CLINICAL TRIALS ADMINISTRATOR

An essential resource for managers of

2011 Salary Survey included in this issue.

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AHC Media

Technological changes give CR sites more options for running business

Training has increased for monitors

Clinical research technology continues to evolve at a pace that's difficult to fathom. Everything from study recruitment to budgeting to operations are changing and evolving because of technological advances.

Some areas are transforming rapidly as major research and health care organizations invest in electronic data collection solutions and make paper-based research processes increasingly obsolete.

"Universal electronic medical records have the potential to transform research," says **T. J. Milling**, MD, FACEP, director of medical research at Hospital Physicians Clinical Research (HPCR) in Austin, TX.

"In the last couple of years we've set up email alerts based on certain lab values or presentation of complaints, which is easier than sifting through every patient record," Milling says. "Communication by email and cell phone calls takes less real time than a few years ago with the ability to text back and text pictures."

At Dana-Farber/Harvard Cancer Center in Boston, MA, the health system's electronic data capture (EDC) system has reduced research data entry workload, improved data quality, reduced turnaround time for study analysis, and increased efficiency, says **Marina Nillni**, PMP, EDC program manager at DFHCC. Dana-Farber/Harvard Cancer Center is a consortium of Harvard University-affiliated hospitals.

The EDC also has led to an annual increase in clinical trials since the EDC was installed six years ago, Nillni says.

But it's the improved efficiency that most impacts research staff.

"The electronic data capture system allows us to do an electronic check, so we can correct problems right away," Nillni explains. "In the paper world, two months would go by before you'd get a [corrected] data form."

As a result, investigators are able to publish and submit grants faster, she adds. *(See story on Dana-Farber/Harvard Cancer Center EDC system, p. 102.)*

For clinical research organizations (CROs) and monitors, technological changes have ramped up their need for continual training in recent years.

"When I started as clinical research associate 10 years ago, we had one or two areas of technology we had to keep up with: one was in training and

the other was where we wrote our reports," says **Laurel Bonner**, RN, BSN, principal CRA with PPD, a Wilmington, NC-based global clinical research organization.

"In the last three-to-four years I can count upwards to 10 different technological systems I've had to learn proficiently in order to do my job," Bonner says. "It continues to evolve."

Each new technological solution also comes with a new challenge, experts say.

One of the chief issues involves interoperability or collaboration between entities using the systems, says **Dan Kerpelman,** chief executive officer of Bio-Optronics Inc. of Rochester, NY. Bio-Optronics develops software products and information technology solutions for the health care and clinical trial industries.

Technological advances in clinical trials are increasing as sponsors, contract research organizations (CROs), and sites increasingly adopt electronic management for data, operations, inventory, labs, projects, and customer relations, Kerpelman says.

"There is an increase in penetration in all of these systems in clinical trials, but these are not matched by an increase in interoperability or collaboration between all of these systems," he explains. "The increase in adoption creates greater need for interoperability and collaboration, but the industry has not followed with this."

One reason for the lack of interoperability is that in a free market economy, companies will select solutions that work best for their particular organization, which does not translate into a solution that is compatible with potential collaborators or competitors, Kerpelman notes. *(See story on technological integration in research, p. 101.)*

"Coming up with a solution that ensures the system interoperates with other systems in the clinical trial enterprise is not just the responsibility of technology providers, it's also the responsibility of technology users," he says.

Even if technology companies were able to design interoperability between research electronic data capture systems and hospital electronic medical records, there are major obstacles to this working in any useful way, Nillni says.

For one thing, the two types of data systems collect information in different ways to suit different purposes. For research, data must be very systematic and organized in a way that facilitates statistical analysis and comparison. For health systems, electronic records are more descriptive with more free text because they are used for documentation and not for analysis, she explains.

Secondly, large research organizations might have clinical trials around the world. An interoperability solution that works in the United States likely would not work in Canada, Europe, Asia, or Africa, she says.

"So the challenge is there has to be some level of abstraction from the medical record," Nillni says. "I don't think we'll see that type of integration anytime soon."

Some of the latest technological advances hold promise for seamless clinical trial marketing and

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advertising. For instance, CR sites find that Internet advertising for a new trial can provide a very efficient and quick link that sends interested parties directly to the trial website where they can easily request to be contacted via email or a phone call. Some basic screening also can take place this way. This approach reaches only the people who pay attention to advertising online, however.

Now there's a possible new approach that would provide the same seamless link between potential recruits and CR sites in public locations. So, people who are waiting at a subway station, walking by a billboard, or browsing through a magazine could directly link to the CR site's recruitment page. It's called 2D barcode technology, which consists of large data barcodes that look like a square blot matrix.

For instance, research sites could place billboard advertisements in public places frequented by a target audience that relies on mobile phones for communication and Internet needs. As people walk by the advertisement, they could point their phone at the advertisement's 2D barcode, photographing it. Then the code will direct them to a website where they could learn about the new study. The study site's computer would send the person a text message that requests a reply if they are interested in hearing more about enrolling in the study.

"We do patient recruitment using short codes now, but no one is doing the 2D barcodes yet," says Tim Davis, BSc, chief executive officer and cofounder of Exco InTouch Ltd. in London, England. Exco InTouch is an interactive mobile technology company that designs technology solutions for clinical research recruitment, compliance, and data collection.

This technology could pass IRB muster because the individual's consent can be implied by the act of photographing the 2D barcode, Davis says.

"If they wanted to add a second step, they could [have a pop-up] ask, 'Are you sure you want to do this?'" he adds. *(See story on the latest in new CR technology, p. 100.)*

Technology also exists to allow research study visit encounters between a subject and study coordinator who might be 500 or 5,000 miles apart.

"The potential is there, and we're looking into it," Milling says. "You could have interactive face-to-face conversations."

While there might be some initial regulatory barriers to this, it is possible technologically, he adds. "The regulations will follow; the high speed Internet is there, the technology is there, and it'd be a shame not to use it."

Another new step is to use eDocument technology for signatures.

"Our industry is awash in paper, and it takes time to get paper to the right person to sign," Milling says. "Being able to get the signature by email will save time; we have the software for this, and it should be up and running in the next few weeks."

One of the benefits of the research industry being late adopters of electronic technology is that it requires slightly little less staff training when new electronic systems are implemented, Milling notes.

"Everybody we hire is skilled at email and word processors and spreadsheets," he says. "Most people have been working on those things for 10 to 20 years." ■

SPECIAL REPORT: Common Rule Changes

[Editor's note: This is the first in an occasionally reoccurring series of reports about the proposed changes to the Common Rule. As the U.S. Department of Health and Human Services (HHS) receives and posts comments, Clinical Trials Administrator will provide more in-depth coverage of what these changes might mean to research organizations.]

HHS: expand Common Rule privacy protection

HIPAA would cover just about all CTs

Clinical trial investigators soon will need to follow more stringent data security and information protection standards, according to a notice of proposed rulemaking, published in the *Federal Register*, July 26, 2011.

The U.S. Department of Health and Human Services (HHS) has proposed a number of changes to human subjects research protections and what is called the Common Rule. One of the most significant changes involves establishing mandatory data security and information protection standards for identifiable information.

HIPAA's reach would be expanded under the proposal to cover studies that now are exempt from the regulations.

"The HIPAA rules apply to the use of 'protected health information' by 'covered entities,'" says **Jerry Menikoff**, MD, JD, director of the Office for Human

Research Protection (OHRP).

"Many research studies either do not use protected health information or do not involve covered entities," he adds. "Subjects participating in those studies deserve to have appropriate protections."

Specifically, the proposed change calls for the establishment of mandatory data security and information protection standards for all studies that involve identifiable or potentially identifiable data.

HHS is considering three specific requirements to strengthen the protection for research studies that pose informational risks, the proposed rule states.

These are as follows:

• Research that involves the collection of identifiable data, including data in a limited data set form, could be required to adhere to data security standards modeled on HIPAA.

"For research using limited data sets or de-identified information, investigators would be strictly prohibited from attempting to re-identify the subjects of the information," the proposal states. "Requiring that investigators implement and adhere to these standard data security and information protection measures would lessen the need for investigators to enter into data use agreements to protect the limited data set, as is currently required under the HIPAA Privacy Rule."

• The new proposal would have data considered de-identified even if investigators see the identifiers but do not record them in the permanent research file.

• HHS is considering strengthening the Common Rule enforcement mechanisms by having periodic random retrospective audits.

Patient privacy is one of the biggest issues in new technology, notes **T. J. Milling**, MD, FACEP, director of medical research at Hospital Physicians Clinical Research (HPCR) in Austin, TX.

"We have to be very careful with the security of email and texting," Milling adds. "Emails are secured and encrypted with no patient identifiers."

Some technology organizations already meet the most stringent privacy and security standards, says **Dan Kerpelman**, chief executive officer of Bio-Optronics Inc. of Rochester, NY.

"The Common Rule changes would apply to HIPAA, and we've been following HIPAA and Safe Harbor for European organizations," he says. "Most providers would do the same.

One change might require a technology focus, and that's the area of focusing on de-identified data and following new standards in using it, Kerpelman says.

It's not a major technology challenge, however, he adds.

"Our technology can allow the contract research organization to see the status patient by patient of a trial without identifying a single patient or characteristics, and the way de-identification is done is bulletproof," he says. "But if the standard calls for a specific recipe for de-identification, we'd have to make sure our approach is compliant with that."

Bio-Optronics and other technology companies will be watching the Common Rule changes unfold to see how detailed they become, he adds.

[Editor's note: Clinical research professionals who would like to comment on the proposed changes to the Common Rule can submit comments through the Federal eRulemaking Portal at http://www.regulations.gov or by mailing their comments to Jerry Menikoff, MD, JD, OHRP, 1101 Wootton Parkway, Suite 200, Rockville, MD 20852.] ■

Smart phones: calling up apps for new CR uses

New technology works globally

The vanguard of new technology includes multiple uses of mobile phones during the clinical research process. These devices have a penetration that laptops and land lines will never have, and so they are becoming an important tool for use in recruiting and monitoring subjects, an expert says.

Clinical trial recruitment that uses new mobile telephone technology is especially important in many areas of the world where cell phones can be found in four-to-five times as many homes as land phone lines or computers, says **Tim Davis**, BSc, chief executive officer and co-founder of Exco InTouch Ltd. in London, England.

In resource-poor countries the land line technology is poor, but it has been easier to install mobile phone networks nationwide, so these countries leaped ahead to mobile technology, Davis explains.

"When we do clinical trials in South Africa or Kenya, it's incredibly simple to use mobile phone networks, which are reliable and easy to work with and can support all different languages across the networks," Davis says.

For example, mobile phones can be used when research participants keep electronic diaries. They can transmit data from home across their phone networks, and a central site can review that information remotely.

"If they have patients in South Africa or China, the information is transmitted across real time across

mobile networks, and then the principal investigator can log onto our secure reporting and review that data, taking appropriate action," Davis explains.

"We're looking at integrating medical devices without a platform, such as glucometers and those kind of devices that could have blue tooth technology associated with them," Davis says. "There could be the ability to connect to those devices so when a patient is at home, you could take a peak flow reading remotely."

Using mobile phone technology, remote research nurses can monitor study participants for problems, such as infections. They can track their temperatures through a transmission across the mobile network in real time and alerting the investigator if there's a finding that indicates a health problem, he adds.

Another progressive use of new technology is that clinical research organizations can do remote verification of clinical trial site data, says **Laurel Bonner**, RN, BSN, principal CRA with PPD, a Wilmington, NC-based global clinical research organization.

"You actually see what the site has entered into the system before you get there," she adds. "Another aspect that's excellent is seeing your old reports and site issues prior to the visit."

A monitor can run the report and let the site know there are issues still outstanding at the site, so the site can address these before the next visit.

With new technology, there is a lot monitors can do prior to a site visit so their time is spent more productively when they do travel to the site, Bonner says.

"Your time can be spent actually doing the source data verification, data entry, looking over the regulatory documentation and investigational product accountability," she explains. "These things you do as a monitor at every visit, and now you have time to do a higher quality review within the time frame you have available." ■

Tech integration, alliances slow to improve

Integration within partners is happening first

There's a resounding cry in the research industry for better technological integration and clinical research collaboration, but the movement in this direction has been very slow, an expert says.

Horizontal technology integration could lead to the widespread dissemination of best practices and electronic solutions, but there are no incentives to make this happen, says **Dan Kerpelman**, chief executive officer of Bio-Optronics Inc. of Rochester, NY.

"Say a site is working with a contract research organization or sponsor on a trial, and the site has information that's relevant to other sites such as enrolling patient volunteers," Kerpelman says. "One site reaches capacity recruitment, but has patients who are available for the study, so why not offer up these patients to other sites that have openings?"

The answer is the site with extra potential volunteers has no motivation or incentives to share that information with other sites, he says.

"So they're probably not asking their IT [information technology] vendors to provide better horizontal integration so they can integrate with their peers, who also are their competitors," Kerpelman explains. "That's one issue that leads to a lack of collaboration."

The lack of integration has led to some ever-evolving job skills in some areas of the clinical research industry.

For instance, clinical research organization (CRO) monitors now have to learn a wide range of electronic systems in order to work with a variety of clinical trial sites and sponsors, says **Laurel Bonner**, RN, BSN, principal CRA with Wilmington, NC-based PPD, a global CRO.

"Within the last couple of years the amount of systems you need to learn has escalated," she says. "The more you use them the more familiar you are with their little quirks, but there's definitely a learning curve there."

Technological integration in the research industry is still a distant hope rather than a reality.

"It's been very slow simply because you have so many different systems out there, and to open that portability and connection with every single system is almost impossible to imagine," Bonner says.

A clinical trial monitor might be working with eight research sites and of those five are using electronic systems, and four of these might be entirely different systems, Bonner explains.

"So you have to know how to use each one so you can verify their data," she says.

"The training PPD provides us for every new technological system is pretty extensive," she says. "We are constantly evolving in this business, but it eventually will come to the point where we're technologically saturated, and then it's just a matter of keeping up with the changes within that [electronic] system, which may be upgraded because it's constantly being tweaked."

In the case of vertical integration there are some

incentives, but the technology provider industry in general does not address these well, Kerpelman says.

One solution is for research IT vendors to build collaborative tools that move up the network, starting at the research site level, he says.

"It's easier to move up from the site than from the sponsor on down because of the sheer volume of sites and the experience you gain in doing this and understanding how sites work," Kerpelman says. "The reality is that trials win or lose at the site level, not in the headquarters of large multinational pharmaceutical companies, because the biggest risks are around things like recruitment, which happens by and large at the site level."

Companies like Bio-Optronics can improve vertical integration by facilitating work flow data management and financial management at the site level. As more sites adopt these solutions, they'll also appeal more to clinical research organizations (CROs) and ultimately to sponsors, he says.

For example, Kerpelman's health care and CR software company has a collaborative enterprise clinical trial management system (CTMS) called Clinical Conductor Enterprise that provides clinical trial management across studies and sites. This CTMS system, which is integrated across the clinical trial enterprise, manages and tracks everything from patient recruitment to financial management, Kerpelman says.

"For example, once a contract is awarded, the protocol is encoded in a language that allows it to be used in an automated fashion and to guide workflow for trial recruitment, such as eligibility, screening processes, enrollment, randomization, etc.," he explains.

Monitor visits can be governed by the electronic system, collecting and aggregating data from visits.

Another area in which collaboration and data integration are important involves billing for research activities versus hospital clinical activities.

"Say you have a health care practice or hospital department that provides health care, but also participates in clinical trials," Kerpelman says. "They have to be careful they don't mix and match billing accidentally."

It could have major repercussions if a Medicare patient's Medicare payer is billed for something that should have been paid as part of a clinical trial, he explains.

Research organizations could use two separate billing systems to ensure they are keeping these bills separate, but this is resource intensive and unnecessary when they have a large overlap of patients/volunteers, Kerpelman says.

The solution is to build technological bridges to the existing health records of the patients and volunteers, so there won't be mistakes made that has a procedure being billed to the wrong payer, he says.

"You flag whether a procedure is trial-related or not and that allows the two systems to branch off independently of one another and then come back together for internal bookkeeping," he explains. "This is collaboration between a health care provider and the clinical trial site." ■

Organization achieves success with EDC system

It eliminates paper, automates corrections

A major research organization in the Northeast successfully uses an electronic data capture (EDC) system with hundreds of clinical trials each year.

Dana-Farber/Harvard Cancer Center in Boston, MA, has used an EDC system for research since 2005, achieving better quality and improved turnaround time and increased efficiency, says **Marina Nillni**, PMP, EDC program manager for the DFHCC.

"We conduct a lot of our own research," Nillni says. "Investigators do their own trials with sponsorship from the government, and these EDC tools are used to manage data and conduct principal investigator-initiated studies."

The sponsored trials are conducted with whatever electronic tools the sponsors use, she adds.

Nillni outlines these benefits from using an EDC system for clinical trials:

• **No more paper case report forms:** Using electronic case report forms can save time over the long haul when compared with using paper, printing, mailing, and faxing, Nillni says.

"You also do all of the work upfront," she says. "In EDC you spend a lot of time building those case report forms and analyzing the needs of investigators."

The payoff is when the trial is up and running, the workflow runs smoother, saving time, she adds.

There also are some cost savings, although the electronic solutions have an expensive upfront cost, Nillni notes.

• **There can be a reduction in queries to the**

study teams: "We've definitely seen a reduction," Nillni says.

One reason for the reduction is that the EDC has built-in parameters that prevent some common errors involving putting in the wrong decimal point, she says.

"The EDC can fix data with the wrong decimal point rather than having someone send out a query," she says. "A lot of data is immediately corrected by the data entry person."

The EDC system also can correct immediate errors related to data that indicates treatment for the wrong diagnosis. When the wrong diagnosis is plugged into the EDC, it will be identified as an inconsistency and can be immediately corrected, Nillni says.

"Quality assurance happens simultaneously," she explains. "As soon as a person has data there is a query and the person has a chance to respond right away."

EDC users can program automatic and complex checks in the system, according to the common mistakes they've identified.

• **The EDC has system integration within the research organization:** "The protocol registration is integrated with the EDC," Nillni says.

"Because we are both site and sponsor, we have a centralized registration system for all our patients participating in clinical trials," She explains. "So any patient who comes through for participating on a clinical trial or even patients who maybe be on a different site all get registered through a centralized registry, and that piece is integrated."

For example, if a subject is enrolled today on a new study, that enrollment is put in the EDC tool that night.

"Every night we populate demographic data, date of birth, case number, gender, all into our EDC tool," Nillni says.

Also, the EDC can send some reporting information to external regulatory agencies and insurance companies, she adds.

The system's integration capability is limited to demographic information, and it doesn't extend to the hospitals' electronic medical systems because these do not capture data in a systematic way that would work for use in clinical trials, Nillni points out.

"In an EDC tool, every data point is coded; we don't take free text because you can't do an analysis at a statistical level on free text," she says. "Medical records are not structured in that way." ■

Putting profits to work in CR side of business

CR sites can make money, and here's how…

No one asks large pharmaceutical companies to develop and market new drugs as a non-profit venture. So why would anyone expect clinical research sites to operate at a loss?

Yet, this is how research organizations sometimes operate, even when it's not their intention.

When Piedmont Hematology Oncology Associates of Winston-Salem, NC, first began clinical research, it was so physicians could offer their patient population a potentially better treatment option. They never paid much attention to the research budget and costs, says **Don McCall**, RN, CCRC, research manager.

"A lot of sites are naïve like we were," McCall says. "The sponsor sends you a budget, and you just accept it; you don't know it's negotiable."

That all changed for Piedmont Hematology Oncology Associates in 2000 when McCall began to look at the profit and loss statements for the research side of the business.

"We looked at it as a separate entity and did cross-accounting for the whole department," McCall says. "A lot of centers don't do this at all, and they don't know what their profit margins are in research."

When McCall and investigators took a close look at the business' financial numbers, they discovered that they were doing research at a significant loss. The research income was not covering the costs of research salaries, benefits, office space, technology, etc.

"We have to look at the numbers," McCall says. "Like any business, our goal is to have a robust research program with trials underway all the time."

McCall used cross-accounting information the next time he received a sponsor's proposed budget for a clinical trial.

"I told a sponsor that we can't accept this budget, and the sponsor was okay with that," McCall recalls. "That opened up the door for us."

"Research is a business, and everyone else involved in research runs their program as a business except for sites," McCall says. *(See McCall's budget strategies, p. 104.)*

"I see our sponsors as our customers," he says. "We provide them with the best service we possibly can, but that service comes with a price because in order to do good service, it is costly, and in order to do research according to GCP [Good Clinical

Practice] guidelines, it's extremely timely and costly."

Research is labor intensive, and regulations add even more time to the work.

"All of the time physicians spend in research and providing proper oversight of clinical trials is an immense amount of their time, and they should be compensated appropriately," McCall says.

Clinical trial coordinators and data managers also spend a lot of time handling documentation, even when everything is done electronically.

"Electronic data collection takes three times longer," McCall says.

"Sponsors think it's quicker, and it is quicker for them because they don't have to take the information off paper and enter it into the system," he explains. "But it takes a lot longer for us because we get queries for silly things, such as verifying things on case report forms."

The electronic data capturing systems kick out automatic queries; clinical research organization (CRO) data managers send out queries, and CRO monitors send out queries. Often these are redundant and unnecessary, he says.

"Sometimes our study coordinators don't know what the sponsor or CRO is asking for," McCall says. "So the monitors come in and explain what they want. But six months and eight patients later, the monitor comes back and says, 'No, they want us to do it this way,' and you have to go back and redo your work."

Another thing that sponsors and CROs sometimes underestimate involves the amount of time it takes to do a procedure. For example, a subject is brought in for an infusion. It's not possible to just give the person the infusion and then send him or her home. The subject has to wait at the clinic for an hour for observation to make sure they do not experience any immediate adverse events or problems, McCall explains.

"Sponsors often do not want to pay for that observation time," he adds.

Since sponsors typically underestimate the amount time their study will take at the clinical research site, there budget also underestimates the site's costs. So there are few trials where Piedmont Hematology Oncology Associates accepts the sponsor's budget as it is written, McCall says.

"The product of the research site is data," McCall says. "Sponsors underestimate the value of our information, and I think they do that across the board."

Sometimes, sponsors will underestimate the costs of certain procedures," he explains. "We want to be paid by the sponsor what the insurance company pays us for a procedure."

Other budget negotiation conflicts arise over the definition of "standard of care." Sponsors often add more procedures into standard of care than what could be legitimately billed to an insurance company, McCall says.

Clinical trial sites also make mistakes. They forget to add in the cost of the equipment and technology they need to do research.

"We need copying machines, exam rooms, refrigeration, ECG machines, and all of these things are costly," McCall says.

"I don't believe it's up to a site to be paying for these things," he adds. "These costs should be coming out of the budget created for the business." ■

BUDGET STRATEGIES

Here's expert's advice to develop a solid budget

Watch for discrepancies

Budgeting is a complicated process, but you can make it work well by following thorough and well-organized, step-by-step strategies.

A first step could be to invest in a clinical management system, says **Don McCall**, RN, CCRC, research manager at Piedmont Hematology Oncology Associates of Winston-Salem, NC.

"The CTMS helps keep you from spending a lot of time doing budgeting," McCall says. "And it's good to be standardized."

McCall, who has spoken about clinical trial budgets at national conferences, says that his personal experience working in all facets of research helped immensely when he began writing study budgets.

"I've worked in every area of the department: data management, regulatory, coordinator, everything that could be done in a research trial, so I understand how much time it all takes, and that helps us do well," McCall says.

McCall offers this advice on how to improve a trial site's budgeting:

• Closely examine the protocol when developing budget.

"First look at the table of events in the protocol," McCall says. "Most sponsors give you a spreadsheet."

The key is to review and compare the protocol and study budget.

"It takes me almost a day to look at a good oncol-

ogy study budget," he adds. "I have two widescreen monitors in front of me, and I have a protocol on one and a budget on another."

The budget template should look like the table of events in the protocol, so it's important to compare the two, looking for discrepancies.

"Sometimes you'll find something that's not in the budget, but it's in the table of events," McCall says. "The sponsor might leave something out that maybe is nothing, but it also could be something that costs you money, so you should look for it and scrutinize both the budget and table of events."

The most costly errors can occur when sites and sponsors underestimate how long a study will take.

"The study could go on for two years while your budget went on for three months," McCall says. "Make sure the wording is appropriate in the budget."

• Involve the research site's billing office.

Billing office staff can be helpful in analyzing costs and preparing the budget.

For example, when a research manager determines the cost of a specific procedure, it helps to know what the billing office charges an insurer for the same procedure. The billing office also can help with calculating the research office's overhead costs, which could range from 20% to 40%, although sponsors will pay at the lower end, McCall says.

Set procedure costs should be updated on a regular basis, as should drug and other item costs.

"Exam costs might change yearly, but some things like drugs could change quarterly," McCall says.

McCall checks on prices twice a year. He emails or calls the billing department as he updates the costs.

• Physician investigators review the protocol.

After McCall takes a look at the protocol, he sends it to the research site's physicians to see if it meets their scientific criteria.

"I just look at the structure of the protocol to see if this is something our center can find patients to enroll," he says. "Physicians check the protocol to see if this is something they'd want to give to their patients."

They check to see if the study is asking appropriate questions and whether the questions are relevant. They see whether the endpoints are important for the patient population, McCall says.

• Assess study's enrollment potential.

Research sites like Piedmont Hematology Oncology Associates have electronic medical records that could be accessed to determine the patient population for any particular study. This provides a good baseline for determining any particular study's potential to succeed in enrollment.

But there are other considerations, as well.

"Our screen failure rate has doubled over the last two years," McCall notes. "The inclusion/exclusion criteria these days are very targeted with specific issues, including interactions with other drugs."

In oncology, many new drugs could cause blood clots, so patients who already have blood clots typically are excluded from oncology trials, he says.

Also, many patients have cardiac arrhythmias, and investigational drugs often could cause problems for these patients, so they also are excluded from clinical trials, he adds.

"Patients who have had any other type of cancer, such as men who have a history of prostate or lung cancer, and women with cervical or breast cancer, also can be excluded," McCall says.

So it's crucial to carefully examine the inclusion/exclusion criteria and estimate based on these how narrow or broad the potential recruitment pool might be.

"If you don't enroll, you lose money, so you have to enroll," he says. "You realize every site has the same issues, so the sponsor has to expect low recruitment numbers, and I'll open a trial if I think I can enroll even three subjects."

On rare occasions, the research site might even take a trial in which only one patient could be enrolled, he adds.

• Learn to handle the negotiators.

McCall recommends returning the sponsor's budget with changes highlighted in red, letting them know that the site manager is happy to discuss the changes. It's important to return budget changes in a professional manner, using an Excel spreadsheet so the sponsor will see that the site manager knows what he or she is doing.

"They can tell whether you have been doing this a long time by the way you return the budget," McCall says.

Sponsors sometimes contract with clinical research organizations (CROs) to negotiate contracts and budgets. Research site managers might assume that the CRO has financial incentives to negotiate low budgets, so they should understand how to handle these negotiations, McCall says.

"The CRO always will tell you, 'The sponsor's limit is this amount,'" he says. "And I say, 'What I need you to do is submit the budget as I wrote it to the sponsor because when I submitted this budget it was conservative, and it's my bottom line.'"

Typically, things will work out once the site's budget is sent to the sponsor, he adds.

"You have to be willing to speak directly and not be nervous about it," McCall advises. "This is a busi-

ness deal, just like buying a car; you tell them what you need, and you don't get emotional; just be polite and professional."

Sponsors and CROs sometimes try to appeal to a researcher's benevolence, asking the clinical trial site to take on a study that might cost more than its budget for the sake of helping their patients. This is an erroneous assumption because no clinical trial can guarantee a personal benefit to subjects, McCall says.

Occasionally, McCall finds that a CRO or sponsor negotiator is taking the process too personally and is upset that McCall rejects the initial study budget. When this occurs, McCall finds someone else to deal with.

"I will send an email, saying, 'I can't work with this person; they're too emotional and are taking it too personally,'" he says. "So I'll request a different person, or I'll ask the person to stop that line of reasoning that this study is for the patient's benefit."

The key is to think of the clinical trial as a partnership between sponsors, CROs, and research sites. Each party wants to achieve the same objective: successful trials with robust data.

"Both sides understand they need to look out for one another," McCall says. "If I gouge the sponsor they won't come back to me with more studies, and if I'm losing money on the study than I won't be able to do research much longer."

• Walk away from the study when the numbers do not work.

"My goal is to not walk away from a study, but I will walk away," McCall says. "I don't want any bad feelings, and I won't get personal with budgets; these are business and nothing else."

Sometimes contract negotiations reach an impasse, and the research site has to decide whether there are any positive factors that make it worth taking on a trial that will lose money. For instance, is this a case where it will create good will with a new sponsor partner, and the long-term relationship could prove more financially profitable? Or perhaps this is an investigational product that patients, who have exhausted existing treatments, have been asking about.

But if there are no compelling reasons why the site should take on a study that will lose money, then the site manager should just say, 'No thanks,' and walk away, McCall suggests.

"Pharmaceutical companies have been making profits for years and years, and research centers have not," he says. "But in order for us to do good research, we need to make a profit, and we need to compensate our staff well for their taking on the kind of stress they have in doing clinical research." ■

BEST PRACTICES SPOTLIGHT

Site develops incidental findings report model

Protect confidentiality in process

The first step was a mandate by the institution. The Mind Research Network (MRN) requires researchers to report incidental findings to subjects in a systematic way that protects confidentiality and is sensitive to the emotional impact of receiving the news.

The mandate evolved over a year's period and was fully implemented several years ago, says **John P. Phillips**, MD, medical director of the Mind Research Network in Albuquerque, NM.

"I just became the medical director in 2006 when we were developing a system about how to look at and classify incidental findings," he recalls.

At first, people focused on reporting significant findings, but then changed the focus to incidental because the same brain scan results could be either significant or not, depending on the patient's history and background, he explains.

"How do we know if something won't become significant in the future?" he says. "I thought to be consistent and fair to subjects, the subjects should have an opportunity to decide what they feel about the findings themselves."

The process provides all research participants with results. According to the Mind Research Network's evaluation of the program, it has resulted in about 8,500 scans with incidental findings from the radiological review process in 34% of these. Of the reviews with incidental findings, nearly one-third needed no referral, and only 0.9% required an urgent or immediate referral.

"Results go to every single person unless they say they don't want to receive their report," says **Jody M. Shoemaker**, MS, CIP, CCRP, director of research at the Mind Research Network.

"Participants usually are eager and appreciative to receive their radiology review," she adds. "The report will say any of these: no abnormal findings, no referral necessary, routine referral, urgent referral, or immediate referral."

Each letter sent to participants includes a comments section that explains details about the nature

of the finding. And they can request a copy of their brain scan to take to their community providers. The research site's IRB approved the language in the letters, making certain subjects wouldn't be confused, thinking this was a full clinical scan instead of a research scan, Phillips notes.

"MRN drafted the consent language in conjunction with the IRB," Shoemaker says. "We have standardized informed consent language for anyone using our facility as we want consistency across the studies."

The Mind Research Network has built HIPAA-compliant database that generates a random number to assign to each scan before they're reviewed by a radiologist, she adds.

"Then an email is sent with the coded number to the investigator and coordinator on the study, and a hard copy is generated and mailed to the participant," she explains.

The reviews are sealed with a sticker that says "radiology review." If the review has no abnormal findings, it's mailed to the participant as is. If there is an abnormal finding, then it's forwarded to Phillips who contacts the subject by phone before the letter is mailed, Shoemaker says.

The research site tested the process for quality, and has addressed concerns from investigators and other research staff.

Phillips met with principal investigators to hear their suggestions and to answer their concerns.

"Some were uncomfortable with this and needed a little time to feel like this was an okay thing to proceed with," he says. "They worried that we were causing too much anxiety in subjects."

The system is being tested for use at the University of Colorado in Boulder, Shoemaker notes.

"The systems we put in place could be adopted anywhere," she says. "We've created a template, and John will serve that role in contacting participants and investigators."

One logistic that had to be overcome involved the imaging scans. How could these be analyzed and communicated in a way that might be useful for research subjects, but not prohibitively expensive? MRN decided upon a process that costs only $20-$25 per scan.

"We contracted with a licensed radiologist to read our scans," Phillips says. "It started off as a mandate from our external IRB, so if someone had a study where the scans wouldn't be read, it wouldn't be approved."

The radiologist's cost is built into the scan cost and has a set rate that includes paying for Phillips' time.

Every subject who has neuroimaging results has a radiological review through customized software. It sends an electronic report to the principal investigator and generates a copy for research subjects. If a neuroradiologist determines there's a need for an urgent or immediate referral, the scan results are brought to Phillips' attention, and he contacts the subject to explain the results and to arrange follow-up clinical care.

"I offer to take the burden off the principal investigator for all subject contact," Phillips says.

"They don't have to worry about it, and just have to pay a little more up front," he adds. "It's a painless system for everyone involved, and it can be easily

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.

To earn credit for this activity, please follow these instructions.

1. Read and study the activity, using the provided references for further research.
2. Log on to **www.cmecity.com** to take a post-test; tests can be taken after each issue or collectively at the end of the semester. *First-time users will have to register on the site using the 8-digit subscriber number printed on their mailing label, invoice or renewal notice.*
3. Pass the online tests with a score of 100%; you will be allowed to answer the questions as many times as needed to achieve a score of 100%.
4. After successfully completing the last test of the semester, your browser will be automatically directed to the activity evaluation form, which you will submit online.
5. Once the completed evaluation is received, a credit letter will be e-mailed to you instantly. ■

COMING IN FUTURE MONTHS

■ Experts analyze how proposed Common Rule changes could impact CR sites

■ Design a better source document template

■ Jumpstart your site start-up process with expert's tips

■ Research director of small CR site offers best practice advice

adopted by other centers."

Phillips calls research participants when the findings appear to be urgent.

"As I follow up on the phone people can be nervous; it's an anxiety-provoking experience," he says. "People are appreciative to hear the findings even though there might be a time of anxiety." ■

CNE/CME QUESTIONS

33. The U.S. Department of Health and Human Services has proposed major changes to the Common Rule. Which of the following describes proposed changes regarding data privacy and security?
    A. Research that involves the collection of identifiable data, including data in a limited data set form, could be required to adhere to data security standards modeled on HIPAA
    B. The new proposal would have data considered de-identified even if investigators see the identifiers but do not record them in the permanent research file
    C. HHS is considering strengthening the Common Rule enforcement mechanisms by having periodic random retrospective audits
    D. All of the above

34. One of the chief ways research technology is spreading to resource-poor nations is through which type of electronic technology?
    A. Laptop computers and the Internet
    B. Mobile phones
    C. Thumb-sized paging devices
    D. All of the above

35. According to a clinical research budgeting expert, which of the following strategies is not recommended for a best practice in preparing a clinical trial budget?
    A. As for help from the research site's billing office
    B. Have physician investigators review the protocol for scientific criteria
    C. Copy the sponsor's budget and adjust a few items according to your site's capacity and costs
    D. Assess the study's enrollment potential

36. After a research site called the Mind Research Network began to provide research participants with their incidental findings from a radiological review process, they found that one-third of these findings needed no referral. What percentage required an urgent or immediate referral?
    A. 0.9%
    B. 2.2%
    C. 6.1%
    D. 7.6%