CLINICAL TRIALS ADMINISTRATOR

An essential resource for managers of clinical trials

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Research industry's trends beget more challenges for trial sites

CT globalization key part of change

The last five years have been tumultuous years for the clinical research industry due to the global economic downturn and other trends that are dampening revenues, experts say.

"There's a looming patent cliff," says **Ken Getz**, MBA, a senior research fellow and assistant professor at Tufts Center for the Study of Drug Development at Tufts University in Boston, MA. Getz also is chair of the Center for Information and Study on Clinical Research Participation in Boston.

"The engine that delivers resources invested in research and development (R&D) has been under attack by generic erosion, softer consumer demand in a down economy, and the introduction of products into the marketplace that are targeting smaller markets," he explains.

Sponsors are losing their blockbuster drugs as patents run out and few drugs can replace these, he adds.

"It's forced sponsors to re-evaluate how they can optimize every dollar they spend on R&D, and it has direct translation into the clinical trials arena," Getz says.

This means the clinical trial (CT) business is becoming harder for sites, says **Norman M. Goldfarb**, CRCP, managing director of First Clinical Research, editor of the Journal of Clinical Research Best Practices, and chair of MAGI – the Model Agreements and Guidelines International, all in San Francisco, CA.

"When the economy went down in 2009, the clinical trial business got a lot harder," Goldfarb says. "So it's been a tough environment, and there are some sites that will say 2010 was tougher than 2009."

CT sites feel a lot of the same pain pharmaceutical companies feel, but they experience it in different ways, says **Dave Handelsman**, senior industry consultant at SAS Health and Life Sciences in Cary, NC. SAS provides advanced analytics to solve scientific and business problems.

"Clinical trial sites are being held more accountable to meeting their milestones in terms of recruitment and quality," he adds.*(See story on improving site efficiency, p. 51.)*

Research organizations can use business analytics to help them improve their operations. Analytics can help them design better trials, target

patient recruitment, optimize operational activities, etc., Handelsman says. *(See story on improving trial design, p. 52.)*

As research organizations plan ahead for 2012, they should take note of these current trends:

• **There is more focus on CT site data collection:** Sponsors increasingly are using site report cards in which they have collected data on sites involved in a study, Goldfarb says.

"They create a small digest and send it to sites so sites can see how they're doing during the study and how they did after the study," he says. "The report card will tell them whether they're in the 57th percentile, and it will give them feedback so they'll do better."

Sponsors and clinical research organizations (CROs) are following the philosophy that you can't manage what you can't measure, Getz notes.

"So there's a real focus on having sites collect start-up metrics, recruitment metrics, and all kinds of metrics around the review and approval of the IRB," he adds.

Since many sites still have very poor recruitment experiences in studies, enrolling one or no subjects, sponsors or CROs might take a look at a site's historical performance before including them in a study, Handelsman says.

"Pharmaceutical companies need to know and collect those metrics," he adds. "Some CROs are more active than others on doing this."

Also, sponsors increasingly are demanding that sites provide more metrics, and they're using these data to better select sites that will be successful in study recruitment and meeting enrollment deadlines, Getz says.

• **Generic drugs have gained more market share:** "The majority of prescription drugs that are sold each year now are generic versions," Getz says.

"These are not just drugs developed in an emerging country, but also drugs for large markets that have now lost patent protection, including drugs for high blood pressure, heart disease, and even some widely-taken drugs for psychiatric illnesses and neurologic diseases," he adds.

As these blockbuster drugs become open to generic drug competition, these competitors are eating into critical revenue streams that the pharmaceutical and biotechnology fields once relied upon, Getz says.

"A lot of treatments moving through the pipeline are also targeting smaller markets, so companies have to figure out how to create a larger portfolio of drugs to recoup the lost sales from the blockbuster drugs that now are generic," he explains. "It's true that they're always trying to diversify their portfolios, but in the past a single successful drug would generate enough revenue to recover costs."

Sponsors need to improve their drug success pattern. They no longer can afford to have only one drug brought to market for every five in clinical research, Getz says.

"That probability of success has to improve because the drugs in the market are not generating

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enough revenue to cover the high cost of failure," he says. "This is forcing companies to assess how to lower the cost of R&D or accelerate the time it takes to get a drug to market."

• **Sponsors want greater clinical research efficiency**:This trend often translates into cost pressure on CT sites, but it does not solve the underlying revenue problems sponsors face, Goldfarb notes.

"You can use the auto industry as an analogy," he explains. "When it started getting pressure from Japan and Japanese automakers, it decided it had to reduce its prices and costs, and you could do that by negotiating lower prices from vendors."

While that helped, it didn't solve the problem, so the government stepped in when there was a big crisis, he adds.

"So the pharmaceutical industry is still largely in that phase of putting price and pressure on its vendors," Goldfarb says. "It's doing a little bit with partnerships with CROs and partnerships with sites, but these won't solve the problem."

Sponsors are giving CROs greater autonomy because it saves their resources to trust the CRO's site monitoring and to avoid redundant oversight, Getz says.

"The CRO seems to be poised to drive an even higher level of integration and management influence over the site's operations," he adds.

The likely resolution will involve the industry's financial situation getting worse until the industry decides to take dramatic steps, including adopting standards that can save money and time, he says.

"Sponsors have the pressure to develop more products faster and cheaper, so clinical trials need to be faster, cheaper, and have quality data," Goldfarb says.

• **Globalization of trials will continue**: Goldfarb estimates that about half of CT sites and more than half of CT subjects are overseas, especially in developing countries.

"Sponsors are saying, 'If I can get research done overseas with additional costs and headaches, but a lot cheaper then why not do it,'" he says.

"In terms of an overall trend for globalization, my guess is the United States will end up with a 25% market share of clinical trial studies eventually," Goldfarb predicts. "Twenty years ago, 98% of the trials were done in the United States, and that has worked its way down about 2% a year."

This globalization trend likely will continue until it reaches the point where some of the advantages of having trials in the developing world go away, he adds.

"At some point there will be fewer naïve populations, more competition for subjects in those countries, and their costs will go up closer to U.S. costs," Goldfarb says. "It will take a while, and it will be very painful for U.S. research sites, but the market share will stop changing."

Handelsman also predicts a continuation of the globalization trend for clinical trials.

"There's a belief that you can get more patients enrolled in trials overseas," Handelsman says. "There are different costs associated with it and different regulatory issues, but there is a ton of work going overseas, and we won't see that declining soon to any extent." ■

Down economy obliges CT to improve efficiency

Protocol complexity increases

Clinical trial (CT) research is moving toward a performance-driven model in which sites increasingly will compete with top-performing U.S. sites and lower-cost sites in developing nations overseas.

At the same time, studies are becoming more complex, which puts a huge burden on sites and is harming their performance, says **Ken Getz**, MBA, a senior research fellow and assistant professor at Tufts Center for the Study of Drug Development at Tufts University in Boston, MA. Getz also is chair of the Center for Information and Study on Clinical Research Participation in Boston.

"You have a down economy that's putting pressure on all of these different players: sponsors, clinical research organizations (CROs), and sites," Getz explains. "At the same time, sponsors' own portfolios and composition of products require higher efficiency, and these needs are transferred to third parties."

The result is pressure on CT sites to deliver a higher level of efficiency under more difficult and complex programs, he adds.

Research industry statistics clearly show clinical research inefficiency.

Most CT sites in 2008 and 2009 enrolled one or fewer patients, costing the industry an average of $50,000 to open and close each unsuccessful site, says **Dave Handelsman**, senior industry consultant at SAS Health and Life Sciences in Cary, NC.

"Only about one-third of all sites in a given trial meets or exceeds the enrollment goals of the trial," Getz says. "We know that when looking across

a large sampling of studies that it is taking 30% to 40% longer to complete the programs than it did for the prior four-year period, so it's getting slower at a time when speed is even more precious."

Sponsors are trying to change things, but it seems that each change creates more complexity, he adds.

"I've been hearing from sites that they're frustrated with the ways they're introduced to trials and how often they put in effort to prepare for a trial and engage staff to gear up for a study, and then it doesn't happen," he says.

Across every phase of clinical research there has been a dramatic and significant increase in the complexity of protocols, Getz notes.

"We've seen the number of procedures and their frequency rise rapidly, and we've seen the number of eligibility criteria rise rapidly," he explains. "All of this additional complexity is creating a burden on the operations and feasibility of the trials, so it's harder to find people to enroll, and it's harder to keep them in the studies."

CT sites get caught up in the cycle of having to accept studies they should turn down because they need the work and then failing to succeed partly because of the study's complexity.

"Right now the complexity is winning out, and it's actually hurting efficiency," Getz says.

It's difficult for sites to survive in this environment, but it can be done.

For instance, sponsors and clinical research organizations (CROs) are placing more emphasis on sites producing quality data, and some are tracking sites' success rates, Handelsman says.

"There will be more done to identify sites that are real rock stars," he adds. "And sponsors will make sure they're involved in the recruitment process."

CT sites can improve their recruitment numbers by doing groundwork to more accurately predict their enrollment potential before they accept a trial, Handelsman says.

This might also mean asking for a more realistic budget.

Both sites and sponsors could use a model and simulation approach that more accurately predicts the study's likelihood of hitting recruitment and milestones, Handelsman suggests.

Sponsors have a wealth of trial data available, and they are beginning to realize it can be mined for the purpose of informing enrollment and clinical trial site decisions, he adds.

"We're seeing a lot of effort to bring data together to make it more actionable," Handelsman says. "There's a wealth of knowledge out there, and it's an important step."

It helps if sites collect their own performance data. They could use their metrics to better pinpoint their potential recruitment numbers. If their experience shows they would be unable to produce enough subjects for a particular trial, then they can turn it down. Or perhaps their numbers show they could meet enrollment goals and bring in the study on time, but it would be costly to do so.

"It's also about quality and cost," Handelsman says. "Maybe a site could do what they say they're going to do, but it will cost 50% more than a site with less of a track record."

Sites can implement better management controls and more accurately estimate their own resource requirements, Getz says.

"They should do a more realistic estimate of their own budget requirements and pass those on to the sponsor or CRO," he adds. ■

Key to research success: designing better studies

Adaptive trials is one new model

Clinical research experts largely agree on the clinical research industry's problems. It's more difficult to find a consensus on potential solutions. However, one strategy often mentioned these days is for the industry to design better clinical trials.

"We're closer to designing better trials, and the technology has been available for a while," says **Dave Handelsman**, senior industry consultant at SAS Health and Life Sciences in Cary, NC.

"What's lacking is the will to change," he adds.

The industry's problems of patent and revenue concerns and poor performance are growing and soon will be unmanageable.

"When you're in the pharma industry and revenues are growing, efficiency is less important," Handelsman says. "But when revenues are not growing and when Lipitor® and many other drugs and billions of dollars will disappear from the top pharma revenue stream, it's time to look at different business models."

One way is to design and apply smarter clinical trials, he adds.

"It takes too long to get a drug through the approval process, and late phase III failures are huge cost problems," Handelsman says. "A lot of

trials don't meet their endpoints for a variety of reasons."

Better study design also could solve some of these problems.

Sponsors could use data and information technology tools to better assess the likelihood of a clinical trial's success. They could use this information, as well as simulations of different study designs, to design a trial for optimal demonstration of safety or efficacy, Handelsman says.

For instance, one new study design strategy involves adaptive design clinical trials. These work differently than conventional clinical trials by including a prospectively planned opportunity for modification on a specified aspect of the study design, based on analysis of interim data, according to the U.S. Food and Drug Administration's "Guidance for Industry, Adaptive Design Clinical Trials for Drugs and Biologics," a 50-page draft guidance published at www.fda.gov in February, 2010.

"You design it to make changes in the protocol, like adding a dosing arm or removing a dosing arm," Handelsman says. "There are prespecified changes along the way with the goal of having a more effective research program."

Adaptive trials are not the same as studies that are changed as a result of information obtained from outside study results or other external data and events.

There have been case studies on how adaptive trials help improve clinical research, but they are difficult to implement, Handelsman says.

"The math is complicated, and there's an operational piece that doesn't necessarily fit pharma companies' style," he says.

It's challenging for sponsors to get the drug to different sites in different doses than what was originally planned. Also, clinical trial sites have to get data in quickly so the protocol can be adapted, and that's difficult to accomplish, Handelsman says.

Plus it takes longer to get a complex, adaptive trial approved by institutional review boards and other committees, he adds.

"But there is a lot of opportunity there," Handelsman says.

Pharmaceutical sponsors have had the most interest in adaptive trials, according to the FDA's draft guidance.

Some of the possible study design modifications that can be planned in an adaptive trial include these listed in the FDA guidance:

- Study eligibility criteria for either subsequent enrollment or for a subset selection of an analytic population
- Randomization procedure
- Treatment regimens of the different study groups, including dose level, schedule, and duration
- Total sample size of the study, including early termination
- Concomitant treatments used
- Planned schedule of patient evaluations for data collection, such as the number of intermediate time points, timing of last patient observation and duration of patient study participation
- Primary endpoint, including outcome assessments, time point of assessment, use of unitary versus composite endpoint, or the components included in a composite endpoint
- Selection and/or order of secondary endpoints
- Analytic methods to evaluate the endpoints, including covariates of final analysis, statistical methodology, and type I error control.

Other ways studies might be designed better involves gathering more data in clinical trials for the purpose of identifying genetic bases for diseases and finding subpopulations that have responded well to treatment even when the general study population does not have positive findings, suggests Ken Getz, MBA, senior research fellow and assistant professor at the Tufts Center for the Study of Drug Development at Tufts University in Boston, MA.

"There is a lot of talk now about stratified medicines," Getz adds.

Stratified medicine research is where investigators use biomarkers to identify patients who are more likely to benefit from a particular drug or who are most likely to experience an adverse event. Clinicians could match patients with therapies with this type of information, and some trials are collecting these data.

"We're still at a critical place where companies are looking to gather more data, identify biomarkers, validate biomarkers, and collect genetic tissue to help them identify genetic bases for diseases," Getz explains.

These types of studies can lead to treatment breakthroughs and are beginning to transform early stage innovation through integrated partnerships with academic organizations for the purpose of identifying new and promising drug candidates, he adds.

"The sponsor will provide data on failed compounds and let scientists at the university cull through the data to see if they can find a subpopu-

lation that might have responded well to the treatment," Getz says. ■

Genomics R&D requires updated understanding

Ethical, other issues come into play

Genome research and accumulated knowledge is changing the way we understand disease and treatment, which, in turn, is changing clinical trials, an expert says.

"For many years we conducted clinical trials with new drugs, and we'd see some responders and partial responders and some with no response, and nobody understood why," says *Joan Rankin Shapiro*, PhD, MD, an associate dean for research and a research professor in basic medical sciences at the University of Arizona College of Medicine in Phoenix, AZ.

The answer is that not all tumors are the same – even when they're located in the same place.

"We would think of somebody with a diagnosis like breast cancer or lung cancer as having the same kind of tumor," Shapiro says.

"Now, what we have come to appreciate is that whatever transformation is that begins the process, these tumors can evolve down different pathways," she says.

With this knowledge and new technologies, researchers have the ability to look at the complete genome of an individual, searching for abnormalities that exist in that patient's tumor, she explains.

This genetic information can inform both clinical trial studies and treatment. Studies will show which types of tumors respond to certain medications and doses.

"We're now gravitating toward more personal medicine," Shapiro says. "Most clinical trials are taking that more into consideration because of our ability to analyze genomics."

Investigators can analyze the genome for specific changes in patients' tumors. These changes tell them how to more accurately direct a drug to that individual and how to develop a subset of patients based on the abnormalities they have within their tumor, she adds.

"It is the kind of thing that allows us to look more in depth into a clinical trial involving a drug," Shapiro says.

Having the knowledge and ability to conduct this research is not enough. There are ethical and practical logistics that are daunting.

For example, HIPAA privacy rules govern how tissue can be used once it's extracted from a patient.

"Who is going to receive this information?" Shapiro says.

Tissue used in research might be moved from one site or company to another or used in multiple studies.

"When running a clinical trial, and they request tissue from patients, investigators need to know the laws and regulations, including that patients need to know what will be done with their tissue," she says.

The National Public Radio (NPR) and other media outlets have publicized the case of the woman whose tissue was used in studies and laboratories for years without her knowledge, Shapiro notes.

"No patient should donate any tissue without knowing what it's for and what is being used and what is going to happen to it," she says.

HIPAA rules make it more complicated.

"HIPAA says you can store tissue in a bank or take the tissue as long as you tell the patient what it's being used for," Shapiro says. "But if you store it in the bank and then take it out five years from now then how do you let the patient know what it's being used for?"

One way might be to ask patients up front about their tissue being used for research. They might ask these questions:

- Are you willing to donate tissue for Study X at this time?
- At some time in the future would you be willing to donate this tissue for future experiments related to this diagnosis?
- Would you like to be contacted each time there's a potential use for your tissue?

"You could ask the patient right up front what they would like done with the tissue," Shapiro says.

Investigators need to keep in mind that HIPAA does not permit them to consent a patient for the future, she adds.

If they check the box that says, 'Do you wish to be informed if in the future your tissue is to be accessed?' then that means someone needs to call them if the tissue is to be used in a study.

"Even if they leave the box blank most hospitals and universities have compliance policies that will require someone to make that call to the person," Shapiro says.

"The big clause is that maybe they give their tissue to a tissue bank, but five years from now they decide they don't like what the tissue bank is doing with these tissues and they want to withdraw their tissue from the bank," she adds. "Investigators have to put that in the informed consent form – that patients have the right to withdraw their tissue at any time, and investigators have to return it unless patients say it has to just be destroyed."

Most people will agree to donating their tissue to research, but they need to understand they will not benefit personally, but that someone in the future might benefit from its use in research, she notes.

"There's always the hope they will benefit someday, so we have to make people understand they won't benefit from this," Shapiro says.

"And maybe their particular tumor has a receptor that is important to developing a particular drug," she adds. "The patient may never benefit from that drug being marketed 10 years down the road."

So it's very important to be clear in informed consent about how the patient probably will not receive any physical or financial benefit from the use of their tissue in research.

In the past, researchers were less attentive to communicating this message, but now it's important from a regulatory standpoint, as well as from an ethical perspective, that they clearly inform patients about how the process works, what their personal protections are, and how they will or will not benefit from the research.

Investigators also have to be aware of the requirements when a breach of privacy occurs with biospecimens.

"If for any reason their tissue is identified, and there's a breach of confidentiality that exceeds 50 people, then we have to report it to every person involved in the breach," Shapiro says. "If the breach impacts more than 500 people then we have to report it to the federal government and the media."

This requirement puts pressure on researchers and sponsors to protect information very carefully to ensure there is no breach of confidentiality.

The simplest strategy is to de-identify biospecimen samples.

"There's a lot of understanding between the industry and science to make sure we can get as much information as we can get, but still not have the possibility of samples being identified," Shapiro says.

Another issue involves how biospecimens are stored.

Researchers previously have used local freezers, but this increases the risk of a breach of confidentiality, she notes.

"They are now developing biodepositories, " Shapiro says.

The National Cancer Institute (NCI) and the Food and Drug Administration (FDA) have guidelines for repositories. These detail how they are to be stored, how biospecimens are shipped, and how their integrity can be retained, she explains.

Clinical trial sites and investigators should become accustomed to living in a time when many rules apply to how they handle human biospecimens, Shapiro says.

"We live in a litigious society, and in order to protect not only the patient but the investigator and institution, we need to make sure we don't violate these rules," she adds. "You don't want your institution to end up in headlines, saying that 'XX is selling body parts.'" ■

Improving site-to-staff/ PI/doctor relations is key

Enhance staff and MD morale

Managing a clinical research department is challenging for a variety of reasons. One of the most difficult issues involves staffing communication and retention.

Also, research sites need to develop relationships with physicians in the community who might become study referral sources.

The key is improving communication skills and strategies, says **Linda Sherriff**, RN, MHA, CCRC, a research coordinator at Columbia Cardiology in Columbia, SC. Sherriff also has served as department manager over clinical trials, overseeing research coordinators, regulatory coordinators, and others at a large health care institution.

Research sites should keep lines of communication open with investigators and develop close relationships with physicians, Sherriff says.

One strategy for larger clinical trial (CT) sites would be to hold educational luncheons for the department or hospital in which a physician would speak about the clinical trial.

If study participants are recruited from the emergency department or intensive care unit (ICU), then the educational session could be held

at different times to catch all shifts, Sherriff suggests.

"You could pull in nursing staff, residents, and other physicians," she says. "It helps for them to get to know the investigator, and it helps with back-and-forth communication."

Here are some other strategies for improving staff retention and satisfaction, as well as research staff-physician communication:

• **Find ways to enhance staff morale:** One of the common management flaws that dampen staff morale involves letting employees stay in a rut.

Managers sometimes fail to use all of their staff's abilities, Sherriff says.

"Part of the problem is they do not assess employees' skills," she adds. "Also, managers might not realize that the more you can encourage others to develop professionally, the better the department would be."

Another way to improve morale is to encourage positive comments and compliments through a kudos' board.

"So if somebody did something nice then another employee would write it down and put it on the bulletin board," Sherriff says. "After a while it becomes a challenge of 'Who can think of the most positive things?'"

This type of program is particularly helpful during economic downturns when employees do not receive annual raises and some other benefits are withheld, she notes.

• **Identify the right people through team interviewing and team input:** Sometimes the best way to ensure high staff morale is by hiring the right people in the first place. With team interviewing, a research site can more thoroughly assess a potential new employee's skills and personal attributes.

"We utilized team interviewing with each of us focused on different areas," Sherriff says. "We had a regulatory coordinator who represented the legal aspect and looked at the organizational skills."

Another person on the team had long-term

CLINICAL RESEARCH NEWS

OHRP publishes international protections info

Five countries added to compilation

The Office for Human Research Protections (OHRP) of the U.S. Department of Health and Human Services has published online its 2011 edition of the "International Compilation of Human Research Protections."

The 100-page document can be found at the OHRP website at http://www.hhs.gov/ohrp/ by clicking on the "international" link.

The compilation lists more than 1,000 laws, regulations, and guidelines from 101 countries. These are related to human subjects research and include standards from various international and regional organizations. The compilation's purpose is to offer information for investigators, IRBs, and others involved in international research.

The 2011 edition includes a new sub-section on the laws, regulations, and guidelines on medical device research under its "Drugs and Devices" section, and it includes the laws, regulations and/or guidelines for five new countries, including Belarus, Grenada, Pakistan, Rwanda, and Tunisia.

The compilation's table of contents lists each country and has these categories of standards:

• General, related to most or all types of human subjects research
• Drugs and Devices
• Privacy/Data Protection
• Human Biological Materials
• Genetic
• Embryos, Stem Cells, and Cloning.
• The information is organized into four columns, which are as follows:
• Key organizations, which include groups that issue regulations or guidelines or that serve in a national oversight role for human subjects protection
• Legislation, which includes statutes, statutory instruments, and legislative decrees, as well as constitutional provisions that relate to human subject protections
• Regulations, which refer to instruments that are created and issued under the name of governmental administrative bodies
• Guidelines that pertain to non-binding instruments.

Many of the listings in the online document include hyperlinks to the source document. ■

research experience and assessed potential new employees' overall personality, she adds.

Employees also can help a research organization better match existing staff with their untapped skills and potential.

For example, a new employee might be hired to work in a critical care area when another nurse gets to know her and says, "Did you know she also had this background in public relations before she came into nursing?" Sherriff says.

This type of information helps a research organization better use its employees' skills and talents.

• **Employ the Studer method to learn more about staff**: Some hospitals follow Quint Studer's rounding strategy for learning more about employees and boosting staff morale.

Studer, a chief executive officer of Studer Group, is author of the book, *Hardwiring Excellence: Purpose, Worthwhile Work, Making a Difference*, published in 2004 by Fire Starter Publishing. His leadership techniques include what he calls the magic of rounding.

"Each month you have rounding and talking with staff, connecting with individuals, as well as with groups," Sherriff explains. "Managers can find out what it is employees want from them and also say what it is they need, hopefully making a match."

Studer's writings describe his rounding method as having a department manager, CEO or vice president make rounds to check on the status of employees. It is about gathering information proactively and in a structured way in order to reinforce positive behaviors. More details about the method can be found at his website: www.studergroup.com.

• **Assess physicians' satisfaction and communication needs**: Research directors might offer to meet with physician investigators on a one-by-one basis to discuss any important issues or to find out the best ways to communicate with them during ongoing trials.

"Some like emails but want you to keep it short and to the point, maybe listing the first three things you want them to do," Sherriff says. "Some just say, 'Call me.'"

When meeting with investigators, the key is to keep the agenda short and to the point.

"Go over the highlights and talk about the current study quickly," Sherriff suggests. "If there is limited time you could make sure papers are signed or the coordinator could talk with the physician, discussing site initiations, completed surveys, and asking if there's anything else they want us to do."

Twice a year, a research director could send out a satisfaction questionnaire, asking investigators how the department did, how coordinators did, and what everyone could do better, she says.

• **Provide adequate awards for physicians**: For physicians, an organization could hold a "Doctor's Day" in which staff makes cards and cookies for them as a simple thank-you message, Sherriff says.

When physicians speak at research or department meetings, this is a way of thanking them for their time.

Also, a research division could hold monthly luncheons. These are opportunities where staff could increase their understanding and educate employees.

When physicians make referrals to studies, research departments could put their names in a hat and pick one to reward with a pizza, Sherriff suggests.

"It would be something simple and you might get approval through the IRB," she adds.

Research departments could even put up a board with doctors' names on it and starts next to their names after referrals are made. One hospital-based research site did this, and it made a big impact with physicians, she notes.

"They had little stars but were tickled," Sherriff says. "Every time they made a referral, whether or not the patient met the criteria, they'd get a star."

• **Enhance customer service**: "In our area there are a lot of customers," Sherriff says. "They could be physicians, each other, and ancillary departments in the hospital, such as radiology and labs for some studies."

Communication strategies are needed for working with the various departments/customers.

As research departments handle studies, these have a potential impact on many different departments, and all of these people should have some knowledge and interest in the research.

When studies are complicated, the research staff could hold small group meetings with key players. Nurses, physicians, and pharmacists could provide some of the education about the research project.

At smaller sites, internal customer service is simpler.

"When you have eight physicians and a nurse practitioner, it's much easier to find time with physicians, and it's easier to get to know the doctors quickly," Sherriff says. "You're a visible face to them, so it's easier to develop a relationship." ■

Clean your own house before OIG knocks

Repay overpayments in 60 days

The U.S. Department of Health and Human Services' Office of Inspector General (OIG) now expects research institutions to monitor their own regulatory compliance and identify errors and overpayments. While voluntary disclosure has been an option since the 1990s, the OIG has made it a bigger focus lately, a regulatory expert says.

Voluntary disclosure involves having research institutions conduct internal reviews, find errors, and report them, says **Pat Marion**, CFE, principal of Compliance Concepts Inc. of Philadelphia, PA. Marion worked for the OIG for more than 20 years. Compliance Concepts is a 14-year-old health care compliance firm.

"This is always a much better way to find and correct problems," he says.

When a research organization discovers a billing error, it can report this and adjust payment to the Medicare carrier, accordingly.

"If you find an issue that potentially contains fraud, then those cases you take to the Office of Inspector General," Marion says.

Marion offers these suggestions for how to handle various compliance issues:

1. Listen to research participants' complaints about billing issues.

Occasionally, a research participant will receive a bill from Medicare that the person thought would be paid by the clinical trial. Perhaps they were told the trial would cover all costs.

Investigators might answer this complaint with a casual, "Don't worry about it." But this is precisely the type of situation a research compliance office should review, Marion says.

"When you get these complaints and ignore them they can turn into a bigger problem," he explains. "And sooner or later you're going to have OIG knocking on your door."

The research organization's research administrator should review the claim and then return to the patient with an explanation about why Medicare was billed for this item, he adds.

If the item billed to Medicare was not for standard of care and was billed inappropriately, then this should be corrected with a refund made to Medicare.

"Find out why it happened: was there a breakdown in Medicare coverage analysis? Did somebody not do something they should have?" Marion says. "Don't let this escalate to something bigger."

2. Pay close attention to effort reporting.

"One issue that people don't tend to be as mindful of is effort reports in universities," Marion says. "I think there is a huge liability if effort reports are not correctly filled out."

Marion has seen cases where researchers only keep track of their federal research time, a practice that is noncompliant with regulations.

"In the government's mind there is no such thing as a 40-hour workweek in an academic research setting," Marion says. "You have to report 100% of total university effort, including federal and nonfederal research time."

Researchers lose sight of this requirement and fail to complete accurate effort reports. But this is a compliance issue the federal government takes seriously, he adds.

"They have to include research time, instruction time, clinical time, and administration time," he says.

In one investigation Marion saw the investigator listed his time on the effort report as 100% for the federally-sponsored research. In reality, the investigator had other job responsibilities, including chairing a department, heading five committees, so it was impossible for him to have spent 100% of his time on just the research.

"The government takes great exception to that," he says.

3. Report all awards to the National Institutes of Health (NIH).

Researchers often list only their NIH awards on the support application, but the federal government wants to know of all of their awards – both public and private ones, Marion says.

"The government wants a thorough and accurate answer," he says.

The federal award process judges want to know how much time you might have available for the federal grant for which an investigator is applying.

"They want that information listed so they can make a decision about the full breadth of what a researcher is doing and make a decision on that basis," Marion explains. "If you have three other awards, the decision might have a different outcome than if you have 30 other awards."

But if investigators do not list all of their awards and NIH discovers this omission it could result in

NIH asking for its grant money to be returned, he adds.

4. Collect co-payments properly.

Research institutions cannot arbitrarily waive co-payments, Marion says.

"That's always an issue in any program," he says. "You can't bring somebody in and say, 'We'll waive any co-pays on that.'"

For instance, the research participant receives an x-ray that is covered under Medicare's standard of care. There's a Medicare co-payment associated with that treatment. The researcher can't say this co-payment will be waived, he explains.

"We will have to disclose to people which things will be standard of care and might require a co-pay," he says. "You need to tell people what they will be responsible for, and you can't promise them the world."

5. Disclose errors discovered during internal review.

The first thing a research institution should do if it discovers an error during an internal review is disclose the mistake and return the funds, Marion says.

Some investigators question why they should return the money and why it isn't adequate to simply change the practice moving forward so that mistake won't recur, he notes.

"The answer is, 'No. If you know you have Medicare or Medicaid payments that are overlapped with research services, then you have to pay that money back within 60 days,'" he states.

"We've seen some investigations where organizations knew they had issues and did not correct them or pay back the money they should have paid back," Marion says. "In the future, it will get worse for these organizations."

"Make sure you close the loop and get that money back to the awarding agency or Medicare or wherever that overpayment came from," he adds. "That 60-day deadline to pay it back starts when you identify the overpayment through an internal investigation."

6. Follow three steps in reporting mistakes.

- Step 1: If it's a simple mistake in billing, then return payment to the carrier.
- Step 2: If it's an issue that is potentially intentional or the result of fraud, then report the case to the OIG.
- Step 3: If it's a case where someone might have clear criminal conduct, then report the case directly to the U.S. Attorney's office and the Department of Justice, Marion says.

"For example, we were involved in an embezzlement case where we knew from the third day that there was theft of money, embezzlement involving federal dollars," he recalls. "Because of the nature of the investigation and activity, it was clearly a criminal case and was reported directly to the U.S. Attorney's office."

The institution also brought in outside counsel to conduct an internal investigation and to make the disclosure about the findings.

In cases like that one, institutions often enter a corporate integrity agreement in which they agree to pay back the money overpaid and describe how they will operate for the next five years to prevent future problems.

"It includes designating what your corporate

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

- Design thorough study audit process
- Enrollment strategies that work
- Operationalize compliance at sites
- Working with data safety monitoring boards
- Managing multisite, global trials

compliance program should look like, the requirements for training, and some of these have a clause for having an outside auditor come in and look at claims for the next three to five years," Marion says. "If the federal government does an investigation and there's a settlement, then there's a 99% chance you'll receive a corporate integrity agreement." ■

CNE/CME QUESTIONS

17. Which of the following describes an industry trend that is leading to difficult financial times for research and development?
A. Generic erosion
B. Softer consumer demand in a down economy
C. New products that target smaller markets
D. All of the above

18. What is one new study design strategy some sponsors are using in clinical trials?
A. Endpoint prolongation clinical trial
B. Midpoint modification study
C. Adaptive design clinical trials
D. None of the above

19. Which of the following is not a question investigators could ask patients when requesting the use of their tissue for research?
A. Are you willing to donate tissue for Study X at this time?
B. Would you be willing to have your tissue used for any unanticipated clinical trials without anyone notifying you at the time of the proposed use?
C. At some time in the future would you be willing to donate this tissue for future experiments related to this diagnosis?
D. Would you like to be contacted each time there's a potential use for your tissue?

20. True or False: If an academic investigator keeps careful track of all time spent on his or her federal research grant and records this in the efforts reporting log, then this fully satisfies the federal effort reporting requirement?
A. True
B. False

Answers: 17. D, 18. C, 19. B, 20. B *(They also have to include nonfederal research time, instruction time, clinical time, and administration time)*