# CLINICAL TRIALS ADMINISTRATOR

*An essential resource for managers of clinical trials*

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## IN THIS ISSUE




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**DECEMBER 2008**
**VOL. 6, NO. 12 • (pages 133-144)**


# CT site's unique research model reaps success and contented PIs

*PIs receive needed CR support services*

Everyone agrees that these are difficult times for physicians who wish to start working in clinical trials. They often have trouble enrolling in new trials, and the budgeting and documentation realities may lead to disillusionment before their first studies are completed.

There is hope, however.

A new clinical research (CR) model takes away principal investigators' (PIs') headaches and gives them the freedom to pursue the type of research they desire, while still making a fair return for their time investment.

This model has been successfully employed by HOPE Research Institute (HOPE) of Phoenix, AZ, which has 25 staff CR employees, 12 physician PI contractors, and four partners, says **Patricia Adams**, managing partner and co-founder.

"HOPE was started in 2002 with three partners, and we added an investigator as we were growing," Adams says. "There has been a constant growth curve since we started with five clinical trials."

Now the CT site handles 50 clinical trials and anticipates growth to 75 CTs by 2010, Adams says. Also, the organization has been profitable continually since its sixth month of operations, she adds. **(See related story, p. 135)**

The CT site pays investigators a percentage that is above the industry's average for CT work, Adams says. "It's up to HOPE to make sure the trial is running efficiently and that there's a little profit left after all the overhead expenses," Adams says. "The physician doesn't have to slow down in his clinical practice, and it makes it easier for him to see a research patient while also seeing clinical patients."

For all of these reasons, the CR model has been popular among physi-

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cians who've worked with HOPE Research Institute, says **Jeffrey Gitt**, DO, principal investigator and a partner at HOPE Research Institute.

"This is something I'm sure will catch on because people know we're successful, and we're very excited about this," Gitt says.

HOPE Research Institute recently received full accreditation from the Association for the Accreditation of Human Research Protection Programs (AAHRPP) of Washington, DC.

"We do classic sponsor-supported clinical research that grassroots America is involved in," Adams says. "We strictly do the research, and our investigators provide clinical care and function as both clinicians and investigators."

HOPE Research Institute provides any CR staffing, documentation, and other support an investigator needs, she notes.

"Our investigators are very excited to work with HOPE because HOPE makes sure they're doing a good job, and we can help them handle audits," Adams adds.

## Opportunities in many specialties

The model creates opportunities for researchers to do research in different specialties, Gitt says.

"So we do research in my area of neurology, but also have research in general medicine, podiatry, ophthalmology, and others," Gitt says.

"The other advantage is we have a group of very bright people, each of whom has a different role," Gitt explains. "We have people who do study acquisition, looking for new studies; people who market studies; people who handle regulatory concerns and the IRB."

The clinical research environment has changed a great deal since the 1980's, when Gitt first became a researcher, he says. These days, any doctor who gets involved in research because he or she wants to make money won't be happy, Gitt says.

"The time investment and commitment to doing a study can be larger than they expect, and frustration in getting all the paperwork completed can be far greater than they anticipated," he explains. "You have to like research and getting involved in cutting edge technology, and research has to be somewhat altruistic."

One of the drawbacks for physicians who are interested in research is that they may not have staff with the right skills to engage in clinical research, Gitt notes.

"For an individual doctor to obtain studies, get regulatory approval, do all the paperwork, and get everything done, including recruiting patients and getting it to flow from a financial perspective is almost impossible," he says. "If they don't have the right help and aren't savvy, they'll fail."

So HOPE Research Institute provides these individual physicians with the research expertise they often don't have.

"Having the right people in place allows us to free ourselves up to take care of our patients, rather than worrying about clinical trials details," Gitt says.

**Clinical Trials Administrator** (ISSN# 1544-8460) is published monthly by AHC Media LLC, 3525 Piedmont Road, Building Six, Suite 400, Atlanta, GA 30305. Telephone: (404) 262-7436. Periodicals postage paid at Atlanta, GA 30304 and at additional mailing offices. POSTMASTER: Send address changes to **Clinical Trials Administrator**, P.O. Box 740059, Atlanta, GA 30374.

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The model also provides a possible answer to some goals in the research roadmap promoted by the National Institutes of Health (NIH) of Bethesda, MD.

According to NIH meeting minutes in 2007, **Elias A. Zerhouni**, MD, NIH director, has a top priority and passion of finding new investigators. He acknowledges the common barriers to engaging new investigators, including lack of time and training.[1]

"Many mom and pop research organizations don't succeed," Adams says.

So HOPE Research Institute's model is attractive to physicians interested in clinical trials, Adams says. "They ask me how to put together a research organization," she says.

Often these new investigators will attempt to build their own CR site from the ground up, but typically they end up quitting when they become frustrated with the realities of the day-to-day CT work, Adams adds.

"It's easy to assume that people with medical and clinical expertise could easily go into research, but research requires unique skills," she says.

There are a number of reasons why the model has done well, but two stand out:

**1.** Adams envisioned the enterprise as being flexible and moving with CR trends, and it's been successful in doing so.

**2.** Investigators have learned not to choose trials where they anticipate problems with enrollment.

"We do not take trials that we don't believe we can succeed in," Gitt says. "I have had 70-80 trials, and I've had none where we have not enrolled any patients."

Gitt has turned down trials that he doesn't believe are in the patient's best interest or where he doesn't believe in the investigational product or when the CT would be in competition with another CT that HOPE Research Institute has underway.

"Part of our success involves PIs like myself taking on studies where we are honest and believe we have a patient population where we can find people," Gitt explains. "It helps if you've done research before and you have a long track record."

### Reference

1. Department of Health and Human Services, National Institutes of Health, Office of the Director, Office of Portfolio Analysis and Strategic Initiatives, Council of Councils Planning Meeting, Nov. 8, 2007. Meeting minutes. Web site: http://opasi.nih.gov/council/110807minutes.pdf. ■

# CR model works for AZ investigators

*PIs commit to honest enrollment appraisals*

When the founders of HOPE Research Institute of Phoenix, AZ, began to envision their new clinical research (CR) organization, they relied upon both their past successes and challenges in drawing plans.

"This is the second research site I've built," says **Patricia Adams**, managing partner with HOPE Research Institute. "I've learned lessons from the first one."

For one thing, Adams learned that if you build a clinical trial site around a certain type of medical specialty area because there's a strong pipeline of studies in that field, then you might face a major downturn when the pipeline changes directions.

"In starting a new organization and wanting a consistent pipeline, I looked at creating a business with a multi-specialty approach," Adams says. "So if there is a lot of work available in neurology, then we put efforts in that direction, and when that dies down, we'll go to gastrointestinal studies or pain management research."

Developing a multi-specialty site was crucial to creating a CR business that would survive in the long term, she adds.

"We started with podiatry, women's health, and neurology, which are our three physician partners' specialties," Adams says. "As we grew, we added other therapeutic areas, including orthopedics, dermatology, gastrointestinal, pain management, urology, ophthalmology, and others."

Physicians who contract with HOPE Research Institute are spread out in the CT site's geographical area. They can use the HOPE Research facility to see trial participants, or they can use their own offices, Adams says.

Principal investigators also can use the institute's clinical trial coordinators at the Hope facility or have the coordinators visit their own practices, she adds. Here are some more details about how the model works:

• **The PI decides how many or few support services to use:** Principal investigators decide when and how to delegate the CT work. "They might delegate data entry to one of our study coordinators," Adams says. The PIs are in charge of the study, but they rely on HOPE's experienced team to assist them in areas where their

expertise is thin, such as regulatory, contract negotiations, and/or budgets.

HOPE Research Institute also can provide PIs with assistance in budgeting, training coordinators, psychometrician services, contract negotiation, study accounting, personnel issues, and regulatory services, she says.

"We'll partner with the PI to put all pieces together to get a complete picture and to conduct the trial according to the protocol," Adams says. "The thing that clinicians like about that is that they can count on HOPE to provide them with qualified personnel."

• **CT site expects investigators to meet their obligations:** When physicians discuss building a relationship with HOPE Research Institute, Adams discusses their own responsibilities in making certain they'll meet study enrollment deadlines.

"We have straight talk about the requirements for working for HOPE," Adams says. "I've had investigators who have not been able to enroll or fulfill responsibilities seriously, so I'll then end our relationship with them."

Sometimes it's apparent early on that an investigator is not going to be a good partner, she notes.

"If you bring someone on who doesn't book time for coordinators or to attend investigator meetings, then I can see it's not going to work out," Adams says. "Those who have worked with us have consistently met their enrollment needs."

Occasionally, even the most seasoned PI will take on a study in good faith and then discover that the enrollment is not going to work as well as anticipated, Adams notes.

But for the best investigators, this is a rare experience, she adds.

Another expectation the CT site has is that investigators will become trained in clinical research.

"Just because you're a great a clinician doesn't make you a good investigator," Adams says. "For the investigator, it takes time and training to be a good clinical researcher."

• **Study acquisition team reviews proposed protocols:** "First, we ask investigators what they're interested in doing," Adams says. "We let investigators know that just because you're interested in this doesn't mean that there are studies of it right now."

But there might be other studies that will interest a particular investigator, so the CT site pairs investigators with the studies that are available.

"We take a look at the industry and see if we can find a match," Adams says.

"We gather feasibility information and contact the sponsor," she adds. "Then we review the protocol requirements."

For every five clinical trials the site reviews, about one is selected, Adams says.

• **CT site helps PI prepare for trial:** "After we obtain the sponsor's commitment, we have a pre-study visit, get the facility ready to do the trial, and make sure the PI has the appropriate storage facility for study drugs, including temperature logs," Adams says.

"We help them get their facility ready to conduct clinical research," Adams adds. "We make sure the PI has knowledge about the protocol and processes and clinical practice and is meeting the FDA's requirement for compliance."

The CT site makes certain PIs are trained on policy and procedures and have study coordinators with whom they are comfortable.

"The contract negotiation process will go on at the same time in a different department," Adams says. "We have the contract negotiation and budgeting work going on at the same time."

This way the time-consuming study paperwork process is underway before all of the approvals are in place, she adds.

• **Study enrollment begins:** "Once we have a strategy, and all approvals are in place, we'll start enrolling in the clinical trial," Adams says. "This may involve a chart review, getting involved actively, having a coordinator in our office talking with patients, and sometimes the coordinator will partner with the clinical office and scheduler to identify potential subjects for the study."

If there's a need for advertising, the CT site has staff handle the ad calls, and full-time recruitment coordinators write the ads and place them with the media, Adams says.

"It's really a team effort to make the CT successful," she says. "The trick in enrolling in CTs is to have an active investigator." Investigators who delegate all active recruitment to coordinators will not be as successful, she notes.

"Sometimes new investigators don't understanding how challenging that will be, and no matter how much you explain it, they'll say, 'This is a lot harder than I thought,' and it doesn't work for them," Adams says. "But those who work in CTs a lot are very successful in recruiting."

• **Site director works with investigators and CT staff:** "We have an executive site director who works with the investigator and coordinator, and

he and the financial director track screening efforts and enrollment efforts weekly," Adams explains. "We keep our finger on the pulse as we go along."

If a coordinator appears to be not making much of an effort or time investment, then the CT site's staff will meet with the coordinator to try to rekindle the coordinator's interest or to troubleshoot problems the coordinator is facing, Adams says.

"We do this in real time because if we let weeks and weeks go by, you'll miss the boat," Adams says. "So it's checked every week through processes that see what kind of activity went on in the screening and recruitment."

The CT site also makes sure study participants are fully protected and that they are compliant with study requirements.

"We have policy and procedures that are in place about how to care for those individuals," Adams says. "We make sure our investigators and coordinators understand the requirements and ensure subjects' safety." ■

# More harm than good? Fed database stirs controversy

*Critics: Database opens CTs to second-guessing*

The clinical research industry is bracing itself for the next phase of the federal government's ClinicalTrials.gov research database and the addition of CT results.

The Department of Health and Human Services (HHS) is expected to release proposed rules about how sponsors and research sites should comply with the requirement, which was part of the Title VIII of the Food and Drug Administration Amendments Act of 2007 (FDAAA, Public Law 110-85, section 801), to provide greater transparency in clinical research.

Originally, the Food and Drug Modernization Act (FDAMA) passed in November, 1997, mandating that the National Institutes of Health establish and operate a public resource for information about clinical trials. NIH established a data bank located on-line at ClinicalTrials.gov, in 2000. The data bank reached its 1,000th CT listing in 2003 and has continued to grow to more than 60,000 trials listed.

The FDAAA requires CT sites and sponsors to submit data after a trial is completed to provide summary results statistics for drugs, medical devices, and biological products that have been approved by the FDA.

The results database will build on the existing ClinicalTrials.gov listings, allowing sponsors and principal investigators to submit basic results summary data for public view.

Soon there should be federal rules for how the CT industry can expand its listings in the data bank to include results. And this is what worries some in the industry.

"Both as a lawyer and a consultant in the world of clinical research, I've been asked by many clients how they can comply with these requirements," says **Mark Barnes**, JD, managing director of Huron Consulting Group, which is headquartered in Chicago, IL, and also located in Boston, MA, and New York, NY, as well as other cities.

"People wonder what the ultimate ramifications and consequences would be for these requirements," Barnes says.

So far there is no results database, but some preliminary information about it is expected in 2009 or 2010.

The 2007 legislation requires the registry of clinical trials to include both results and the occurrence of adverse events, Barnes says.

"This is something that has never been done by the government before, although there are pharmaceutical companies that have begun to put results of trials they sponsor on their own Web sites," he says.

### *Transparency goal clouded*

Congress' theory for this legislation is that it will create a lot of transparency in research, Barnes notes.

"But the problem is that there are a lot of badly-designed trials out there, and a reader who looks at the results data will not know which is the well-designed trial and will be published in a peer-reviewed journal and which is not," Barnes explains. "The bottom line is that less is often more."

The legislation requires all results to be listed regardless of whether the results ever are published, and this creates a number of problems, Barnes adds.

"Whenever there's a bad outcome in an approved medication or medical device the media are going to go to the results database to look to see if there were ever any bad results from clinical tri-

als, and, of course, there were bad results," Barnes says. "There always are bad results."

So the results database will be used to second-guess CR decisions, and it will be used against the industry by the media and plaintiff's malpractice lawyers, he adds.

"The ultimate result might be an even greater timidity for drug companies and device companies and biotech companies to test innovative products and take them to market, Barnes says.

"This is widely thought to be a potential consequence of this legislation," Barnes says.

Even worse, there might be a chilling affect on academic research as well, he says.

"Trials might be designed in the first place to minimize negative results and to maximize positive results," Barnes explains. "Think about it: if you are a drug company are you going to want to do risky trials?"

This is why the mandate for more information could lead to even less information, he says.

"There are multiple secondary and tertiary consequences to mandating secondary actors using NIH funds or institutional resources to listing CT results," Barnes adds.

"What has happened here is Congress in a stampede toward disclosure as a panacea for all these ills has taken a meat ax when a scalpel will do," he says. "If the FDA is being denied essential information it needs in deciding approval of these drugs, then we can get to that information without mandating disclosure on public Web sites."

In fact, the FDA already has the right to look at unpublished CT data, he notes.

"What has deterred the FDA is the lack of staff to investigate and run down all the information they need to find," Barnes says.

"We're all waiting for the proposed rules to come out, and that's when the fight will begin," Barnes says. "They won't be proposed until the new administration comes in, and there are lots of variables between now and then." ■

# Advice to improve informed consent

*Three different approaches outlined*

There are a number of ways clinical trial (CT) sites and investigators could improve the informed consent process, and CT experts offer a variety of suggestions for how to make this happen.

Here are some of their ideas:

- Make certain potential participants do not harbor therapeutic misconception;
- Check consent forms for the eight basic elements included in the federal mandate of 45CFR46.116;
- Use the consent form as a tool to assist with a lengthy informed consent discussion.

"The whole notion of informed consent is so important, yet so difficult to figure out," says **Robyn Shapiro**, JD, a partner who specializes in health law at Drinker Biddle & Reath in Milwaukee, WI.

Principal investigators and CT staff struggle with how to meet all of the informed consent requirements and how to provide IC effectively, Shapiro notes.

"Part of the challenge has to do with the complexity of the research, and part of it has to do with the difficulty of counteracting the therapeutic misconception," Shapiro explains. "Therapeutic misconception is most prevalent in cases where you have desperately-ill patients who are thinking about very early phase trials when not a lot of other options are available, and the procedure is complex."

To some extent, therapeutic misconception is always an issue because a patient might benefit, but then, again, might not because this is research and not clinical treatment, she adds.

With a little discipline and extra time, CT sites can make certain all informed consent documents include the eight federally-mandated basic requirements.

It's a good strategy to create a template or checklist listing those eight requirements, says **Judi Kuhl**, CIP, BS, quality improvement coordinator in the office of research integrity at the University of Kentucky in Lexington, KY.

### *True to the code*

According to the Code of Federal Regulations (45CFR46.116), the eight mandatory elements of informed consent are listed verbatim below:

1. A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental;
2. A description of any reasonably foreseeable

risks or discomforts to the subject;

3. A description of any benefits to the subject or to others which may reasonably be expected from the research;

4. A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;

5. A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained;

6. For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained;

7. An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject; and

8. A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

One challenge for some investigators is including these eight elements in less formal informed consent documents, such as letters that are mailed out with surveys when the waiver of documentation of informed consent has been approved by an IRB, Kuhl says.

"A survey cover letter is a little different than an informed consent form for diabetes research," Kuhl notes. "The most effective cover letters are the ones that are like a conversation between a person and less technical."

So it's difficult to include the eight mandatory elements while writing the letter in this conversational tone, she adds.

This is why the University of Kentucky is working on a template for a cover letter that could be used with research and in the event of a waiver of documentation, Kuhl says.

Sometimes it's difficult for investigators and CT staff to view the informed consent document as a tool to facilitate the informed consent process and not as an end to the discussion.

"The consent form is really nothing more than a tool, and it's used in the context of what is supposed to be a discussion between an investigator and the subject," says **Stewart A. Laidlaw**, PhD, an associate vice president for compliance at the Los Angeles Biomedical Research Institute at the Harbor-UCLA Medical Center (LA BioMed) in Torrance, CA. **(See story on IC strategies, below.)**

"The investigator should explain what's involved in the study and do it at a much lower level than what's in the consent form language," Laidlaw says. "Conscientious investigators will spend considerable time with each individual subject, attempting to communicate what's involved in the study." ■

# Simplify IC form is first idea — here are other strategies to follow

*Don't use exculpatory language*

If you believe the informed consent process truly is a process and not just a multi-page document to get someone to sign, then it's important to develop strategies for improving both the process and the IC form.

"The consenting process itself is a dialogue between the investigator and the potential subjects," says **Stewart A. Laidlaw**, PhD, an associate vice president for compliance at the Los Angeles Biomedical Research Institute at the Harbor-UCLA Medical Center (LA BioMed) in Torrance, CA.

"So the investigator explains what's involved in the study and explains about risks and potential benefits, and the potential subject asks questions to clarify issues that he or she is not clear on," Laidlaw says. "This theoretically goes on until it reaches a point where the potential subject decides he or she will take part in the study or will not take part in the study."

This process is complemented by the informed consent document, which ideally is simple, highly readable, and provides clarity to the points the CT coordinator or principal investigator is making about the study.

There are at least two points of view on how an ideal consent form should be written.

"There's always a dynamic tension between those who wish to simplify it and make it understandable versus those who wish to make it complete," Laidlaw notes.

If the form is simplified and readable, then it could serve its purpose.

On the other hand, sometimes it's a good idea

to add short explanations of background clinical trial information in the consent form, says **Robyn Shapiro**, JD, a partner who specializes in health law at Drinker Biddle & Reath in Milwaukee, WI.

"I've been thinking about this, and I know it goes against the comments that are popular and valid lately that these consent forms are just too long," Shapiro says. "Nonetheless, I think it would be a good idea to do a short explanation of the various trials in clinical research so that you can help people understand."

For example, an IC form could include this boilerplate information, Shapiro suggests:

- Phase I studies are small studies of an experimental intervention, usually the first time the intervention is used in humans, with the primary purpose to test for safety, harms, and discomforts and how these change at different doses;
- Phase II studies are mid-size studies designed to begin a more complete evaluation of the effectiveness of the intervention-at a dose level thought to be safe, based on earlier studies-and also to continue to test for harms, discomforts, and side effects;
- Phase III studies are large studies to gather data to prove or disprove safety and effectiveness, and reconfirm optimal doses and routes of administration.

LA BioMed uses an informed consent format that has a standard section, Laidlaw says.

"There is standard language in any consent form that relates to what an IRB will look for in an informed consent document," Laidlaw says. "This includes what will happen in the event of an emergency, contact numbers, and the fact that the participation is voluntary."

When plaintiffs suing CT investigators and sponsors prevail, it's sometimes related to informed consent claims, Shapiro notes.

For instance, in 1990 there was a case decided by the California Supreme Court regarding a leukemia patient named John Moore. His spleen cells were used to develop and patent an anti-cancer drug, but Moore claimed that he never gave permission for his cells to be used in medical research.[1]

The California Supreme Court ruled that a patient does not have property rights over body tissues used to develop new treatments, but that Moore had not received adequate informed consent, Shapiro says.

"He lost on the property claim, but won on the informed consent claim," she adds.

The case applied only to California law, but has had wider implications for research scientists.

After this lawsuit, CT investigators wanted IC documents to say that participants were giving up their blood and tissue samples and relinquishing all legal rights and interests to the items, Shapiro says.

"But that's the kind of exculpatory language you can't use," she says. "No informed consent written or oral can include exculpatory language if your institution is subject to the Common Rule."

This means that subjects cannot waive their legal rights or release the investigator or institution or sponsor from liability or negligence under federal regulations, Shapiro explains.

"So that precludes a lot of language that lawyers otherwise would like to put in informed consent forms," she adds.

Instead, California institutions and others might say: "The tissue we get from you in this research may be used to develop a product that could be patented and licensed. There are no plans to provide any financial compensation to you if this happens," Shapiro says.

"So far this wording has stood up because it leaves a loophole," Shapiro adds. "You're just saying, 'We're not planning at this moment' with the subtext of 'We won't pay compensate you for the tissue unless we have to in a court of law.'"

From an ethical perspective, it's important for investigators and CT staff to remember that research participants are volunteers who are putting their lives on the line for the research, Laidlaw says.

"The study is being done to answer a question of whether this treatment is effective or not or more effective than another treatment," he says. "So it's important to treat subjects with an enormous amount of respect because they are the actual heroes of the medical research enterprise."

### Reference

1. Blakeslee S. Patient's right to tissue is limited. New York Times. July 10, 1990;1. ■

# Boost recruitment efforts by building up referrals

*Be ready with updates and thank you's*

For clinical trial enrollment success sites need to have solid, long-term relationships with

clinicians who refer patients to studies.

"You need to know doctors on a colloquial level," says **Pamela Normandin**, RN, MSN, CCRC, clinical nurse specialist in the office of research at Iowa Lutheran Hospital in Des Moines, IA.

"What you do is mentor those relationships," Normandin suggests.

Iowa Lutheran Hospital was the top enroller for a study about a tumor necrosis factor (TNF) antibody drug to treat sepsis, and the sponsor attributed the hospital's success to the personal relationships Normandin and other clinical trial (CT) staff developed with emergency room clinicians, she says.

"We were able to tap into every sepsis patient who came in the door," Normandin says. "We enrolled 126 patients over a couple of years."

Here's how the CT site meets enrollment goals:

**1. Build trust with referral sources.**

Normandin met with nurses and physicians in the emergency room, attended their unit meetings, and discussed the study's goals of improving medical care for sepsis patients.

As the study began enrolling, Normandin would update emergency department staff about the study's progress and how many patients were enrolled.

"One time at a meeting I showed them a bar graph of enrollment and said, 'I was aiming for 26 patients, and you've already given me 18,'" she recalls.

"I would make cookies and bring them to the nurses and put them in the break room," Normandin says. "I'd thank them for their help and say, 'I saw how busy you are this weekend, and I know I added to your workload, so I appreciate all you've done.'"

Another way CT staff could thank referral sources is by finding something they like and having a drawing with the item as a prize, Normandin suggests.

"One time an investigator put all of the nurses' names in a hat and gave the winning nurse a critical care textbook that was worth $100," she says. "Then he bought a few textbooks for the intensive care unit and critical care units."

When a referral source is particularly helpful it's important to acknowledge this.

"I had one nurse who went above and beyond, and I wrote her a personal thank-you note," Normandin says.

These small actions make a huge difference to overworked health care professionals, she notes.

"Some [CT staff] will go to the unit and add to their workload, but they don't understand from the nurse's perspective how hard and laborious it can be to have to gather more data and to do more things because of a research project."

**2. Educate referral sources about the study.**

Normandin attended residency meetings to discuss the study with physicians representing various disciplines.

"I'd go to their meetings and tell them about research we're doing and the inclusion/exclusion criteria," she says. "Then I'd go through the protocol and tell them that if they thought they had a patient who could be in our study, then they should make sure it was okay with the attending physician to refer the patient."

When studies have inclusion/exclusion cards, these can be handed out to residents and other physicians to carry in their lab coat pockets, she adds.

Normandin also spoke with emergency department staff before the sepsis study began enrolling to make certain they understood the study.

She made sure they knew that the study provided an investigational treatment to patients, but this was an enhancement over the treatment they already were receiving, Normandin says.

"With sepsis patients, we'd give them the same antibiotics and treatment, but we'd add the study treatment," she explains.

Then she kept an eye out for sepsis patients as they came through the ED doors and would meet with ED staff immediately, she says.

"With sepsis, you have such a short time frame," Normandin notes. "I worked with this intensivist who also was a pulmonary specialist, so when someone was diagnosed with sepsis, the patient was referred to him, and we'd be right there."

Normandin also met with medical helicopter crews.

"We're a pretty rural state, and this is a high referral hospital, so with our trauma center we have a helicopter that's sometimes sent to pick up sepsis patients from smaller hospitals that could not manage their care," Normandin explains. "So I'd talk with the helicopter crew about sepsis inclusion criteria so they could alert the physician and say, 'Were you aware of this trial?'"

Then the referring physician would contact Normandin to request that the patient be screened for the study.

For studies where it wasn't as critical to enroll

patients immediately upon ED arrival, the CT staff would wait for an ED physician to call with the referral, she adds.

"But, again, in very short time frames, I'd go down to the emergency room and do the initial screening by speaking with the patient or family," Normandin says.

**3. Prepare for all informed consent possibilities.**

If CT staff found sepsis patients before they lost consciousness, they could provide their own informed consent, she says.

With others, Normandin would meet with the family to discuss the study.

The CT site followed state laws regarding informed consent and family members, and this issue was discussed at lengths by the hospital's ethics group, Normandin says.

She would explain to the family how the investigational treatment would be in addition to the standard treatment and how the research could help stop the escalation of the disease. ■

## CR and FDA News

# Four new NIH centers in alternative medicine

Four new Centers of Excellence for Research on Complementary and Alternative Medicine (CERCs) have been added by the National Institutes of Health's National Center for Complementary and Alternative Medicine (NCCAM).

The new centers are as follows:

• **Wisconsin Center for the Neuroscience and Psychophysiology of Meditation**: Located at the University of Wisconsin in Madison, WI, the center's research team, headed by **Richard J. Davidson**, PhD, will examine the impact on the brain and body of two forms of meditation: loving-kindness/compassion meditation and mindfulness meditation. Potential health applications include biological and behavioral processes linked with emotions and stress, including recurrent depression.

• **Metabolic and Immunologic Effects of Medicine:** Located at the University of California, San Francisco, the site will study a program combining mindfulness meditation, mindful eating, and a diet and exercise program for use in obesity and metabolic syndrome. **Frederick M. Hecht**, MD, will lead the research team as it tests whether this program helps alter participants' hormonal responses to stress and helps enhance and maintain weight loss.

• **CAM as Countermeasures Against Infectious and Inflammatory Disease**: Principal investigator **Mark A. Jutila**, PhD, at Montana State University in Bozeman, MT, will head a project that focuses on the effects of botanical extracts from apple polyphenols, which are located in apple skins, and from yamoa, which comes from the bark of an African gum tree, on white blood cells. The project will use models of infection and inflammation of the intestinal mucosa.

A second project will examine two models of influenza and stomach virus, and a third project will focus on bacterial products to see how they treat autoimmune diseases, such as arthritis.

• **Center for Herbal Research on Colorectal Cancer:** At the University of Chicago in Illinois, principal investigator **Chun-Su Yuan**, MD, PhD, and colleagues will examine the anti-tumor effects of different preparations of the herbs American gingseng and notoginseng. Their goal is to learn more through laboratory and animal studies of how these herbs act upon cellular and molecular pathways of the mechanisms of cancer inhibition.

The NCCAM grants are for five years, and there now are 11 CERCs. For more information, visit the Web site: nccam.nih.gov/training/centers/, or call 888-644-6226. ■

# ACRP comments on FDA draft guidance

The Association of Clinical Research Professionals (ACRP) of Alexandria, VA, wrote to the Food and Drug Administration (FDA) on Sept. 26, 2008, to address questions about the FDA's draft guidance on FAQ - Statement of Investigator (Form FDA 1572).

Thomas L. Adams, CAE, president and chief executive officer of ACRP questioned the wording in four items, including the following:

• **Item #5: What are the minimum qualifica-**

**tions of an investigator?**

According to Adams' letter, ACRP believes mentioning a concreted example of achievement, such as a physician investigator certification, would provide an example of the "general recognition that this would include familiarity with human subject protection requirements…"

**• Item #17: How should an investigator's name appear on the 1572?**

"The guidance mentions the use of the legal name on Block #1. Some believe that the name must match exactly how their name appears on their medical license (i.e., "James A. Smith, M.D." versus "James Smith, M.D."). Is this the case?" Adams writes.

**• Item #30: Who should be listed as a subinvestigator in Block #6?**

Adams' letter recommends deleting the sentence in lines 321-323, which reads, "In general, if an individual is directly involved in the treatment or evaluation of research subjects, that person should be listed on the 1572." Adams makes this recommendation because the sentence seems to be inconsistent with the clarity of "direct and significant contribution to the data" as it implies that many people, including hospital nurses who pass the study drug or a radiology technician, would need to be on the 1572 as they are involved in the treatment of the individual, the letter states.

**• Item #31: Should research nurses, other nurses, residents, fellows, office staff, or other hospital staff be listed in Block #6?**

Adams' letter asks the FDA for an example of what kind of statement should be made with regard to lines 337-338, which state that if there are staff residents on rotation, a general statement can be made regarding their planned participation.

"Additionally, many settings such as psychiatric hospitals or specialty clinics, contract with physician groups to perform physical exams and care which may be used as data for the study," Adams writes. "Under these arrangements, it is not easily predictable as to which physician in the group will show up that day to perform the care." ■

# FDA opening offices in Asia, Europe, Latin America

The U.S. Department of Health and Human Services announced in October that it will send Food and Drug Administration (FDA) staff to China, India, Europe, and Latin America before the end of 2008.

HHS Secretary Mike Leavitt says the goal is to better safeguard the nation's food and medicine supply.

The department already has begun implementing product safety agreements with China and other key trading partners, and there have been upgrades to labs and equipment, as well as additional staff hired. ■

## CE/CME Objectives / Instructions

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

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

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

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

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

## *COMING IN FUTURE MONTHS*

- ■ OHRP issues revised human subjects research guidance
- ■ Try these strategies for improving subject recruitment
- ■ Know your obligations under federal wide assurance
- ■ Start a mentoring program for PIs
- ■ Avoid common mistakes and educate through short videos

# CE/CME *questions*

21. A new clinical research model requires investigators to fulfill certain responsibilities. Which of the following is the chief responsibility of a principal investigator, according to this model?
    A. To hire CT staff and write policies and procedures
    B. To ensure compliance with federal and state regulations
    C. To meet enrollment goals
    D. All of the above

22. Which of the following is a good example of language to include in informed consent forms with the goal of improving subjects' understanding of clinical research?
    A. Phase I studies are small studies of an experimental intervention, usually the first time the intervention is used in humans, with the primary purpose to test for safety.
    B. Phase II studies are mid-size studies designed to begin a more complete evaluation of the effectiveness of the intervention-at a dose level thought to be safe.
    C. Phase III studies are large studies to gather data to prove or disprove safety and effectiveness, and reconfirm optimal doses and routes of administration.
    D. All of the above

23. Critics of the FDA Amendments Act of 2007 say they fear it will result in some unintended consequences, including:
    A. The general public and media will see results of both badly-designed and well-designed trials, and they will not be able to distinguish between the results.
    B. The media will check the results database to look for bad results and will second-guess scientists and the FDA.
    C. Both A and B
    D. None of the above

24. A good strategy for improving a CT site's relationship with potential referral sources is to offer personal financial rewards to physicians who make referrals to a study.
    A. True
    B. False

**Answers: 21. C; 22. D; 23. C; 24. B.**

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*An essential resource for managers of clinical trials*


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