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IN THIS ISSUE

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AHC Media

Research sites should update their disaster preparedness

Focus on communication, data security

As the past year's devastating tornadoes, unexpected flooding, and other disasters have shown, it is impossible to predict when and where a natural disaster might interrupt a city's business as usual.

Areas where research professionals have never experienced major flooding now can find their offices knee-high in water. Places where tornadoes left small, infrequent damage now can span a mile radius and wipe out entire towns within seconds. Hurricanes once meant broken windows; now they can incapacitate a major academic research complex for months.

Disaster planning has become more urgent and personal in the past decade, and research offices are responding with preparations that in an earlier time might have seemed excessive.

Some experts who have lived through one of the recent major natural disasters say it is especially important for clinical research institutions to fully prepare for an event that could wipe out usual communication, prevent access to offices and computers, and disrupt clinical trials for an extended period of time.

In June, 2001, the IRB office at the University of Texas Health Science Center (UTHSC) in Houston, TX, had concluded business as usual on a Friday evening, and by the next morning the basement research facilities had 23 feet of water, and the IRB offices on the ground floor were flooded to the second filing cabinet drawer, recalls **Paula Knudson**, UTHSC special advisor and former director of the committee for the protection of human subjects.

"Tropical storm Allison brought four days of severe rain," Knudson says. "The water rose up from underground springs, so we didn't know that was happening, and no one expected this disaster."

The research building lost all electricity and climate control. The research lab animals housed in the basement were killed by the floodwaters, and the resulting decay created an unbearable odor. No one could stand being in the IRB office for more than half an hour at a time when they were trying to retrieve files and anything else that wasn't destroyed by water, she recalls.

Knudson and other experts learned the hard way how ill-prepared they were for a major disaster. So they offered these suggestions for other research institutions:

• **Set up a communication plan:** From a clinical trials office perspective, communication with subjects is the first disaster planning procedure to consider, says **Alicia Pouncey**, MEd, managing director of Aureus Research Consultants of Metairie, LA.

When Katrina struck the New Orleans area in 2005 it took at least several days to re-establish some communication with staff through an Internet voice mail system. Finding patients is even more difficult, so research organizations need to plan for a major communication disruption, she suggests.

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EDITORIAL QUESTIONS

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"One facility in New Orleans put together a database after Katrina where they sequestered parts of their emergency medical record system," she explains. "And several individuals, who were considered first responders, could access these data across all studies at the facility to identify study patients who might need a follow-up care and a re-supply of medication."

Others used the research institution's website as a communications hub.

"We put information in our health science center website asking subjects to contact the institution with their contact telephone numbers so we could try to get them in touch with the clinicians running clinical trials," says **Kenneth E. Kratz**, PhD, director of the office of research services at Louisiana State University Health Sciences Center (LSUHSC) in New Orleans, LA. Kratz witnessed the aftermath of Hurricane Katrina in August and September, 2005.

After flood waters prevented Kratz and other staff from returning to work in New Orleans, they found that employees, investigators, and research subjects were scattered far and wide. There was no access to landline phones, and cell phone use and Internet contacts were limited, so it was very difficult to re-establish communication.

"We put notices in newspapers in cities like Houston where many of the people had landed, and we hoped that might facilitate their being able to establish communication with investigators," he adds. "We also told our investigators that the IRB would not be able to meet for probably two months, so it couldn't process new studies of any sort."

The Internet provides an opportunity for fast and more easily accessible communication after a natural disaster.

"We moved our email to an offsite server," Pouncey says. "Prior to the storm we had our own server, and we still do, but part of our evacuation plan and disaster standard operating procedures is to switch over operations and go along with the email that's already offsite."

Since Katrina, the LSUHSC research office has educated staff and researchers on procedures to follow during a disaster, including visiting LSUHSC's website for emergency information and directions.

"Many people didn't know to do that six years ago when they left the city," Kratz says. "Now we make sure all of our investigators and employees are aware of it."

The website lists contact information for investigators and research coordinators. It has an emergency preparedness link for investigators. The link tells investigators to inform subjects when they enroll in a study that they if they should have to leave town for

any reason they should call this toll-free number, he says.

"Investigators are asked to give subjects a wallet-sized card with the name of the institution, name of the trial, and contact information, including this toll-free number," Kratz adds.

"My staff monitors that number, and it has a voice mail system located in Shreveport (LA)," he says. "So there's no danger of there being a problem with the phone system."

Once subjects contact the research office through the toll-free number, they are given advice on how to proceed with their treatment, and they're asked to provide their out-of-town contact information," he says.

Communication problems also arose in Houston when Allison hit, Knudson says.

"It's tremendously important to remember that we are responsible for people in studies, so we need to be in touch with our principal investigators to see how they are managing the emergency with their study subjects," Knudson says.

So a good strategy is to start an emergency contact tree. Research offices should obtain all staff and investigators' telephone numbers, including cell phones and contact numbers of family members they would visit if they were to suddenly leave town.

"I have cell phone numbers for each of my staff members, and we make sure they can receive text information," Kratz says.

"One interesting thing after the storm was one day a text message came in from a coordinator," he recalls. "I didn't know how to do text messaging then, but that's how I communicated with her."

Sometimes cell phones might lose their ability to receive incoming phone calls, but they can still receive text messages, which transmit digitally and more quickly, Kratz notes.

Some research institutions plan to use text alert systems in which students and staff are sent a text message with instructions in anticipation of a hurricane or after a disaster.

• **Design research data security measures in anticipation of a physical site disaster:** After Hurricane Katrina, LSUHSC's research office lost much of its electronic information because the IRB building's servers were destroyed due to electrical and heat problems, Kratz says.

"The buildings had high humidity, and temperatures were up in the high 90s and 100 degrees," he explains. "Fortunately, almost all of the information on the servers were backed up at other places, and they were able to reconstruct everything, but that took our IT department a long time."

Since then, the institution has improved its data back-up system so information is stored at multiple sites, he adds.

"My understanding is it's much more secure now," Kratz says. "As a result of the tragedy in New Orleans, the information on servers would not be affected if there were another storm, but it was a significant problem back then."

Offsite data backup and data cloud services are good ways to provide protection against a local disaster, but they can pose other security problems that research sites should address, says **Elizabeth A. Buchanan**, PhD, endowed chair and director of the Center for Applied Ethics at the University of Wisconsin-Stout in Menomonie, WI.

"Seek out external storage sites – that's the future," she says. "Few of us can store our data on just one device anymore."

Cloud services are emerging as a popular option for research sites, but they're also raising some other data security issues.

"As we are putting more and more data in cloud services, saving things in places we're not necessarily in control of, it's creating an interesting contradiction for IRBs," Buchanan says. *(See story on data security in the age of clouds, below.)*

In recent years, many research institutions have moved to web-based systems for IRB and other work, and this creates flexibility in the event of a local disaster, Pouncey notes.

"At any given point they can sign on and access information, and this is a big change," she adds.

There remain data security issues, but things have improved considerably since Hurricane Katrina, Pouncey says. ■

Risks of managing data in the cyber cloud age

Cyber disasters are potential risk

Clinical research sites impacted by hurricanes, flooding, or other disasters a decade ago faced daunting challenges in retrieving files and irreplaceable study data because they either relied on paper or were early in the transition to electronic files.

Now most research sites are invested in electronic files or back-up and so they can protect themselves better against a large, destructive local event. But how protected are they from a cyber-disaster?

Cyber problems could include cloud services that

are hacked into or are suddenly closed down, as well as having natural disasters impact their physical locations.

"If you rely on a third party storage device certainly you have the potential loss if that company goes under, and then what becomes of your data," says **Elizabeth A. Buchanan**, PhD, endowed chair and director of the Center for Applied Ethics at the University of Wisconsin-Stout in Menomonie, WI.

"On the one hand it's a whole lot safer to put data in a cloud and have it backed up somewhere," she explains.

Cloud computing involves a network of remote servers that store and process data. Some in the information technology industry predict there will soon be a time when very few personal computers store their own data and everything will be handled via cloud storage.

"But you have to be very careful of cloud storage because you lose control of data from a disaster perspective."

For instance, the cloud network could be compromised or data could be destroyed, which is why research institutions should make certain their data back-up contractor has its own disaster plan and back-up. Also, research institutions could buy cyber insurance, so if the third party loses data there would be some form of protection, Buchanan suggests.

There are no guarantees, but research institutions can follow some steps to protect their data and subjects in the event of a cloud service disaster, including these:

• **Require strict protections:** "Be sure the cloud has strict protections in place," Buchanan says.

Third party cloud service sites should have strong back-up systems in the event of a large scale disaster, she says.

"By virtue of data being networked, the potential for sharing it is much more enhanced," she says. "We tell subjects their data will be secure; their data will be safe, and we'll protect your identity, but sometimes that might not be 100% accurate anymore."

Researchers can run into ethical challenges when they use outside contractors for storing data, so they need to ensure these entities are taking appropriate precautions against data loss or release.

"There's the rule of three that archivists have talked about for years: original data, back up of data, and back up of the back up," Buchanan says.

Computer server farms where enormous amounts of data are stored are increasing nationwide, a trend that suggests offsite data storage will only increase, she notes.

"I think this is the way it's going to be from now on," Buchanan says.

And data stored in cloud services, maintained in server farms, is fine, as long the highest level of protections are in place.

Researchers need to understand how this works and how it may impact data security. They also should be able to explain this clearly to their research participants, she adds.

• **Create data security procedures and rules:** Research sites should create data security rules that address privacy and confidentiality, risk, and variances from security requirements, which might require IRB approval.

Harvard University has a model data security plan that outlines key responsibilities and procedures, Buchanan notes.

Available online at http://security.harvard.edu, the provides for five tiers of data sensitivity. It also requires investigators to disclose the nature of the confidential data they collect to the IRB for data risk assessment. Investigators also are responsible for preparing and implementing study data security plans and procedures.

IRBs are encouraged to work with information technology staff when assessing the adequacy of researchers' confidentiality provisions.

Harvard's five tiers include a level 3 in which information has individually identifiable data that could be damaging to a person's reputation if disclosed, and a level 5, which describes data that could cause major harm to an individual, including incarceration, psychological damage, and loss of work or insurance.

"Each level has different requirements, and if you reach a level 5, they call this extremely sensitive research information about individually identifiable people," Buchanan says. "And it must be stored and processed only in physically secured rooms and not in an information network outside of that room."

The idea is that some data should not be placed in a network environment, she adds.

"Harvard's data security plan is a very useful model in helping people understand the range of data security issues," Buchanan says.

• **Educate researchers on definition, processes:** Research institutions should ensure investigators are fully aware of how data are handled and what various data security terms mean, Buchanan recommends.

For instance, the Harvard model data security plan includes a glossary link in which various terms

are defined. One example is the term "identity key," which Harvard's glossary defines as a "code used in place of personal identifier(s) in a research data set." This is followed by "identity-mapping file," which is defined as a "data set that can be used to associate identity keys with individuals."

Defining words and terms is important since many researchers may be unaware of this language, Buchanan notes.

Once when Buchanan was speaking in a room of research professionals, she mentioned the term "cloud storage," and someone asked her what that meant, she recalls.

"I asked if they use Google email or Drop Box," Buchanan says.

"People are using these tools, and they don't know what they are," she adds. "We share data in different places, and we're not sure what the rules are when we get into clouds."

• **Consider geopolitical factors when selecting data storage services:** Data concentrated in single large places, called server farms, can be handled more efficiently, securely, and safely during day-to-day operations. But there is always the risk of a major disaster or cyber-attack that could disable the entire server farm.

Research institutions should consider this potential when they select data management service.

For instance, does the country or region in which the server farm exists have any geopolitical vulnerabilities to risks of cyber terrorism, government espionage, major natural disasters, or interrupted electrical power?

Server farms use enormous amounts of power and need to have back-up plans for continuing climate control even when a disaster has incapacitated the local energy grid.

Another factor involves political risk, Buchanan notes.

"There was a great story from Canada of a company that was looking at servers in the U.S. to store bibliographic research material," she says. "Some Canadian researchers said they were uncomfortable storing their bibliographic material in the U.S. when the Patriot Act had just been passed."

They were afraid the U.S. government could use the act to search through their data, effectively compromising any privacy, she adds.

"It's a major consideration for researchers to find out where their servers are located and whether they have to worry about someone looking at their data," Buchanan says. "So researchers need to be aware of different legal boundaries, as well." ■

Common Rule tissue changes elicit objections

Collateral damage could be high

One of the more controversial proposed changes to the research Common Rule involves strengthening informed consent protections related to research involving biospecimens. Some researchers predict these changes could shut down much of their work and result in major collateral damage to the research enterprise.

"I think the changes being proposed will have a major impact on our ability to do research," says **William E. Grizzle**, MD, PhD, professor of pathology at the University of Alabama at Birmingham in Birmingham, AL.

Researchers now can conduct research with existing biospecimens without obtaining informed consent when they've stripped the specimens of identifiers. The proposed changes in the advanced notice of proposed rulemaking (ANPRM), published in the Federal Register on July 25, 2011, would require written consent for research use of biospecimens even when they have been stripped of identifiers.

"They're asking us to consent 30,000 to 50,000 patients a year," Grizzle says. "We estimate it would take three or four fulltime individuals who would do nothing but informed consent, costing us up to $300,000 more to be able to continue doing research at the level we're currently operating."

HHS would be mandating this extra expense at the same time the National Institutes of Health (NIH) has cut its support of research, he adds.

"My budgets now are decreased by 5% to 10%, so we'd have to greatly reduce our service to the research community," Grizzle says.

The U.S. Department of Health and Human Services (HHS) has proposed that researchers obtain consent with a standard short form. It would provide open-ended consent for most research uses of biospecimens, including clinical specimens collected at a hospital.

The rationale behind the change, according to HHS is that changing technology in genomics has increased the amount and nature of information that can be obtained about individuals. Plus, HHS says that surveys show that people want to be able to decide whether or not their specimens can be used in research.

Although HHS' goals may be laudable, some experts commenting on the proposed changes, say

the consequence of the proposed change would be dire.

"This would have a calamitous impact on medical research in this country," writes **Helen P. Cathro**, MBChB, MPH, associate professor in the department of pathology at the University of Virginia in Charlottesville, VA. Cathro submitted a personal comment on the proposal to the Office for Human Research Protections (OHRP). All comments are published online at www.regulations.gov. *(See story with comments to OHRP, p. 127.)*

Obtaining informed consent from every hospital patient who might have tissue used in research is almost impossible, Cathro says.

"It would cost a huge amount of money," she adds. "We've actually tried to get a hospital to do this, and we've had no success at all."

Most of these patients are facing surgery and already have to read multiple pages of documents, she explains.

"So you have to get someone to explain to them all of the ramifications of what will happen to their tissue," Cathro says. "And unless hospitals are forced to pay for this, it won't happen. Research budgets have no money built in for this expense."

There are huge ramifications for the scope of medical research across the United States, Cathro adds.

Without continued access to thousands of tissue samples, some research publishing will slow, the medication pipeline will grind to a halt, and academic researcher careers will stagnate, she predicts.

"If the general patient population were polled on the proposed measures and educated as to the likely implications for U.S.-based research, I have no doubt that they too would oppose it," Cathro writes in her comment. "Using de-identified tissue for research imposes a minimal risk to patients and provides potential large benefit to the future patient population."

The proposed change will have its greatest impact on research involving remnant tissue, Grizzle says.

"One thing I'm sure [regulators] have not looked at is the issue of how various types of bio-depositories will be affected," Grizzle says. "You have one issue when a biobank or depository has specimens from patients who are part of a cohort or epidemiological study because the biobank has an ongoing relationship with the patient."

Bio-depositories that collect remnant specimens that are left over after a clinical diagnosis and would otherwise be thrown away will have a major problem with this change, he notes.

"A big portion of research today is performed on remnant specimens, and that's where they'll have a problem," he adds.

Everyone in the research world agrees that investigators need to obtain informed consent in clinical trials or during any research in which there is a direct interaction with a patient or the potential of harm, says **Christopher A. Moskaluk**, MD, PhD, David Harrison Distinguished Teaching Professor of Pathology at the University of Virginia Health System in Charlottesville, VA.

"The issue is for research that is utilizing both archival tissue specimens and clinical data," he says.

"The proposed rule changes will affect both," he adds. "Right now it is possible to use archival tissue specimens and have access to patient's medical records for certain research projects if the IRB reviews them and feels there will be no direct interaction with the patient and no subsequent consequences to clinical care, and no risk of the patients being associated with the study's data."

IRBs can allow a waiver of informed consent in those instances, he says.

These waivers are especially important when investigators are using many different tissue samples or medical records that may involve hundreds of individuals and samples that date back decades, Moskaluk explains.

"The effort to track down individuals to obtain informed consent would take more effort than the actual investigation, and that's why a waiver is allowed right now," he adds.

For instance, suppose a pathologist or researcher suspects a certain biochemical pathway is activated in breast cancer and this hypothesis should be investigated, Moskaluk says.

"The researcher would get a sizable cohort of maybe 100 cases to see if this bio-pathway is activated," he explains. "But trying to get retroactive informed consent from those 100 individuals is quite difficult to do, and HIPAA regulations would prevent you from doing it directly."

Instead, the researcher would have to contact each patient's doctor and ask them to contact the patient.

"It's a quite laborious, multistep process to obtain informed consent for something that would have no direct impact on the patient's care," he adds. "The goal would be to find something that could move the medical knowledge toward finding new drugs and therapies, so it would be for the good of society."

Also, research involving tissue samples has no inherent associated risk, he says.

"Advancing medical knowledge with no impact in terms of subject risk is something that can be done relatively easily with IRB review when they allow for a waiver of informed consent," he adds. "But

this won't happen in the future under the proposed Common Rule changes."

HHS says that the proposed informed consent changes would apply only to biospecimens collected after the effective date of the new rules. This grandfather clause is critically important if the rules are approved as written, Grizzle says.

"All paraffin block collections in any institution would no longer be of any use unless they're grandfathered," he says. "Trying to consent those patients would be an impossibility."

The Common Rule changes as written would result in a 30% to 40% decrease in available specimens, Grizzle predicts.

The impact on translational investigation would be negative and unnecessary, Moskaluk notes.

"The waiver of informed consent is not a huge insult to the autonomy of individuals," he says. "How much autonomy should people be granted to be involved in research?"

On the other hand, regulations that create onerous restrictions on research can also create harm, he adds.

"If research really is minimal risk and it uses retrospective materials and data, then having to get informed consent could create a financial and logistical burden that would prevent a lot of this research from occurring, and that is a harm to society." ■

Organizations add input on IC with biospecimens

Most oppose wholesale changes

National research organizations and individual researchers have weighed in on the government's proposed changes to the Common Rule, saying regulators should reconsider their plans for requiring informed consent for all biospecimens.

In a comment to the Office for Human Research Protections (OHRP), the American Association for the Study of Liver Diseases writes that the issue of biospecimens is of significant concern to its members.

"We urge HHS to work with interested parties in crafting the policy governing the biospecimens," writes **W. Ray Kim**, MD, AASLD clinical research committee chair, in a letter submitted Sept. 23, 2011.

"We would like to highlight that many of the seminal discoveries made in our field were based upon biospecimens obtained from purposes other than the questions they ended up answering," Kim writes. "We believe it is possible to strike a good balance between fostering opportunities for new discoveries based on archived biospecimens and ensuring protection of private information of research subjects."

If the Department of Health and Human Services (HHS) continues with the proposed requirement of requiring all studies involving biospecimens to obtain informed consent of people from whom the tissue was extracted, the end result will be fewer researchers and research institutions, writes **Helen P. Cathro**, MBChB, MPH, in a personal comment to OHRP. Cathro is an associate professor in the department of pathology at the University of Virginia in Charlottesville, VA.

"This requirement would increase the time and resources by orders of magnitude, and put many smaller academic centers out of the business of research altogether," Cathro comments. "In addition, the cost of funding grants will also increase exponentially, further impacting an already stunted research atmosphere."

The Mayo Clinic of Rochester, MN, in a letter sent to OHRP in September, 2011, comments that HHS has raised an important issue with regard to informed consent and biospecimens, particularly because the current Common Rule requirements are not clear and can lead to inefficiencies.

"Of the possibilities mentioned in the ANPRM, Mayo Clinic believes that a notification and opt-out process would strike the best balance," writes **Robert A. Rizza**, MD, executive dean for research and William J. Tremaine, MD, director of the institutional review board.

"If DHHS considers a notification and opt-out process, Mayo Clinic suggests that it also consider the fact that many biospecimens are not collected by the research institution," Rizza and Tremaine write. "For example, physicians may send biospecimens to a hospital for testing, but the hospital may never interact directly with the patients."

So it may not be feasible for researchers to contact patients, they add.

The Mayo Clinic suggests that HHS consider these options:

- Permit a waiver of informed consent where the biospecimen is not collected from the individual by the research institution
- Make the notification process a national effort, giving individuals who wish to opt out the opportunity to register in a single location. Researchers would submit a query and presume a biospecimen could be used if the individual had not opted out. ■

BEST PRACTICES SPOTLIGHT

Be a nitpicker when it comes to IC form details

Check all signatures & dates

Thirty seconds is all it might take to prevent a weeks-long regulatory hassle.

That's what **Eunice Newbert**, MPH, tells clinical trial staff at Children's Hospital Boston (MA), where she is the manager of education and the quality improvement program.

Study coordinators should spend 30 seconds reviewing each signed informed consent (IC) form to make certain research participants signed these on the designated lines and dated these correctly, she says.

"If someone is asked to sign an informed consent form, they might sign the wrong line if they're given an option," Newbert says. "Parents might sign a witness signature line, and then the form is invalid, and you can't use that patient's data."

Researchers can correct these mistakes after the fact by reporting a deviation and then fixing them, but that takes much longer than a quick little review that is done before the subject leaves the room, she notes.

When research involves children or others who are unable to provide informed consent and need a guardian or other representative to sign the form, additional issues can arise. *(See story on handling guardian signatures, p. 129.)*

Newbert offers these best practice tips for the IC process:

• **Organize the IC template to reflect what the regulations require:** Research sites could prevent common informed consent form mistakes through better organization of their informed consent template.

"Tailor the form for your study and to facilitate your consent process," Newbert suggests.

"This could be by changing the order of the signature line," she adds. "A lot of times principal investigators will sign the form before the subject, and that never makes any sense because the principal investigator (PI) or an organized consenter has to attest that the consent process happened correctly."

When the IC template has the PI's signature first, then people doing consent will obtain signatures in that order, so it makes sense to make the template reflect the process steps timeline, she says.

• **Train staff to avoid fixing subjects' missing date lines:** Another common mistake is for clinical trial staff to date a subject's signature when they discover this was left blank, Newbert says.

Again, that 30-second review could have prevented this problem. But if researchers discover blank date lines after the subject has left the building, then correcting the problem by adding in the date themselves could land them in regulatory hot water.

"I have read FDA warning letters, and next to the problems of enrolling ineligible subjects, the FDA has suspicions of researchers dating another person's signature," Newbert says. "The signature date is one of the few ways the FDA has to determine if the study began prior to the informed consent process."

Although study coordinators might believe it's a trivial difference — their putting in the date right after the subject signs the form, it is no small thing to regulators.

"It's supposed to be the subject attesting to the fact that they are signing the consent form on this date, prior to the first study procedure," Newbert explains. "If you are dating it, how do regulators know that the subject signed it prior to the first study procedure?"

The same reasoning applies if the subject has written in the wrong date.

"It's better to write a follow-up memo, saying, 'It was noted that the subject misdated it, however they attested to signing it on this [correct] date,'" she says. "Just don't correct it for them."

• **Create an IC checklist:** When clinical trials sites begin a quality improvement process to increase regulatory compliance they might create an informed consent checklist, Newbert suggests.

This should list every activity that needs to be done, including signatures, dates, parental permission, and assent, she says.

"Make it as specific as you like," Newbert says.

The checklist also should direct research staff to make routine back-up documentation of the IC process.

"If you lose a case report form you should be able to go back into your files, look at the medical records and verify that data," Newbert explains. "But if you lost the original consent form how would you know the consent process happened?"

• **Require back up IC documentation:** Invariably, there are studies with a missing consent form, so research sites need to prepare for that eventuality.

If a study coordinator loses a consent form, then he or she should have some other way of verifying the informed consent process took place, Newbert says.

"Go back into the medical records or clinical

notes and say, 'At this date the informed consent was obtained,'" she suggests.

Then if a consent form is lost, the researcher should report it to the IRB, sponsor, and applicable agencies as a deviation. The study site might also obtain reconsent from the subject, but these actions are in addition to having the original consent process documented in other records or notes, she adds.

• **Know when to reconsent subjects:** If there is a change significant enough to influence subjects' decision to participate, subjects should be reconsented, Newbert says.

This change could involve adding study visits to the schedule or discontinuing a procedure that might have resulted in a personal benefit to the subject, she notes.

"Give subjects the choice of whether they want to continue," she adds.

• **Always use the most up-to-date consent form:** Even if an informed consent document was not changed, but an updated approval occurred during the continuing review process, study staff should use the form that has the latest IRB approval, Newbert says.

"This is one of the most common mistakes I would see," she says.

If a study coordinators has a new subject sign the earlier version of the IC form, then it's a deviation.

One way to prevent the use of dated forms is to build safeguards into electronic links to downloadable IC forms.

"What our institution did was create an informed consent library for the purpose of minimizing the use of nonactive consent forms," Newbert says.

"Researchers log into this IC library and download only the most recently approved version," she explains. "The link is available only on the IRB website, and we ask people to print out one or two copies."

The library will not permit the download of previous versions of the IC form, which solves one problem but raises two other issues, she notes.

One is that sometimes investigators lose their previous copies, which need to be kept on file, and they return to the library, thinking they can find the older version there. But the library cannot be used for that purpose. Researchers need to keep their own files of older versions of the IC form, Newbert says.

Secondly, on rare occasions, the IRB makes a mistake and has an incorrect version listed as the latest IC document, Newbert says.

"I tell PIs they're responsible for making sure that whatever they're downloading is current," Newbert says. "I tell them to not blindly use the form on the website because they still have to check it." ■

Be cautious when asking guardians to sign IC forms

Relationship status is key

Research sites need to be especially cautious about signatures when they work with children or other populations that are unable to provide informed consent and must have a guardian or legal representative sign the IC form, an expert advises.

It's important for clinical research staff and investigators to check the IC form for what the representative has written on the line that asks them to specify their relationship to the patient/subject, says **Eunice Newbert**, MPH, manager of education and the quality improvement program at Children's Hospital Boston (MA).

"Since we're a pediatric institution, we have a lot of legal guardian signatures," Newbert says. "Whenever there's a parent signature line, there's one next to it that says, 'Specify relationship to the child.'"

Study coordinators should make certain that line has been completed, and they should ensure that the person who is signing the IC form is the person who answers the question about the relationship to the child.

To demonstrate how important this item can be, Newbert relates the story of a situation when study coordinator realized in a panic that the person who had signed the IC document was the nanny and not a legal guardian.

The nanny had brought the child to the appointment and then signed the form, but had left the relationship line blank. The coordinator thought she was the mother, so she filled in the line for her.

"That's a good example of why you should never fill in any information for anybody," Newbert says. "You never assume a relationship."

The situation worked out all right because once the coordinator realized her mistake and called the child's mother and legal guardian, the mother provided the required informed consent, she adds.

In other cases, the adult signing the form could be the child's stepparent, but not a legal guardian. And the step-parent status is indicated on the relationship line. These are situations that should be handled with sensitivity, Newbert notes.

"You don't want to question the person about their guardian status," she says. "We will just report this [to the IRB] and ask for guidance on how to handle it."

In one case, the principal investigator had to have

the stepmother fill out a form, and the father, who was the legal guardian, also had to sign the informed consent form.

"This is why you should make sure people complete the form and you evaluate it," Newbert says. "In that 30 seconds it takes for someone to scan the informed consent form, you can pick up these things."

Other issues can arise when a child's parent has a different last name.

"I'm seeing more and more that the mother and father do not have the same last name," Newbert says. "So if you want to look at the consent form a year later, how would you connect the child and the signed consent document based on the signature alone?"

When this situation occurs, the solution might be to make certain the subject's name is documented on the form, something that at times is overlooked, she adds. ■

Collecting site metrics; do you know what they say?

Ask sponsors, CROs, FDA for feedback

Sponsors, clinical research organizations (CROs), and others increasingly are collecting site-level metrics, along with other data pertaining to clinical research performance. If clinical trial sites are not finding out what their metrics show, then they're missing a good opportunity to improve their operations.

"It's not about the numbers or that red-green-yellow dashboard," says **Liz Wool**, CCRA, CMT, president and chief executive officer of QD – Quality and Training Solutions in San Bruno, CA. Wool is a member of the board of trustees of the Association of Clinical Research Professionals (ACRP).

"It's about establishing metrics and having a series of questions and assessments," Wool says.

The goal is to find a quality site scoring tool, enter in your site performance data, obtain a score, and learn what your risks and areas needing improvement are.

For example, the Metrics Champion Consortium (MCC) of Carmel, IN, provides members with access to a clinical trial metrics tools and activities, including process improvement meetings. MCC's website is located at http://www.metricschampion.org.

"MCC has a lot of presentations that could be a good resource," Wool says. "I have encouraged sites to join the MCC and be at the table as metrics are being developed for clinical trial performance."

Clinical trial sites also could obtain information about their performance metrics from their study sponsors and CROs, she suggests.

"There are companies that keep scorecards on your performance in a clinical trial, and that is the information I've heard that sites would like to know," she says. "I believe sites need to ask sponsors if they utilize a scoring tool, dashboard, or scorecard to evaluate performance, and after the study they can ask for a copy."

Research sites need to know what those indicators are so they can be responsive to improving performance and acting on identified problems, she adds.

Another place where sites could obtain metrics and quality data is the Food and Drug Administration (FDA).

"The FDA has been presenting at conferences for the last year about site inspections for marketing approval," Wool says. "It's called the PAI – pre-application inspection where the FDA gathers information they might have about a site."

The FDA's list of attributes include complaints that have been made about investigators, the number of investigational new drug (IND) permits, and other information collected from sponsors, she explains.

In past decades, the FDA would trust sponsors' analyses, but now the agency has the funding and time to go over a study's metrics, Wool says.

"The FDA runs the database through its own statistical analysis to confirm its conclusion that the drug is safe and effective," she explains. "And they're now analyzing site level data and assigning risk to performance using that information."

Analysis from the Clinical Trial Site Selection Tool results in each site having a risk score that the FDA's Center for Drug Evaluation and Research (CDER) uses to determine which sites will be inspected, she adds.

According to CDER, the different levels or risk attributes are the application level, the study level, and the clinical site level.

For instance, at the clinical site level, the metrics would involve enrollment, protocol deviations, adverse events, subject deaths, site specific efficacy, financial disclosures, complaints, inspection history, enroll/screen ratio, and data about subject discontinuations.

The FDA information is free, so sites can obtain it and use it to assess their own performance, Wool says.

Everyone involved in the research enterprise has a

stake in high quality metrics, which is why a number of sponsors and others have joined the MCC to be engaged with its efforts to create high quality metrics that will be used to identify best practices and improvement needs throughout the industry, Wool notes.

"At MCC there are no politics or posturing," she says. "Everybody is there about the quality of the metrics we want to deliver, and there are respectful collaborative teams."

For example, the MCC also is looking at metrics for measuring protocols.

"Sponsors routinely do not send protocols to sites for feedback on whether they're viable or not," Wool says. "That's an issue we're developing in an MCC working group; that's why we have a protocol scoring tool." ■

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.

To earn credit for this activity, please follow these instructions.

1. Read and study the activity, using the provided references for further research.
2. Log on to www.cmecity.com to take a post-test; tests can be taken after each issue or collectively at the end of the semester. First-time users will have to register on the site using the 8-digit subscriber number printed on their mailing label, invoice or renewal notice.
3. Pass the online tests with a score of 100%; you will be allowed to answer the questions as many times as needed to achieve a score of 100%.
4. After successfully completing the last test of the semester, your browser will be automatically directed to the activity evaluation form, which you will submit online.
5. Once the completed evaluation is received, a credit letter will be e-mailed to you instantly. ■

COMING IN FUTURE MONTHS

■ Experts discuss improving public perception of research

■ Here's how to respond to draft site visit reports

■ Check out these tips on improving the IC form

■ Best practices in using adaptive technologies in CTs

■ Implement corrective actions efficiently

CNE/CME QUESTIONS

1. According to several clinical research experts who have dealt with natural disasters impacting their workflow and offices, which are two top priority areas to consider when creating a disaster preparedness plan?
   A. Transportation and environmental protection
   B. Electricity and computer access
   C. Communications and data security
   D. None of the above

2. The proposed changes to the Common Rule, published in the Federal Register on July 25, 2011, would make what kind of change to regulations regarding research using biospecimens and informed consent?
   A. Researchers would be able to conduct research with existing biospecimens without obtaining informed consent when they've been stripped of identifiers
   B. Researchers would need to obtain written consent for all biospecimens even when they have been stripped of identifiers
   C. Researchers would have to require clinical doctors and hospitals to obtain a research informed consent of all patients who might have a biospecimen sample used in future studies
   D. None of the above

3. When research subjects forget to add the date after signing an informed consent form, what is right way to fix this problem?
   A. Check the form carefully after they sign it to catch the omission and to have the subject add the date
   B. Write in the date for the subject
   C. Write a follow-up memo, noting that the subject misdated it, but attesting to their having signed it on the correct date
   D. Both A and C

4. True or False: Clinical trial sites can have the adult who brings in a child patient for a research study visit sign the informed consent form.
   A. True
   B. False

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