CLINICAL TRIALS
ADMINISTRATOR
An essential resource for managers of clinical trials

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IN THIS ISSUE

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Site relationship management: Sponsors help sites be more productive

Will fewer, high-performance sites get the lion's share of work?

Whether they call it investigator or site relationship management, it seems that big pharma thinks it's just plain old good business. Something they openly admit they hadn't been focused on.

Intentional relationship building

These initiatives, according to **Beth Harper**, BS, MBA, president, Clinical Performance Partners, Keller, TX, are focused efforts by sponsors to intentionally improve relationships with sites for mutual benefit.

"There is site relationship management [SRM], which I prefer, and investigator relationship management [IRM]," notes Harper. "Focusing on the investigator is one piece, implying more of a sales approach. I think focusing on the site recognizes the broader sense of how clinical trials get done," she added.

Being part of the solution

Sponsors have now acknowledged that sites need help meeting contractual milestones. They know, for instance, that an incredibly high percentage of sites overpromise and underdeliver when it comes to subject enrollment. A great many never enroll a single subject.

Add to the mix increased competition over a declining number of investigators and, according Harper, "pharmaceutical companies realized that they had to make efforts to support and protect their business, which includes clinical sites — and to begin to relate to them as suppliers and customers."

Frustrations — and finger pointing — aside, sponsors are increasingly recognizing that they share a common goal with clinical sites, namely to produce regulatory-compliant and acceptable clinical data in a timely and efficient manner. As a result, many of the big pharma players have spent significant time and resources determining how they might help sites work better.

And big pharma has a big stake in helping sites become better performers. Better data, produced more quickly with fewer redundancies translates into speedier NDA submissions to the FDA.

So this year, many companies, including Wyeth, Sanofi Aventis, and Eli Lilly, are rolling out their IRM and SRM programs. They all have their own unique names, but they all share some common (and complementary) principles:

- **Help sites function better.** Sponsors have been working to improve and facilitate communication between sponsors and sites and have made available extensive training and "tool kits" to help sites with trial start-up and ongoing monitoring.
- **Keep trials moving efficiently.** Streamlining, by way of designating a specific sponsor contact, involving investigators in protocol development, and simplifying payment processes, keeps trials on track and running smoothly.
- **Increase investigator retention.** Happy investigators and clinical sites are more inclined to continue working with the sponsor, and with improved function and efficiencies, may be able to conduct more studies. And if one sponsor can monopolize a particular site, that site might get even better — not having to juggle processes and systems from more than one sponsor.

Sanofi Aventis: Partners

Sanofi Aventis' program began at square one. They surveyed more than 5,000 sites to find out where to focus their efforts. The sites were clear in what they wanted: more effective communication between the site and sponsor, better payment processes, properly trained and professional sponsor representatives, and help during trial start-up.

Wyeth: Site Management Breakthrough

Wyeth's program, called Site Management Breakthrough, is a high-tech throwback to the past in some ways. It calls for more sponsor/clinical site communication, but creates a focused internal contact point to streamline the information-sharing process.

With the technology component, Wyeth hopes to cut months off the amount of time sites spend getting started. But in something much more forward thinking, Wyeth is soliciting investigator input on protocol design to decrease delays encountered with IRBs and protocol amendments.

Eli Lilly: Portfolio Sites

The focus at Eli Lilly hinges upon determining the criteria for identifying high-performance sites. Eli Lilly calls these sites Portfolio

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Sites and plans to forge intense relationships with them — sites with the right performance may even be offered right of first refusal on future trials.

Eli Lilly recognizes the potential for several economies of scale with their initiative and envisions that it will reduce paperwork associated with contracts and negotiations, reducing start-up time and allowing investigators to focus on other aspects of the clinical trial such as enrollment.

Good business practices

From a strictly business perspective, this paradigm seems to make intuitive sense and there's no shortage of examples of this kind of customer relationship management in other industries. So what took big pharma so long to see the light?

"There are so many fundamental reasons why it took so long," explained Harper. "Much of it has been organizational and a result of the demands placed on CRAs. Often they were simply focused on managing protocols and data, in a very heads down approach, and lost sight of this side of the supply chain."

According to Harper, to successfully implement SRM initiatives, the role of the CRA must change. "In addition to the core functions, CRAs will be called upon to run point on a new set of skills," she notes. Harper calls these skills the "eight ATEs": collaborate, advocate, negotiate, educate, communicate, appreciate, motivate, and evaluate.

Some also thought that technology would save the day and focused on electronic data capture. According Harper, "technology has helped, but hasn't proven to be the panacea some had hoped for."

Proving performance

With the focus on helping sites improve efficiencies and produce better outcomes, everyone wins, right? Not necessarily. While part of SRM clearly cuts to the heart of finding and nurturing the highest-performance sites, it also means weeding out the underperformers. Eli Lilly's aim to consolidate trials — perhaps even portfolios — with a right of first refusal to those sites that perform best is shared by most sponsors breaking into IRM and SRM.

So what does this mean for John Q. Site? It's time to leverage what the sponsors have to offer. Big pharma calls it a site market, in much the way the housing market is a buyer's market. Sites, especially those with demonstrable performance history, should ask sponsors for access to the tools and resources available in their programs.

Then sites need to continue to prove their value by achieving performance milestones. That appears to be the best guarantee of continued (and perhaps increased) collaboration. ■

NCI provides ethical, legal guidelines for handling biospecimen resources

NCI officials explain recommendations

The National Cancer Institute of Bethesda, MD, decided to address a deficit in quality of biospecimens collected for research purposes with the recent publication of improved recommendations.

"The underlying need of personalized medicine is to have particularly reliable methods to detect certain biomarkers for cancer and other diseases," says **Jim Vaught**, PhD, deputy director of the office of biorepository and biospecimen research at NCI.

"There are a number of initiatives within NCI and elsewhere that led the NCI to believe that or confirm that the quality of biospecimens collected for research purposes is not uniformly high," Vaught says. "And we need to address them on a more consistent basis than has been done before."

The National Cancer Institute Best Practices for Biospecimen Resources, published last summer, provides a blueprint for both clinical trial sites and IRBs with regard to handling research in which biospecimens are collected and studied.[1]

"The ethical and legal issues address five main areas," says **Nicole Lockhart**, PhD, a biospecimen technology program specialist in the office of biorepository and biospecimen research at NCI.

These are the custodianship of biospecimens, recommendations for informed consent, privacy protection, access to biospecimens and data, and intellectual property and resource sharing, Lockhart says.

"What we try to do in this document is discuss existing federal regulations and guidance,"

Lockhart explains. "We would like everyone to adhere to existing guidance and regulations."

While NCI doesn't mandate or recommend a specific plan, the goal is to raise awareness of the issues involved in collecting biospecimens, Lockhart says.

Here are the main areas of ethical, legal, and best policy practices that researchers might need to keep in mind:

• **Responsible custodianship.** "Custodianship is something we are trying to investigate further," Lockhart says. "We held workshops in 2007 dedicated to the issue of custodianship, and we're working on some publications derived from those workshops to try to answer more specific guidance to investigators."

NCI focuses on making any policies transparent so research volunteers know exactly what is happening with the biospecimens.

One of the aspects of custodianship that is difficult involves how the courts have addressed ownership of biospecimens, she notes.

"This gets into the issue of ownership and how the courts have addressed this issue," Lockhart says.

One landmark court decision was the case of *Moore v. Regents of the University of California*, Lockhart says.

The Supreme Court of California decided in 1990 that John Moore had no property rights to a cell line that was developed and commercialized from his hairy cell leukemia biospecimen.

Another case was *Catalona v. Washington University* in which a Missouri judge ruled in March, 2006, that the university, and not the researcher or patient, owned the biological samples under dispute.[2]

"I think what an IRB could do is maybe clarify custodianship when they're looking at a protocol," Lockhart suggests.

NCI uses the term "custodianship" rather than "ownership" because the word better describes the research institution's role in caretaking of the specimen, she adds.

"In most cases the development of a drug involves the use of thousands of specimens, so for any one participant to derive some financial benefit is a stretch," Lockhart says. "If you go down that road you'd never get any new treatments."

• **Informed consent issues.** NCI recommends that the informed consent document should say something about how the research participant would not derive any financial benefits from the development of a drug or treatment that results in part from use of the biospecimen, Lockhart says.

"A lot of patients are fine with that," she adds. "They've seen some of these blockbuster drugs developed for diseases like breast cancer, and they want mass treatments available to help their family and loved ones."

Another informed consent issue is whether the volunteers will receive research results.

"We're not advocating that research results be returned," Lockhart says. "It's a very complicated issue, and people are still trying to determine whether it's appropriate."

But participants should know whether they'll receive study results, she adds.

"We are again advocating transparency," Lockhart says.

"Participants should know whether their data will be shared," Lockhart says. "Researchers need a lot of samples, and research participants need to know whether their samples are shared at their own institution or shipped across the country and used in a collaboration."

The key is to make certain the informed consent document is clear on this subject.

"Some informed consents are specifically for tissue banking, and they might be written in a broader way where the patient consents to donating tissue to a tissue bank," Lockhart notes. "Sometimes the informed consent form will say something about future research use, but these vary in specificity."

Sometimes the informed consent document will say the tissue may be used for future research projects, but these projects will be approved by an IRB, Lockhart says.

"I think as long as the informed consent is well designed and whatever future research is within the bounds of the informed consent, and so long as it doesn't result in additional risk then it should be sufficient," Lockhart adds.

• **Privacy protection.** "Part of our recommendations describes HIPAA and how it relates to biospecimen resources," Lockhart says.

One issue of concern is whether a study can have a general authorization for use of protected health information under HIPAA, Lockhart says.

This issue is an ongoing question, so it's something that investigators and IRBs will have to think about thoroughly.

"Investigators will need to think about what type of data they need and how it will impact how they structure their informed consent,"

Lockhart says.

"Breaches in privacy and confidentiality are rare, but institutions are taking a very protectionist role and being cautious," she adds. "I'm fairly certain that there are public health exemptions, such as a public health emergency."

Protocols should be compliant with all HIPAA regulations, including data encryption and identifiable information, she says.

"HIPAA is not the end-all of privacy," Lockhart says. "There are other means of protecting people."

For instance, privacy and confidentiality can be protected through the use of intelligent bioinformatics and encrypting data, and investigators might use these methods.

• **Access to data and biospecimens.** "We advocate having transparent policies so a researcher who would like to use biospecimens in their research can find out where they can obtain the specimens from and what access policies are in place," Lockhart says.

"Not all resources will be in a position to share samples, but everyone should have defined policies that are equitable and determined scientifically and clearly communicated," Lockhart says. "Generally, an access committee serves the role of reviewing these policies."

The access part of the recommendations was put in the NCI paper because NCI felt there were uneven policies about access across biospecimen resources, Vaught says.

"We want to encourage more open policies about access," he says.

"Not only does NCI feel like the quality of biospecimens access has been inconsistent, but that access to biospecimens has sometimes not been as open as it should be," Vaught says.

For example, some investigators and institutions might be storing specimens and not making them readily available for research for as long as they should, he says.

"We're encouraging access to be more open and specimens to be more available," Vaught says. "They should be more openly available to be used by other researchers."

In general, the NCI paper provides IRBs, research institutions, and investigators with ethical issues to consider and some guidance to best practices.

It should also help IRBs and investigators look at biospecimens in a less clinical way than their scientific backgrounds would encourage.

"Not everyone can see tissue and biospecimens in that way," Lockhart says. "Some cultures place a very high value on any part of their bodies, and in some cases they see it as part of their soul."

Also, there are ethical, religious, and cultural differences in philosophy about biospecimens, and investigators and IRBs need to be sensitive to these, she adds.

"People do feel sometimes an inherent attachment to what's attached to themselves, and there might be some misunderstanding as to the importance of biospecimens," Lockhart says.

"There is a lot of research going on, but if the general public doesn't realize those molecules come from tissues, and if people don't donate blood or let their remnant tissue be used for research, then research won't continue," Lockhart says.

"We want to raise awareness of these issues so there can be greater communication," Lockhart adds. ■

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Do staff speak up when safety or compliance is in jeopardy?

Openness must be part of culture

The health care community has long endorsed staff and patients speaking up when necessary to protect patient safety, but in the heat of the moment, a staff member can be intimidated by superiors and fearful of rocking the boat.

How can you tell if your colleagues will speak up? Finding the answer requires some digging, according to **Grena Porto**, RN, MS, ARM, CPHRM, senior vice president with Marsh, a health care management company in Philadelphia. Employees quickly get the message that the correct response when patients or subjects are at risk is to speak up, but that doesn't mean they really feel empowered to do so, she points out.

"A lot of people want to just say, 'We'll train them, tell them what to do, and they will do it.' In fact, they don't," Porto says. "The culture really needs to support what you're telling them to do.

Encouraging Openness: Is It Just Lip Service?

The health care industry is complex. And to overcome that complexity, we hear much more today about openness and transparency, but are these efforts getting people to speak up?

2006 Internal Audit of the Department of Psychiatry at the University of Minnesota

Following the 2004 suicide of a research subject in a clinical trial investigating the effectiveness of anti-psychotic drugs came four years of litigation — and questions about conflict of interest, recruiting pressure, coercion, ability to give consent, and lack of oversight. In February of this year, a judge ruled that the University of Minnesota had statutory immunity and that there was no evidence that the sponsor's drug caused the death. In the midst of these inquiries, the university launched its own review of internal processes.

Statistics from the internal audit of the Department of Psychiatry revealed many concerns, but with regard to openness and the willingness of staff to speak up, here's what the audit found:

- 39% of the Department of Psychiatry staff responding to the auditor survey said they did not believe they would be protected from retaliation for blowing the whistle on a suspected violation in the department.
- 35% of the Department of Psychiatry staff said in the survey they didn't think their managers provided adequate oversight.

When you're not heard, then what?

More than ever, employees are protected if they come forward as whistleblowers.

In a recent example, the spinal unit of Medtronic will pay $75 million to settle a whistleblower lawsuit alleging that it defrauded Medicare by telling doctors they could bill for an inpatient stay when a cheaper outpatient visit would have sufficed.

The allegations were originally made against Kyphon, which Medtronic bought in November for $4.2 billion.

Medtronic said that the settlement agreement reflects its assertion that neither Kyphon nor its employees engaged in any wrongdoing or illegal activity. The company will sign a corporate integrity agreement (CIA) with the Office of Inspector General for the Department of Health and Human Services, as part of the deal. The CIA focuses on training about appropriate reimbursement advice to customers, and also requires maintenance and implementation of standard compliance processes.

Kyphon charged $3,500 to $5,500 for a surgery kit to treat spinal compression fractures caused by osteoporosis, cancer, or lesions. It was able to keep prices that high by persuading doctors and hospitals to keep patients overnight, which allowed hospitals to charge Medicare up to $10,000 per procedure — even though the patients typically had fully recovered within a few hours, said **Mary Louise Cohen**, a Washington attorney with Phillips & Cohen. Cohen also said Kyphon would only train doctors who had admitting privileges at their hospitals.

The lawsuit was brought under the federal False Claims Act, which allows whistleblowers to sue on the government's behalf.

Phillips & Cohen said it filed the whistleblower lawsuit in 2005 in federal district court in Buffalo on behalf of **Craig Patrick** and **Chuck Bates**. Patrick, of Hudson, WI, was a reimbursement manager for Kyphon, and Bates was a regional sales manager in Birmingham, AL. Patrick left Kyphon after complaints he made about its sales strategy went unheeded, the firm said.

According to an *Associated Press* report, Patrick went to a Medicare fraud conference in 2005. He said he recognized Kyphon's practices in what he saw at that conference.

"At that moment it just became very clear to me: What we've been doing the whole time was Medicare fraud," he said.

Patrick said he presented the situation to Kyphon's VP of reimbursement and general counsel and was told he was not a team player. He eventually took a different job, with a sharp pay cut.

According to the Department of Justice, Patrick and Bates will share $14.9 million. ■

Organizations that want to put all their focus on training the staff are missing the boat, because you have to create a systemwide culture."

Nurses and other staff are astute observers of the employer's culture and will respond accordingly, she says. They are quick to recognize that leaders are preaching about the virtues of speaking up for safety or compliance but at the same time dismissing staff concerns or even punishing those who speak. "It only takes one or two instances to undermine your whole effort. The staff will say they're not going to speak up because they saw what happened to someone else who opened their mouth," Porto says. "Of course, they'll still tell you that they will do the right thing and speak up, because that's what you want to hear. I see that a lot."

Be an agent of change

For a "stop-the-line" culture, in which even the lowest-ranking employee can intervene when patient safety or compliance is threatened, that attitude must be modeled across the board, up to the highest levels of management, Porto says.

At the *Clinical Trials Administrators Conference: Fresh Perspectives on Fundamentals* held in March in Atlanta, **Woody Woodaman**, president & CEO, Synergy Clinical Research Centers, San Diego, CA, recounted a favorite story that illustrates this kind of behavioral modeling.

While working as an administrator in a hospital setting years ago, Woodaman conducted his own informal experiment. It wasn't about direct patient care, but more about the work environment and the image the institution was giving patients and visitors.

"To create change I knew I needed to be a visible example of the change I wanted to create," he said. "So from time to time when I was walking down a corridor, I would bend over and pretend to pick up something and then go throw it away in the trash can."

The results were impressive. "It only took a few times before others had observed my behavior and began picking up after themselves. It was a spark that helped create the ownership and accountability we wanted in our staff."

Local culture can be important

The effort to encourage staff to speak up is worthwhile because each instance of an error, near miss, or policy violation is an opportunity to improve patient safety or compliance, says **Lori A. Paine**, RN, MS, patient safety manager at Johns Hopkins Medicine in Baltimore.

"If we merely see nurses as the executors of provider orders, we miss the opportunity for the nurses to be that final check," she says. "That's how we see nurses, as a vital part of the system, sometimes the last gatekeeper for safety. If they are not empowered to speak up and if we don't listen to them, the organization misses a huge opportunity to improve safety."

Paine points out that, while organizational culture is important, the "local" culture of a staff member's unit or work area can be the driving factor in whether someone speaks up. Even if the overall culture of an organization is on the right track, there may be considerable variability from one unit to another, she says.

"We see this sometimes in our event reporting, which we watch carefully and mine for any signs of problems that we need to address," Paine says. "Sometimes we will see reports that a nurse or supervisor is resistant to reporting from others, or we may also see a sharp discrepancy in the number of event reports coming from one unit. That can suggest that the staff in that particular unit are feeling discouraged from reporting these events to us."

Follow through with support

Staff must be assured that they will be supported by the institution when they act on behalf of a patient or regulatory concern, says **Christy Dempsey**, BSN, MBA, CNOR, previously vice president and director of perioperative services at St. John's Regional Health Center in Springfield, MO, and now senior vice president of clinical operations for PatientFlow Technology, a health care consulting firm in Boston.

"From a management perspective, that's what I did to encourage people to speak up and act," she says. "I told them that as long as they followed the proper procedures [and acted in the best interests of the patient, the institution, or the project], I would stand by them completely and support their actions. I wanted them to feel that they weren't going to be out there by themselves if they stuck their necks out."

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Translational science consortium sets out to improve process

Task force sets sights on multicenter studies

A new consortium of research institutions is seeking to transform the process of translational research, in hopes of progressing more efficiently from scientific breakthrough to patient treatment.

Funded by the National Institutes of Health, the Clinical and Translational Science Awards (CTSA) have taken on a number of areas of concern, including training and mentoring for researchers and designing new clinical informatics tools.

James A. Moran, JD, CPA, is executive director of the Center for Clinical Studies at Washington University in St. Louis, MO, and chairman of the CTSA's Regulatory and Ethics IRB Taskforce, which seeks to work with CTSA institutions — currently numbering 38, but set to increase to about 60 by 2012 — to come up with better ways to achieve multisite IRB review.

Because of the CTSA's goal of improving the "bench-to-bedside" process, Moran says it was an obvious choice to focus on issues surrounding IRB review of multicenter studies.

"We're anticipating an increase in the number of clinical trials we're going to do, and we anticipate they will be done largely through other CTSA recipients," Moran says. "If you have 10 or 20 different sites, all academic, the IRB approval process is a major area of interest, in terms of how long it will take to enroll your first subject."

Faster and better

He says the task force's goal is to find ways to break through institutional bureaucracies to better handle investigator-initiated multicenter clinical studies.

"Not only faster, but better," he says. "That includes the quality of the research itself and also the protections given to our research participants."

Individual institutions have received CTSA grants to work on their own ideas for improving translational research. Moran says his task force hopes to take the best of those ideas and promote them across the CTSA network.

But he says the members of the task force have expressed a desire to go further.

"We've been talking about doing some research on the research process itself," Moran says. "It would mean looking at practices at some of the institutions that are part of this task force and seeing what are the value-added steps, what are the high-quality things that we do, and what things maybe provide more burden than quality — burden to the investigator, burden to the institution."

Currently, he says, the committee doesn't have funding for such research, but Moran says the task force is looking at how they might carry it out.

Articles and regulatory advice

In addition to his new position with the IRB task force, Moran also serves on the consortium's Clinical Research Management Taskforce, which plans to establish a common set of measures across CTSA organizations. One of them would look at the length of the IRB approval process.

"Very soon after we start tracking in a common, consistent way how long it takes to get things done, the next question is how we can improve that," Moran says. "I think that's really the role of this IRB task force — to come up with some concrete things we can do based on the research and based on the available evidence."

Moran says the task force members hope to be able to publish a white paper or journal articles to help disseminate what they learn as they examine the IRB systems at the CTSA institutions.

The task force also could work through common IRB issues arising at its various member institutions.

"When we have common questions that all of the institutions are dealing with, rather than coming up with 24 different ways to do something, there could be a common approach that might be

able to be replicated across institutions," Moran says.

Beyond that, armed with data from the CTSA institutions, Moran hopes the task force could provide some suggestions to regulatory agencies to help form future guidance for other IRBs.

The IRB task force only began meeting in March and Moran concedes that it could be a while before they can achieve all of their goals.

"There are certain things that we can do fairly quickly," he says. "If we were looking at something that an institution did particularly well as a model practice, we can get those model practices out there fairly quickly in the next six to 12 months.

"But these bigger picture things — doing the research, coming back with data, and talking to the regulatory authorities — that's going to be a much longer time frame."

Despite the task force's interest in regulatory issues, Moran says, the goal of this process isn't more requirements.

"The outcome here, we hope, is to come up with a more logical framework across institutions," he says.

Although this is hardly the first effort to address issues raised by multisite review, Moran says he's optimistic that the unique nature of the CTSA consortium can lead to success.

"The collaboration between organizations is very high in the CTSA," he says. "I think that's really a unique approach. Rather than just working on a problem, we're also being tasked with getting the work done — that's what makes us different.

"The CTSA, in order to be successful overall, is going to have to do more clinical trials," Moran says. "We're working on an issue that we think could be an impediment to doing that. So I think these institutions are now motivated to work together to come up with a way that we can do this better."

For more information about the National Institutes of Health's Clinical and Translational Science Awards, visit the consortium's web site at: www.ctsaweb.org. ■

Bridging the Gap Between Research and Practice

Unfortunately, we know that even when an intervention is proven to be efficacious and applicable, it's not always applied," says **Catarina Kiefe**, MD, PhD, professor of medicine and biostatistics, and director of preventive medicine at the University of Alabama at Birmingham, one of 14 new 2008 members of the CTSA consortium.

"The goal of translational research is to bring basic science findings to fruition to better the health of all people. Whereas phase 1 translational research studies the efficacy of interventions with rigid protocols and highly selected populations, phase 2 translational research [implementation research] brings the results of phase 2 studies to large populations and the 'real world,'" explains Kiefe.

"Implementation research is a subset of translational research," continues Kiefe, "and its goal is to bridge the gap between large randomized clinical trials and direct patient care and interventions.

"For example, 10 to 15 years ago, we knew that every heart attack patient should receive an aspirin as soon as they arrive in the emergency room. But only about 60% of heart attack patients were getting that aspirin. Today, it's still not up to 100%. It's probably around 90%," said Kiefe.

"This is a straightforward example, but an important one that illustrates the need for research to facilitate changes in practice patterns," Kiefe explains.

Based on implementation research, investigators play a part in facilitating generalizabilty at the community level. "Consideration must be given to defining exclusion criteria as narrowly as possible," Kiefe says. "Clinical endpoints could be more patient-oriented, as well," she adds, "using health-related quality of life measures, not just physician-defined morbidity and mortality."

How results are presented in the peer-reviewed literature is another way of facilitating incorporation of clinical research into clinical practice. "The discussion section of a paper should address the relevance of the data to clinical practice," Kiefe says. "And the methods section needs to spell out exactly what was done so the practicing clinician can determine whether the results apply to his/her patient population." ■

Laptop theft points to need for checklist to deal with data breach

Consider if and how to notify participants

In this digital age, a breach of personal data about clients or customers is the nightmare scenario for any business, conjuring specters of identity theft and public relations woes.

But for a research institution, the worries go deeper. In addition to financial information, a breach of data from a research project could compromise private medical information about thousands of subjects.

Then comes the decision of whether and how to notify participants about the breach.

That scenario was played out earlier this year in Maryland when a laptop computer was stolen from the car trunk of a researcher with the National Heart, Lung, and Blood Institute (NHLBI) in Bethesda, MD. The computer contained unencrypted research information — including names, birth dates, hospital medical record numbers, and cardiac MRI data — from about 2,500 participants from an NHLBI study conducted between 2001 and 2007.

In a statement released March 24, the NHLBI's director said that the laptop was turned off and password-protected, but that the information shouldn't have been stored on a laptop computer without encryption.

"When volunteers enroll in a clinical study, they place great trust in the researchers and study staff, expecting them to act both responsibly and ethically," says **Elizabeth G. Nabel**, MD. "We at the NHLBI take that trust very seriously and we deeply regret that this incident may cause those who have participated in one of our studies to feel that we have violated that trust."

According to NIH spokesman **John T. Burklow**, the Feb. 23 theft was reported to the NIH information technology department the same day and to the NHLBI's IRB on Feb. 26. Burklow says NIH policy requires primary investigators to report to the IRB any unanticipated problems that could present a risk to subjects.

At its next scheduled meeting, March 4, the IRB voted unanimously to inform participants about the theft. On March 20, the IRB approved a letter to be sent by overnight mail to all participants for whom current addresses were available. Participants were told they should contact the NHLBI if they had concerns about the theft.

The letter explains the incident, points out that Social Security numbers and other financial data were not involved, and reassures participants that the theft "poses a low likelihood of identity theft or financial implications."

"It is, however, an unfortunate breach of our commitment to protect the confidentiality of your research records," the letter states.

Burklow says about 80 participants have called or e-mailed the NHLBI since the letter was sent, about a third of them expressing concern over the incident or wanting more information.

"Several individuals sent e-mails expressing their appreciation for the notification," he says.

In the wake of the incident, Nabel says the institute is ensuring that all NHLBI laptops are encrypted, and that staff have been told never to keep patient names or other identifiable medical information on laptop computers.

In addition, Burklow says, the IRB is clarifying the notification process when a breach occurs.

Breaches common

Kirk J. Nahra, JD, a health care attorney who is co-chair of the Confidentiality, Privacy and Security Workgroup at Wiley Rein LLP in Washington, DC, says such security breaches happen all the time, in every industry.

"There's obviously lots in the health care industry, there's a ton in the academic community," he says. "I take from that a couple of principles — one is that everybody's got to pay attention to this. And a lot of what paying attention is, if it's going to happen, what can I do to reduce the problems from that?"

Nahra says institutions need to think about the problem of data security from two angles: reducing the risk of breach and knowing what to do if one occurs.

"One question is on the front end," he says. "Should they be factoring security issues more into the front-end approval process? The bulk of those approval principles have typically involved privacy issues rather than security issues."

For example, Nahra notes that laptops are stolen every day. For that reason, he says, encryption should be the norm for laptops containing research information.

"I can't tell you it's formally a legal requirement anywhere, but they should be doing it, and

if it's encrypted, you don't have to worry about some of the notice issues."

He says it's also important to pay attention to what is being kept on laptops, and whether sensitive details such as patient names really belong on computers that so easily can go astray.

"You're not going to say don't use laptops," Nahra said. "But if we're recognizing that people use laptops and they're moving around with their laptops and there's sensitive data on them, encrypt them."

To report, or not?

Once a breach has occurred, Nahra says the institution next must decide how serious it is and what reporting is required — either legally or ethically.

He says 42 states currently have laws requiring that customers, clients, or patients be notified in the event of certain security breaches, usually involving the unauthorized release of financial information such as Social Security numbers.

Last year, California expanded its law to include medical information.

Nahra says state laws usually do not require notification if the information was encrypted.

He says the HIPAA Privacy Rule itself does not require notice to study participants if their health information is breached. But it does require that covered entities mitigate, to the extent they can, any harmful effects caused by disclosure of personal, private health information in violation of the Privacy Rule.

"Sometimes mitigation of harm would make you give notice — and it might make you give notice in situations where the state laws wouldn't," he says. "Let's say you have a security breach of [information about] AIDS patients. HIPAA might tell you to give notice even though the state laws might say you don't have to."

Nahra says an institution has to make a complicated judgment when a breach occurs to determine whether participants need to be notified.

"You have a set of incidents where you have to notify, there's another set of incidents where you should probably notify anyway and then there's a set where maybe you'll make a judgment not to," he says. "It requires an assessment every time there's a breach as to whether these obligations are triggered and what it is you're going to do."

If, for example, a laptop is stolen, but the information on it is encrypted, Nahra says an institution might make the decision not to notify participants.

Nahra usually advises clients not to have a set procedure for how to handle a breach, but rather to have a list of questions to ask first.

"Who do we notify? How do we fix it? Who do we get involved in the investigation? How do we figure out what kind of information was involved?" he says. "It's not a one-size-fits-all response."

"If you say, 'We will always give notice of every security breach,' that's not a good answer,"

CNE/CME Objectives / Instructions

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

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

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

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

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

COMING IN FUTURE MONTHS

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- The impact of FDAAA on data stewardship principles
- CDISC standards and research site processes
- Keys to establishing best practices for accelerated study start-up

Nahra says. "There's a negative to giving notice, which is you scare people. And so if there's really not a problem, don't scare people." ■

CNE/CME *questions*

1. With site relationship management programs, sponsors are focused on which of the following efforts?
   A. More effective and frequent communication
   B. Reducing start-up time
   C. More efficient payment processes
   D. All of the above

2. The National Cancer Institute's recent guide on handling biospecimen resources emphasizes one important goal for IRBs and study sites when considering the various ethical and regulatory issues. What is this overarching goal?
   A. Documentation
   B. Transparency
   C. Compliance
   D. Reduce liability

3. To encourage openness among staff, it is important to:
   A. Make an example out of complainers
   B. Create silos to address and contain complaints
   C. Model openness at all levels of the organization
   D. Ignore negative reports from staff

4. The goals of the Clinical and Translational Science awards include which of the following?
   A. To train and mentor researchers
   B. To reduce institutional bureaucracies
   C. To create a logical regulatory framework across institutions
   D. All of the above

Answers: 1. d, 2. b, 3. c, 4. d.