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An essential resource for managers of clinical trials

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Infuse best practice strategies into managing multisite trials

The key? Improve communication between sites

When clinical trials administrators are working on a study that is part of a multisite trial, the biggest challenge is communicating with everyone involved.

There are many areas in which best practices in communication might improve coordination of multisite trials, including at the beginning of the process when it's important to make certain everyone is implementing the protocol the same way, says **Mark Thornquist**, PhD, senior staff scientist at Fred Hutchinson Cancer Research Center in Seattle.

"We set up systems to do a distribution of responses through an online system to which everyone involved in the study has access," says Thornquist. "We track inquiries and ensure the response is sent out to all sites to make sure all are interpreting the protocol in the same way."

When it's necessary to hold teleconferences, time differences can form a barrier to effective communication.

"You have to be flexible because you might have sites throughout the country, and we have to be very aware of time differences," says **Cim Edelstein**, COMPASS coordinating center manager of Fred Hutchinson Cancer Research Center.

"You have to be careful to set up meeting and conference calls that can accommodate the people in different time zones," she adds.

When a study has trial sites around the world, the time difference is just one factor that makes communication more challenging. Another problem is dealing with multiple languages, says **Jennifer Yahne**, contracting projects manager at Fred Hutchinson.

Yahne works with the HIV Vaccine Trials Network, which coordinates clinical trials of potential HIV vaccine candidates at 30 sites in the United States, Africa, South America, the Caribbean, and Asia.

"We try to operate our particular part of the operation 12 hours a day from 6 a.m. to 6 p.m.," reports **Banks Warden**, MHA, chief operating officer of the HIV Vaccine Trials Network at Fred Hutchinson. **(See story on handling international trial sites, p. 28.)**

"We've tried to hire people who have [foreign] language skills, and we have the people who work in our travel office and conference call

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office also have significant language skills, " he says.

When one site is coordinating the multisite study, it's important that the site's IRB establishes effective communication with the other sites and IRBs involved, says **Karen Hansen**, director of institutional review office at Fred Hutchinson Cancer Research Center.

"If your site is the main coordinating center for a study, it's really important for the IRB to communicate and work with lead investigators early on to identify the roles of all players and to make it clear who is participating in what level of activity," she advises.

Hansen and the other experts offer these additional guidelines for establishing best practices in coordination of multisite clinical trials:

1. Hire a central coordinator.

"Having a central coordinator for multisite trials is critical," Edelstein says. "You have to have a designated person who is the coordinator of the project, not multiple people coordinating activity."

Multisite trials need one project leader who is making sure everything necessary is done at all sites, Thornquist says.

A central coordinator or project manager might not have all the answers when inquiries arise, but will know who to contact to find the answers, Edelstein adds.

For instance, if a trial site encounters a programming glitch, then the project manager will talk with the information technologies staff; or if there's a scientific question, the project manager will meet with the trial's executive site committee, she explains.

Another good reason for having a project manager is because one designated person could establish relationships with investigators and staff at multiple sites and with sponsors, IRBs, and institutional staff, Edelstein says.

"I've been in this business for 20 years, and you find that you keep running into the same people. That's helpful if you're developing relationships where you know these people, and they know you," she adds.

2. Answer everyone when one person asks a question.

When multiple sites are conducting a clinical trial, it's important to make the flow of information as efficient as possible by sending information and responses to questions to every site when one person involved in the project makes a request, Thornquist says.

One way to do this is through e-mail messages

that are sent simultaneously to all involved.

For example, a research coordinator at one site might ask how and when a particular device is to be used. Once the answer comes from the principal investigator, it can be sent to every clinical coordinator and investigator, Thornquist explains.

Better yet, all inquiries and other updates could be stored in a central electronic location for referral throughout the trial, Thornquist says.

"Where there are clarifications to protocols or to modify protocols because the practice has been changed, we indicate a date of inquiry so from that date forward all information follows the date of that inquiry," he explains. "We call it our information management system."

The information management system tracks all internal review and stores questions and answers so the information will be useful when research staff need it, Edelstein says.

"Sites report they read these, and they use these as part of their training," Thornquist says. "They are required to go to the information management system daily."

Fred Hutchinson research staff had used a paper information management system before switching to an electronic version, and the electronic version is more efficient because it can get out common responses to inquiries much faster, he notes.

"Everyone has access to reading and submitting a question," Thornquist says. "The program looks through the database and pulls out those that may be similar to see whether the question has been asked before and whether it has been answered so it won't be duplicated."

Get everyone on the same page

3. Create a manual of operation.

Fred Hutchinson's institutional review office started a manual of operation for one study, and now it's reviewed by the IRB each year, Hansen reports.

The institution keeps the manual current with information about all multisite clinical trial partners, standard operating procedures, sponsors, coordinating centers, IRBs, and it details all aspects of human subject protection and who the point person is for making certain all approval dates are in place, she says.

"It enables the IRB at the coordinating center level to have a solid footing on all activity that's going on," Hansen explains.

The manual outlines all of the material that needs to be reviewed by the IRB, including every human subject protection measure that would be required by the Office of Human Research Protections (OHRP), she adds.

"This is a good mechanism when you have a multisite trial and your coordinator wants to have a handle on what's happening at each site," Hansen explains.

Formatted in an Excel spreadsheet, the manual includes details, such as the OHRP memo of engagement, informed consent for subjects, regulatory operations center duties, the program medical officer's role, and references, she adds.

4. Consider futures uses of collected data.

Too often in the past, clinical trial investigators and administrators had tunnel vision and thought only of the immediate uses of the data that would be collected during a course of a study, Edelstein notes.

Now, research professionals realize that sometimes the most important use of collected data might not be imagined at the time of a particular study, so it's important to keep options open for future uses.

"For people who start any multisite trial, you have to look broad because the opportunities are very real," Edelstein says. "You have to think about that when you're writing consent forms and think about that when you're developing a tracking system."

Also, clinical trials staff will need to consider ownership issues and develop policies and procedures that can handle ancillary studies coming from a multisite trial, Edelstein says.

For example, a study of 10-20 years ago might have collected blood samples for the purpose of looking at the effect of certain vitamins on lung cancer, but then the potential to analyze genetic information occurred, and the same samples could be used for research that has more far-reaching potential, Edelstein notes.

"So you have to anticipate that science will change as you collect those samples," Edelstein says. "Twenty years ago, there was less concern about particular analyses being done on samples, but now it's possible for consent to be open-ended, depending on the consents you allow."

Of course, all of this needs to be handled under the privacy rules of HIPAA, including obtaining IRB approval for all new uses of data, Thornquist notes.

"With HIPAA, the biggest impact has been ensuring that when you do share data or specimens that you do so with information or

specimens being de-identified," Thornquist says. "The site receiving the information cannot determine specific individuals that the information came from."

Also, before investigators are given samples of data they are required to sign a privilege of received data form that will document what specific analyses they are permitted to do and that will inform them of the process they have to go through if they want to do additional analyses, Thornquist adds.

Another consideration is whether investigators will be able to use existing data effectively, and this might require a formal collaboration in the case of long studies in which the protocol has been modified many times over the years, he says.

"Sometimes, the only reasonable way to share data is through a formal collaboration so we can make sure they're using the correct data elements, interpreting data right and interpreting it based on other data published in a consistent manner," Thornquist says. ■

Going global? Watch out for cultural divide

Respect for differences a good first step

When clinical trial administrators and staff are dealing with multisite trials that include international locations, there is a lot to consider, including time and language differences.

"You encounter issues with communication and people who don't speak English and the translation of study materials, and that's one aspect of it," says **Jennifer Yahne**, contracting projects manager for the HIV Vaccine Trials Network, which is based at Fred Hutchinson Cancer Research Center in Seattle.

Multisite trials that involve international sites require a great deal of flexibility on the part of the coordinating center site staff because time differences can be substantial. For instance, clinical trial sites in Thailand are 15 hours ahead of Pacific Coast time, she says.

"So doing conference calls requires flexibility just to get everyone on the phone at the same time," Yahne says. "Communicating with a group of that size and spread geographically has its challenges."

Yahne arrives at work at 6:30 a.m. and will work late when it's necessary to schedule a telephone call at 4 p.m. to include East Coast clinical trial staff at 7 p.m. their time and Thailand clinical trial staff at 7 a.m. their time.

Good will goes a long way

Other issues to consider include cultural differences and political obstacles to conducting international clinical trials, says **Banks Warden**, MHA, chief operating officer of the HIV Vaccine Trials Network.

"Some things we've learned is that no matter how good your principal investigator is in a particular location, if you don't have political good will in the country then, in general, it's very hard to have a successful operation," he says.

By political good will, Warden refers to having the cooperation of the country's ministry of health or other high-ranking government officials who have influence over research conducted in the country.

"A lot of countries have regulatory operations that are well developed, and they have to be convinced that we're doing ethical research and that we're doing it in a way that protects the safety of the citizens of their country," he says.

To satisfy these concerns, it's important to conduct an exploratory visit prior to developing a site and meet with the people whom the principal investigator has identified as being key in establishing political good will, Yahne says.

This includes ministries of health officials and representatives of nongovernmental organizations in the community, she notes.

"We also try to place trials in places where they have a basic lab and other infrastructure, but that's not always possible," Warden says.

Once a site has been selected, the next step is to develop a community advisory board for the clinical trial, he says.

The community advisory board is separate from the IRB, which also is established at the local trial site, Yahne notes.

"We find that has been a very successful part of our strategy to make sure the community knows what we're doing," Warden says. "The community advisory board is there to provide insight into what the community is thinking and insight into cultural issues that we may not have appreciated when we first went there."

Also, a local board can help educate the community about the disease associated with the clinical trials, such as HIV in areas where HIV

clinical trials are conducted, Yahne says.

"The board also is there to help us identify the populations from which we could recruit participants for the trials and to make sure we're treating them fairly and answering ethical concerns," she adds.

For some international trials, such as the HIV/AIDS Vaccine Trials with which Yahne and Warden are familiar, there are recruitment and screening challenges.

"In early trials, we looked for people who are at low risk of acquiring HIV, so reaching out and bringing in those populations is challenging at times because some of the same sites also are used for recruiting people who are at high risk for HIV infection," Yahne says. "And we have a vigorous screening policy; so even if you qualify initially, you could be turned down as screening progresses."

Of course, the IRB is the chief body to review ethical concerns, she adds.

"There can be multiple IRBs for a given site, especially internationally where the funding is going through the United States and a local institution, which still has to get approval in the U.S. and at the international site," Yahne explains. "And usually in other countries, there's a governmental level approval necessary at the ministry of health level, so it can take quite a while to get all approvals in place."

When economies clash

Contract negotiations also can be tricky when an institution's dealing with international sites, Warden says.

"One thing we've run into fairly recently is the exchange rates," he explains. "We can negotiate contracts for certain amounts of dollars, but then our study will run for 18 months to five years."

If there are dollar fluctuations as there has been in recent years, then the value in exchange rate can create problems, such as undermining the value of what has been negotiated for pay at international sites, Warden says.

"This last period has been more difficult because the dollar has been devalued so much against so many other currencies, so if a site really is having difficulty with the financing we'll go back to work with them over their finances," he notes.

Still, when the contract amount is fixed, clinical trial administrators have to be creative in finding solutions, such as reducing some expenditures at the core office so that the site might receive a little more funding, Warden says.

"Any manager in this business will need to have some sort of small contingency fund because you're always going to have problems you didn't expect," he adds.

Other problems might include the logistics of getting supplies and equipment into foreign countries, Yahne says.

For instance, it's very difficult to get equipment through customs in Haiti; this makes timing a clinical trial more difficult, she notes.

"So it's important to plan ahead for trials and know what sorts of items they need, and if the item is a special freezer then you need to know ahead that it could take six months to get it through customs," Yahne says. "All of these logistical issues are just a matter of planning ahead and communicating with the site to make sure you get items to them and the things they need." ■

A good template improves trial budgeting process

One research hospital's best practice

One of the keys to accurately projecting costs of a clinical trial is to have a working budget template that captures every single cost, but which avoids duplications that could lead to regulatory problems, an expert says.

"A working template helps us understand how the budget needs to be constructed," says **Bill Caskey**, PhD, director of research and grants administration at The Children's Mercy Hospital in Kansas City, MO. Caskey spoke about clinical trials budgeting at the 2004 Annual Meeting of the Society of Research Administrators International, held Oct. 23-27, 2004, in Salt Lake City.

The template provides the backbone of the budgeting process. To obtain accurate cost estimates, principal investigators and research coordinators need to provide clinical information that is as accurate as possible, he says.

Since the institution has had success with its budgeting template, the research and grants office is able to determine the actual costs of conducting a clinical trial or other research study, putting a cost on every item and service provided, including pencils and pens, Caskey reports.

"We do this day in and day out, and we probably get a better budget for investigators than what the investigators themselves would," he says. "Our

research cost is what our real cost is, and that's what we charge the federal government."

The Children's Mercy Hospital's efficiency in research budgeting has been a factor in its tremendous research growth within the past eight years, including an increase in external funding from $1 million to $10 million this past year, Caskey says.

Research expenditures have increased from about $2 million eight years ago to about $15 million now, Caskey says.

The institution will break even on research contracts with the NIH, he adds.

You get what you pay for

When Caskey begins negotiations with a pharmaceutical company or other private sponsor, the negotiations typically are a little different. "The first offer is what I'd charge an insurance company for the same interventions," he says.

"We're a pediatric hospital exclusively, and with the renewal of the Drug Labeling Act for pediatrics, pharmaceutical companies are seeking sites to place a pediatric study," Caskey explains. "Our case completion rate approaches 100% in accuracy. I've been here eight years, and I don't remember a study where we didn't enroll all the subjects we said we'd enroll."

So when sponsors complain about the research charges, he responds, "You get what you pay for, so if you want a study done well and fast, you'll come here."

Caskey provides these best practice guidelines for improving accuracy and success in the budgeting process:

• Capture the best information possible from investigators.

Investigators are asked to check boxes for each of the possible interventions and services provided for a study, which means that they either need to have experience or need to receive input from someone who does have experience with a particular type of protocol, Caskey says.

After research coordinators and investigators select the interventions that will be done for each research subject, then those interventions are matched with hospital codes, while facility charges are separated, he explains.

For instance, if the investigator has indicated that a subject will need a complete blood cell (CBC) count, then the working template already has a calculation for the charge associated with use of the examining room and what the charge is for that intervention, based on whether the intervention is a Level 1, 2, or 3. The level of intervention is dependent on the time spent and equipment needed for the exam room, Caskey explains.

"We separate facility charges from actual treatment or tests being done," he adds.

When these calculations are made, they're shared with the research coordinator or the physician investigator who review them and approve them, Caskey says.

"Once we identify those charge codes, we can create an Excel spreadsheet that closely resembles the study schematic in the protocol," he says. "Then we can provide the total costs for all CBCs done for a study."

Also, the finished spreadsheet can be transferred to the sponsor's budget forms, and the information is easy to decipher when budget negotiations begin, Caskey says.

"It really helps with negotiations because it's a clear presentation of what it actually costs us to do the study," he says.

Delineate patient care, trial charges

• Keep research enrollee charges separate from patient care admission charges.

The institution uses separate enrollment screens for clinical studies, and these are different from the ones used for admission of patients for patient care, Caskey says.

When a patient is enrolled in a study, the research coordinator involved knows how to separate standard of care and send charges to the right place, whether it's Medicaid, a third-party payer, or a clinical study, he says.

Then each month, the bills are sent to research coordinators who review them to make corrections and make certain that research charges are not also billed to Medicare or Medicaid, Caskey reports.

"No research charges go to a third party, and no standard of care charges go to the research account, and that policy coupled with enrollment screens helps us to minimize mistakes," he says.

Research coordinators tend to be detail-oriented, so this monthly review has worked well, Caskey notes.

"We set this up with the hospitalwide training program, and when somebody new comes on we train them on how to use the research screens," he says. "The director of clinical trials administration holds a meeting once a month with all research coordinators and they talk about issues and new

policies and anything that comes up related to that."

Through working with research staff, administrators found a solution to what has been a common research charge problem for other institutions: the charge for blood draws.

Instead of making a blood draw a separate charge from the CBC, for example, it is included in the CBC charge, Caskey says.

Accounting experts amortized the cost of blood draws across different lab charges, so part of the cost is attributed to the CBC and part is attributed to other chemistry panels, he says.

"At the end of the year, based on our statistics, we break even on the cost of the blood draws," Caskey says.

Better yet, this policy has eliminated the potential problem of a single blood draw that is done for both research and medical care purposes being charged accidentally to both the federal government and to a clinical study, which could trigger a federal fraud investigation and hefty fines, he reports.

Account for time

• **Dig up all hidden costs.**

Physician and research coordinator time are the most hidden of costs, Caskey notes.

"You can calculate the amount of time someone will need on a visit, but it's the follow-up time and paper time to do reports and such that are difficult to calculate," Caskey says. "So we developed a spreadsheet that we use with coordinators and investigators."

When the spreadsheet calculations have grossly underestimated actual costs, this is documented so the mistake can be prevented the next time.

"The manager of clinical trials has developed this spreadsheet over time by working with investigators and research nurses," Caskey says. "It was developed through trial and error."

Among the hidden costs that are captured in the spread sheet are the following:

— how long it takes to review a protocol by investigators and research coordinators;

— how long it takes to set up a study;

— time and travel for pre-study meetings;

— IRB admission costs, including the time either the investigator or study coordinator spends at the IRB meeting in which the protocol is reviewed;

— cost of subinvestigator staff;

— advertising costs, shipping costs;

— time spent for closeout and archiving;

— time spent for study administration, monitoring visits, study maintenance, scheduling clinical visits, follow-ups when a patient is a no-show; follow-ups for other problems, etc.

Once all questions are answered regarding research staff time, the time is translated into dollar costs based on each research employee's base salary plus fringe benefits, Caskey says.

• **Make payment schedule work economically.**

"As we work through the spreadsheet, and once we agree to numbers and the sponsor agrees to numbers, we have an investigator and coordinator sign on the budget," Caskey says. "Generally, it will have a per-patient charge, and we carry that over and have a summary page that shows the anticipated number with the charge per subject and the upfront charges, including the IRB fee, the study coordinator time, and the investigator time."

Then there's an additional section of study charges, and if the sponsor has an unusual requirement for document storage, for instance, that is included here, he says.

"We also need a lot of IRB amendments for pediatric studies, so we budget for two amendments of $200 each," Caskey says. "We charge $1,500 for the review and $200 for each amendment."

It's important to ask for all upfront fees to be nonrefundable and to be paid at the time the contract is executed, he says. "Sometimes that includes the IRB fee, and sometimes the IRB fee is invoiced separately, depending on how the company handles that."

Then screen failures are estimated, and with experience this can be predicted fairly accurately, Caskey says.

Sponsors usually request that a portion of the fee is held until all the case report forms are completed, and typically that amount is 10%, he says.

Then the other payment dates are set according to study milestones, such as each time an X number of patients are enrolled, Caskey adds.

Finally, if a clinical trial is losing money, it's important to go back to the sponsor to request additional funding, he says.

"That has happened only two or three times," Caskey notes.

When a budget has been thoroughly estimated, including even the miscellaneous supplies, such as paper, pencils, etc., there should be few occasions when the clinical trial falls greatly under or over budget, he says. ■

Are difficult scientists creating waves?

Here are tips for dealing with them

Every clinical trial administrator has encountered the occasional investigator who causes staff to pop antacid pills the minute he or she walks into the room. And while large research institutions tolerated such personalities in the past, with today's tighter focus on research compliance and ethical concerns, such personalities now can be a real problem.

There are several common personality and behavior problems that clinical trial staff might encounter among investigators, including the following:

• "Rules don't apply to me."

"One of the biggest concerns is a scientist who feels the rules don't apply to him," says **Cindy Kiel**, JD, CRA, director of sponsored projects at the University of Nevada, Reno.

"A lot of times these are brilliant people," she explains. "When dealing with cutting-edge research, what most researchers are doing is pushing what is known, disproving what people thought they knew."

Because of the maverick personality needed to succeed in this type of research, often the successful investigators also are people who are more creative than bound to rules and conventions, Kiel explains.

"Sometimes that can flow over into the compliance world where an institution might end up with legal and liability concerns if the individual feels the rules don't apply to him or that they were made to be broken," she says. "There are times when you need to think outside the box and times when you need to play inside it."

The solution to dealing with investigator who refuses to follow rules and regulations could be terminating the person's position or contract; although with university tenure tradition, that is extremely difficult to do, Kiel notes.

"If the person causes extreme liability to the institution then you need to go down that road, but if the person will listen to reason, then the team approach sometimes will work," she suggests.

By this Kiel means that research administrators assemble a group of people at the institution to sit down with the investigator, explain what the problem is and why it's a problem, and let the person know that if things don't change there will be severe repercussion, such as a job dismissal, she says.

"Hearing stories about extreme examples of what happens with noncompliance does help," Kiel says.

For instance, when federal officials brought criminal charges against faculty at another institution because of their inaccurate effort reporting, that got the attention of researchers, Kiel notes.

"When our faculty saw their colleagues facing criminal sanctions they started calling our office to say, 'Tell us what the rules are because we want to follow whatever the rules are, and we don't want to get close to the edge,'" Kiel says. "It has much more of an impact when it's someone they know who gets into trouble."

• "Don't bother me with details."

"A second variety of difficult scientists is the individual who feels like, 'I'm only here to do my science, and don't bother me with the business details — that's not why I was hired,'" Kiel says. "They don't want to pay any attention to budgets and paperwork and procedures and bureaucracies, and they don't feel like it's even their duty or role."

The most effective way to cope with these types of personalities is through proper training of the roles and responsibilities, especially when the person is first hired or learning to become a researcher, she says.

"Whenever you accept funding there are strings attached, and some faculty simply don't want to have to deal with that and haven't been trained in it," Kiel says. "So the solution is to train them to accept the fact that when they accept money they do have a role to play in day-to-day management and regulatory compliance."

This is another type of investigator who might learn from some extreme examples. For example, there was the situation where an investigator was using toxic chemicals, including anthrax, and he didn't bother with the paperwork that tracked the substance, so when federal officials began to investigate the use of the substance, they filed criminal charges against the scientist, she says.

• "It's not my world, and I don't want to have to do it."

Then there's the type of investigator who simply refuses to follow some rules and obligations, such as taking time for mandatory training courses, Kiel says.

"A lot of institutions have made training mandatory, and those sometimes are the ones

who have been hit with legal or audit findings," she notes. "That gives them the clout on campus to say, 'We will make this training mandatory.'"

Still, there are always the scientists who will say the rule shouldn't apply to them because they haven't gotten into trouble or because they are so low on the federal radar screen that no one will be looking over their shoulders, Kiel says.

One solution is to make the training as pertinent and valuable as possible for investigators, so they cannot use the argument that they wouldn't learn anything from it.

Another solution in dealing with scientists who refuse to cooperate and follow documentation rules is to assign them an administrator who will help them out with the paperwork load, Kiel suggests.

"If the investigator is bringing in decent amounts of outside grant funds, then your overhead return can be used to apply to those resources," she adds.

• **The abusive scientist.**

Typically, the personnel department should handle the investigator with an abusive nature, although it might be impossible to turn this type of situation around, Kiel says.

"I've heard of faculty who are abusive to students and other faculty to the tune of even assaulting another person," Kiel says. "These are people who have difficulty working with other scientists."

When clinical trial staff have to work with such a person, it's probably a good idea for the administrator to be present, she notes.

Also, an administrator, who no doubt will hear warnings about the abusive investigator before first meeting the person could be proactive in defusing the situation by inviting the scientist out for coffee in an off-campus location, Kiel suggests.

"Get to know the scientist as a person first," she suggests. "Take that approach: Get them off-campus and outside of the work arena, pay for their coffee, sit down and say, 'I'm really interested in your science and what you're doing and what benefits you're providing to the community, and I really want to hear about it.'"

This builds a rapport with the individual that will make it easier to talk with the person when a problem arises, Kiel explains.

Another strategy is to change one's own attitude toward the difficult personality, she says.

"When I'm dealing with someone I just want to strangle, I picture a relative who is like that but is someone whom I love," Kiel says. "You can't take these people personally, and while they'll sometimes attack you personally, you can't take it personally."

A third strategy is to tell the clinical trials staff that before they get to the point of wanting to scream and yell and react angrily to such a person, they should forward the person on to their supervisor, saying, "Why don't you speak to our director?" she says.

Often when an angry person is sent to someone new to handle the situation, the person will tone it down a little, Kiel says.

It's also a good idea for administrators, and maybe even the staff, to learn communication skills that could help in dealing with difficult and angry people, she suggests.

Such skills could follow the judo model of defense/offense in which if someone is arguing about something, you agree with them on some element of their complaint because this will disarm them, she says.

"Find that element and agree on that because they're not expecting it," Kiel says.

For example, if an investigator calls to complain about a delay with a proposal, the research administrator could say, "I agree; three days seems like an awful long time for a signature," she says.

This approach pops the balloon of their aggressiveness and prepares the situation for the second phase in which the research administrator compliments the angry investigator by saying, "Most people wouldn't have called in to let me know they were upset, so I think it took a lot of courage to call in," Kiel says.

Now that the person's anger is defused, it's time to get to the root of the problem because they'll be willing to listen, she adds.

"You have no control over another person and you can't change their mind, so throw away that expectation up front," Kiel says. "What you can change are your own attitudes."

If a mistake has been made, then own up to it, and if not then there's no reason to let the other person's accusations affect how one is feeling, she says.

• **Cultural misunderstandings.**

Sometimes the difficult scientist is someone who comes from another country and culture, and the main reason for the difficulty involves vastly different worldviews.

For instance, research staff sometimes encounter difficulties when dealing with scientists from

nations where women are expected to follow proscribed roles regardless of their position and training, Kiel says.

Kiel heard of an extreme example of this type of difficulty: An investigator from a country where women always walked 10 paces behind men and who never sat in the same room as a man refused to have any contact with a female administrator, who was trying to talk with him about the problems he was having with other staff, she says.

"Because the man wouldn't come to her office, the administrator tried to speak with him outside his office, but he kept walking ahead of her, and as he walked faster, she walked faster until she was chasing him," Kiel recalls.

Finally, the administrator called him on the telephone and said, "I understand that in your country it makes you uncomfortable to be this close to a woman, but we really need to discuss the issue because this is the United States, and what you're doing is considered to be discrimination," she says.

The administrator further noted that she and the scientist needed to figure out a way that he could interact with female colleagues without making this an uncomfortable situation, and so they decided that he could stand in the doorway of the administrator's office when they needed to have a discussion, Kiel adds.

"Usually, you don't know about cultural differences until something happens," Kiel says. "So this is a hard one."

However, it can help if a research administrator has traveled around the world and understands how it feels to be a foreigner, she notes.

It also helps if the foreign scientist has someone discuss potential differences and conflicts up front and to tell the person what is expected to happen in this country, Kiel says.

"There are circumstances where we will call upon department chairs and deans to solve the situation," she adds. "The vast majority of faculty are very nice and will make changes if told about the problem." ■

Compliance Corner

Improve compliance processes with audit

Committee provides continuous oversight

Developing a thorough self-audit process is one-way research institutions can improve research and clinical trial compliance and prevent small problems from becoming regulatory nightmares, according to a research compliance expert.

"We have a well-established compliance office within the health system, and over the past year we've developed a campuswide research compliance program that includes a research compliance committee," says **Lynne Chronister**, MPA, associate vice chancellor of research for the University of California-Davis.

"What's important is to promote a culture of integrity, and while that sounds so easy to do, it's difficult to define and implement," she says. "But you can have wonderful compliance policies and internal controls and programs and forms to fill out, but if the culture doesn't promote a culture of compliance, then those are just processes and are not as meaningful as they should be."

This is why a good way to improve a compliance program is through the development of an audit that provides a status report of every compliance area that needs improvement, she suggests.

"We went through the entire campus and medical center and looked at what we have done and where we are," Chronister says.

The audit report gave them a good idea of where the institution's gaps and where additional policies, processes, and resources are needed, she adds.

Through this extensive process, which took about a year, research officials identified three important areas for improvements, including IRB, conflict of interest, and financial accountability, Chronister says.

Here's how the auditing process worked:

1. Identify priorities:

Several key compliance people worked on the audit boilerplate over a three-month period, and then a compliance committee carried out the audit, Chronister says.

"First we had to go through and identify every area that's critical to the broad area of research compliance, and then we had to go back and fill in the critical components of those areas of research compliance," she explains.

The next step was to identify the people

responsible for each of those areas and find out what the compliance requirements were and whether they were being met, Chronister notes.

"Then, we prioritized those areas where we needed to improve, and we're in the stage of requesting resources for those areas," she says.

2. Establish a continuous improvement process:

"What we plan to do annually is have an ongoing committee with continuous oversight look at those areas where we thought we needed improvement," Chronister says.

For instance, the oversight committee will view the audit chart and updates and see what has been accomplished over the year, she says.

"We will use the results of our audit and do a self-assessment on an annual basis, prioritizing those areas we felt needed attention first and those will be the ones where we'll spend most of our resources in the coming year," Chronister explains. "We have high-risk, medium-risk, and low-risk areas."

The committee, which also conducted the audit, meets every two weeks, but soon will switch to a one-a-month meeting schedule, she says.

Update, update, update

3. Make changes where needed:

As a result of the audit, the institution's staff are rewriting the policy on conflict of interest and have already rewritten the scientific integrity policy, Chronister notes.

"It's important to come up with a process that works for a particular institution because federal policy says we have to manage, reduce, or eliminate the conflict of interest in research or in any study," she says.

For most institutions, it's probably best to keep the policy somewhat flexible, Chronister adds.

For example, a policy that is prohibits all conflicts of interest in which a researcher has an overlap with his or her research and some company in which he or she has a personal interest could be too restrictive, she notes.

"Some campuses will say, 'You can't work on that project on campus or have ownership in that company,'" Chronister explains.

And with clinical trial research perhaps it's best to have a strict conflict of interest policy, but an option for other types of research is to have a policy in which some of these types of conflicts of interest are permitted, so long as they are managed with oversight, she says.

"At our institution generally, we would not allow conflicts like that in clinical trials," says Chronister. "But suppose you have a surgeon who develops a new process for thoracic surgery and he has started a company using that process, and the doctor is an expert but has a vested interest — so do you want that surgeon to do surgery or to have someone else do it?"

With animal studies, the institution typically tries to manage conflict of interest with oversight, she says.

Another area that the compliance program found in need of some changes involves the IRB, Chronister says.

New research issues arise regularly and require some adjustment to policies involving IRBs, she notes.

For example, research institutions in California now have to deal with the issue of embryonic stem cell research since voters approved the state's Proposition 71 in November 2004. The state now will invest $300 million a year in human embryonic stem cell research, which could create new research opportunities statewide, but also requires additional policies and rules, Chronister explains.

The new law requires that all human stem cell research be approved by an IRB, and this means that IRBs will need to obtain appropriate expertise to deal with this new area of review, she notes.

"So who do you consent, and at what level is IRB approval needed?" Chronister asks. "We emphasize high ethical standards and some other IRB issues that are important are the selection of subjects and ensuring that appropriate subject populations are used." ■

COMING IN FUTURE MONTHS

- Improve financial compliance following these guidelines
- Establish best practices in effort reporting
- Use humor to improve staff performance
- Here's the latest technology in clinical trial processes
- Learn more about OMB circulars A-21 and A-110

CE/CME instructions/objectives

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.

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. ■

CE/CME *questions*

9. When a clinical trials office is working with international sites, it's a good idea to develop a community advisory board that is separate from the IRB. Why is this a good practice?
A. It helps to ensure that the community is aware of the clinical trial and its purpose.
B. The community advisory board can provide insight into the community's perception of the trial and the community's cultural issues.
C. The community advisory board can assist in educating the community about the disease associated with the clinical trials.
D. All of the above.

10. When writing an estimated budget for a clinical trial, which of the following is not a hidden cost that needs to be included?
A. How long it takes to review a protocol by investigators and research coordinators
B. Time and travel for pre-study meetings
C. CBC charges and other lab costs
D. Cost of subinvestigator staff, advertising costs, shipping costs

11. Clinical trial and research administrators sometimes have to deal with investigators who have difficult personalities. Which of the following is a good strategy for coping with the type of scientist who doesn't bother with the details, such as filing regulatory paperwork?
A. Provide investigator training about regulations, and provide investigators with examples of scientists who faced criminal charges because they had neglected to file federal paperwork related to their research studies.
B. Fire investigators who fail to complete paperwork twice.
C. Submit the investigator's name to a federal regulatory agency for sanctions.
D. All of the above.

12. Which of the following is a good strategy for ensuring that a research institution is in full compliance with policies and regulations?
A. After a federal audit, make the necessary changes to improve the mistakes discovered.
B. Develop a comprehensive audit process that provides a status report of every area that needs improvement, and then follow that up with continuous monitoring.
C. Ask each research employee to complete a form that asks for their analysis of their own compliance with research rules and regulations.
D. None of the above.

Answers: 9-D; 10-C; 11-A; 12-B.