CLINICAL TRIALS
ADMINISTRATOR
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IN THIS ISSUE

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CR organizations bring subject recruitment to new, creative levels

Recruitment begins with public service campaigns

The clinical research industry's enrollment failures are more complex and have greater repercussions than delays, experts say. "Take a step back and look at clinical trials that fail," suggests **Joan A. Chambers**, BS, director of strategic marketing and development at Tufts University's Center for the Study of Drug Development in Boston. "The industry is aware that maybe the protocol is poorly designed, or the site has conflicting studies," Chambers says. "There might be poor patient compliance and retention, and you take all of that into consideration, and that's what our industry is witnessing."

About 80 percent of the estimated 50,000 clinical trials in the United States are delayed at least one month because of enrollment difficulties, and the amount of time needed to develop new drugs has nearly doubled in the past 40 years, according to statistics by Thomson CenterWatch of Boston.

One of the reasons why so many sites have trouble recruiting subjects is they have a plan A for recruitment and no plan B, says **Louis C. Kirby**, MD, medical director and founder of Pivotal Research Centers in Peoria, AZ.

"If a site's database doesn't generate patients, then what are the contingency plans?" Kirby says. "And if a site has none, then there's only so much it can spend out of the [clinical trial] budget."

Add to these common problems the broader picture of having a media splash whenever a major study problem occurs, and the public perception appears negative, she adds.

"With the popular culture, it seems that on TV you don't hear a lot about positives and what research can do for patients," Chambers says. "You hear the term 'guinea pigs,' and then there are movies like "The Fugitive" and "The Constant Gardener" that portray the industry as corrupt and greedy."

So it's little wonder that national surveys reflect a public that is conflicted about clinical trial research, she says.

This is why clinical research recruitment needs to begin in the broader public arena with people who know almost nothing about

research studies other than what they see on TV or in the movies, says **Christine Pierre**, RN, founder and chief executive officer of RxTrials and RxTrials Institute, which now includes ForeSite Publishing, all of which is in Ellicott City, MD.

"I believe if we would educate the general public, their willingness to participate would increase," Pierre says.

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Editor: **Melinda Young**.
Vice President/Group Publisher: **Brenda Mooney**, (404) 262-5403 (brenda.mooney@thomson.com).
Editorial Group Head: **Lee Landenberger**, (404) 262-5483 (lee.landenberger@thomson.com).
Managing Editor: **Leslie Hamlin**, (404) 262-5416 (leslie.hamlin@thomson.com).

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Editorial Questions

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Chambers, Kirby, and Pierre offer these suggestions for improving study recruitment and retention:

1. Make the most of patient charts.

Two-thirds of clinical trial sites have a medical practice attached, and these sites can check patient charts for diagnoses and other possible qualifications for a study, Kirby says.

"Using patient charts is the most juicy aspect of getting subjects," Kirby says. "If you have a practice, you know what medicines they're taking, and you also have information about your lab and other things to see if a patient is qualified for a trial."

While this is the easiest and cheapest way of getting patients, many studies are not filled by the patient population the site already has, he adds.

"Close to 15 percent of all sites are dedicated research centers, which is what mine is, and it's not attached to any practice," Kirby says. "So we have to have advertising money."

However, even dedicated research centers keep study participant information in a database, which they can use for screening purposes before calling past participants about new studies, Kirby says.

"That's pretty efficient for us — way more than advertising in the media and fielding phone calls," Kirby explains. "But that only gets us a portion of patients because a majority of people will fall out of the study criteria." And this is why advertising often is essential.

2. Know what to expect from recruitment advertising.

Give study sponsors a proposal for print and/or radio advertising, and tell them how many participants this will generate, Kirby suggests.

"They'll fund a portion of that budget, and then they'll give you more money as patients enroll," he says.

Sponsors typically do not like to give sites large sums of money toward advertising up front because they think it could be wasted and unending, Kirby says.

Also, pharmaceutical companies sometimes make assumptions that are not accurate about how a site finds patients, Kirby says.

For example, a sponsor might think that it will work only with sites that already have the desired patient population, but even those sites may run out of patients, causing enrollment delays and resulting in last-minute advertising, he adds.

Once a site has established a good relationship with a sponsor, it's easier to tell them that it will take more time and money to recruit the patients they require or to ask them to change study criteria, Kirby notes.

Also, investigators and clinical research professionals need to know which types of studies will not have success with advertising, such as acute fever blisters, Kirby says.

"On studies we think we can do, we talk to the sponsor up front and say, 'This is what it will take for us, as a dedicated center, to do this study,'" Kirby explains. "It will require advertising money, and if you don't have it, then we're a poor choice for you."

Clinical trial professionals and investigators also should learn the nuances of advertising, including how to buy it and negotiate for the best price, how to add recruitment ads to the site's Web site, how to monitor advertising results, and how to make changes mid-stream if enrollment becomes a problem, Kirby adds.

3. Be careful when selecting studies.

"Sites need to be very careful about what they say 'Yes' to," Kirby says. "If they can enroll and have experience in enrolling, then they should say 'Yes,' but if not then they have to turn down the study and walk away."

Sites will save money by not putting their resources into a study in which they'll have trouble enrolling participants, Kirby says.

"You make no money other than your expenses if you've not enrolled subjects," Kirby says. "And you've lost an opportunity, so sites have to be very careful, and some are not as careful as they should be."

Sites need to be honest with themselves and with the pharmaceutical company about how well they are capable of performing on a particular protocol, Kirby adds.

"If sites spend time understanding themselves then the outcome is far better, and the sponsor is likely to have a better group of sites that are more likely to find patients," Kirby says.

4. Educate the public, as well as potential participants, about clinical trial research.

"You're trying to reach out to [the general public] because they have low awareness about clinical trials," Chambers explains. "You plant the seed and reach out to them and build that awareness, so when they see a clinical trial advertised, they will recognize what it's about."

Chambers uses a four-stage model to describe the public and clinical research. The first stage is the pre-participant stage, which describes people who have never been involved in clinical research and know little about it. This is followed by prospective participants, study participants, and past participants. (See story about four stages of CR awareness and participant recruitment below).

Companies that succeed with recruitment do a lot of upfront planning and have a very targeted message to potential study volunteers, Chambers says.

5. Provide results of study to participants, whenever possible.

This often is a low priority because by the time a study's results are available, the clinical trial site has moved on to other research, Pierre notes.

"The study is long over, and researchers could be 10 studies down the road," she says. "But it's important to know that 87 percent of participants want to hear the results, so we should make it an expectation we impose on ourselves."

Clinical trial professionals should tell participants that when they learn of the results they'll tell them, Pierre suggests.

Then when the results are available, the investigator and site should mail participants letters telling them of the results, she says.

The letter could use phrases like 'This drug has made it to market and it's marketed under this name, and if it wasn't for people like you participating in the research, then the drug never would have gotten through the regulatory process,' Pierre says. ■

Recruitment begins long before the study's first visit is scheduled

Think of participants in four categories

When clinical trial sites seek participants for a particular study, they often think of study subjects in one concrete way, rather than looking at the bigger picture of building a base of potential research volunteers.

"We actually have four target audiences," says **Joan A. Chambers**, BS, director of strategic marketing and development at Tufts University's Center for the Study of Drug Development (CSDD) in Boston.

For each of these audiences, there are specific ways the clinical research industry can enhance their involvement in research, she says.

The four categories are:

• **Pre-participant:** This person has heard little about clinical research other than what is in the popular media, Chambers says.

• **Prospective participant:** This target person is familiar with research, but hasn't participated yet, she says.

• **Study participant:** The study participant is someone who has participated in research and continues to volunteer in a clinical trial.

• **Past-participant:** Although this person has participated in a clinical trial previously, the site and sponsor have not followed up with this person, and so there is no current study involvement, Chambers says.

"When you divide it up like that, it helps to know who your target audiences are and how you are going to position your promotional material," Chambers says. "When you're trying to recruit for a new study, you may want to target the message very differently: the study participant group versus the past-participant group or the pre-participant group."

Here are some strategies for engaging each of the four groups:

1. Understand what pre-participants know.

For example, Tufts CSDD research has found that 94 percent of Americans believe clinical research is important for advancing medical knowledge, and 69 percent of the public has seen an advertisement seeking trial participants, Chambers says.

But only 21 percent of Americans believe they have a basic understanding of why and how clinical research is conducted, and less than 5 percent of Americans say they feel confident enough to begin searching for information about clinical research trials, she says.

These statistics show how there's a great deal of potential for expanding the research volunteer base if clinical trial sites and the research industry were to reach the pre-participant group.

For example, the Center for Information and Study on Clinical Research Participation (CISCRP) of Dedham, MA, has a variety of public education materials available to study participants, researchers, and others at the center's Web site: www.ciscrp.org. CISCRP also holds educational sessions in a number of U.S. cities, calling them AWARE for Annual Workshop to Advance Clinical Research Education.

Another way to reach the general public is to have professional education and outreach programs for medical professionals to distribute to their patients, Chambers says.

"These can help them educate patients about clinical research," she notes.

2. Have doctors help you reach prospective participants.

Prospective participants are the elusive group that everyone wants to understand and reach.

"Prospective participants know the risks and benefits of clinical research, but they haven't taken the initiative to participate," Chambers says.

This group can be reached most efficiently through their physician because 78 percent of them consider their physician the most trusted source for medical and health-related information, Chambers says.

"The question is, 'How can we provide information to these physicians in order for them to share it with their patients?'" Chambers says.

One solution would be a newsletter that is sent out to patients.

ForeSite Publishing of Ellicott City, MD, has developed an educational newsletter that can be mailed to a clinical research site's patients and distributed in doctors' offices. Called ForeWard, the four-page newsletter is full-color and includes engaging articles about clinical research, says **Christine Pierre**, RN, founder and chief executive officer of RxTrials, RxTrials Institute, and ForeSite Publishing.

The summer 2006 issue includes a cover story called "What is Clinical Research?" and an inside column called "Volunteer's Voice." A blue-boxed bullet points section answers the question "Why do they do it?" with very short answers, including "To find a cure for a disease they have."

Another section provides a short article that highlights a particular researcher and his work, and this interview-based story is how the newsletter is customized for its subscriber site, Pierre explains.

"The physician interview is on each and every one of their customized newsletters, including their names, logos, and studies," Pierre says.

"For the volunteer's voice, we have a library of volunteers we've interviewed on various aspects of research," Pierre says.

Sites can buy copies of the newsletter in increments of 1,000 per quarter, and these can be sent to patients, physician offices, or to organizations in the community, she adds.

One hundred patients selected randomly were

asked to fill out a questionnaire about clinical research and their willingness to participate, and then they were sent the newsletter for three months, Pierre says.

Before receiving the newsletter, 40 percent of the patients said they were willing to participate in research, and 60 percent said they were not willing, she says.

After receiving the newsletter, the patients were asked again about their feelings toward research and, this time, the numbers had reversed with 60 percent of the patients saying they would be willing to participate in research, Pierre adds.

3. Help study participants stay invested in clinical research.

"One way to keep participants engaged is to have ongoing communication with them," Pierre says. "What's most beneficial is they really want to know the results of their participation, so having a letter that you've written, thanking them for their participation, builds an incredible relationship."

There is no immediate fix to the recruitment problem, but clinical research sites can build a foundation to a stronger relationship with subjects and future subjects, Pierre says.

"So you have a study and need to populate it, but you should be doing these foundational activities all the time," Pierre adds. "That's just good business."

The degree of emphasis that should be placed on retention is directly related to how long the subject will be on the study, Pierre notes.

"If the study is for 12 weeks, then you can do basic customer service, including being prompt, accommodating their schedule, and showing appreciation and respect of their contribution as research subjects," she says.

"If you have a study where you'll need the subjects for a year or five years, then you will need some retention strategies and programs," Pierre says.

These might include sending out birthday cards to participants, remembering them on their anniversary, maybe giving them small boxes of chocolates on the special occasions, Pierre suggests.

All of these activities will require IRB approval, and it doesn't matter how strong or grand the activities are, Pierre says.

CISCRP has promoted a "Heroes" program in which clinical trials participants are recognized and thanked for their contribution to research, Pierre notes.

"Another group gives out t-shirts that say, 'I'm part of the solution,'" she adds.

Sites that have long-term studies will need to provide some sort of recognition for participants. These could be divided into six month intervals and involve giving participants inexpensive gifts, such as t-shirts, cards, or sponsor items, such as water bottles, bags, clocks, or other items with the study's name on them, Pierre suggests.

"It's an incredible amount of time commitment on participants' part," Pierre says. "And we ask them to do a whole lot more than if they were receiving standard care in most instances."

4. Don't lose sight of past-participants.

"Unfortunately, from our survey results, we found that 88 percent of past-participants say they would participate, and 87 percent want to know the results of the study they participated in, but 79 percent say they never received any updates after the trial ended," Chambers says.

"That's a huge percentage of participants out there that had participated for a length of time and wondered about study results, but never heard back," Chambers says. "How would that make them feel about being approached again?"

This shows how there should be an initiative taken to send out follow-up notices and to say, 'Thank you for participating; we're able to share the results,' or 'We're not able to share the results,' Chambers says.

"If they're approached for a new study, and they hadn't received the results from the last one, then the new researcher can give them those results," Chambers adds.

Past-participants need some kind of closure, and they want to be treated as if they were important, she says. ■

Develop comprehensive hiring and training plan for new staff at a clinical research site

Expert offers outline for competent hiring and training

Clinical research is more complex these days, and so is the hiring process. Clinical trials sites and others in the

industry now have a variety of options when hiring new personnel, including the latest option of hiring staff that are fresh out of a clinical research degree program.

As such, it's a good idea to review the hiring and training objectives and update and revise these where necessary, an expert advises.

"Over the last two years, we've implemented a position-specific training program," says **Kathleen S. Badeaux**, MS, CCRA, clinical research associate for MedTrials Inc. of Dallas. MedTrials is a clinical research organization, and Badeaux spoke about creating a training needs analysis and resultant training matrix at the Drug Information Association's 42nd annual meeting, held June 18-22, 2006, in Philadelphia.

"Our training program is created at the organizational level, but it can be individualized for each employee based on the person's previous experience and/or education," Badeaux adds.

One way to do this is to create a training needs analysis that encompasses both initial employment and continuing education and training, Badeaux says.

Badeaux explains how to create such an analysis, as follows:

1. Write a detailed job description.

"We saw a need for ongoing training in our organization, and so we thought the best way to address that issue would be to address it according to the job description," Badeaux says.

An institution's or company's job descriptions should be made at the organizational level in which the company decides what basic knowledge, skills, and abilities they want in each job, Badeaux suggests.

"Our job descriptions are pretty extensive," Badeaux notes. "To have a thorough job description, it has to be done at the highest managerial levels."

The key is to identify first the skills required to help the company meet its own goals, she says.

"Then hopefully, your position's job description will follow from that," Badeaux adds.

The MedTrials' job descriptions typically are two pages long and include job functions and qualifications, which increase in length as the job level increases.

For instance, a job function description for a clinical research associate (CRA) level 1 position will be shorter than the job function description for a CRA level 3 because the level 3 description includes the same function descriptions noted in levels 1 and 2, plus additional items, she explains.

"Our qualifications are very specific initially, and then they become more general," Badeaux says.

Also, there is some flexibility in hiring objectives.

For example, for a CRA level 1, the typical job function requirement is for the employee to have two years previous clinical research experience, Badeaux says.

"But a lot of times we'll hire someone and let them be an in-house CRA where they can learn the nuts and bolts of the job, work with filing and document management until they have a firm understanding of the regulations, and then they can start looking at monitoring reports from other CRAs," Badeaux says. "They are responsible for filing those and tracking them, and they're exposed to a lot of the facets of the CRA level 1 position, and then they can go out and co-monitor with a CRA before becoming a CRA themselves."

For higher CRA levels, the years of experience requirements are less flexible, she adds.

"We also require degrees and want at least a bachelor's degree, although many of our employees have higher degrees," Badeaux says. "We usually require CRA certification for levels 2 and, especially, 3."

The skills required are built from there, including managerial skills, drug and device experience, communication skills, and organizational skills, she says.

2. Divide potential employees according to experience.

"We take the core competencies required in the job description and we correlate those with the experience and education each individual brings to the job," Badeaux says.

"We do a functional analysis and look for employees' demonstrable skills and individual differences in past training, any pre-conceived ideas they bring with them, and their level of motivation," she explains.

Using a CRA level 1 as an example, MedTrials would expect the new employee's knowledge to include competency in good clinical practices (GCPs), all research regulations, guidelines, industry standards, and company or project/sponsor-specific standard operating procedures (SOPs), Badeaux says.

"So that's the general knowledge that we want for a CRA level 1," she adds.

A new hire's past experience usually falls into one of four categories:

• Position experience — This requires shorter training time, less training expense, quicker productivity, possible bias, and higher salary;

• Industry experience — This employee would need medium training time, moderate training expense, quick productivity, possible bias, and moderate salary;

• Inexperienced/CR education — This employee will need medium to extensive training time, moderate training expense, reasonable productivity, minimal bias, low to moderate salary;

• Inexperienced/no CR education — For this employee, the training time and expense are extensive, and there is delayed productivity, but no bias, and a low salary.

3. Know your own organization's goals.

A company must know what needs to be accomplished, what's driving the company's goals, and the job description should flow from those goals, Badeaux says.

"The goals and job description represent what we want in our employees as representatives of our company," Badeaux says. "We have always prided ourselves on providing a quality product, so we stress quality, and that's why we implemented this type of training program to make sure when we hire people their work helps us provide the best possible product we can provide."

So for MedTrials, the job descriptions flow from the company's chief goal of producing a quality product for clients, she adds.

4. Make assumptions based on employee type.

Based on the four different types of employees, some basic assumptions can be made, Badeaux says.

"Each individual is different, so we want to give them a little bit of time to show us what they can do," she adds. "But we had to make basic assumptions when we designed specific educational modules, or we wouldn't know where to begin."

For example, for employees who already are CRAs, managers assume the new employees have knowledge about GCPs and industry practices, Badeaux says.

"Someone who has clinical research experience, but not as a monitor, probably has been exposed to GCPs, as has the graduate of a clinical research education program," she says. "But the completely inexperienced individual, who has no real monitoring experience, would probably not be conversant in GCPs, industry practices, or SOPs."

Another assumption would be that an experienced CRA would have some monitoring mechanics, would be computer proficient, and would have good communication skills, Badeaux says.

So when a company creates education and training requirements for new employees, it's important to chart according to an employee's assumed knowledge, skills, and abilities for each of the four types of education/experience scenarios, Badeaux says.

5. Document specific training dynamics based on perceived deficiencies.

Once basic assumptions are on paper about each position and level of experience, then it's time to chart training requirements for each scenario.

"So we started with CRA level 1 and developed a CRA level 1 book of knowledge," Badeaux explains.

This requires answering the question, 'What are the critical elements we want them to know to do their job?'

"What we came up with is we definitely wanted staff to be knowledgeable in GCP; we wanted them to know our company and project-specific SOPs," Badeaux says. "We also want them to possess specific monitoring skills, good communication techniques and soft skills, such as critical thinking skills."

The company also has specific ongoing job requirements and considerations for them as well, she adds. (See chart of position-specific training needs analysis, p. 116.)

For example, these are some ongoing training considerations:

• For inexperienced staff: Allow sufficient in-house time to develop familiarity with all aspects of clinical research and company policies, and provide training modules both before field monitoring has started and shortly thereafter;

• For experienced staff, repeat initial and more advanced training modules at least once per year;

• For all staff, provide resources and references for refresher courses and questions in field or in practice.

6. Provide staff education modules and position-specific training.

MedTrials' training sessions involve instructors who hold workshops lasting from one-half a day to two days in duration, Badeaux says.

Each workshop consists of modules, lasting from one hour to 1.5 hours.

"We have an outline of all of our modules, and we've identified how long they will run," she says.

Position-Specific Training

Training Needs Analysis Based on Knowledge, Skills, Abilities

New Hire	GCPs	SOPs	Monitoring Requirements	Communication, IT Capability	Soft Skills (Analytical,
Position Experience	Refresh	Yes	Co-Monitor: Subsequent PST	Company Specifics Communication Methods	Varies
Industry Experience	Refresh	Yes	PST and Co-Monitor	Company Specifics Communication Methods	Varies
Inexperienced But Clinical Research Education	Assess Refresh	Yes	PST and Co-Monitor	Company Specifics Communication Methods	Professional Practices
Inexperienced No Clinical Research Education	GCP "*Boot Camp*"	Yes	PST: Before/After Co-Monitor	Company Specifics Commu nication Methods	Professional Practices

All new monitors will take the interim monitoring workshop, and then they'll continue to take it as part of their continuing education, so they will always remain proficient in monitoring, Badeaux says.

"We allow two full days for the interim monitoring workshop, and we have seven sessions within that workshop," she says. "All four levels of staff take this workshop, and we tailor it to our way of doing monitoring."

MedTrials also provides inservices to help employees hone their hard and soft skills, including their communication skills and IT skills, Badeaux says.

"We also have weekly inservices where we provide continuing education to all employees," she notes. "Every Friday we have lunches provided to staff, and sometimes the inservices are based on federal regulations, therapeutic areas, or ethical issues."

"That's a real benefit to our organization and employees, and that's in addition to the formal modules we have," Badeaux adds.

Depending on an employee's education/training level and position, there will be a variety of other modules required. These additional modules include the topics of regulatory review and source document verification, Badeaux says.

Each required module is based on what the company expects the employee to be able to do on the job, she explains.

"The training program is about what we need to provide them so they can perform that job well," Badeaux says. "We want to make sure they will be able to perform their job to our standards and how we want it to be done." ■

Site level considerations in study completion speed

Expert's research highlights main issues

[Editor's note: in this Q&A story, ***Jeffrey James DiFrancesco****, MSc, MEng, CSSBB, an assistant professor of pharmaceutical business in the College of Graduate Studies, University of the Sciences in Philadelphia, Philadelphia College of Pharmacy in Philadelphia, PA., and a partner with PrécisTrial LLC in Blue Bell, PA, discusses his research into study completion performance. DiFrancesco's co-author in the study is* ***Harold E. Glass****, PhD, professor of pharmaceutical business, University of the Sciences in Philadelphia, Philadelphia College of Pharmacy.]*

***CTA*:** Would you please provide background information about your research?

DiFrancesco: Seven companies took part in the study: Bristol-Myers Squibb, GlaxoSmithKline, J&J, Novartis, Pfizer, Sanofi-Aventis, and Wyeth. The study focused on several indications: Asthma/COPD, Depression, Schizophrenia, Bipolar disorder, Hypertension, Diabetes and Menopausal Syndrome. The global study included data from 521 phases 2 and 3 studies at 4,092 sites and were completed after 2002.

All phase 3 studies were multinational, involving the U.S., and at least one western and one eastern European country.

***CTA*:** What do you see as the main site level considerations in study completion speed?

DiFrancesco: When we began our research, we interviewed each sponsor to gather what they subjectively believed were the site level considerations in study completion speed. One of the strongest and most consistent assertions made by the sponsors was the importance of the quality, experience, and availability of the site's clinical research coordinator, and equally as important on the sponsor's side — or contract research organization — the quality, experience, and availability of the site monitor/clinical research administrator. This effectiveness of site monitor and study coordinator was together as important as the effectiveness of the principal investigator.

Was the relationship between site monitor and/or study coordinator effective, and was study completion statistically significant? Unfortunately, we were unable to determine this. The dilemma is that these types of site data are rarely collected or retained by most sponsors during clinical trial operations. Our research did, however, provide inference to support these assertions. For example, we were able to show statistically that the higher the number of prior studies the site had conducted for the sponsor or the greater number of prior studies (1572's) the principal investigator had participated in correlated with greater site performance. Another site specific variable was country: non-US sites typically had slightly higher number of patients enrolled per site than their US counterparts.

***CTA*:** How can clinical trial sites help eliminate the barriers to a faster completion time, and what are the actions that would have to be taken by the sponsor or another organization?

DiFrancesco: I like to answer this question operationally in two ways: first from a site planning perspective and then as an in-study site management perspective. For site planning, our research indicates sponsors need to structure site study grants to incorporate milestone-based payments, and further, structure site study enrollment goals to be competitive. These results are supportive intuitively, that market and competitive-based incentives are effective in influencing site level behavior and their resulting performance.

A counter intuitive result pertained to grant payments. Our research revealed that higher grant payments are not related to faster study completion times, although some sites may enroll faster when non-refundable start-up payments are incorporated. However, there is no clear evidence that higher payments alone insure higher quality.

Pertaining to in-study site management, our research shows simply that higher performing sites will typically have grant agreements executed earlier in the study than other sites, and or once a grant agreement is executed early, the time to first patient first visit is typically less. When you think about it, this makes sense. The earlier a site is initiated, the longer time they will have to enroll patients, provided the study's last patient first visit milestone remains fixed: more enrollment time, more patients enrolled, more site performance and faster study completion! Furthermore, these results infers that the time to grant agreement execution, as well as grant agreement to first patient first visit are statistically good early in-study indicators of site performance.

***CTA*:** What are the results and data about phase 3 studies that you made public at the DIA conference, and is there anything new to report?

DiFrancesco: Many of the preceding conclusions are new; however, most importantly we have shown statistically significant the relative explanatory power among site's different dependent variables as compared to the site's resulting performance. We will be publishing our quantitative conclusions and the results of further analysis later this year and next year in peer reviewed journals.

***CTA*:** As the research industry becomes more fully outsourced to international sites, do you see the clinical trial completion speed improving in the short term or long term?

DiFrancesco: Our research did not incorporate this question explicitly other than, as earlier stated, non-US sites seem to show a slightly higher number of patients enrolled per site than their US counterparts.

Subjectively, my only comment is we have to stop seeing outsourcing or internationalization of sites as the panacea for speeding study completion. I suggest that we need to think in supply-chain terms: strategically, countries and sites represent a global supplier network; tactically, patient enrollment is controlled by actively adjusting number of sites and countries; and operationally, near real-time feedback of actual performance along with the willingness for early intervention "continuous course correction" enables meeting or exceeding planned patient enrollment deadlines. It's called management!

***CTA*:** Clinical trial experts say there appear to be no immediate solutions to the problems of inexperienced investigators and sites and their

common difficulty in recruiting subjects. Do you know of any long-term solutions to this problem?

DiFrancesco: Research studies have indicated that typically 30% of sites participating in a study will enroll 70% of the eligible patients. The reasons for this high variability in site performance are numerous. Because of this essentially irreducible variability in individual site performance, we need to look at participating sites as a portfolio, and manage them as a portfolio using statistical methods.

Our research, as discussed earlier, shows that the number of prior studies a sponsor has with a site is a determinate factor, as is the experience of the principal investigator. However, when we looked at the relative weight of these types of site selection variables relative to others, the site "inexperience" is not as prominent as you might expect. For instance, site planning and site in-study management variables (as discussed previously) have a much more important role and impact, than site experience.

Pertaining to subject or patient recruitment, the short-term as well as long-term solution is to incorporate the patient recruitment strategy early into the protocol and study design. This will result in a more deterministic enrollment plans, a more targeted site selection process, and a set of effective indicators to actively manage site and country enrollment during study conduct.

***CTA*:** Are there any other problems or trends that you would be interested in commenting on?

DiFrancesco: Numerous research studies indicate the vast majority of studies fail to achieve their planned study deadlines. Furthermore, other studies indicate over the past decades there has been little improvement in study cycle-times. I assert we have to focus more on site planning and in-study site management than site selection alone. Furthermore, earlier in site planning process we have need to be more collaborative among sponsors, clinical research organization, site management organizations, patient recruitment firms, and prospective sites for site planning and in-study site management. We have great rigor in how we design clinical trials and their endpoints, but lack this same rigor in our operational planning and in-study management of studies. For instance, we need to look for more effective means to plan and manage the statistical variance inherit when conducting studies. Site performance will always be limited in its ability to significantly improve study completion speed if the planning of sites and the in-study management of them are systemically inadequate. ■

Communication skills and PI involvement are crucial to improving site's informed consent

IRB approval is just the beginning

Investigators are responsible for ensuring the informed consent process is done properly, but too often they delegate the task to clinical trial staff, an expert says.

"The informed consent process is not just a form and being told, 'Read this, if you like it, sign it,'" says **Michael Hamrell**, PhD, of MORIAH Consultants in Yorba Linda, CA.

"There needs to be a better attitude about the process," Hamrell adds. "Investigators should sit down with subjects, talk about the study and things related to it, and document the process."

Instead of spending most of their effort on getting consent forms approved by the IRB, investigators should consider the actual informed consent form as documentation of the complete informed consent process, Hamrell explains.

"The last thing you should do is say, 'This reiterates what we've discussed, and you may sign it,'" he says.

"The investigator is legally responsible for the informed consent process and has to be involved," Hamrell says.

"It's fine if a site has someone who is really good at talking with people, a patient educator or patient advocate," he notes. "But since many studies involve highly technical and scientific issues, the person who is most knowledgeable needs to be available to answer questions as part of the consent process, and this should be documented."

Hamrell has seen cases where complex studies are explained by a nurse, who obtains the participant's consent.

"They will say the doctor came in and answered the patient's questions," he adds. "Then, shouldn't the doctor be the one who got the consent; shouldn't the investigator's name be on the form?"

There are many other situations where investigators' names should be on consent forms, but they are missing, Hamrell says.

"While the regulations do not require the investigator to personally obtain consent or sign the form, investigators are responsible for making sure things are done right," Hamrell explains.

"The way some people who wrote the regulations envisioned it is to have investigators be involved in the consent and seeing that it's obtained," Hamrell adds. "But what's happened over the years is that medicine is much busier, and clinical research is more complex, so informed consent gets delegated."

Once investigators change their attitude about the informed consent process and realize that their responsibility continues long after the form is approved, then they might be less inclined to delegate the process. Or, if they do have an experienced clinical research educator sit with subjects, then the investigator also will be available to answer any specific questions about the study, Hamrell says.

Physician investigators have an additional burden when speaking with clinical trial participants than they do with their patients, he notes.

"It's not that they shouldn't explain medical issues in detail to patients but, when you have a clinical trial, there's an additional regulatory burden," Hamrell explains. "Without it you'd say, 'Did you understand? Yes or No?' and then they'd sign their name, and that's all you'd need."

However, the trust physicians expect from patients when they prescribe a medication or suggest a procedure can be a problem in clinical trials because they need participants to be fully informed and not make a decision based on their trust of the physician, Hamrell says.

"In our society, the layperson would say, 'If this is what my doctor recommends, he wouldn't recommend something that's not good for me,'" Hamrell says. "They say they trust their doctor and if he recommends a study then it's okay with them."

The other problem is that physician investigators need to learn how to speak about complex medical terms in simpler language than they're accustomed to using.

"Part of this is making sure there's a process that goes on and includes a discussion in which someone is spending time with the patient and explaining things, answering questions," Hamrell says.

Since patients are often overwhelmed by their own disease, some research suggests the best strategy is to have an initial discussion with the patient about the study and then suggest the patient think about it and come back in a couple of days with questions, and then make a decision, Hamrell says.

If the process is truncated to a single presentation then a site runs the risk of the patient saying, 'I don't know what to ask, but I think it sounds okay,' Hamrell says.

Clinical trial sites should stress better communication skills in both face-to-face discussions with participants and in the informed consent document, he notes.

In the informed consent document it is important to translate medical terms into layman words, and the actual sentences need to be structured more simply, Hamrell says.

"I work with sites and say to them, 'This language looks awfully complex,' and they say, 'We've dummied it down,'" Hamrell explains. "Then they check the reading level [such as MS Word's readability check] and discover their text is written at an 11th or 12th grade level, which shocks them."

Another strategy for improving informed consent is to help patients use available educational tools to facilitate the process, Hamrell suggests.

For example, some sites or study sponsors might prepare a videotape that describes the procedure and shows a model undergoing the process, he says.

Then the clinical trial staff can sit down with the participant and explain the study, answer questions, and ask the person to sign the consent form, Hamrell adds.

There has been interactive educational material available, as well.

"All of these things are good; anything that explains the process is good," he says. "Any of these tools help the understanding process." ■

COMING IN FUTURE MONTHS

- Check out these informed consent strategies
- Learn more about NIH roadmap and data standards
- Recover "lost" patients following these tips
- Find out more about new personnel in CR
- Design a formal research compliance program

CE/CME Objectives / Instructions

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

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

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

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

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

CE/CME *questions*

13. According to a recent survey, what percentage of people who had previously volunteered for a clinical trial said they had never received any updates after the trial ended?
A. 79 percent
B. 62 percent
C. 46 percent
D. 22 percent

14. Which of the following categories is not a typical one in which a new hire's past experience can be described?
A. Position experience
B. Industry experience
C. Inexperienced/clinical research education
D. All of the above

15. A recent study of clinical trial site completion speeds had which of the following findings?
A. Site performance was poorest for sites that had fewer than 10 physicians on staff.
B. Statistically, the higher the number of prior studies the site had conducted for the sponsor or the greater number of prior studies (1572's) the principal investigator had participated in correlated with greater site performance.
C. The data showed that sites with past experience of fewer than 500 clinical trials were far less successful in completion time than those with greater than 500 clinical trials experience.
D. None of the above

16. According to statistics and expert opinion, what is the one thing clinical trial participants want most often at the end of the trial, but too few receive it?
A. The study's results
B. A letter thanking them for their participation
C. To be asked to participate in another trial
D. A parting token gift, such as a t-shirt or tote bag

Answers: 13. (a); 14. (d); 15. (b); 16. (a)