinical research standardization effort is saving money

Effort could save industry billions

For about seven years, clinical research leaders and the FDA have collaborated to develop research submission data standards in an effort to improve clinical trial efficiency, reduce costs, and cut delays.

"We're all volunteers," says **Mary Lenzen**, BA, MS, a principal consultant with Octagon Research Solutions Inc. of Wayne, PA. Octagon Research is a leader of electronic transformation of clinical research and development and is a service provider for the pharmaceutical industry.

"The standard we produced is SDTM — Study Data Tabulation Model for electronic submissions," Lenzen says.

The nonprofit organization called CDISC (Clinical Data Interchange Standards Consortium), located online at cdisc.org, is focused on establishing worldwide, industry standards, Lenzen says.

Lenzen says clinical trial data standards could shave months and millions off the cycle of bringing a new drug to market.

The SDTM is being used by some companies to transmit information to the FDA, and it's expected to become a regulation within the next few years. The FDA published a Federal Register notice about standardized electronic study data on April 24, 2006. The notice said that the FDA is proposing to amend the regulations governing the format in which clinical study data are submitted for new drug applications, and other applications.

As of June, 2006, the FDA had received seven submissions using SDTM, Lenzen says.

"This is the closest we've come to an industry standard for clinical trials," Lenzen says. "It's expected to reach into healthcare and not just clinical trials."

Since there is no industry standard, most research companies create their own standards, so when SDTM becomes the industry standard, these companies will need to adapt to the new standards, Lenzen says.

Octagon has already assisted SDTM conversions for 54 studies in the areas of oncology, central nervous system, cardiovascular, and endocrinology, Lenzen says.

The benefits to individual research organizations who implement SDTM conversions depend on how much they change, Lenzen notes.

"The earlier you go upstream, the more impact it will have on internal processes, including work flow, data collection systems, and analysis programs," Lenzen says. "Right now, because most people have legacy data and have not implemented SDTM at the data collection point, they're making the conversion right before submission."

However, there are a number of benefits to organizations that implement SDTM early in the process, including quality improvements and efficiencies, Lenzen says.

For clinical trial institutions that plan to implement SDTM at the point of submission, they'll first have to understand what they're going to map and what resources they'll need, Lenzen says.

"An understanding of source data is important," Lenzen says. "They'll need to find a commercial product or develop their own, but the hardest part is the mapping."

For example, if an organization decides to include gender as part of a demographics data set, conforming this to SDTM, then there are some choices in terms used, including gender and sex. And there are values assigned to the term sex, including male or female, Lenzen explains.

"Your database might have had this in numbers or with male spelled out and female spelled out," Lenzen says. "Or it could be A for male and B for female."

So the key is to look at the structure, list the responses you have, and then have this mapped to SDTM structure and terminology, Lenzen says.

"It can be two-fold: You may have called it gender in your database, but it's called sex in SDTM," she adds. "Mapping is making your structure and terms fit into theirs."

For organizations that are not standardized, the change could be very time consuming, Lenzen notes.

"When you lack standards, the more time it's going to take because you have this variety to deal with within your own company," she explains. "So for companies that are products of mergers and acquisitions, that's a real challenge because they inevitably had more than one standard based on the fact there was a standard or acquisition."

Once the data are mapped to SDTM and data are submitted to the FDA, the impact is all positive, Lenzen says.

"The FDA knows what to expect for the data because of the standard format, and they know what the target is for each company," Lenzen says. "Everyone is talking the same language and working off the same specifications."

Although the standardization submission regulations still are a few years away, many research organizations are starting to think about making the change, Lenzen says.

"If I was starting my own little company for pharmaceutical or biotech purposes, I would start with those standards," Lenzen says.

Existing companies will need to plan for the change, and there is no way to predict how long it will take or how much it will cost, Lenzen says. ■

COMING IN FUTURE MONTHS

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CE/CME Objectives / Instructions

The CE/CME objectives for *Clinical Trials Administrator* are to help physicians and nurses be able to:

- **review** pertinent regulatory mandates;
- **develop** practical clinical trial oversight strategies;
- **review** best practices shared by facilities that successfully conduct clinical trials.

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

Participants should select what they believe to be the correct answers, then refer to the list of correct answers to test their knowledge. To clarify confusion surrounding any questions answered incorrectly, please consult the source material.

After completing this activity at the end of each semester, you must complete the evaluation form provided and return it in the reply envelope provided to receive a letter of credit. When your evaluation is received, a letter of credit will be mailed to you. ■

CE/CME *questions*

21. An expert in enrolling minorities in clinical trials advises sites to follow which of the following strategies when recruiting African Americans?
A. Go into the community to meet and talk with key people.
B. Stress your health background and provide a long-term commitment.
C. Educate providers and the public about clinical research.
D. All of the above

22. For the past five years, the proportion of women physicians conducting clinical trials has decreased. Which of the following is not a possible explanation for this decline?
A. In general, the turnover among clinical investigators is at an all-time high.
B. Regulatory and financial burdens in conducting research are onerous.
C. Fewer women are graduating from medical school than five years ago.
D. Financial rewards in clinical research are not nearly what they were five years ago.

23. What is the primary reason why IRBs review the scientific merit and research design of a protocol?
A. A poorly designed study could place participants at increased risk.
B. Federal regulations require IRBs to be responsible for reviewing a study's research design
C. Both A and B
D. None of the above

24. Clinical research leaders and the Food and Drug Administration (FDA) have collaborated to develop research submission data standards in an effort to achieve what benefits?
A. To improve clinical trial efficiency, reduce costs, and cut delays.
B. To pave the way for electronic submissions
C. To improve clinical trial quality
D. None of the above

Answers: 21. (d); 22. (c); 23. (c); 24. (a)

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