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Research sites can improve compliance by forming centralized CT operations

CT research has become more complex

Large research institutions can help clinical trial (CT) investigators and staff improve their study operations and regulatory compliance by providing clinical research staff services through a centralized office.

Best practice examples and current regulatory pressure have combined to make centralized CT offices a viable and attractive alternative to the traditional approach of each department having its own CT operation, experts say.

Centralized CT offices can oversee compliance and billing issues, as well as provide support services to investigators and research sites. Centralized CT offices might provide contracting services, a staffing pool, and assistance with the IRB submission.

"When you do things independently, you don't have the mentorship and training support that centralized offices provide," says **Tammy Anderson**, CCRC, CCRA, CRCP, director of the clinical trials office at the office of the vice president for health sciences, Virginia Commonwealth University in Richmond, VA. Anderson speaks about centralizing the IRB office at national conferences, including the MAGI Clinical Research Conference — West, held Oct. 24-27, 2010, in San Francisco, CA.

"We can go into departments where they have new coordinators and provide them with mentors and training to make sure everything is set up properly," she explains. "We make sure new coordinators learn how to document properly and know which things are applicable to the conduct of research."

Without this training it's very difficult for a person coming in as a research coordinator to know which regulations, competencies, and training are necessary to their work.

"Protocols have become much more complex; the number of case report form pages has increased," Anderson says. "It's becoming more

difficult for coordinators to do everything."

These issues contribute to start statistics: 80% of all investigators conduct only one clinical trial; 38% of physicians do not return to the clinical research enterprise within any given year, and 61% of current study coordinators held their position for less than three years, Anderson explains.

"This is a nationwide issue," she adds.

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Research compliance is a bottom up process. It relies on front-line research coordinators and other staff adhering to regulatory requirements and best practice guidelines in their day-to-day jobs, says **Kelly Willenberg**, BSN, MBA, president of Synergism, LLC of Chesnee, SC. Synergism provides research compliance, including billing and program compliance services for clinical research sites.

However, research sites need help with compliance issues, which is why it's important to have a centralized research office or a designated billing or compliance manager to oversee compliance, education, and monitoring or audits, she adds.

Look for the deeper issues

Research investigators and staff often fear they have made mistakes in billing, but compliance issues can run deeper than this.

Often, research institutions have decentralized clinical research, conducted in departments that lack communication, training, and consistency, Willenberg says.

"They have undefined roles and responsibilities for staff," she adds. "They have all of these risks because they don't even know they have a risk."

Forming a centralized research office is one answer to this problem.

"Some sites are forming a centralized office because it's cost-effective," Willenberg says. "If you don't have a centralized office to handle clinical trials, billing compliance, and operations then you end up with a lack of consistency across an institution."

One model research institutions sometimes use involves having a centralized office for all research, except for studies conducted by the institution's cancer center. This occurs because cancer centers typically have been conducting research studies for decades. Often they have a clinical research process that is better evolved than other departments.

However, there is a big risk when the centralized office and the cancer center lack communication and consistency, Willenberg says.

For instance, pharmaceutical sponsors might be concerned when they see that research is being conducted differently at the same institution, she adds.

The solution would be for the institution to establish policies and procedures and standard operating procedures that are consistent from one department or research entity to the next. And

the centralized office should have a clear avenue of communication with any remaining research offices.

If one department of a research institution has a good CT operation already, then it wouldn't make sense to fold that operation and make the department start over with a new centralized office, Willenberg acknowledges.

"You need to take the model you have in the cancer department and grow it across the institution," she says. "Then proper oversight will become a fluid process."

Also, when institutions form a central clinical research office they should look for ways to eliminate duplication. Perhaps a cancer department could keep its coordinator hiring and training process, but would be open to merging its billing process with the centralized office's billing.

Before Virginia Commonwealth University formed its centralized clinical research office, Anderson spoke with industry sponsors and others to determine what worked and what didn't.

"We set up several steering committees and groups to look at what clinical trials means from the different perspectives of billing, compliance, etc.," she says. "We looked at all different angles and aspects to determine where our gaps were and what were the needs."

The existing practice was for each university department to handle CT operations and budgeting separately. Each study coordinator hired would be in charge of study enrollment, IRB submissions, subject visits, documentation, and meeting with study monitors.

"If someone wanted to do clinical research, they'd hire someone to be a coordinator or nurse, and the only thing centralized in our university was the contracting aspect," Anderson says. "All contracts had to go through the office of central programs."

But studies sometimes ran into problems when new coordinators could not keep up with study enrollment, as well as all of the other daily tasks. *(See related story, right.)*

This created potential compliance issues since new research staff typically did not have the benefit of working with an experienced mentor. They also lacked the comprehensive type of training that would be available through a centralized research office, she adds.

"Prior to our creating the centralized office, it was very difficult for a person coming in as a research coordinator to know what the regulations and competencies and training were needed to work as a study coordinator," Anderson says.

Free up the coordinators

Virginia Commonwealth University's new centralized research office now offers investigators expertise in each area of CT operations. Investigators can contract to have a recruitment coordinator assist with their study's enrollment, and they can use one of the centralized office's regulatory specialists to assist with IRB submissions, case report form documentation, handling monitor visits, and other regulatory/documentation issues.

"This frees up their coordinators to screen patients as they're identified and to conduct visits," Anderson says. "They have time to see more patients."

The office, which opened in April 2010, now has five departments and nine investigators using its services.

Forming a centralized office is one good strategy for improving research compliance, particularly because it results in better consistency and communication, Willenberg says.

Research institutions with multiple CT offices can achieve better compliance, but only if they have everyone following the same process and budget template, she notes. *(See related story on p. 125.)*

"When I go to a site, even if there are two or three different areas, I make sure they're all using the same budget-development templates and guides and have standardized pricing," she says. "This way you have better consistency with what you're doing, and compliance automatically increases because the flow of documentation is better." ■

Improving compliance consistency via training

Specialized CR positions, budget templates

Clinical research (CR) organizations should focus on two key areas when targeting compliance: First, they should centralize their clinical trial operations or make the decentralized system more consistent; secondly, they should put more resources into CR education and training, experts say.

Here are some ways research sites can improve their consistency, compliance, and staff training:

• Put adequate resources into staff education.

"Because of the economy, people don't have funding, so research employees sometimes are put into these jobs without enough training," says **Kelly Willenberg**, BSN, MBA, president of Synergism, LLC of Chesnee, SC. Synergism provides research compliance, including billing and program compliance services for clinical research sites.

"Study coordinator jobs are extremely demanding, and there are a lot of regulations and things you need to know to do it well and to be accountable," she adds. "Training and education are key, and so many sites do not offer enough training, and I think research is going to suffer for it in the long run."

Online CR courses are fine, but these shouldn't be a one-time educational effort.

CT coordinators need continuing education and mentoring. Their education should focus on all aspects of clinical trials and not focus solely on human subjects research protection, Willenberg says.

"The better the education and training, the better the culture of compliance an institution has," she adds. "When everyone is well-trained the process will flow better, and there's no denying that."

Research sites could hold monthly training and continuing education sessions for coordinators, says **Tammy Anderson**, CCRC, CCRA, CRCP, director of the clinical trials office at the office of the vice president for health sciences, Virginia Commonwealth University in Richmond, VA.

"We have coordinator training on the last Friday of each month," she says. "We provide a monthly topic discussion about the conduct of clinical trials."

Virginia Commonwealth University also provides an Association of Clinical Research Professionals (ACRP) training course with detailed and complex training for advanced coordinators. This course assists them with taking their certification exam, Anderson says.

"We also provide individual training, as needed in the different departments," she adds. "We have a checklist of competencies and training we require of all staff when they're hired, including human subjects protection, good clinical practice guidelines, and HIPAA training."

• Create a career ladder that encourages experienced staff to stay.

One problem research sites encounter involves high staff turnover. Better education and training can help reduce turnover, but so can dividing professional roles in a way that reduces employee frustration and increases opportunities for career advancement.

Virginia Commonwealth University's new centralized CR office has created a model for this type of study coordinator career ladder by dividing jobs into specialty positions of recruitment specialist, regulatory specialist, study coordinator, and others.

For instance, the regulatory specialist position is a good beginning job for new study coordinators. They can start with this job, gain experience and learn more about how clinical trials work.

"We train our regulatory specialists to be backup to the coordinators and assist with visits," Anderson says. "They can move up the career ladder to assistant coordinator and then, after two years of experience they can sit for a certification exam and become certified."

Regulatory specialists make certain all paperwork is available during coordinators' visits. They process lab work, enter data into electronic databases, copy source documentation, and set up patient binders.

A next level up are the entry level coordinators who can perform patient screening and patient visits, but are generally assigned to less complicated protocols under the supervision of an advanced coordinator, Anderson explains.

Advanced certified coordinators work directly with the departments involved in a study to coordinate multiple departmental issues and needs, including scheduling and developing more complex study protocols or inpatient studies. All of these roles can be held by non-RN research staff, depending on their level of experience, training, and education.

A parallel career track includes an entry level RN coordinator and an advanced certified RN coordinator.

Recruitment coordinators are certified coordinators because this role requires a professional who fully understands study exclusion and inclusion criteria and how to conduct clinical trials, she notes.

"The recruitment coordinator position is equivalent to an advanced coordinator," she adds.

Research assistants are at the very bottom of the career ladder in the centralized office, and this role typically is held by volunteers or students, Anderson notes.

"These are the ones who take paperwork around to get signatures; they make copies, run the mail, and perform basic office duties," Anderson says. "We take advantage of federal work study programs at the university so that financial aid programs pay most of their salaries." ■

Integrate best compliance practices in CR operations

Assess, educate, monitor billing compliance

Clinical trial (CT) sites need to do system-wide risk assessments of the CT process to see where they need to improve policies, procedures, and operations, says **Kelly Willenberg**, BSN, MBA, president of Synergism, LLC of Chesnee, SC. Willenberg works with sites to improve research compliance, including billing and program compliance services.

"From my experience, I see that different things work for different places," she says. "It can be challenging to assess the state of your operational engine."

CT sites sometimes have a vague sense that they have a billing compliance risk, but they don't realize how big the risk is, she says.

"I see the biggest problems in billing compliance," Willenberg notes.

But sites also might have conflict of interest and human subjects protection issues.

"They don't have a solid informational infrastructure to build on," she says. "And they're just kind of muddling along with no standard operating procedures (SOPs), plan for the future, or an effective self-monitoring plan because they don't know what they have."

Willenberg suggests sites follow these steps to improve their compliance practices:

• **Establish effective billing compliance practices**: Sites often fail to realize that it takes a multidisciplinary team to do billing coverage analysis and the budget process, Willenberg says.

"They sometimes don't know they have problems because they don't know how to set it up to start out," she explains. "Their first priority should be to have someone in a position who is designated to be responsible for research billing."

This person needs to be very knowledgeable about the regulations and the institution's rules, as well as understanding key compliance principles.

The billing compliance point person also should have the authority to make decisions and changes as needed.

If a site is unable to hire a billing compliance manager, then it would be a good idea to contract with an expert to provide risk assessment and auditing services.

• **Provide adequate investigator and staff training:** Sites often fail to provide adequate and ongoing staff training.

If investigators and study coordinators do not understand the regulations then it is difficult for them to ensure complete compliance.

"Maybe they never had the proper education and training to even know what they should be doing," Willenberg says.

This training should include human subjects protection, best practices, good clinical practices (GCP), clinical trial billing compliance, and other compliance issues.

• **Define your institution's specific compliance needs**: "Some places will find their need is billing compliance; some will need better consent form documentation, and other people might find their need is consistency and integrating compliance into their research operations," Willenberg says.

A CT site might need a process improvement action plan that is communicated to all staff.

"A lot of times what's lacking is communication," Willenberg says.

Most CT sites would benefit from making certain all policies and procedures are written down and defined.

"Then assess and document what educational training is required for all personnel involved in research," she says. "When people are well-trained and receive education on a routine basis, then role delineation and responsibilities are carefully and better outlined for people."

P&Ps can explain who has the authority and responsibility for various research tasks.

"There's a price to pay if you're not doing all this," Willenberg says. "You have potential financial risk and regulatory problems, and the institution's values might be compromised."

• **Conduct self-monitoring and risk assessments:** Sites need to monitor their open studies and look for trends.

"Some institutions will do random self-monitoring, working with a compliance department or internal audit department," Willenberg says. "They'll interview key principal investigators and personnel and assess where they are at that point in time."

If they're assessing the billing process, here are some questions to ask:

— Is the institution charging Medicare for research activities?

— Did the institution bill appropriately to other payers?

— Did the institution bill the sponsor for screening failures or items and services done for research purposes only?

— Were the proper codes and modifiers put on bills that went to Medicare?

"There's a process research sites have to follow at the beginning of a trial to see which activities qualify for Medicare and should be billed," Willenberg says.

"Ninety percent of the time what I see is the accounts receivable are lower than they should be because sites are not billing appropriately," she says. "They're not collecting their accounts receivable and monitoring what should be coming in and what is not billed appropriately."

Before a study begins, a CT site should determine which payer is responsible for each activity, and this information needs to be included in the informed consent form that the patient signs, she adds.

Sites might do a careful coverage analysis before opening a study. This will help them identify holes in their compliance program, especially in billing.

Self-monitoring also means that the site will conduct random review of bills, segregating charges and matching these with what was included on the patient's informed consent.

"In the standard review process, this will ensure you are doing billing compliance in the way you should be," Willenberg says. "You can have a great system, but if someone is not checking how you're segregating charges then who knows if it is being billed correctly." ■

Recruitment specialists can increase enrollment

Specialist takes time to build MD relationships

Study recruitment is an increasingly difficult role that requires relationship-building work among community providers and other skills that clinical trial coordinators might lack.

"Most doctors call our office because they have problems with recruitment, which is the number one problem nationwide," says **Tammy Anderson**, CCRC, CCRA, CRCP, director of the clinical trials office at the office of the vice president for health sciences, Virginia Commonwealth University in Richmond, VA.

"What I have found is that the personality and experience that makes a good RN and study coordinator does not necessarily make a good recruiter," she adds.

Study recruitment has changed for many principal investigators in recent years. While they once might have received dozens of phone calls from a radio or newspaper advertisement, now they find the phones are quiet and finding potential subjects to screen is a challenge. But sponsors still allocate only a limited amount of resources to recruitment, so many studies flounder with no or too small enrollment, Anderson says.

One solution is to hire a contract study recruiter through a research institution's centralized research office, she suggests.

"Our university is supportive of our clinical trials office, and we were given funds to get started so we could provide the role of a recruitment coordinator," Anderson notes. "But it's interesting to me that the key factor sponsors need is recruitment, yet none of the sponsors will pay for a recruiter or marketer; they'll pay for advertising, but they won't pay for a site to have someone dedicated to recruitment."

The problem likely is that sponsors still operate under an older system that expects investigators to recruit easily through traditional advertising methods, despite evidence that the old way is not working well in the 21st century, she explains.

"In 2000, sponsors were spending $400 million a year in recruitment advertising; in 2008, that figure was up to $515 million," Anderson says. "Yet inquiry rates have dropped to less than 1% from 3%, and randomization rates declined from 75% of screens to less than 60%, and completion rates are running two-thirds to less than one-half."

A best practice way to handle recruitment is to build relationships with clinical practices and have staff that can focus just on recruitment, Anderson says.

"We need to find a way to get sponsors on board with supporting the physical recruitment efforts and not just the advertising costs," she adds.

Some research institutions are facing the reality of study recruitment challenges and are devoting their own resources to hiring recruitment specialists.

The Virginia Commonwealth University's new centralized CT office offers researchers a wide range of services, including contract staffing for

the purposes of study recruitment. This role has proved invaluable to some investigators.

For example, one long-time investigator who typically had 20 to 30 ongoing studies per year had been cutting back because her research coordinators could not keep up with enrollment work, Anderson explains.

"She originally had two or three coordinators who would do all of the IRB submission work, handle advertisements and call scripts, do all visits, complete case report forms (CRFs), coordinate monitoring visits, handle regulatory information and continuing reviews," she says.

What would happen is they'd begin to enroll for a new study and then get so bogged down with the other duties they wouldn't have time for aggressive recruitment practices when enrollment slowed down, she adds.

So this particular physician investigator was having problems with recruitment and called the clinical trials office for help.

Anderson assigned a recruitment coordinator to work with the physician, and this person handled telephone calls and met with physicians at local primary care offices and specialty clinics to identify patients who might meet the study's criteria.

The recruitment coordinator had built trust with community providers and their staffs. So when patients came in who might meet the study's criteria, the staff would ask if they'd like to speak with a research recruiter, who happened to be sitting there.

Then the recruitment coordinator would make appointments for patients to come into a satellite research clinic to be screened for a study.

"Our recruitment coordinators spend all of their time recruiting for all of the studies we have that are open for recruitment," Anderson says. "They might recruit for several different physician investigators, and they suggest to clinic nurses that a particular patient might be a candidate for a study so they would give the patient a brochure."

Since the recruitment coordinators carry around Blackberry phones, they are able to respond quickly to any recruitment calls or emails they receive, she adds.

"They've already done the legwork to have relationships with physicians," Anderson explains. "But it's important to have someone be physically there in the doctor's office, serving as a constant reminder to the clinic team."

These specialized recruitment services had an immediate impact on the investigator's study enrollment: within six weeks, the recruitment coordinator had enrolled 12 study participants in trials that had been unable to enroll even one person over a number of months, she says.

The investigator had been at risk of losing three projects because she couldn't enroll patients in these studies. The recruitment coordinator had identified three to four patients in each of those studies, meeting two 30-day deadlines.

"The phones are ringing off the hook, and the recruitment coordinator has a list of patients responding to ads," Anderson adds. "We're identifying patients daily who are interested in participating in clinical trials." ■

iPhone app makes trial adverse event grading more efficient, easy

Toss the laminated information cards

Researchers and informatics specialists at The Children's Hospital of Philadelphia (CHOP) of Philadelphia, PA, have found a novel way to connect a research tool to popular telephone or hand-held computer technology, making the grading of adverse events (AEs) more efficient and faster.

Although it was developed for use in oncology clinical trials, the tool could be adapted for other types of studies, as well, says **Peter White**, PhD, director of the Center for Biomedical Informatics (CBMI) at The Children's Hospital. White also is a research associate professor in the division of oncology at the University of Pennsylvania in Philadelphia.

The new tool was developed as an application for iPhones, iPods, and iPads, and it's available for a free download on iTunes online.

The standard classification system for adverse events in oncology research is the *National Cancer Institute's Common Terminology Criteria for Adverse Events* (CTCAE), a 200-page handbook.

The CTCAE standards help investigators quantify the severity of toxicities from anticancer drugs used in clinical trials, says **Frank M. Balis**, MD, director of the Clinical Cancer Research Center for Childhood Cancer Research and director of the division of oncology at The Children's Hospital.

"The iPhone app developed at The Children's Hospital displays these standardized toxicity grad-

ing criteria in an easily searchable and very portable format," Balis says. "We have loaded the app on iPod touches for our clinical research associates, who collect data for our clinical trials."

Research associates then can take their iPods to rounds and ask clinicians to grade their patients' toxicities based on descriptions of the various grades, he adds.

"This allows us to collect these data in near real time while the information still is fresh in the clinician's mind," Balis says.

This type of tool lends itself well to new mobile technology, White notes.

"The reason we were interested in doing this is because some time ago we figured mobile applications would play a significant role in the hospital here," White says.

The informatics center staff had discussions with oncologists about how to create a clinical trials database and registry. One oncologist was trying to figure out a way to standardize how the adverse event reporting occurred.

The oncologist wanted to find a simple and fast way to make the CTCAE information available to clinical trial investigators and coordinators as they observed AEs in study participants, White explains.

"One suggestion was to create a series of laminated cards and make these available to individuals," White says. "While the oncologist was having this discussion with our informatics developers, Mike Italia and Lauren Frazier, he was idly playing with his iPhone on the desk."

Eureka!

The informatics developers suddenly realized that researchers commonly used this technology, and that the CTCAE could be turned into an application on iPhones.

They decided to develop it for Apple's telephone technology because these were homogenous in terms of hardware platform, and only one version would be necessary.

"It's a little more of a controlled environment than the android environment with several different manufacturers and different versions of phones," White explains.

Plus Apple's iPod Touch is relatively low cost, he adds.

The portability of the app also makes the tool convenient. Although it was developed as a research tool, it has crept into use in patient care as clinicians use toxicity grades to determine drug dose reductions in patients receiving anticancer drugs, Balis says.

"The iPhone app is very intuitive so essentially no training has been required," Balis says. "Most people can pick it up and use it because it follows the same conventions as other iPhone apps and the iPhone OS."

The tool is efficient, taking a few seconds and several taps on the keypad to find a CTCAE answer to any adverse event inquiry, White says.

"Especially if you rely on a mobile device for several aspects of the clinical trial then it becomes almost second nature that you're using it, so it saves time," he adds.

Programs like the CTCAE app that bring research tools to the clinical space increasingly will be important to the future of clinical trials.

"Unlike the CTCAE book, you always have it with you if it's on your phone, and you can use it when unexpected problems arise," Balis says.

The next step would be to make adverse event reporting as simple and easy.

"It would be exciting to enter data directly into this system wirelessly using the PDA functions of an iPhone or iPod touch," Balis says.

"Most centers are moving towards paperless systems for patient care and management of clinical trials and the data that they generate," he explains. "Here, we are working to ensure our electronic medical record and clinical trial management system can communicate with each other directly."

An iPhone app that permits data input for clinical trials would help reduce the potential for data input errors, but the transition has many system barriers.

For instance, a device that records AEs from study subjects who also are patients in a hospital's clinical care could be viewed as a medical device by regulatory authorities, White says.

"We haven't explored that option yet," he says. "There's a whole business process you go through to create medical devices, and this would have to be regulated by the Food and Drug Administration (FDA) if we reported it."

Ideally, research sites would have access to a clinical trial management system that is associated with mobile applications, White says.

"There could be an interface between the CTCAE applications we've developed that integrates with a clinical trial management system," he explains.

The key step to take before a clinical trial sites installs new technology is to sit down with investigators, study coordinators, and other users to determine how the change will impact their workflow, White suggests.

"Otherwise you'll build a tool and they won't use it," he adds. "That's happened to us, as well." ■

Improving site coordinator, study monitor relationship

Talk among thyselves

The sponsor and sponsored site have a relationship that is tended during a study by the study coordinator and the study monitor. If their communication and trust are good, then the study benefits from this relationship. If not, then there could be problems.

"Communication is key," says **Stacey Basham**, RN, RQAP-GCP, president of Rialto Quality Group of Alexandria, VA.

Site coordinators should talk with monitors during site visits, quickly address any corrective actions, and document everything, she says.

Here are some of Basham's other suggestions for how to improve the coordinator — monitor relationship:

• **Know which questions to ask a monitor and which questions to answer:** "Generally you should know the scope of the visit based on earlier communication from the monitor," Basham says. "For example, the monitor might say the focus of the visit is accountability."

Monitors check during the visit to make sure the site is doing drug accountability correctly, and coordinators should follow-up with monitors to make certain their site is on track and doing the accountability correctly, she suggests.

For example, if a trial participant says he took 20 doses of a study drug and this comes in a pack of 25 doses, coordinators should have five doses left in the pack to verify the numbers match, Basham explains.

Return or destroy?

Plus coordinators should know or ask monitors about whether they should return remaining product or destroy them at the site. And the monitor should check these drug packs before completing the visit.

"If you have a collection of drug pack returns, know where they are in accountability and how soon you can send them back," Basham says. "These are important to know when you are sitting down with your monitor."

The monitor is responsible for making sure accountability records reflect what's at the site so every pill and dosage is accounted for, she adds.

When the monitor has finished the visit, the study coordinator might ask for information about any findings that possibly could be corrected while the monitor is still there, she suggests.

"I know everyone is busy, and you don't want to be disruptive, but the coordinator should try to do an end of the day meeting with the monitor before the monitor leaves," she says. "Try to learn some of the findings at the visit instead of waiting for a letter to arrive later."

Then if there are some findings, the coordinator should ask the monitor for suggestions on how to resolve these issues.

"Maybe the protocol is asking for documentation of telephone contact, and it doesn't say how to do this, so the coordinator could ask the monitor for a suggestion," Basham says. "Also, find out when the next visit will be and when the monitor will need to meet with specific staff members, such as the pharmacist."

• **Make time for the monitor during site visits and facilitate smooth communication:** "Try to put that visit into your work practices," Basham says.

During a site initiation visit or the first meeting with the monitor, a study coordinator should sit down with the monitor to discuss how they want communication to flow. This prevents miscommunication problems.

For instance, if a monitor says she'll send out findings about a week after a site visit, then the coordinator should follow-up with an email after six or seven days, saying the report hasn't arrived.

"Make sure you know the monitor's expectations and the monitor knows yours," Basham says. "Find out when the monitor will want to meet with the principal investigator — is it every visit or every third visit?"

"If a monitor likes to communicate by email on Thursday afternoons, then that's how it should happen," Basham says. "Find out how the monitor will provide follow-up."

An ideal communication plan within the monitoring plan is having weekly communication between the monitor and site, Basham notes.

"Email is the most advisable because it's written down and it stays there," she adds. "I don't recommend texting."

There will be some phone calls between coordinators and monitors, but coordinators should keep in mind that emails provide verification that your message was heard and remembered.

"If a monitor is boarding a plane and sees her email about a visit, then she knows that as soon as she reaches her destination she can add the appointment to her calendar," Basham explains. "Plus it's an easy way to respond."

Consider all options

Other communication options include how sites should respond to monitors' follow-up letters and findings.

"Once the follow-up letter is received, the site may communicate with the site monitor how they'll follow-up with the items," Basham says.

Also, coordinators should ensure there is open and ongoing communication between themselves and monitors. If a monitor's follow-up letter includes items that a coordinator doesn't clearly understand, the coordinator should contact the monitor and ask for a clarification.

"It might be the subject listed is number 139, but the letter says number 193," Basham says. "You should have good communication so you can say, 'Did you mean this patient or that patient?'"

Coordinators should identify the quick fixes and then document how they made them, she adds.

"If something is missing, or if there's a data transcription error, then go in and change the eight to a nine," Basham says. "Or if something further is needed, add a progress note."

All documentation should identify what the issue was, what was done about it, and explain everything clearly and concisely.

It's also up to coordinators to resolve issues with monitors who are behind in communication.

If a monitor's follow-up information remains slow despite a coordinator's repeated emails and calls, then escalate the issue by talking to the next manager, Basham suggests.

"If the monitor consistently is showing up for another visit while you're waiting for a follow-up from six weeks ago, then go to the monitor's manager," she says.

At the close-out visit, study coordinators or other representatives at the site should be aware of any monitoring, follow-up letters received in which there are unresolved questions or issues.

"Make sure everything has been closed out, including what's in the follow-up letters and set time parameters," Basham says. "Make sure any findings that have not been addressed are taken care of." ■

FDA beefs up safety reporting during CTs

Clinical trials now will have to report a number of safety incidents that previously were not reported, according to a final rule issued by the U.S. Food and Drug Administration (FDA). The regulation deals with reporting safety information during clinical trials of investigational drugs and biologics.

The rule is intended to expedite the FDA's review of critical safety information and provide better protection for clinical trial participants, the FDA said in a statement issued Sept. 28, 2010.

Research sites will have 15 days from being made aware of an occurrence to report the following types of events:

- Findings from clinical or epidemiological studies that suggest a significant risk to study participants;
- Serious suspected adverse reactions that occur at a rate higher than expected;
- Serious adverse events from bioavailability and bioequivalence studies, which are conducted for generic drugs.

These bioavailability and bioequivalence studies are used to determine what percentage of drug is absorbed in the bloodstream and whether the drug has the same strength and effects people the same way as the brand name drug.

The final rule provides examples of evidence that would suggest that an investigational product may be the cause of a safety problem. Under current regulations, drug sponsors often report all serious adverse events, including those that likely were not caused by the product being studied. The FDA seeks to eliminate the "noise" or unnecessary data from its database to simplify the task of detecting safety signals.

Now clinical trial sites have some concrete examples addressing when a single event should be reported or when there is a need to wait for more than one occurrence.

Also, the final rule revises definitions and reporting standards to make these more con-

sistent with the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use and the World Health Organization's Council for International Organizations of Medical Sciences. The FDA's changes are designed to ensure harmonized reporting of global clinical trials.

Researchers and others in the industry could find more information and advice about the new requirements through the FDA's draft guidance and by visiting the website: www.fda.govssLINK/ucm226358.htm. ■

CNE/CME OBJECTIVES / INSTRUCTIONS

The CNE/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

■ Negotiate CT budgets like the pros

■ Learn to navigate FDA audits

■ Hit the ground running in site start-up process

■ Manage risk through better informed consent

■ Tips on handling site visit follow-up

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PS Form 3526, September 1998 (Reverse)

CNE/CME QUESTIONS

17. What are two of the key areas to focus on when the goal is to improve clinical trial site compliance?
A. Write informed consent forms in lower reading level and have staff attend sponsor's investigator meeting
B. Moving to an electronic documentation system and contracting best practices
C. Organizational consistency or centralization and staff education/training
D. All of the above

18. When assessing a clinical trial site's billing process, which of the following are questions that need to be asked?
A. Is the institution charging Medicare for research activities?
B. Did the institution bill appropriately to other payers?
C. Did the institution bill the sponsor for screening failures or items and services done for research purposes only?
D. All of the above

19. Researchers and informatics experts at The Children's Hospital of Philadelphia have developed a free iPhone application that displays standardized toxicity grading criteria according to the National Cancer Institute's Common Terminology Criteria for Adverse Events.
A. True
B. False

20. Which of the following is a good strategy for improving a clinical trial coordinator's relationship with study monitors?
A. Meet early with monitors to learn how they would like to communicate and how long it will take to receive reports after site visits
B. Call monitors at least every other day until site visit reports arrive
C. Refer all of the monitor's questions to the principal investigator
D. All of the above

Answers: 17. C; 18. D; 19; A; 20. A.