CLINICAL TRIALS ADMINISTRATOR

An essential resource for managers of clinical trials

THOMSON
AMERICAN HEALTH CONSULTANTS

IN THIS ISSUE

Financial Disclosure:
Editor Melinda Young, Editorial Group Head Lee Landenberger, Managing Editor Alison Allen, and Nurse Planner Elizabeth Hill, DNSc, report no consultant, stockholder, speaker's bureaus, research or other financial relationships with companies having ties to this field of study. Physician Reviewer Stephen Kopecky, MD, is a consultant to GlaxoSmith-Kline and has a research affiliation with Bristol-Myers Squibb.

NOVEMBER 2005
VOL. 3, NO. 11 • (pages 121-132)

Special Report: SoCRA Conference Coverage

One size does not fit all when it comes to the consent process

[Editor's note: In this issue of Clinical Trials Administrator, *there is coverage of some of the important issues discussed at the 14th annual Society of Clinical Research Associates (SoCRA) Conference, held Sept. 23-25, in Lake Buena Vista, FL. The cover story in this issue and a follow-up story in the December issue look at how research sites can work toward obtaining fully informed consent. Also, inside is a story on best practices in managing clinical trial sub-sites.]*

Develop multiple strategies for minorities and the elderly

Clinical trial sites continue to struggle with finding the best strategies for executing an informed consent process, although there are many good ideas employed at research institutions across North America.

Several speakers at the 14th annual Society of Clinical Research Associate Conference (SoCRA), Sept. 23-25, in Lake Buena Vista, FL, discussed best practices in consenting minorities, older adults, and in monitoring the informed consent process.

With clinical trials and research making headlines lately, there is a heightened awareness of ethical considerations in clinical trials, but informed consent has long been a very important part of research, says **John Wright**, BS, CCRC, IRB administrator at the Baylor College of Medicine in Houston. Wright spoke about working toward fully-informed consent at the SoCRA conference.

Sometimes an important strategy in providing informed consent is to acknowledge past research problems, particularly if these are on people's minds from news articles reporting deaths among research subjects, suggests **Lyndon V. Evans**, CCRP, RN, research manager with CancerCenters of the Carolinas in Greenville, SC. Evans spoke at the SoCRA conference about going beyond the document in informed consent.

Also, new research presented at SoCRA highlights how important it is for researchers working with older adults to spend more time with

NOW AVAILABLE ON-LINE! www.ahcpub.com/online.html
For more information, call toll-free (800) 688-2421.

Clinical Trials Administrator (ISSN# 1544-8460) is published monthly by Thomson American Health Consultants, 3525 Piedmont Road, Building Six, Suite 400, Atlanta, GA 30305. Telephone: (404) 262-7436. Application to mail at periodicals postage rates is pending at Atlanta, GA 30304. POSTMASTER: Send address changes to **Clinical Trials Administrator**, P.O. Box 740059, Atlanta, GA 30374.

Thomson American Health Consultants is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

Thomson American Health Consultants designates this educational activity for a maximum of 18 credit hours in category 1 credits toward the AMA Physician's Recognition Award. Each physician should claim only those hours of credit that he/she actually spent in the educational activity.

Thomson American Health Consultants is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center's Commission on Accreditation. Provider approved by the California Board of Registered Nursing, provider number CEP 10864. This activity is approved for 18 nursing contact hours.

Opinions expressed are not necessarily those of this publication. Mention of products or services does not constitute endorsement. Clinical, legal, tax, and other comments are offered for general guidance only; professional counsel should be sought for specific situations.

Subscriber Information

Customer Service: (800) 688-2421 or fax (800) 284-3291, (ahc.customer service@thomson.com). Hours of operation: 8:30 a.m. -6 p.m. Monday-Thursday; 8:30 a.m.- 4:30 p.m. Friday.

Subscription rates: U.S.A., one year (12 issues), $299. Outside U.S., add $30 per year, total prepaid in U.S. funds. Discounts are available for multiple subscriptions. For pricing information, call Steve Vance at (404) 262-5511. **Back issues**, when available, are $50 each. (GST registration number R128870672.)
Photocopying: No part of this newsletter may be reproduced in any form or incorporated into any information retrieval system without the written permission of the copyright owner. For reprint permission, please contact Thomson American Health Consultants. Address: P.O. Box 740056, Atlanta, GA 30374. Telephone: (800) 688-2421. World Wide Web: www.ahcpub.com.

This publication does not receive financial support.

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: **Alison Allen**, (404) 262-5431, (alison.allen@thomson.com).

Copyright © 2005 by Thomson American Health Consultants. **Clinical Trials Administrator** is a registered trademark of Thomson American Health Consultants. The trademark **Clinical Trials Administrator** is used herein under license. All rights reserved.

THOMSON
AMERICAN HEALTH CONSULTANTS

Editorial Questions

Questions or comments?
Call **Alison Allen** at (404) 262-5431.

subjects than usual during the informed consent process, says **Lorraine Frazier**, DSN, RN, NP, an associate professor in the School of Nursing at the University of Texas in Houston. Frazier spoke about informed consent and understanding of genetics among older adults and at the SoCRA conference.

Frazier and **Menayra Caro**, BS, CCRP, IRB/regulatory specialist at the Lakeland Regional Cancer Center in Lakeland, FL, offer these ideas for improving informed consent when working with minority or older populations:

• Improve the consent process for minority populations.

For those who believe translating an informed consent document into a foreign language is as simple as hiring a contracting translation service, Caro would like to burst their bubble.

"Most translators are not aware of the federal [research] guidelines, and even though the English version strictly follows those guidelines, when it's translated into Spanish, they may disregard the guidelines," Caro says.

Caro, who is Puerto Rican, once reviewed an informed consent document that had been translated from English into Spanish, and she saw a very strange difference: In the English version, a description said the subject would be injected in a thigh, while the Spanish version said the subject would be injected in a muscle.

"When the translator was requested to correct it, she said the thigh was the muscle, but the problem is that not every muscle is a thigh," Caro recalls.

Another problem has to do with selecting a reading comprehension level for minority patients, Caro says.

"A lot of people are not aware that the reading levels for the Spanish-speaking community is third grade," Caro says.

This means a consent form would need far simpler language than what commonly is used and even simpler than federal regulations, which request a fifth-grade reading level, Caro notes.

Some consent forms continue to be written and translated into language that's so technical that even trained research professionals like Caro can't understand them, she says.

Another problem that crops up with clinical trial sites work minority subjects is finding good verbal translators, Caro says.

The most common practices for translating for the Spanish community are to have a patient's relative act as an interpreter or using a bilingual

physician or other health care professional as a translator, Caro says.

Using a family member might be the very worst translation method because the research site is putting the family member in the role of acting in the subject's best interest, when there might be other personal motivations that get in the way of the person fulfilling that obligation, she says.

"Are there any financial interests? And how will the person effectively describe procedures to the patient?" Caro asks.

Having a bilingual physician translate also poses problems because some patients might feel intimidated or coerced by a physician who is describing the clinical trial, Caro says.

"So the most feasible practice is to have a bilingual health care professional, who is not related to the patient and not connected to the physician investigator, but who works at the site with patients, be the translator," Caro suggests.

At the very least, clinical trial sites should make an effort to hire bilingual staff whose language skills correspond with sites' minority populations, Caro says.

"Having this staff promotes and establishes trust," Caro adds. "So that's the biggest and best thing sites need to do if they want to enroll minorities, recruit them, and retain them."

• Keep informed consent simple when working with older adults.

Clinical trial coordinators and investigators need to pay particular attention to informed consent language when working with adults over age 65, particularly when a clinical trial involves genetics, Frazier says.

With a $10,000 grant from PARTNERS, a University of Texas sponsor that funds nursing research, researchers conducted a focus group study to find out how well older adults understood research terms and informed consent, Frazier explains.

There were 23 subjects with a mean age of 78, and they were divided fairly evenly between Caucasians who lived in an assisted living facility, African Americans who received meals and education at a community support center, and Hispanics who visited a medical clinic, Frazier says.

"For the long term we wanted to develop a culturally sensitive approach and design materials to work with those populations when we asked for consent to genetic research," Frazier says.

Five themes came out of the focus group sessions, and they were as follows:

— Older adults defined genetics as something passed down from one generation to another, as well as something that can skip a generation and which is affected by the environment.

"For example, African Americans suggested it was a family curse; the Hispanic group thought it was an illness caused by someone who didn't like you, perhaps like witchcraft," Frazier says. "And Caucasians saw it as a family weakness."

— The older adults would justify genetic testing only if they trusted the research and the institution, Frazier says.

Despite their views, participants routinely said they would have genetic testing if their doctor recommended it, and it didn't matter what else they learned about it, Frazier says.

"For research, they said they would participate if they trusted the researcher and the institution," she adds.

— Older adults also had concerns about disclosing clinical trial information to their families.

"They didn't want to worry about diseases they didn't know they had, and they had some suspicions of the medical community," Frazier says. "And some were worried about family issues, including insurance, jobs, and prospective marriage partners for grandchildren and whether genetic information would affect that."

While some participants said they wanted their families to know what was going on, many said they would tell only their children and leave it to their children to tell the grandchildren, Frazier notes.

— Another concern expressed by older adults was that the informed consent process be communicated on an individual basis. The participants expressed an interest in hearing stories and seeing pictures to illustrate what was being told, Frazier says.

"Principal investigators need to be aware that this population is very vulnerable, particularly in an acute care setting, and they need to take more time with them," Frazier says. "Use less or no medical jargon, and they like the use of stories to explain things."

For example, a story might tell of a lady who had this type of disease with this genetic variation, and she went on to do fine, while another person with similar disease didn't do as well, Frazier says.

— A common phrase that came up with older adults was "acting my age," Frazier says.

"They used that term a lot," Frazier says. "'At my age,' they'd say, they'd want to give back to society, and developmentally, this was appropriate for their age."

Their motivations for considering participating in research were altruistic, and this also makes them vulnerable, Frazier notes.

"They were not interested in genetic tests for clinical testing only, but were interested in something that could help future generations," Frazier says. "It's a good reason for participating, but we need to be sure they understand the risks and benefits to them and to their family members."

One other finding of the focus group study is that the older people were concerned that their blood samples might be used for something they didn't want them to be used for or that they would be subjected to bad needles, Frazier says.

"I never would have thought about that as a concern," she notes.

"They also didn't want information asked of them that was too personal, and they were concerned about the lack of transportation and parking costs," Frazier adds.

What these findings suggest is that clinical trial coordinators and investigators need to keep the informed consent process simple, allowing plenty of time for older subjects to ask questions, Frazier says.

"I think that older people tend to trust more and tend to like people in authority to be more directional, and they tend to trust other people to make decisions for them more than younger populations," Frazier says. ■

Special Report: SoCRA Conference Coverage

Sub-sites help to meet recruitment challenges

Check out these accountability challenges

For many larger research institutions it is more efficient to contract with other research sites to be sub-sites in a particular study than it is to try to enroll subjects entirely at the main location.

The recent trend of declining clinical trial enrollment because of the negative publicity about drugs being pulled from the market after serious illnesses and deaths occurred has made it even more challenging for a single site to meet its recruitment goals alone, says **Sylvia Dickinson**, RN, MSN, CCRP, research clinical specialist at Vanderbilt-Ingram Cancer Center in Nashville. Dickinson spoke about coordinating clinical trial sub-sites at the 14th annual Society of Clinical Research Associate Conference (SoCRA), Sept. 23-25, in Lake Buena Vista, FL.

"Also, requirements for consenting patients are getting tougher, and you have HIPAA [Health Insurance Portability & Accountability Act], and it all makes it harder to accrue even one patient at one center," Dickinson says.

One solution is for the site that originates the trial to become a coordinating center, contracting with sub-sites. When this happens a trial involving a rare population might finish enrolling patients in a year or two, instead of five years or more, saving money in the process, Dickinson says.

"One of the main reasons for doing sub-sites at any level is to get your numbers of accrual and to get them as fast as possible, so you'll have lower expenses, faster data, faster results, and quicker approval for drugs," Dickinson says.

The advantage to sub-sites is they might have something additional to offer patients who have exhausted existing treatment options, and they won't have to refer them to a facility out-of-state for the research trial, Dickinson adds.

Dickinson, who is part of a regulatory staff of five, manages 24 sub-sites for various studies at Vanderbilt-Ingram Cancer Center, and the center probably has more than 40 sub-sites total, she says.

Also, a for-profit organization connected with the center has a couple hundred of trial sub-sites, Dickinson adds.

For years, the large consortiums, including the Eastern Cooperative Oncology Group, the Radiation Oncology Treatment Group, and others have looked at all phases of cancer and worked with smaller institutions that lacked the resources to conduct the more complicated studies on their own, Dickinson explains.

"What's been falling through the cracks is how does an investigator who has a cutting edge idea for a research study get it off the ground?" Dickinson says. "Not many study sites have the expertise or equipment required to do these higher-tech studies."

Investigators at Vanderbilt-Ingram Cancer Center commonly come up with new ideas for cancer drugs and treatment and are required to file new IND applications or cross-reference INDs with the FDA, Dickinson notes.

As such, the cancer center becomes the coordinating site when principal investigators contract

with researchers at other institutions to enroll subjects in their clinical trials, she says.

While most clinical trial administrators are familiar with regulatory requirements for being a clinical trial site, they may not be as comfortable with what's required as a clinical trial coordinating center, so Dickinson offers these strategies for improving the coordination of clinical trial sub-sites:

• **Simplify requirements for sub-sites.** A coordinating center may follow good clinical practice (GCP) guidelines unfailingly, but it would be very time-consuming for the center to monitor and ensure that all sub-sites follow every detail in GCP guidelines, Dickinson says.

So it's important to focus on ensuring sub-sites follow all federal regulations, she says.

"Everyone who is doing clinical trials has to adhere to FDA rules, but the guidelines, the good clinical practice guidelines, are guidelines, so I'm not going to nitpick over the guidelines," Dickinson says.

"We get a lot of sponsors coming in and monitoring us, and they all have their own standard operating procedures [SOPs] on how they want to have things done," Dickinson adds. "It gets to be very time consuming, and the federal regulations do not go into the detail that pharmaceutical companies and clinical research organizations [CROs] would like to require."

Dickinson says she keeps that experience in mind when dealing with sub-sites, who might view detailed monitoring as a harassment.

"I try to keep an open and friendly communication with sub-sites because I know down the road that the study might be audited, and I may need to ask them to send me stuff STAT," Dickinson explains. "And they need to know that when they get a fax from me they have to pay attention to it and not think, 'She's calling wolf again.'"

• **Keep a thorough tracking system.** Dickinson uses an electronic tool that's accessible throughout the hospital, so nurses can access it when enrolling a patient in a trial and data managers and study coordinators can use it to check on each sub-sites' progress.

The tool is an electronic spreadsheet that holds multiple layers of data that can be accessed and understood by all involved, Dickinson says.

"The trial coordinator can pull up information to see if a sub-site is activated to enroll their first patient," Dickinson says.

The data manager receives information on eligibility screening logs, and then they have to track worksheet eligibilities for different amendments, Dickinson says.

For example, a sub-site may have been approved for amendment two, while the coordinating center has already been approved for an amendment three. The data manager's job is to make certain the sub-site is enrolling subjects under the amendment two and doesn't inadvertently use three's eligibility, Dickinson says.

"Only the approved versions can be out and about at any one sub-site at any one time, and you have to know which version they're using," Dickinson says.

While Vanderbilt-Ingram Cancer Center has no formal auditing program for sub-sites, the data manager and other clinical trial staff collect enough information to be able to catch any regulatory problems that might arise, Dickinson says.

"If needed we can require all of the information from the sub-site to be sent to us so an audit can be performed without going out to the site," Dickinson says.

• **Communicate clearly and efficiently.** "I educate them on what it is important to know about regulations, new amendments, and accrual numbers," Dickinson says.

Dickinson has created a fax cover letter that is designed to get sub-site staff's attention and ensure their immediate response. The fax cover letter doesn't focus on a study's protocol number as the identifying feature. Instead, the fax letter has a bold-faced title, printed typically in 16-point Arial font, she says.

"The sponsor investigator's name is there because a lot of people will link their train of thought to that too," Dickinson says. "And I make sure I list my name and contact information. I'll also, in the comment section, bullet what's included in the fax because sometimes not all the paper comes through."

The fax list quickly tells recipients the order of importance and when Dickinson needs the information returned.

"I try to make everything standardized so all forms look the same that go out to them," Dickinson says. "I have several reminder sheets so when the site alerts us that they are interested in being one of our sub-sites, I send this out about how to do an initial IRB submission."

Sub-sites occasionally don't include a list of the documents that they are submitting to their IRB, but this is an omission that could prove costly since it's usually something an auditor wants to see.

• **Maintain monitoring control.** Since coordinating centers are responsible for each sub-site, it's important for the sub-sites to get the IRB submission information up front, Dickinson says.

"When a PI gives a sub-site to contact, I will send them an electronic form to fill out," Dickinson says. "That gives me contact information, tells me about their center, and then I know who I'm going to deal with from a nursing or regulatory perspective."

Also, Dickinson lets sub-sites know that the coordinating center will need to see their HIPAA document for the study, draft of informed consent, and other sub-sites' IRB submission information before it's sent to the IRB for approval.

This requirement is to ensure that the language used in the consent and HIPAA forms will not prevent the sub-site from sharing data with the coordinating center and to make certain they meet all FDA and other contractual requirements, Dickinson explains.

Likewise, the coordinating center is responsible for the dispersal of IND safety reports related to the study to all sub-sites, as well as keeping everyone on the team, including the nurse, data manager, and principal investigator, on the same page as to where the study is in the approval process, Dickinson adds. ■

FDP participation benefits smaller research programs

Important benefit: Access to federal ears

Institutions with small research programs have watched in recent years as their regulatory burden has increased, even though they often lack the resources to handle the extra workload.

While not much can be done to change regulations that already exist, some research directors at smaller research institutions have found that they can have some impact on future regulations if they are involved with the Federal Demonstration Partnership (FDP).

"The whole purpose of the FDP is to establish demonstration projects designed to help streamline the administrative processes between the federal government and research institutions in order to maximize cost effectiveness, without sacrificing good stewardship," says **Richard Keogh**, PhD, a consultant with InfoEd International of Albany, NY, and a senior advisor for research administration at Rhode Island College in Providence.

Three years ago, Rhode Island College was the first Emerging Research Institutions (ERIs) to join the FDP, Keogh says. The FDP's roots date back to the mid-1980s, but it wasn't until more than a decade later that the FDP began to focus on smaller research institutions, Keogh says.

"Their voices were not being heard, and they were not participating in these demonstration projects," Keogh says. "So the FDP, when it moved into phase IV, has begun to remedy that and bring in representatives of institutions from predominantly undergraduate institutions and others who do research."

With three years remaining on the FDP's phase IV, the only institutions still eligible to join the FDP are those qualifying as ERIs. ERIs are defined by the FDP as those whose annual federally supported research and development expenditures are less than $15 million.

ERIs do not have to pay an annual fee for participation in the FDP, and their input will be heard on phase IV issues, including continued streamlining and standardization of research administration process and suggesting equitable methods for providing and documenting cost sharing and direct effort.

However, the time commitment and travel arrangements might be imposing for institutions which might have only one person in charge of research administration, says **Vijaya L. Melnick**, PhD, a biologist and director in the office of sponsored research and programs at the University of the District of Columbia in Washington, DC.

Larger research institutions may have the luxury of sending 10 people to FDP meetings, so they can be represented in each committee, Melnick notes. "For my institution, I'm the only person who goes to the meetings, except sometimes an engineering professor might attend a faculty-oriented committee," Melnick says.

Also, small institutions might find it expensive to pay the travel costs of sending staff to the FDP meetings, Melnick notes.

However, when ERIs choose to participate, there are some considerable benefits, she says.

"We find out about new policies being considered by federal agencies, and so we're able to prepare for those and respond to whether these will be an onus for our institution," Melnick says.

For instance, compliance regulations are a big issue for small institutions because they have a

small pool of people involved in research, and this same group would have to be on all of the required committees, including IRBs, Melnick explains. Until the FDP actively sought input from ERIs, the perspective on these requirements came primarily from the nation's largest research institutions, Melnick notes.

Keogh and Melnick list some of the other benefits for ERIs to joining the FDP:

• **FDP participants hear first about new tools and developments.** One of the FDP projects was a simplified subcontract form, Keogh notes.

"It's a much simpler and more streamlined subcontract form between institutions, and, initially, you had to be a member of the FDP to participate and use this form," Keogh says. "I found out about it as a result of the college being an ERI, and adopted that format and form, which saved the institution a great deal of time and effort."

The form became the institution's standard form, and later it became a standard form for research institutions across the United States, Keogh adds.

Also, Keogh learned about developments in transmitting research proposals electronically to the federal government by sitting at the same table as some of the largest research institutions, which were in on the early developments of the process, he says. "This is a streamlining effort that the FDP is heavily involved in so research institutions don't have to submit multiple submissions to multiple agencies," Keogh says.

• **ERIs can model policies already created at larger institutions.** For ERIs that have new or understaffed research offices, one of the benefits to participation in the FDP is having access to policies and procedures that someone else has already developed, Melnick says.

For example, Melnick needed a new misconduct policy, and so she located one that other participants in the FDP had recommended.

"I took that model and made the necessary modifications," Melnick says. "So it's very useful in the sense that I don't have to re-invent the wheel."

While many of these policies may be available on the Internet at various institutions' Web sites, a research administrator might not know where to look or feel comfortable borrowing from these without first having a conversation with someone from that institution, Melnick notes.

Since Melnick is involved with the FDP, she was able to hear about model policies and obtain other FDP participants' permission to use them.

• **FDP participants hear first about proposed federal regulations.** Through meetings on the various committees, FDP members hear about possible federal guidelines, policies, and changes from federal staff, Keogh and Melnick say.

"When new guidelines are being discussed and promoted, and these might be put into a ruling down the road, there are significant advantages to being there first to hear about these," Keogh says. "It helps to keep a research institution on their toes."

ERIs participating in the FDP have a little extra time to prepare for new policies, and also have a more effective forum for responding to what's proposed by federal agencies, Melnick says.

Most small institutions have no say over proposed policies until they're already published, Melnick notes.

But it's much more effective to have the opportunity to respond to such policies when they are first being shaped and discussed, and that's what FDP committee participation offers, Melnick says.

• **ERIs can develop a network for collaboration.** "There's an opportunity for collaboration through the FDP," Melnick says.

"We're looking forward to identifying grants where we can collaborate with other universities," Melnick says. "If this is worked out properly so that the collaboration does not lead to an unequal partnership then it can be very beneficial for both institutions, and the FDP provides that opportunities." ■

Compliance Corner

Improve quality with a trial monitoring program

Set up a comprehensive program

As federal officials and the media increasingly focus on clinical trials, it's a good idea to take the proactive step of forming an internal monitoring system for study conduct, according to a clinical research expert.

"I think it's fairly accurate to say that most academic medical centers don't have an internal monitoring system for study conduct," says

Bambi Jo Grilley, RPh, CCRP, CCRC, CIP, director of clinical protocol research and regulatory affairs for the Texas Children's Cancer Center and the Center for Cell and Gene Therapy at Baylor College of Medicine in Houston.

The FDA told the institution that ongoing monitoring would be necessary because of its involvement in gene transfer studies, Grilley says.

Since there aren't many existing models for such programs, Baylor officials decided to use the pharmaceutical industry's monitoring programs as a guide, Grilley says.

"We call it QA [quality assurance] audits, but it's really study monitoring," Grilley says.

The most difficult part of establishing the monitoring program was finding funding and deciding how much monitoring could be done by a limited staff, Grilley notes.

"It would be ideal to say every internal study is monitored each month or every three months, but that wasn't practical," Grilley says. "So what we came up with is something where we hope we're catching the bigger problems up front, and through random selection, we're catching other things as they occur."

Last year, the FDA again recommended that the institution make a change. This time the FDA noted that while the QA program with retrospective review was fine, the agency really wanted some prospective monitoring, as well, Grilley says.

"So we came up with the idea of a QC [quality control] program," she says. "The QA focuses on internally-initiated studies with the primary focus on IND studies, where we're trying to decrease regulatory risk." The QC program is more about reviewing particular employees' work than studies, Grilley explains.

"We look at how they're doing studies, whether their research reports are good, what the sponsors find when they come here," Grilley says. "And we're looking for the opportunity to either improve the system or retrain personnel."

Taken together, the two different types of monitoring programs provide a broad overview of how the research institution is doing, Grilley notes. Each program has one full-time employee, and they may be expanded as the need has grown, she says.

"The QA and QC are complementary programs," Grilley says. "The QC program is interesting because it's given us an opportunity to look at numerous employees and say, 'Wow, across the board people don't understand this.'"

Although the monitoring programs first were initiated in the cancer and gene therapy research areas, they've caught on, Grilley says. "We've been asked by other sections of the hospital to review their research, as well," she says.

Here's how the quality improvement programs work:

• **Select studies to monitor.** Under the QA monitoring program, any time an IND study enrolls its first patient, it is audited, Grilley says.

Also there are for-cause audits and random audits. "All internal studies are up for random auditing, and 10 percent are audited each year," Grilley adds. "The QA program could be a lot larger than it is, but we've set up a system that we think allows us to catch the majority of issues we'd be interested in looking at."

The QC program provides ongoing training and orientation training, as well as monitoring of individual investigators, Grilley says.

Under the QA program, each study randomly selected for an audit will be studied over a five to 10 day period, with the monitor checking 10 percent of the patients, Grilley explains.

The institution's data review committee might request a for-cause audit if they see some questionable data, Grilley says.

The QC monitor contacts an investigator and says she will conduct a QC review on these dates, Grilley says.

"The monitor looks at consent forms, data, all components of the work," Grilley says.

If the person being audited is a research nurse, then the monitor will check all phone logs, as well.

"Then she prepares a report and lists each patients reviewed and what the findings were," Grilley says. "If the monitor discovers that someone's research charts are a month behind or if someone doesn't follow standard operating procedures (SOPs), then the monitor will note that in a conclusion to the QC report."

If the monitor finds a more global problem, then she'll discuss that as well in the report, Grilley adds.

• **Determine consequences for problems found.** Monitors report any findings regarding patient safety immediately to the clinical research oversight committee (CROC), and the CROC decides whether the study needs to be closed, Grilley says.

"The more likely scenario is that what they bring to us has their findings divided into minor

continued on page 130

Baylor College of Medicine's Quality Assurance Audit Checklist for Patient Data

Auditor: _____
Principal investigator: _____
Protocol: _____
Patients audited (initials & study ID): _____

Consent:
- ❒ Are all required signatures and dates on consent form (legal guardian, patient, person obtaining consent, translator)?
- ❒ Are all pages in the original consent?
- ❒ Is patient name on all pages?
- ❒ Hand written patient name entered in the text?
- ❒ Patient initials entered in the text?
- ❒ Current IRB approved consent form?
- ❒ Was consent protocol specific?
- ❒ Was short consent form used?
- ❒ Was consent obtained before treatment start?
- ❒ Was consent process documented?
- ❒ Other

Eligibility:
- ❒ Was patient eligible?
- ❒ If no, why?
- ❒ Was eligibility checklist filled out, signed, and dated by PI?
- ❒ Was patient eligibility documented?
- ❒ Other

Randomization:
- ❒ Was randomization documented?
- ❒ Other

Pre-study evaluation:
- ❒ Were all pre-study evaluations done according to protocol requirements?
- ❒ If no, which ones were not done?
- ❒ Other

Treatment:
- ❒ Was dose of study agent administered according to protocol (± 10 percent)?
- ❒ Was dose of study agent modified according to protocol (± 10 percent)?
- ❒ If no, describe deviations.
- ❒ Was study agent administration documented?
- ❒ Were all on-study evaluations done according to study requirements?
- ❒ Other

Off-therapy evaluation:
- ❒ Were all off-study evaluations done?
- ❒ If no, which ones were not done?
- ❒ Other

Accountability of investigational drug:
- ❒ Were agent accountability forms maintained?
- ❒ Were all dispensed study agents accounted for?
- ❒ Other

Response:
- ❒ Was disease assessment documented?
- ❒ Were tumor measurements performed if required?
- ❒ Was protocol-directed response assessment documented?
- ❒ Other

Adverse events:
- ❒ Were protocol-specific toxicity criteria used for toxicities evaluation?
- ❒ Were all adverse events captured according to protocol requirements (grade, type, dates, duration)?
- ❒ Were all captured adverse events substantiated?
- ❒ Were follow-up studies performed when required to assess toxicities?
- ❒ Were all serious adverse events captured?
- ❒ Were all serious adverse events reported to IRB, FDA, GCRC, IBC, sponsor?
- ❒ Was there over-reporting of adverse events?
- ❒ Was there under-reporting of adverse events?
- ❒ Other

Case report forms:
- ❒ Were all corrections made according to GCP guidelines (crossed, initialed, and dated)?
- ❒ Were all case report forms filled out as required by protocol?
- ❒ Was source documentation found for all data entered in case report forms?
- ❒ Was quality of data transcription acceptable (inaccuracies, transcription errors, blank fields)?
- ❒ Was data submission delinquent?
- ❒ Was all data entered in study database accurate?

Source: The Texas Children's Cancer Center and Center for Cell and Gene Therapy at Baylor College of Medicine in Houston. Reprinted with permission.

and major problems," Grilley says. "And if they have a lot of majors, they recommend to the committee that the study be stopped, but that hasn't happened."

There was one situation where a QA monitor conducted an audit and sent the findings to the study's principal investigator, but the PI failed to respond in a timely manner, Grilley says.

"There was serious discussion of whether the study should be put on hold until the issues were resolved, and we were concerned that the PI wasn't responsive," Grilley recalls. "But once the PI found out we were thinking of doing this, we got our response."

In another instance, the monitor found that data collected was delinquent, and the CROC told the investigator that if the problem couldn't be cleaned up within two weeks then the committee would make the study stop enrolling patients, Grilley recalls.

"They cleaned it up," Grilley adds. "We've been very fortunate because we have a lot of support from the top, so when we talk about investigator problems, they know we mean it."

One of the most difficult challenges in having an internal monitoring program is providing to investigators that it has teeth, because if they believe the program has no power to levy consequences, then it won't work, Grilley notes.

However, the monitoring program so far has turned up mostly minor problems, such as the misfiling of documents, Grilley says. "It gives us a good feeling that there's nothing horrible under the rock that will be discovered by the FDA."

The QC monitor provides clinical research staff with a list of deficiencies or errors that were found, and the person is expected to correct the errors, Grilley says.

"If what the monitor discovers is that there's something this person is doing that is generally wrong, then we probably will talk more seriously about how we're going to address that," she adds. "The person is going to need to be retrained, and disciplinary action is needed."

• **Develop an efficient system.** It took a while for the QA program to get off the ground and to develop the necessary forms and policies, Grilley says. "It's the set-up part that's really hard," she explains. "You need someone who can understand the impact of various things."

During the program's development, the staff worked closely with the CROC, going through ideas for how to run the monitoring program and negotiating policies when necessary, Grilley says.

Likewise, developing the QC program took some planning. Initially, some though the QC monitor should audit each investigator each month, but that proved impractical, so the goal became to audit one person per day, Grilley says.

The monitoring programs each have their own written policies, procedures, standard notification forms, checklists, certificates of completion, and written examples of major deficiencies. (See Sample Checklist, p. 129.)

When a monitor discovers a problem with a trial that may indicate a more pervasive problem with particular clinical trial staff, then it's likely there will be a re-audit within three months, Grilley says. "We try to keep these as collegial interactions," Grilley explains. "We say, 'Here's what you're doing wrong, and we'll help you fix it.'" ■

Are unit-based research centers the next big thing?

Collaboration is first step

Research institutions with unit-based research centers will more efficiently meet the needs of their specific research populations and investigators, an expert says.

"If you plug in a system in which you have research advocates or an organization within that unit then your researchers can go to the center and get all the information they need for that specific population," says **Lisa Golec**, RRT, BSc, MHSM, clinical research coordinator at the neonatal intensive care unit at Sunnybrook and Women's College Health Sciences Centre in Toronto, Canada. Golec has spoken about establishing unit-based research centers at North American research conferences.

The institution's unit-based research center was formed about five years ago, after years in which research was conducted without any organizational framework, Golec says. Now the unit-based research center has 11 ongoing studies of which the majority were initiated by the center's own investigators, Golec says.

Why the move to unit based research? The unit-based research center helps keeps all parties well informed. She offers as an example their role in a neonatal medical center where the potential research population is a captive audience because the patients will be there with their families for

weeks to months. "The families are stressed out because they didn't anticipate premature delivery," Golec says. "Then the mother is recovering from delivery, and they're frequently approached about many different studies."

A cancer patient might be asked once about clinical trial participation, families with prematurely born infants might be asked to enroll in studies as many as five times, Golec says.

"It's striking that balance of not taking advantage of them because they're a captive audience and giving them the autonomy to not do the study," Golec says.

This is where a unit-based research center plays a defining role. "We are able to meet the needs of the investigator and the family because we attempt to set a system in place that is going to be protective of the family and their ethical rights. And we're also tuned into the bedside caregiver's opinions," Golec says.

"I know of one center where they don't have a system like this in place, and they have a physician who finds out his patient was enrolled in a surgery study, but he didn't know anything about it," Golec says. "The investigator approached the family, but didn't tell the attending physician."

Golec offers these tips to setting up a unit-based research center:

• Create a realistic budget and expectations.

"Research is an expensive business, and you have to have the infrastructure and administration set up," Golec says.

"Sometimes people bite off more than they can chew, so you have to start small, taking one or two projects, see how they go and then expand from there," Golec advises. "If you're compelled to take on more research, it evolves into too much and the whole thing will implode."

It's wiser to start small, putting a great deal of heart and energy into a couple of projects, and work toward success with those, Golec adds.

Then a site can build upon those successful experiences, sticking to the same areas of research, which will minimize the learning curve, she says. "A lot of people underestimate the amount of work that goes into the study before it starts," she says. "The majority of research work happens before the first patient is enrolled, with the screening and preparation work."

This is why the budget for starting the research center should reflect those upfront costs, since it's less likely sponsors will provide those funds, Golec says. Eventually, a center will have to work into its contracts with sponsors adequate start-up money to support their costs, she adds.

• Provide adequate training to staff and investigators.

Golec gives investigators a package of information about research, and she's working on beginning a two-day clinical research workshop.

"Even though our bedside staff may not be interested in becoming researchers, they're interested in research itself, so we have education days for them with brown bag lunches," Golec says.

Sending staff to certification courses is another option. "A lot of centers that are established have training, and they will fund their staff to take certification courses," Golec notes. "I think there should be certification because it's important for people to know this information, but part of it has to be comprehensive."

• Assist investigators with finding grant and sponsor funding.

It's important to look at different sources of funding, finding them through word-of-mouth and other means, Golec says. "We keep our ears open," Golec explains. "If someone hears of another investigator obtaining a grant, we write it down and apply."

Golec will conduct Internet searches for investigators about grants, and she'll attend conferences, picking up funding pamphlets at various booths.

"You may hear it through the grapevine, but you need to be dynamic because the funding bodies change their criteria, and you need to stay up to date," Golec says.

"Brand new investigators shouldn't go after federal funding, but should get their feet wet with funding from some other sources." While a research institution always needs some outside funding for studies, it's also important to provide some internal seed money when an investigator has a good idea because that may eventually enhance the institution's reputation, Golec says. ■

COMING IN FUTURE MONTHS

- Setting up a QA program
- A strategy for determining protocol feasibility
- Need to know more about HIPAA?
- Expert offers best practice guidelines for trial budgeting

Editorial Advisory Board

Stephen L. Kopecky, MD
Medical Director
Mayo Alliance for Clinical Trials
Rochester, MN

Elizabeth E. Hill
BSN, RN, DNSc
Assistant Professor
Director
Clinical Research
Management Program
Duke University
School of Nursing
Durham, NC

Edwin V. Gaffney, PhD
Executive Director
Clinical Research
Baptist Health System Inc.
Birmingham, AL

LaDale George, JD
Senior Counsel
Health Law Department/
Health Care Business
Counseling Practicing Group
Foley & Lardner
Chicago

Ellen Hyman-Browne
JD, MPH, CIP
Director
Research Compliance
New York University
Medical Center
New York City

Barbara LoDico, CIP
Executive Director
Human Subjects Protections
University of Medicine &
Dentistry of New Jersey
Newark

Tamara Dowd Owens
RN, MSN, MBA
Clinical Research Manager
Governor's Institute on Alcohol
and Substance Abuse
Research Triangle Park, NC

Lynette M. Schenkel
Director
Office for Responsible
Conduct of Research
University of Oregon
Eugene

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 certificate of completion. When your evaluation is received, a certificate will be mailed to you. ■

CE/CME *questions*

17. Which of the following is the best way to translate information to to subjects who speak a language other than English?
A. Have a bilingual physician/investigator do the translating.
B. Have a family member of the subject translate the clinical trial coordinator's words.
C. Have a bilingual health care professional who has research experience, but has no connection to that particular study, translate.
D. All of the above

18. Which of the following is a valid benefit to using sub-sites in clinical trial research?
A. With sub-sites, a clinical trial will accrue subjects more quickly, leading to better data and faster product approval.
B. Clinical trial grant administrators would have a better chance of obtaining certain grants if they use sub-sites.
C. Human subject research administrators will have the opportunity to improve educational processes as they train sub-site research staff, as well as their own.
D. All of the above.

19. Which of the following is NOT a valid reason for an emerging research institution (ERI) to join the Federal Demonstration Partnership project?
A. An ERI could be on the cutting edge of new research technology and federal regulations by sitting in on FDP meetings.
B. An ERI could be the first on the list to receive sub-site contracts with large research sites.
C. An ERI could meet representatives from other ERIs and larger research institutions and possibly form research collaborations.
D. An ERI could model policies and procedures after best practices already developed by institutions that have more resources to develop their own tools.

20. In developing a quality assurance patient data checklist, which of the following is an item that should be listed under the category of consent?
A. Are all required signatures and dates on consent form (legal guardian, patient, person obtaining consent, translator)?
B. Are all pages in the original consent?
C. Was consent protocol specific?
D. All of the above

Answers: 1. C; 2. A; 3. B; 4. D