CLINICAL TRIALS ADMINISTRATOR

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Research center's compliance program makes use of prospective monitoring

Center receives full accreditation with distinction

A prospective monitoring program is not for the faint-hearted, but it can result in better education for clinical research staff and prevent many research problems from occurring, according to experts who've created such a program.

The key is to initiate a prospective monitoring program out of the research compliance office and use this for educational purposes, as well as for achieving compliance goals.

Such a program also can save research resources overall.

"We wanted a group that could do friendly monitoring," says **Philip Cola**, MA, vice president of research and technology management at the Center for Clinical Research of University Hospitals Case Medical Center in Cleveland, OH.

"How can we help investigators take a fresh look at how they conduct research," Cola says. "We don't want to call it auditing."

The center's prospective monitoring program appears to be a success, and it takes pressure off the institution's IRB, which previously was the office where investigators and clinical research staff sought answers to their regulatory questions.

In a recent IRB office audit from the FDA, the institution did very well, Cola recalls.

"It's the best FDA audit I've ever seen in the years I've been here," he says.

Cola attributes the successful audit to a dedicated staff and to the IRB's re-focus on its chief role of reviewing protocols.

"By having this specialized additional resource of a monitoring team, the IRB is doing what it's supposed to be doing," he adds.

Also, the office recently received full accreditation with distinction in June 2007 from the Association for the Accreditation of Human Research Protection Programs (AAHRPP) of Washington, DC.

"I don't think, honestly, we would have been ready to be fully accredited without the full compliance of this monitoring program," Cola says. "That piece is central and critical to what we do."

To many research professionals, the image of an auditor is someone

who shows up and reviews documentation for a couple of days and then disappears, Cola notes.

"I wanted this process to be friendly with a 'We're on your team type of approach,'" Cola says. "Secondly, I wanted it to be in the arena of self-evaluation."

Since the compliance department is in the same institution and essentially on the same team as the investigators, it seems like a better approach to have someone come in from their team to prospectively check their studies for potential red flags, he says.

"In my mind this is a self-evaluation because we're all part of the same institution," Cola says.

The prospective monitoring program is intended to be investigator-friendly, and it includes education support, says **Carol A. Fedor**, ND, RN, CCRC, a clinical research manager of the office of research compliance at the Center for Clinical Research of the University Hospitals Case Medical Center.

"It's a good clinical practice approach that is based on supporting investigators and being proactive," Fedor says.

The center occasionally receives feedback from clinical research sites, and much of it is positive, says **Cristina Ferrazzano Yaussy**, MPH, research compliance specialist in the office of research compliance.

"Most recently, an investigator we monitored commented to another [clinical trial] group that his site had been a part of the monitoring, and it was great because it really taught them what they needed to do," Yaussy recalls.

Based on data recently published, the research institution has saved resources by using the prospective monitoring program, Cola says.

"We actually ended up saving resources that we would have utilized to fix something that went wrong," Cola explains. "Prevention is a better use for resources than riding in [on a white horse] when there's a problem."

The way the compliance office has developed its prospective monitoring program includes the random selection of studies to be part of the review process, Fedor explains. **(See story on strategies for conducting a prospective monitoring program, p. 3.)**

"It's random, but there is a hierarchy in the way they're chosen," Fedor adds. "There are high-risk studies where there's an increase of risk to participants, and those are generally part of the group that is chosen more frequently for monitoring."

Also, studies that involve vulnerable populations, including children and people who are decisionally impaired, and investigator-initiated studies would be more likely to be monitored, Fedor says.

Typically, the compliance office will pick sites for monitoring visits in groups of 10, Yaussy says.

"Once the protocols are chosen we send a letter to the investigator, letting them know they are

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selected as part of the review process," Yaussy explains. "Then I follow up and contact them to schedule a monitoring visit."

When the IRB makes a request that the office monitor a particular study, this visit will be added to the workload, she notes.

"We select areas to focus on based on what we understand to be common areas of noncompliance," Fedor says. "We want to be proactive and prospective in monitoring, so we look at what the federal government finds in their own quality assurance programs, and we look at the literature to see what the trends are."

The FDA's findings tend to be consistent over time, Fedor notes.

For instance, informed consent tends to be a major problem area for clinical trial sites, she says.

"It's the nature of the beast," Fedor says. "The screening and consent process have many details and variability, and errors can occur particularly during those times of the research study."

The compliance office is most concerned about areas that most greatly impact human subjects and their safety, Fedor adds.

For example, to have a person enrolled in a study when the person isn't eligible would be a potentially serious deviation, so the compliance office will review that carefully and consider eligibility criteria a priority area, Fedor says.

"Our aspiration is to use a preventive approach, rather than have the monitoring focus on those required directive requests from the IRB, Fedor says.

Also, prospective monitoring tends to be more cost-effective than directive monitoring, Fedor notes.

The monitors have a great deal of preparation work to do before a visit, Yaussy notes.

"The upfront work includes reviewing the IRB file, the protocol, consent form, and understanding the people who are identified to the IRB as research staff members," Yaussy says. "This is so that we can have an understanding of who is involved in the research, as well as what resources are used."

When discrepancies are discovered during the monitoring visit, the monitors make sure these are addressed at the site with the principal investigator, Fedor says.

"If the investigator chooses to have his staff present, we'd be happy to talk with him as well," Fedor adds. "And we'd certainly plan to schedule further educational sessions to make sure this service is seen as a support to them and not necessarily a punitive approach."

The education component is important because it helps research staff understand what the requirements are immediately and doesn't mean they have to wait for a month to receive a letter that outlines the problems discovered, Fedor says. ■

Use these strategies when providing a prospective monitoring program

Communication, education are key

Research institutions might consider providing prospective monitoring when enhancing a research compliance program.

There are benefits to such an approach, including improved human subjects protection regulatory compliance and the long-term cost savings of a preventive approach, experts say.

The office of research compliance at the Center for Clinical Research of University Hospitals Case Medical Center in Cleveland, OH, has developed a successful prospective monitoring program, following these strategies:

• **Keep monitoring visits time- and cost-effective.** The Center for Clinical Research tracks the amount of time it takes for each monitoring task and has developed a mean amount of time that it takes to monitor a protocol, says **Philip Cola**, MA, vice president of research and technology management at the Center for Clinical Research.

"If we randomly select a protocol it takes about 15 hours to complete everything," Cola says.

If a protocol is being monitored because of a reported problem then the time spent on monitoring increases to an average of 19.5 hours, Cola says.

"It takes four hours longer per protocol when there already is an issue developed versus randomly selecting a protocol," he says. "There is very different resource utilization depending on what's already the history of that protocol."

With a two-person staff, the center's monitoring capacity is about one study per week, says **Cristina Ferrazzano Yaussy**, MPH, research compliance specialist with the office of research compliance at the Center for Clinical Research.

"I'm usually the lead person who does the monitoring, so I'm definitely there for every

single monitoring visit," Yaussy says.

Monitors conduct a variety of pre-monitoring tasks, including contacting investigators and research coordinators to talk about the monitoring process, Yaussy says.

"We make sure the study is actively enrolling participants, and we help the research team up front," she adds. "We make sure the study chosen is appropriate, and then we choose a day and set a time for the monitoring visit."

The pre-monitoring work typically takes about 4.5 hours, Cola says.

"You have to have all of your tools ready and review the protocol with the IRB in some detail," he says. "Then you go out and schedule with the investigator and do a pre-monitoring interview."

The pre-monitoring interview involves sitting down with the research staff, including the coordinator and investigator and talking about the study, Yaussy explains.

This discussion will last 30 minutes to an hour as the monitor tells the investigator which documentation will be reviewed and which records to have readily available.

The monitoring visit takes about seven hours or an entire day for an average-sized study, Cola says.

"Even if there's a larger cohort of patients, you're randomly selecting subjects in the cohort, and that takes about seven hours," he adds.

Monitors use checklists during the visit, Yaussy says. The checklist makes the monitoring process run more smoothly, she notes.

"We look at the regulatory documentation and the regulatory binder relative to IRB submissions," Yaussy says. "If the Food and Drug Administration [FDA] is involved, we look at documentation by the FDA and sponsors."

There also is a separate checklist for the consent process, and this helps the monitors keep track of dates, Yaussy says.

The checklist was developed over time, says **Carol A. Fedor**, ND, RN, CCRC, clinical research manager of the office of research compliance at the Center for Clinical Research.

"We started by looking at what was publicly available at research programs across the country," Fedor says. "Then we streamlined and individualized it so it'd make sense for the type of research we conducted here."

The key is for the checklist to have information that meets the goals of the research program, as well as meets the standards of accreditation, Fedor says.

Finally, the post-monitoring time adds an additional eight hours on average for the study that has been flagged due to problems.

"This is writing up a plan, communicating with the investigator, asking for clarification, looking at grants and contract issues, checking with the investigational pharmacy if it's a drug study," Cola explains. "Then you start a plan for an educational session."

• **Add an educational component.** Monitors send summary letters back to the research group and follow up these letters with education and support, Yaussy says.

"We're available to help them understand why we made the recommendations we made," she says.

"Our approach is to get out there and work with research teams and do hands-on education and monitoring, which is how we assess and evaluate the process," Yaussy says. "We go back and talk with the research team, giving them helpful hints on how to do research responsibly."

The education component was enhanced as the monitoring program evolved.

After the first year or so of conducting prospective monitoring, it became clear that while these were friendly monitoring visits, they were less helpful than they could be, Cola says.

"We left the investigator with a letter that said, 'Here are the things you're doing wrong and that you need to fix,' but it wasn't the way I wanted it to be," Cola explains. "So we added a whole new component, which is education."

Now the monitoring visit is very useful to research groups.

"We say, 'Here are things that went wrong, but here is a program specifically tailored for you and your research group,'" Cola says. "We give examples of how you might do it differently for this study and future studies, and it's amazing how well that's worked."

The volume of educational seminars also has increased dramatically since the monitoring program began.

"We went from essentially offering one education session to the research community at the academic medical center per month to 35 responsible conduct of research education sessions on this campus in three months time," Cola says.

"We've trained about 500 people on some aspect of responsible conduct, and the most experienced investigators are showing up because they're saying, 'If we do this stuff in a proactive way it saves us all time, money, and resources

down the road,'" he says. "We have a staff of 25 full-time equivalents in the areas of grants, IRB, technology management, and research compliance, and these people all end up giving educational sessions."

When compliance monitors go into the field and notice that a research group is having difficulty with some process, such as the informed consent process, then they'll create for that research group an informed consent workshop, Cola says.

Cola says the education component is an essential part of compliance monitoring.

"Without the educational component attached to it, no matter how nice you are, it feels punitive," Cola says.

• **Include investigators and CR staff in planning educational sessions.** A feedback process was begun before the monitoring program was rolled out, Fedor notes.

"We invited a representative from most of the research groups," she explains. "We met with most of the clinical research coordinators and had to work with them to sell this idea."

Research coordinators are the ones who coordinate visits for monitoring, and they're the people the monitors call if there are any issues identified during the monitoring visit, Fedor says.

"So we had focus group discussions from the beginning, talking with coordinators, giving them a brief PowerPoint presentation, and getting their feedback," Fedor says. "I don't think we could have done anything else that was more important."

These feedback sessions empowered research staff to understand the nature of the monitoring visits, and it gave the compliance staff necessary information before they made changes to the monitoring process, she adds.

Research professionals also help plan some of the compliance education.

"We sometimes have investigators and study coordinators help plan the educational sessions because they're experts in the field," Cola says. "With their expertise and our expertise it comes to life."

For example, a research nurse in the emergency medicine department might be asked to speak about the rules in that setting and the practical issues that staff face, he explains.

"So we're utilizing our research environment and training the trainer," Cola says. "We're enabling them to bring all of this to life in the world, and I think that's why we're getting such good responses to the sessions."

An open door policy also helps improve collaboration between research administration and compliance offices and research groups.

Investigators are invited to go through the grant submission with the office, for example.

Also there are open sessions in which the IRB administrator answers questions by clinical trial investigators and staff.

"I make myself available and the manager of the IRB office and I sit in a conference room and say, 'Good morning, what are your questions?'" Cola says. "Also, some of the most senior investigators have come down and answered questions other investigators have about protocols." ■

Better CR sites succeed through faster initiation

Competitive pay and experience also matter

It's a question all sponsors and clinical research sites ponder: Why do some studies and some sites finish significantly faster than others?

A new study provides some answers.

"Good sites start enrolling quickly," says **Harold E. Glass**, PhD, MSc, professor, health policy, of the University of the Sciences of Philadelphia in Philadelphia, PA. Glass also is the president of TTC, a data base company in Philadelphia.

It's almost that simple.

"The amount of time it takes them to sign a contract is shorter, so they're in the field much faster," Glass says. "What happens is not only do they enroll on a weekly rate, but they actually enroll well and have more time to enroll because they're out there early."

Sites that begin enrolling earlier than others have more time to enroll and apparently use this time to improve enrollment, he adds.

"The study ends at the same time for everyone, so the only way to have more time is to enroll more quickly," Glass says.

The site performance study compared research data from 262 phase III studies that involved 2,047 sites in the United States and Europe.[1]

Experience counts

Besides having a faster initiation speed, faster sites also have more experienced investigators,

Glass says.

Researchers looked at the amount of studies that investigators had done for a particular sponsor in the previous three years by calculating the number of investigational new drug forms completed and submitted to the FDA, Glass says.

"We looked up how many times someone's name appeared in [form] 1572 records," he explains. "So sites that did more 1572s on record and did more work for pharmaceutical companies did a better job."

While this would appear to be an obvious finding, it apparently runs counter to conventional wisdom.

"You hear things like, 'Just because someone has done a lot of studies doesn't mean they'll be good in the future,'" Glass says. "Maybe someone will fool lots of people, and no one realizes they're actually terrible, but my guess is they're not bad; they're being selected because they did a good job."

While the better-performing investigators do receive more repeat business, it's also true that the larger sponsor companies are less likely to capitalize on this experience, Glass notes.

"The larger the sponsor company the less likely it is they'll use an investigator for the second time," Glass says. "I suspect it's because they're big companies and there's turnover in people and they lose track of them."

The best strategy would be to mix up the mix of new and experienced investigators, Glass suggests.

"You want new people now and then, but experience counts," he says.

Competitive contracts work best

The study also found that there is no relationship between how fast a site completes its work and how much it's paid, although how it is paid does matter.

"We have a model that determines what is the market rate in terms of clinical grants for the particular work in a country, looking at it in relative amounts," Glass says. "So being paid in the 99th percentile was top payment for comparable levels of work."

When researchers looked at this one measure, they found that how much a site is paid had almost no impact on completion speed, he says.

"If anything, and this is bizarre, it's negative: The more you pay the worse performance you get," Glass says.

"What does matter is how they are paid," Glass adds. "If you have competitive enrollment, then when you get more subjects in, you get paid more, and that makes a big difference in trial speed."

What worked best were competitive contracts.

Sites that were paid competitively, meaning they were paid for performing against certain milestones and if they didn't enroll subjects they were dropped, were faster enrollers, Glass says.

The study also found that sites that received upfront, nonrefundable start-up payments generally completed a higher number of patients.[1]

"Cash flow is important, so you want to make those milestones so you'll get paid," he adds.

Collect performance data

The study's findings have several implications for sponsors and clinical research sites.

First, CR sites should collect their own performance data, and sponsors should develop their own list of top-performing sites, Glass suggests.

"They should develop a list from the FDA of investigators by experience level," he says. "Then they should see what information they can find out about sites."

There already is considerable information available in national databases, but sponsors also have access to valuable site performance information in their own databases, he adds.

"There are lots of ways to construct investigator databases, especially if you find that sites that perform well start early in the process," Glass says.

Sites need to keep their own data because large sponsors have not yet embraced the idea of keeping site performance data and using it in the site selection process, he notes.

"People think these gigantic organizations are well-oiled machines, but they're made up of hardworking people who struggle from day to day," Glass says.

And they make mistakes, including losing or not maintaining their own site performance records.

Also, sponsors need to end contracts with sites that do not enroll or do not enroll quickly, Glass says.

"Sponsors hang on to sites way too long," Glass adds. "It's hard to let them go."

Manage the contract process

Secondly, sponsors and CR sites should work on signing contracts faster and negotiate for faster payments for performance, Glass suggests.

It's important to speed up the contract process,

he says.

"What irritates sites more than anything else is having a problem with cash flow," Glass says. "They need to work out something with sponsor companies to maximize their cash flow."

CR sites can start by being realistic about the financial side of research.

"That's where they get into trouble is by not believing that big companies can take so long to pay," Glass says. "But it does take a long time."

On the other hand, the more successful a CR site is, the more power it has in the marketplace. These sites should be able to negotiate a payment schedule that will serve both sides' interests.

"When sites first start research they have no idea what a hassle it is wait for payments, and they get caught off guard by this," Glass notes.

"What sites have to realize is there is no rule about how much they have to be paid, but it has to be reasonable for the work they're asked to do," Glass says. "There's a lot of variation in fair market rates, so I tell sponsor companies that it's only too much if they won't pay it, or it's not enough if they won't accept it." ■

Reference

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CR field needs better, more consistent training and education

Mistakes are made through ignorance

Clinical trial sites and institutions that want to reduce errors and undesirable audit findings need to invest more resources in educating research staff, an expert asserts.

Traditionally, clinical research professionals are thrown into the fire of research without formal education and training, says **Lisa Mazurka**, president and chief executive officer of Clinical Research Consulting of Boston, MA. Clinical Research Consulting is a niche clinical research organization (CRO) that provides clinical monitoring, project management, and education and training services.

When Mazurka first began working in the clinical research industry 15 years ago, she was given a verbal description of her job and one day with a mentor, who was the person she was replacing.

"In the past, it was a sink or swim education," she says.

But the climate that permitted this lackadaisical attitude toward education has changed substantially in the past decade, Mazurka says.

"People have become more accountable for research mistakes, as we read in the newspaper every day," she says.

These include headlines about deaths or major injuries in clinical trials and investigators and research institutions being suspended by the FDA from doing research, Mazurka explains.

"Many of these incidences could have been avoided if individuals had been adequately trained and educated," Mazurka says.

"We're hearing more and more, including talk at the FDA, about the need for proper education and training for individuals who are coming into this industry," she adds.

However, while improved education and training are being provided to new clinical research professionals, there is no formal requirement or mandate that would make such training consistent, Mazurka says.

"A physician has to go to medical school, and a nurse has to go to nursing school, and they both have to pass an exam to receive a license to practice clinically," she says. "But there is no such requirement for individuals who conduct clinical research."

While there's definitely interest and some movement into the direction of formal requirements, it hasn't happened yet, Mazurka adds.

It is a positive improvement that clinical research certification and accreditation are on the rise as voluntary measures to improve the industry's training and professional competency.

But this trend falls short of a standard and formal requirement.

"I think accreditation and certification are absolutely wonderful things in our industry, but the issue is that to sit for the certification exam, you need two years of experience," Mazurka says. "Where does training and educational experience come in before that happens?"

The handful of universities that have started formal programs to train clinical research professionals should be applauded for their work, but these can reach only a small number of people who are in need of such education, Mazurka says.

"Many individuals who are just starting out in the industry and who would benefit from these

programs don't have time to attend an academic program," she explains.

Likewise, there are many education and training programs available through conferences and on-line curricula, but until these are formal requirements, these will not be accessed by everyone who needs them, she says.

"We're all trying to develop these wonderful programs to solve the problem, but we run into resistance due to budget and time constraints, and it's not mandated," Mazurka says.

"There is a lot of discussion within our industry to mandate some sort of formal education and training, and it is on the table," she adds. "But it's been on the table for many years, so the question is, 'When will we see action on it?'"

It's through education that many common trial mistakes can be prevented.

For instance, Mazurka has often seen examples of clinical research staff making mistakes that highlighted their lack of knowledge about human subjects research regulations.

"One common thing that happens is that a patient is being considered for participation in a clinical trial, and the site actually starts to evaluate and perform tests to determine the eligibility of that subject prior to obtaining informed consent," Mazurka says. "Some of these are routine tests, but if they're truly being used to determine eligibility for a protocol, then the patient needs to have adequate informed consent and needs to have documented informed consent before any procedures are conducted to determine the patient's eligibility."

The regulations clearly state that informed consent must be obtained before any procedure is performed, Mazurka says.

In absence of mandated education, clinical research institutions should develop their own formal education and training programs for all employees, Mazurka suggests.

"We should focus as an industry on documenting training and education for clinical research employees," she says. "They can attend classroom type education and training programs, or if they can't get away from the 40-hour workweek, then on-line education provides an added benefit."

Likewise, research institutions should provide staff with the funds and time necessary to seek certification, Mazurka says.

"We should encourage people upon their two-year anniversary of a job to pursue certification," she adds. ■

Study shows that medical residents lack necessary biostatistics knowledge

Points to problems with knowing research

Medical residents often lack the knowledge and skills they need to interpret medical research studies, which can jeopardize their ability to integrate new findings into their clinical practice, a recent study says.

But it also points to potential problems when these same doctors become researchers.

"We rely on medical literature to keep us up-to-date, and if residents can't understand the methods and results, it could potentially lead to incorrect interpretation and errors and application of what they read," says **Donna M. Windish**, MD, MPH, an assistant professor of medicine at Yale University School of Medicine in New Haven, CT, and at Waterbury Hospital in Waterbury, CT.

There are notable examples of how incorrect interpretations of studies have led to public controversy and changes in clinical practice, such as media reports that exaggerated the coronary risk associated with the diabetes drug rosiglitazone, Windish notes.

Through proper biostatistics and research training, physicians can make their own determinations about the validity of a study's findings, and not rely on headlines in the popular media.

Windish decided to research biostatistics knowledge among residents after noting some educational deficits in her own and in her students' learning experience.

"The study was initially generated through my own teaching at Yale, Johns Hopkins, and when I was a resident myself," Windish says.

"We were expected as physicians to read the most updated literature and interpret the results without having a strong knowledge of the methodology," Windish explains. "I personally found it challenging, and when I became a professor I found the medical students had the same fears and lack of understanding."

Windish conquered her trepidations about biostatistics by learning more as she earned a master's public health degree, but she says that most medical students encounter too few biostatistics courses during their medical training.

"It's very variable," Windish says. "If it's

taught at all, it's taught during the first year or two of training, the pre-clinical years, and that training can last a couple of hours to several courses."

The study, published in the *Journal of the American Medical Association*, surveyed 277 internal medicine residents of 11 residency programs in Connecticut, and found that the overall average percentage correct on statistical knowledge and interpretation of results was 41.4%.[1]

"We limited it to internal medicine trainees, but their characteristics represented trainees from across the country," Windish says.

This compared with an average of 71.5% among fellows and general medicine faculty with research training.[1]

"We looked at 11 programs that allowed us to study their residents, survey them, and give them some training in statistics when we were done," Windish says.

"I heard the same anxieties about statistics from everyone," Windish notes. "If they were taught anything, it was so long ago and not placed in clinical context, so it wasn't meaningful to them."

Researchers created the survey instrument after reviewing the literature for three months, including *JAMA*, and summarized the statistics found in 239 articles, based on which ones were used most frequently, Windish explains.

They wrote questions that best represented the studies' findings.

"Some questions were borne out of biostatistics courses," she says.

For example, Johns Hopkins University gave the investigators permission to use their quizzes and tests, Windish adds.

Altogether the multiple-choice test contains 20 questions, and it's designed to be completed within 20 to 25 minutes, Windish says.

The full test is published as an appendix in *JAMA*, available to other researchers or academics who are interested in it.

The results show that some work needs to be done in improving new physicians' biostatistical knowledge, she adds.

"Residency programs should include biostatistics training to reinforce what was taught prior to residency, if it was taught at all," Windish says. "And they need to make it clinically relevant to their trainees."

Another reason why medical residents should have a firm foundation in biostatistics education is because they might one day want to become researchers.

"Part of the residency training that's mandated by the Accreditation Council for Graduate Education is that all residents have to do some type of scholarly work, and most people try to do research," Windish says. "We see a struggle among our own residents who want to do research, but have a fear they won't be able to analyze the results or even design the study."

Also, there is a national trend of increasing numbers of research studies moving to community settings, where physicians have very little, if any, experience in research. This is another reason why more statistical training is needed.

"Even with our current program, we've been working on developing not only more research methodology training through statistics' courses, but also to give them more formal education and some higher research methods in statistics," Windish says.

This will be a challenge for most educational institutions, she notes.

"It's challenging because even some of our faculty don't have research training," Windish says. "So how can they teach someone else when they don't have the background?"

Windish started a statistics course last year for trainees, and she used the same instrument employed in the study to see whether the training improved the students' knowledge and skills.

"It was only a four-hour course, and those who took the course one time scored 59% on the instrument," Windish says. "Those who took the course a second time, a year later, scored 70%."

These preliminary data support the idea that medical residents don't need large interventions or years of statistics, but would benefit from better information about biostatistics, she adds.

While researchers sometimes do need to consult with biostatisticians to help with study design and statistics, it still is important for medical researchers to demonstrate some competency in research methodology.

"The only other thing we need to consider is whether or not faculty are trained enough in our residency training program to be effective teachers of research and biostatistics," Windish says. "We're trying to work on our own residency training and build a course."

If these efforts succeed, then the information will be distributed to other institutions and training programs for help in developing their own training courses, she adds. ■

Reference

1. Windish DM, et al. Medicine residents' understanding of the biostatistics and results in the medical literature. *JAMA* 2007;298:1010-1022.

Improve your site's relationship with monitors

Coordinators and monitors can compromise

Clear communication and a good understanding of expectations and goals are necessary elements of the relationship between clinical trial professionals and clinical research monitors.

However, each person may have a different perspective and objective, so finding common ground sometimes can be a challenge.

"One thing people need to recognize is that motivations between monitors and study coordinators are different," says **Celine M. Clive**, MBA, president of Polaris Clinical Research Consultants Inc. of Cary, NC.

"Although study coordinators and monitors are both interested in research, study coordinators are focused on clinical care of patients — as they should be," Clive says. "But the clinical care is secondary for monitors."

For example, monitors focus on retrieving data and retrieving regulatory documents, Clive says.

These aspects of research often are of secondary concern to study coordinators who make study participants their main focus, she adds.

"The coordinator does make research a priority," Clive explains. "But most of the time, she thinks that being in this research is the best clinical option for that person."

Study coordinators will find that sponsors each have their own ways of doing things, and adapting to many different expectations can be a challenge, notes **Jane K. Downs**, RN, CCRC, research director of Raleigh Neurology Associates of Raleigh, NC. Downs worked as a monitor for several years in the 1990s, but she missed caring for patients and so switched to the other side of the fence.

"You have dedicated, invested people on both sides, and that can cause conflicts," Downs says.

"The study coordinator will say, 'I've always done it this way,' and the monitor will say, 'I've always done it this way,'" Downs explains. "The key is to compromise and keep your eyes focused on what's really important, which — to me — is the patient."

Most of the time, study coordinators and monitors can find common ground, which is why Clive and Downs offer these tips on how to improve the relationship between study coordinators and clinical research monitors:

• **Help monitors understand the study's science.** New monitors sometimes understand research regulations, but do not understand the science and medicine, Clive says.

Study coordinators typically specialize in one therapeutic area, and so they know that science in depth. Monitors go from study to study and have to be knowledgeable, at least shallowly, on a variety of clinical areas, Clive notes.

"So study coordinators can really help the monitor by actually instructing the monitor on this science and medicine," she adds.

One obstacle to this is time. "Monitors have such a tight time frame that while they may really appreciate the additional instruction, they often have limited time at the site and can't get their work done if they take time for training," Clive adds. "But I think they'd be more effective in their work if they took time for training."

Study coordinators can help by giving monitors any of the patient information about the study, Clive suggests.

"You can take that a step higher and maybe the investigator has published some papers on the disease state studied, and the monitor should be reading the literature that was published by the investigator," Clive adds.

• **Compromise, compromise, compromise.** "If a coordinator and monitor are having a tough time at something, just say, 'Let's look at this from both perspectives,'" Downs suggests.

For example, study coordinators often do not like to file memos because they are red flags to the FDA that something is wrong, Downs says.

"If there's a problem with one patient on one issue, then you should write a note in that patient's chart, and you don't need to file a memo, which should be saved for the big things," Downs explains. "But you find monitors who think memos are the best thing since sliced bread."

When this happens, study coordinators should carefully explain to monitors what the site's policy is with regard to memos, Downs suggests.

Together, coordinators and monitors could reach an agreement about how much should be reported in a memo.

Everyone's goal is to conduct safe and

scientifically valid research that will help to bring a good drug to market, and no one's goal is to complete irrelevant paperwork, Downs notes.

"To promote the monitor-coordinator relationship, I try to make them understand this, and I say, "I'll help you out if you'll help me out," Downs says. "Sometimes they ask me if I'll do this one thing for them because they know [we don't think it's necessary], but they need it."

When coordinators compromise and give in a little to monitors, they might expect something in return.

"I'll do the favor for them, but I'll want them to pick up the phone for me the next time I have a crisis," Downs says.

• **Learn from monitors.** Monitors might need to update study coordinators about regulations, and if both professionals look at their relationship from a collaborative perspective, they'll both benefit, Clive says.

However, coordinators should keep in mind that some of the rules that monitors say are regulations are company policies and not actual government requirements, Clive notes.

"Coordinators will get a variety of instruction and sometimes it's contrarian instruction because of various company policies," Clive explains. "So what happens is the poor coordinator is being told, 'Here you need an original, and here you need a copy,' and it's different according to whom is asking for it."

None of these types of details are driven by regulations, she says.

"It helps to understand where there is flexibility in terms of company policies, versus no flexibility because of the regulations," Clive says. "If coordinators and monitors are building a good rapport, they can foster that understanding."

• **Build rapport.** A lot of information, as well as a better rapport, can be conveyed in the on-site visits, Clive says.

"When the monitor goes to visit the study coordinator, and they're both sitting side by side, it gives them a good opportunity to explain why they're doing it this way and what is needed from both points of view," Clive says. "So I put a lot of stock in the on-site visit."

Also, monitors should be sensitive to the fact that clinical trial coordinators may feel overwhelmed by the documentation and electronic data requirements, Clive notes.

"Electronic case report forms were supposed to make everyone's jobs easier, but it transferred the task of data entry to coordinators, so it resulted in more work for coordinators," Clive explains. "It sped up the data retrieval process, and it may have eliminated things like tracking logs, but it doesn't save coordinators that much time."

Monitors have many pressures that coordinators may not understand, Downs says.

"Monitors might have a standard operating procedure (SOP) at their clinical research organization that says they have to turn in a monitoring report within five days of doing the visit," Downs explains. "If coordinators don't give monitors the information they need for the report

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. ■

COMING IN FUTURE MONTHS

- ■ Improve recruitment of women in research
- ■ Use sleuthing, innovative methods to improve CR recruitment
- ■ Learn ins and outs of clinical trial agreements
- ■ Integrate compliance efforts for better efficiency

then they can't do their job."

Coordinators should keep in mind that monitors have an important job too because the sponsor is paying the site to get the research information, and it's the monitor's job to give the sponsor information for the study, Downs adds.

Finally, coordinators should think of monitors as part of their research team and treat them with patience, even when there's a heated disagreement, Downs suggests.

CE/CME *questions*

1. Which of the following is an essential ingredient of a successful prospective monitoring program?
   A. A two-day on-site visit
   B. Education of site investigators and clinical research staff
   C. Punitive measures for sites with findings
   D. All of the above

2. Which of the following has been found to contribute to a CR site's faster enrollment and successful completion, according to a recent study?
   A. More experienced investigators
   B. Faster initiation of study, including signing contract
   C. Higher pay for site's participation in study
   D. Both A and B

3. What was the average correct score of internal medicine residents in Connecticut on a test of their biostatistical knowledge and interpretation of results?
   A. 41.4%
   B. 59.8%
   C. 71.5%
   D. 82.5%

4. Which of the following best characterizes the chief problem with clinical research education and training?
   A. It's mostly informal.
   B. It's inconsistent and unmandated.
   C. It's employed only after a major disaster occurs.
   D. None of the above

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

"You can't just say 'No' for the fun of it," Downs says. "When monitors get really excited about something, say, "I'll think about that and get back to you,' letting the situation cool down."

Often what seems like a crisis today is not really a crisis and once things cool down, coordinators and monitors can come back to that issue, she adds. ■