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IN THIS ISSUE

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Research site collaboration builds efficient database for CR sites

REDCap saves time and is good fit

Electronic data capture (EDC) systems are supposed to make data collection and analysis easier and more accurate for clinical research (CR) teams. But often CR coordinators and investigators find the systems to be counterintuitive, inflexible, and difficult to navigate.

A new EDC being used by Vanderbilt University of Nashville, TN, and other institutions across North America resolves this dilemma since it's being designed by a group of CR professionals and informatics experts who specialize in research.

Called REDCap for research electronic data capture, the EDC system has been built by a consortium of research professionals, who are using the software and helping to improve it, says **Paul Harris**, PhD, research associate professor in the department of biomedical informatics and director of the clinical and translational science awards (CTSA) biomedical informatics operations at Vanderbilt University. Harris also developed StarBRITE, an electronic portal that assists researchers with finding information. **(See story on StarBRITE on p. 52.)**

"We were finding that everyone now knows how important it is to have audit trails in your data, to have data capture, and to authenticate users and protect confidentiality, etc.," Harris says. "But I find that in basic clinical research studies there is nothing out there that's easy enough for researchers to use on their own."

With the goal of making data capture easier for investigators, Harris began work on an electronic tools project, which eventually became REDCap, in 2004.

REDCap is a user-friendly database for entering information and tracking people, says **Gail Mayo**, RN, a research services consultant in research support services at Vanderbilt University.

CR coordinators can use REDCap to track study participants, see what information is missing, and note where participants are as the study progresses, Mayo says.

"It allows multiple users on the same database," she adds. "So long as you're at an Internet-accessible computer, you can access information."

One of the ways the Internet and various open source software

programs have evolved and improved over the decades is through sharing the systems with the people who will be using them. Everyone uses the electronic system, tweaks it, and submits their improvements for everyone else to use. Harris set up a similar process for REDCap through a consortium of research institutions that share the EDC system.

"We have an expectation that you help us contribute back to the project and make it better," Harris says. "This is why it's one of the best systems I've ever seen."

There are EDC systems available, but often they lack the flexibility required for CR work, he notes.

"Clinical research studies are different in scope and formulization of systems," Harris says. "We need something fast and flexible to support autism studies one day and diabetes or pain studies the next day."

While all EDC systems collect demographic data in similar ways, they need a great deal more diversity for some of the other details collected in clinical research, he adds.

"This system needed to be flexible and fast, and we wanted to offer it to anyone as a free level of support for their research, Harris says.

The Oregon Clinical and Translational Research Institute of Oregon Health & Science University in Portland, OR, got involved with REDCap after responding to a request for collaboration sent out by Harris.

"There was a small group of collaborators in the beginning, and that's been expanding," says **Hannah Howard**, informatics database analyst at the Oregon research institute. "We've been involved in the collaboration for one-and-a-half to two years."

REDCap has some limitations, which collaborating partners are working on, Howard notes.

"The collaboration works really well," Howard adds. "When there's some technical problem to iron out then smaller subgroups work on it."

The main advantage to REDCap is that it's an application that comes from people directly involved with human subjects research, says **Brian Welburn**, BS, clinical trials data manager at the University of Puerto Rico Comprehensive Cancer Center in San Juan, PR.

"All of these collaborators are people who provide services to people who have databases," Welburn says. "This system is specifically developed for research purposes, and I think it incorporates a lot of the experiments of all of these people who have been working in the research community for years."

The University of Puerto Rico became involved with REDCap after a programmer at the institution visited a research meeting for informatics professionals and learned about the system there, says **José G. Conde**, MD, MPH, professor in the school of medicine and an associate director of the RCMI program at the University of Puerto Rico Medical Sciences Campus in San Juan.

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Editor: **Melinda Young**.
Senior Vice President/Group Publisher: **Brenda Mooney**, (404) 262-5403 (brenda.mooney@ahcmedia.com).
Associate Publisher: **Lee Landenberger**, (404) 262-5483 (lee.landenberger@ahcmedia.com).
Senior Managing Editor: **Paula Cousins**, (816) 237-1833 (paula.cousins@ahcmedia.com).

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Editorial Questions

Questions or comments? Call **Paula Cousins** at (816) 237-1833.

"I contacted Paul [Harris], and then we started to develop this collaboration," Conde says.

As part of the collaboration, the University of Puerto Rico is helping to translate the system into a Spanish version, says **Brenda Nieves**, BA, coordinator of research computing system at the Center for Information Architecture and Research at the University of Puerto Rico in San Juan.

"We're in the process of completing the translation," Nieves says. "Most of the program is translated and is already being used in Spanish."

Here are some of REDCap's features:

• **Customization.** As quickly as investigators can define their data, REDCap can be customized for their particular studies, Harris says.

"We can flip [the information] into a web-based database within five to 10 minutes per iteration," Harris adds. "We've had these take less than a day to go into production mode."

Most of the development time is spent as the research team tries to figure out what will be measured, Harris says.

"We support 140 studies right now in the REDCap project, and we take them as fast as we can get them," Harris says.

• **Training research staff.** Research teams receive one-hour training sessions on how to use REDCap.

The training sessions focus on using the tool, validating numbers going into the database, security, and audit trails, Harris says.

"We teach them about HIPAA [Health Insurance Portability & Accountability Act] security rules," Harris says. "We guide them through the process and talk about case report forms and data export in a number of statistical packages."

There's a brief demonstration and an opportunity to ask questions, he adds.

The training includes sending investigators home with an Excel template model and demonstration that instructs them on how to develop an operational database, Harris says.

"If they do the work on it we'll turn it into a real working model and send it back to them with a data dictionary," Harris says.

"We give all of the research team access to that database," Harris says. "We say, 'Work on this as a team.'"

• **Makes informatics staff time more efficient.** "REDCap allows us with our limited resources to help more people," Howard says. "There's not only the time it takes to develop something, but also the time we're waiting."

The research institution has only a few programmers to create custom applications for all research teams, Howard explains.

"We have six projects in production and three more are in development," she adds.

Also, since programmers now spend less time creating new databases for each research project, they have more time to devote to those projects in which REDCap cannot be used, Howard notes.

• **It's web-based and easy to use once the hard decisions are made.** REDCap is a web-based application that is flexible for all types of research and provides an intuitive interface for users to enter data.

"It's extremely easy to use," Welburn says. "The hardest part is agreeing on fields the investigator would like and the organization of those fields into easy form for optimizing the process."

"When we ask the research team to tell us about interesting parts of their process to create the database, everyone says it helps the science," Harris says. "They say it gives a good working model and everyone can participate."

• **Works with a variety of statistical packages.** "In the old system, we've usually custom-created an extract so they can pull data out," she explains. "This usually happens at the end of the development cycle."

This had to be created for each research project, but now with REDCap it has been created once and is automatic, Howard says.

"I don't have to create anything specific — it's automatically there," she says.

"The data can be extracted directly into statistical packages," Howard says.

This feature provides a good benefit to investigators, Conde says.

"They don't have to spend much time writing code and importing the data," Conde says. "You run it and import it into your statistical software."

REDCap supports exports to SPSS, SAS, R, Stata, and Excel, Harris says.

"This is one of our best features, as literally 30 seconds after finishing data collection, you can get a well-formed statistical file with data labels, coded variables, etc., already in place to start the analysis," Harris explains.

For investigators, REDCap is a more natural approach to database management, Welburn says.

"You can select which fields you want to have in your statistical database, selecting just what you want and not everything," Welburn says.

"This is important for investigators," he adds. "They can say, 'This is the database I got three months ago.'" ■

StarBRITE offers quick answers and support

Links CR staff to everything they need

Call it a one-stop clinical research shop. An intranet web site, called StarBRITE, developed at Vanderbilt University in Nashville, TN, gives clinical research (CR) coordinators, investigators, and other research staff immediate access to clinical trials support information.

"It puts information in a central location," says **Gail Mayo**, RN, a research services consultant with research support services at Vanderbilt University in Nashville, TN.

"It provides a place for [CT] support staff to put things for research staff to access," Mayo says.

"I'm an education coordinator, and from the educational perspective we have a combined education calendar listing for five to six different groups," Mayo says. "All of their education sessions are listed in one place."

The idea for StarBRITE came from the process of applying for a clinical and translational science awards (CTSA grant), says **Paul A. Harris**, PhD, director of the CTSA biomedical informatics operations and a research associate professor in the department of biomedical informatics at Vanderbilt University.

"We virtually looked at all aspects of the research organization to find out where we might do a better job, and one area we thought we might improve was in supporting researchers," Harris says.

The idea was to create an electronic portal to assist researchers in finding and connecting information, Harris adds.

"We didn't want to reinvent the wheel," he notes. "Like most academic institutions we have pretty good IRB systems in place, a good contract system in place."

However, there are programs that don't reach their potential, and there are duplication efforts among administrative units, and these problems could be resolved through an electronic portal, he adds.

"We thought that if we built this portal for researchers and their teams and keep it as thin as possible, it would work," Harris says.

So far, the project has been successful with between 30,000 and 35,000 web page hits within the first five months and 1,200 unique users.

Researchers can go to StarBRITE to link IRB system data and clinical research data, extracting the relevant information that they need for their day-to-day work, he explains.

"It's leveraging data across multiple entities with the idea being that we want to deliver to the researcher just-in-time information for doing their jobs today," Harris says.

StarBRITE also lists funding request programs, and it updates staff about policies and procedures.

"In the fall, we'll develop a new set of procedures for study monitors/industry monitors/CRAs to gain access to confidential information," Mayo says. "So when they come from industry to monitor studies and gain access to confidential information, we can make sure it's all done appropriately."

StarBRITE gives the CT site a place to put this new information, Mayo adds.

The web site also provides a template for developing customized action plans (CAPs).

"It asks investigators a series of questions; they answer them, and it helps them determine which application processes they need to move forward for approval of their study," Mayo explains.

This includes IRB approval, biosafety committee approval, etc., she adds.

"StarBRITE helps investigators determine which application processes they need to use," Mayo says.

For example, Vanderbilt has a program that provides seed funding to investigators for pilot studies that could lead to bigger projects funded by government or industry grants, Mayo says.

"The whole program is hosted in StarBRITE," she explains. "It's an amazing portal where investigators and staff go to this one place and find resources that support everything from funding to application to data collection."

StarBRITE is more than a portal with a bunch of links, however.

"There are sections that are just informational in content with static content to show researchers," Harris says. "In many cases, we see the need to build down deeper in functionality."

For example, one of the deep components of StarBRITE is the REDCap database system.

"REDCap is a great tool," Mayo says. "It makes data more reliable and gives you a better vision of where you are with your study and the data you've collected."

Since REDCap was created by research and information technology experts, it's a better system for data collection and data analysis than a

system that most investigators would create for themselves, Mayo adds. **(See cover story about REDCap, p. 49.)**

When researchers and staff first take a look at StarBRITE, they see a colorful screen with button links for research planning and implementation, templates, and other information.

There's a link to a registry where people can sign up for Vanderbilt research studies, and there are links to various funding sources, including the institution's pilot funding mechanism.

"The piece on-line is a micro-grant or voucher where a researcher who needs a little money to see if the concept will work can apply and take it to the next level," Harris explains.

"On StarBRITE, the researcher can find out right now what he needs to do to obtain funding within Vanderbilt," he adds.

The data management link takes one to REDCap, and educational resources provide information about academic workshops involving research, Harris says.

A governance dashboard provides information about registry and REDCap utilization to a select group of users, Harris says.

"The voucher dashboard allows us to look at who is using the voucher system, what level in any month of applications is provided," Mayo says.

The biggest challenge StarBRITE has presented is getting out the word about its features and availability, Mayo notes.

"The big challenge has been getting out the word to investigators that they can look in one place, instead of many different places, for information," she says. "We've done grand rounds and staffing group demonstrations to help them understand they need to take time to investigate it."

Ultimately, the goal is for everyone in the research community to use the portal, Mayo says.

"This is the place that the staff and users can come to for an initial evaluation of their research," Mayo says. "They won't have to search throughout the whole Vanderbilt system to find answers to their questions and needs."

Instead of contacting individual departments, researchers can get on-line and find roadmaps and plans that will help them through the research process from beginning to end, she adds.

"Also, the [research] staff have the ability to access information promptly by going into StarBRITE instead of calling us up with questions and having us send them documents," Mayo says.

For example, if the study will require study monitors to access confidential information, then the study coordinator can go onto StarBRITE and find out step-by-step the details of what needs to be done, she says.

"This allows us time for other projects, like developing more tools and templates," Mayo says. "It should, hopefully, shift and change our roles as support staff." ■

Workshop series gives research coordinators professional updates

Topics range from budgeting to HIPAA

Research coordinators come from such a wide variety of backgrounds and experience that it can challenge institutions to meet everyone's educational needs.

Weill Cornell Medical College in New York, NY, has solved this dilemma with its workshop series called the Research Coordinators Network.

The network originated from an annual IRB submissions orientation program for research coordinators, says **Jonathan M. Cohen**, research integrity coordinator of Weill Cornell Medical College's division of research integrity.

This annual event included speakers from the IRB, pharmaceutical industry, and others, Cohen says.

The sessions, which began a few years ago, quickly drew in more attendees than anticipated, and these included investigators, post-doctorate students, graduate students, administrators, and others, he says.

Due to their popularity, the institution started the monthly workshop series in 2007. A National Institutes of Health (NIH) grant helped the institution start the new research training program to target research coordinators, as well as administrators, new principal investigators, and research staff at other local institutions with whom Weill Cornell has cooperative research agreements, Cohen explains.

Each workshop lasts 2.5 hours and includes PowerPoint presentations and handouts. There's a pizza lunch, and the typical attendance is 60-80 people, Cohen says.

After each workshop, attendees receive an evaluation form that asks for requests for future

workshops. This way the attendees help to direct the topics selected for workshops, he adds.

"There's a lot of turnover in the research community, which is one reason why the ongoing education is so important," Cohen says. "It's a job a lot of people have for only a couple of years and then, maybe, they'll go into graduate school or to work for industry."

One recent session was on the pathology review process, a topic that drew attendees from both the research side and from the pathology department.

"We had a lot of people from the pathology department because they wanted to know what they could expect research coordinators to know about pathology," Cohen says.

Here are some of the workshop topics:

• **Pathology review process.** This workshop covered the study of disease tissues and a very detailed and intensive examination of the disease process, Cohen explains.

"Investigators from many different clinical specialties will rely on pathology services within their trials," Cohen says. "So there's a separate pathology review component of the protocol review process, and pathology has to sign off that they have the facilities to do the microscopic studies that the investigator is calling for."

The pathology department has to make certain the study won't interfere with any pathology obligations the hospital has for patient care and that the department will be paid for its work, he adds.

"It used to be the pathology review was part of the IRB review process, but it was changed to go through pathology as a separate process," Cohen says. "People submitting a protocol to pathology need to know what goes on in pathology and what the department handles so that their forms aren't rejected."

• **Budget process.** This workshop covers grant submissions, contracts related to clinical trials, billing compliance, and budgeting.

"A big part of a grant proposal is budget justification," Cohen says. "You have to account for how the money is spent in terms of personnel and equipment, and various granting agencies have very strict requirements in terms of what are acceptable expenditures."

Once an investigator receives a grant, he or she is accountable to the institution for the money.

"In clinical trials, because you often have medical procedures being done in the hospital and the hospital has to get paid for that, there's a form that describes exactly which procedures the research subject is going to be required to pay for as part of normal care," Cohen explains.

The workshop session also covers budgeting and how budget justification is a part of the grant submission process.

"The investigator describes how the money is spent, including salaries and time," Cohen says.

• **Study organization and compliance.** "Research coordinators need to keep their study organized and ready in case of an audit," Cohen says. "I think the biggest issues with audits tend to be you have to keep clear records of the consenting process."

Study volunteers sometimes say they expected something different than what occurred during the study, he notes.

"To prepare for that possibility, which might be unfounded, you need to show what they consented to, what you did, and how you kept records for the entire informed consent process," Cohen says.

"Since the consenting process is reviewed by the IRB, if you deviate from the consenting process that was reviewed then you're operating an unapproved consenting process," he adds.

Also, researchers need to list all key personnel on the study, including the PI, co-investigators, clinic nurses, research coordinators, and others.

There should be documentation of oral informed consent, and someone needs to keep track of who administered the consent form and make sure that if the IRB-approved protocol says the physician will give informed consent that the physician indeed handle the informed consent, Cohen adds.

• **Data security and HIPAA.** "This office reviews HIPAA compliance for every protocol that will collect protected information," Cohen says.

Investigators have to complete forms listing how the data will be kept, which data will be kept, and how the data will be made secure.

For instance, if there's a paper file, is the filing cabinet located in an area where patients have access, and is the cabinet locked?

"And if it's on a computer, it better not be on a public computer," Cohen says. "Or if it's on a personal computer, is it password protected?"

• **Workplace conflict resolutions.** A previous educational outreach officer had a background in conflict resolution and had worked for the New York City Public Schools for many years, doing conflict resolution workshops, Cohen says.

"So this is a conflict resolution workshop that

discusses interpersonal problems and how to work around them," he explains. "The workshop covers strategies for dealing with a difficult boss and what to do when administrators in other departments don't do what you asked them to do."

The workshop had 52 attendees, he adds.

Some future workshops will cover the topics of hematology/oncology, departmental compliance issues, and research ethics.

"We work on these two months in advance," he says. "This office is working more closely with the department of medical ethics, and the ethics department said when we met with them that they would like to present what they do to the research community network."

In this way, the workshops help to facilitate communication between researchers and study coordinators with various college departments and administrators, Cohen says.

"They want to disseminate what goes on in their department, and they want research coordinators to know what is going on," Cohen adds. ■

Compliance Corner

Here are tips on staying compliant with Medicare reimbursement rules

Systematic oversight is important

Clinical trials administrators and investigators should make certain their processes and practices clearly assign research health care services to the correct payer, an expert advises.

The Centers for Medicare and Medicaid Services (CMS) last year attempted to revise standards for research billing, but ended up leaving the rules as complex as they have been since the last change in 2000, says **Mark Barnes**, JD, counsel for Ropes & Gray of New York, NY. Barnes also is the executive vice president of the Saint Jude Children's Research Hospital in Memphis, TN.

Basically, Medicare will pay for any standard of care services received by a patient who also is a research participant, Barnes says.

"Services that exceed standard of care and those delivered in support of an experimental therapy are not covered," he says.

But this only applies to services that are only associated with the experimental therapy, and are not associated with standard of care therapy, a distinction that was changed in 2000, Barnes notes.

"Under the pre-2000 law, if a patient received standard of care with a regular FDA-approved cancer therapy and also received infusion and hydration therapy for a standard of care drug, then all of this would be covered," he explains.

"But if the same patient had the same diagnosis and same illness and the same standard treatments, but instead of receiving the standard of care drug was receiving an experimental drug, then the old law would say the infusion and hydration therapy couldn't be billed to Medicare," Barnes adds. "So that left a real discrepancy."

The problem was that Medicare had a general rule that any service provided to support an experimental drug or device or procedure would be excluded from Medicare coverage, even if the supporting service was standard of care, he says.

Then in 2000, Medicare decided to eliminate the application of the non-covered services rule and allow patients on experimental protocols to receive the standard of care services and bill these to Medicare, Barnes says.

The biggest challenge research hospitals now face is how to implement Medicare's rules regarding which services should be billed to Medicare and which should be billed to the research project.

"The difficulty is our billing systems for billing insurance are set up in such a way that they don't distinguish between services rendered in standard of care and those rendered in clinical trials," Barnes explains. "They go out by manual processing or automatic servicing."

Institutions need to design a research compliance system that takes into account what is billable to Medicare and what is not, he suggests.

"A hospital or clinic or practice must design a billing system so that it segregates the standard of care services delivered to that patient from the non-standard of care services delivered to that patient and only bill the non-standard of care services," Barnes says.

There are two practical approaches to achieving this system: One would be a mechanized system, and the other is a manual processing system.

"You have to know which patients are on active protocols and which are not," Barnes says. "So the first step is flagging on the paper chart or

electronic records which patients are in the research protocol."

Then the mechanized or manual system needs to decide which services given to the research patient are standard of care and are billable to Medicare, Barnes says.

"One can program this into the electronic billing system form, or you can have a nurse or clerk in the billing coordination process put these in by hand," he adds. "The problem now is that the computerized billing systems, which were designed in the 1960s and 1970s and then revised in the 1980s and 1990s are not designed to do that."

One best practice compliance offices should follow is to have investigators do an analysis from the beginning of a trial about which services in the research protocol are standard of care and which are not, Barnes suggests.

This analysis should occur with both electronic and manual systems.

"Don't err on the side of calling everything standard of care," Barnes says. "There needs to be compliance oversight for the physician, and the physician investigator needs to do this analysis for the entire protocol."

Also, there should be someone checking the investigator's analysis to make certain there's logic in the decision-making process, he adds.

"When you look at literature for what is standard of care, there is a lot of information about addresses established clinical pathways," Barnes says. "These should be compared to the protocol when deciding what is standard of care and what's not."

Finally, even when something is legitimately billable to Medicare, if that service has already been paid for in the research grant or in the research contract, then the investigator cannot bill it to Medicare, Barnes says.

For example, if a major pharmaceutical company has included payment for a particular service into the clinical trial budget and has paid for this service for research participants, then the research institution cannot take that money and bill for that service, Barnes says.

Research institutions that make billing mistakes due to omitting the oversight process run risk of a federal audit, he notes.

"There have been a number of high-profile audits around the country where CMS has investigated inappropriate billing," Barnes says. "CMS is very active on this issue, and it's been on their master work plan published annually for the last several years." ■

Military clinical trials pose unique challenges in subject recruitment

Potential subjects could be deployed

Imagine recruiting for a clinical trial when a big portion of your potential volunteers might be sent to the other side of the world half-way through a study.

Patience is a key philosophy among clinical trial investigators and coordinators for the Naval Medical Research Center (NMRC) Clinical Trials Center in Silver Spring, MD. They need a great deal of patience when dealing with recruiting among a military population.

"When recruiting military personnel, you need to have a supervisor's approval because these individuals are ready to be deployed at any time," says **Victoria Steinbeiss**, BSN, RN, clinical nurse coordinator for the NMRC. The Clinical Trials Center has been involved in Phase 2a trials that test experimental malaria vaccines.

An ongoing trial is designed to assess the safety, tolerability, immunogenicity, and protective efficacy of a multivalent, adenovirus-vectored *Plasmodium falciparum* malaria vaccine. Volunteers are healthy adults who have never been exposed to malaria and who will actively participate in the trial for about one year.

Since enlisted men and women often travel to and from countries where malaria is prevalent, there's an additional challenge in finding malaria-naïve military volunteers who will not be sent to another country during the trial's duration.

"So you have a research study that may go from one year to five years, and these individuals might not qualify because they have to be deployment-ready," Steinbeiss explains. "And, often, their supervisors are not at liberty to give them permission."

Also, civilian staff are required to do the actual recruiting for the trials so there isn't the potential or appearance of undue coercion as there might be if an officer were attempting to recruit enlisted men and women for a study.

Since deployment is a ready possibility for many military personnel during wartime, studies also will enroll non-military volunteers.

"We have a military population, but to have more options we can recruit civilian volunteers,"

says **Jose Mendoza-Silveiras**, MD, Clinical Trials Center director at NMRC.

"But to recruit civilians we need permission through the Secretary of the Navy [SECNAV] that will allow civilians to participate in the studies with a SECNAV designee status," Mendoza-Silveiras says.

Without this approval, studies are restricted to enrolling only military volunteers or their dependents, says **Judith Epstein**, MD, CDR MC USN, a clinical investigator at the NMRC.

"In some of the larger trials it can be difficult to recruit enough people," Epstein notes. "So we give a description of the trial, provide all background details, include the protocol, and a whole packet goes through the chain of command."

Once SECNAV designee status has been approved, the trial can recruit civilian volunteers.

"There are a lot of issues to be dealt with in gaining approval, but for us it means we can open our enrollment to civilians," Epstein says.

Traditionally, military trials have been half civilian volunteers and half military volunteers, she notes. "Now we have more civilians because of the issues of deployment," Epstein says.

Steinbeiss has seen how the recruitment challenges are greater now than they were pre-2003.

"I have seen over the past five years of working in the military research community how there has been an impact [from the Iraq war] in recruiting," Steinbeiss says. "There aren't as many [enlisted men and women] stationed in this vicinity right now because they have been deployed."

Most of the NMRC 's studies have been for the development of a malaria vaccine that could one day be used by the military to protect enlisted personnel, Epstein says.

"Also, we're trying to develop vaccines that could be used in the developing world, where it could be given to children," she adds. "Every minute there are two to three children who die of malaria; this is an incredible tragedy worldwide."

Although there are prophylactic prevention strategies for malaria, there always is the issue of compliance, and these options aren't practical in the developing world, Epstein says.

The NMRC is part of the U.S. Military Malaria Vaccine Program, which has a long-established experimental malaria challenge, Epstein says.

Vaccine trial volunteers are given the malaria vaccine. After several weeks, volunteers are challenged. Five mosquitoes carrying malaria are placed on the volunteer's arm, inside an ice cream cup. The malaria strain used is completely susceptible to the most common treatments, Epstein says.

After the volunteer is exposed to the malaria-infected mosquitoes, the volunteer waits for 30 minutes on site. They may then go home and are followed-up by telephone, she says.

"One week after the challenge we have them check into a location where medical staff will watch them closely. They reside there until approximately 18 days after the challenge," Epstein says. "We follow them very closely and do blood smears every day to see if they've developed malaria."

"During the day and evenings the volunteers are free to pursue their normal activities — it's only at night that they are asked to come to the hotel. It can be a lot of fun gathering in the evenings, eating Chinese take-out together," says Epstein. "Volunteers can avail themselves of the hotel's amenities, such as movies and the fitness center."

"As soon as we document that they have malaria, they receive treatment and we ensure that they adhere to treatment," she says. "Volunteers are always cured completely, although they may feel sick for a day or two during treatment. When finished with the study, they are 100% free of malaria, and to date, no volunteers have had long-term consequences from participation in a malaria challenge conducted by the Navy."

In one trial on two sites, the NMRC is recruiting 44 volunteers, Epstein says.

"We estimate it will take us three months to get the initial 18 volunteers we need to start," she adds. "Prior to their first immunization, we have a three-month screening period."

In the first group of the study, there will be 12 volunteers who will receive the vaccine and six controls who will not receive the vaccine, but who will receive the malaria challenge.

As one site's enrollment is underway, another site's enrollment begins: "We usually have rolling enrollment," Epstein says.

Each volunteer, whether military or civilian, receives some financial compensation per visit, in the range of $25 to $50, Mendoza-Silveiras says.

The amount depends upon the procedures and time required, and the compensation is approved by the IRBs, Mendoza-Silveiras says.

"I came into the military after completing all of my training," Epstein says. "When I first thought of the military doing clinical trials, I wondered if there could be a potential for coercion with young, junior officers participating."

The opposite is true, Epstein says. "The military goes to extreme measures to prevent coercion from occurring," she explains. "They realize there's quite a bit of scrutiny, so auditing and monitoring tends to be of a high standard."

Despite challenges posed by military recruiting, the clinical trial work at the NMRC has been rewarding, say Mendoza-Silveiras and Steinbeiss, who are civilian contractors.

"We have a great team," Mendoza-Silveiras says. "We know each other's jobs, and we're capable of doing everything when somebody's out — we cover each other."

Plus, investigators and study coordinators know their vaccine work is meaningful.

"We're a close team, and we enjoy working on these vaccine studies," Steinbeiss says. ■

Best Practices Spotlight

Informed consent process pays close attention to details, habits

Checklists and logs help

When a research institution is trying to stay compliant and keep track of the voluminous paperwork filed during the clinical trial process, it helps to use logs and checklists that capture each small detail.

CRI Worldwide of Clementine, NJ, has developed a best practice in which logs and checklists help clinical trial staff with study checks and balances.

For instance, the research organization receives many revised informed consent documents, says **Terry Smolenski**, CCRC, director of regulatory affairs at CRI Worldwide.

"We keep track of those by a log I created," Smolenski says. The log notes why there is a change in the informed consent since it was IRB approved, and it details when study coordinators received the revised document, she says.

The most typical reasons an informed consent document might be revised involve a change or update to the study's risks and when an investigator's brochure is updated, Smolenski notes.

"Changes to the consent document are all done through the sponsor," she adds. "If there's an amendment to the protocol, it's done through the sponsor, and so they send it out to the site level."

Before the institution receives an amended change to the consent form, the investigator will have gone to the sponsor and IRB with the proposed change.

By documenting precisely when informed consent document changes were logged in and by whom, the institution stays in compliance with all regulations and rules.

"So before the sponsor audits [the study site], we can look and see exactly what day [the revised consent] was given to the coordinator," Smolenski says.

It's important that investigators and study coordinators do not overlook the latest informed consent revisions, so the institution also has what it calls a "consent-in."

"This is where we go into the consent bin and update documents in there to make sure the most recent was in there," Smolenski says. "We fill out a form and put on a cover sheet that says the protocol number and which changes were made to the consent document."

They further alert staff to the change by using red paper.

"It tells them what's changed in the consent form, so if a coordinator is busy or if somebody picks it up, they'll know exactly what was changed in it," Smolenski says. "We also put tabs on the consent bins so the most recent approval date is there so the staff can look at that and make sure they're using the right one."

Regulatory affairs professionals give study coordinators the changed and approved informed consent document as quickly as possible so they can use it when giving informed consent to new participants and for giving revised informed consent to existing participants, Smolenski says.

The institution's best practices go back even further in the process.

For example, there are quality assurance analysts at the sites. Their job is to monitor the consent process and oversee everything done at the sites to make sure it's all in compliance, Smolenski says.

"They do spot checks on the CRF [clinical research form], and they notify the quality analyst at that site and let them know by e-mail when there's a new consent document," Smolenski says.

This way the quality analyst can make certain the revised document is being used and can make certain study coordinators are re-consenting all participants, using the revised document, she adds.

For another best practice, regulatory affairs professionals refer to checklists when assessing the initial informed consent form.

"When we get the initial consent, we have checklists to go through," Smolenski says. "We go through the consent process and make sure all elements are there and are required by the regulations and HIPAA [Health Insurance Portability and Accountability Act]."

If investigators find some elements missing, they need to return to the sponsor and IRB and let them know about any upcoming changes, Smolenski says.

"It's amazing the things you will catch," she says. "Ultimately you're responsible if you're not using a good consent document."

Smolenski researched what should be on a consent form and perused the regulations on informed consent before creating the checklists.

The checklists include these types of items:

- The informed consent document tells volunteers that their participation is voluntary;
- It tells volunteers that if there is any new information it will be given to them as investigators learn of these;
- The informed consent document should clearly state that the study involves research, explain the study's purpose, and describe the procedures that will be done;
- It should describe anticipated risks and discomfort to the subjects and outline the duration of their participation;
- It should give the approximate number of people who will be involved in the research and describe any benefits the participants will receive;
- The document should provide a name and contact information for someone the participant can reach in the event of research-related injuries;
- There needs to be a disclosure of alternate procedures or treatments to participation in the study;
- Documents should have a description of HIPAA with an end date listed for how long the information might be used, or if there is no end date, then there should be a statement describing how the study is open-ended;
- Also, there should be a statement about the confidentiality of records;
- And there needs to be a statement about how if a participant refuses to participate in the study it will result in no penalty or loss of benefits;
- Finally, there typically is a statement relating to the risk to fetuses and embryos.

"Usually, if I see something is missing from the informed consent document, I'll bring it to investigators' attention, and I'll give them sample language to use," Smolenski says.

The checklist is followed after the study receives IRB approval and all of the IRB's suggestions for change have been incorporated into the informed consent document, she says.

"Once we have everything in place, the informed consent copy is sent to the study

CE/CME Objectives / Instructions

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

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

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

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

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

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coordinator, and it goes into our consent bin at the site," Smolenski says. "So if one of our doctors sees a potential subject, and the doctor feels the person might be appropriate for the study, then he might go to the consent bin and copy the consent form and read it to the patient." ■

CE/CME *questions*

17. Which of the following is an advantage of having an electronic data capturing system that all investigators might use?
    A. It will simplify the process of setting up a new database for each study.
    B. It saves time for informatics research staff.
    C. It's design can make it more flexible and user-friendly than what would otherwise be available.
    D. All of the above

18. Which of the following best describes Medicare's regulations regarding reimbursement for patients involved in a clinical trial?
    A. Medicare will not pay for standard of care services that are given in support of an investigational drug, device, or therapy.
    B. Medicare will pay for any standard of care services received by patient who also is a research participant; services that exceed standard of care and those delivered in support of an experimental therapy are not covered.
    C. Medicare will pay for investigational drugs, devices, or therapies, but only in Phase III clinical trials.
    D. None of the above

19. When conducting a clinical trial that has a duration of one year or longer in a military setting, which of the following is a major challenge?
    A. Recruiting volunteers who will not be deployed during the time period of the study
    B. Finding people who will want to participate
    C. Obtaining IRB approval for recruitment tactics and informed consent
    D. All of the above

20. Which of the following should be included in an informed consent checklist?
    A. The informed consent document tells volunteers that their participation is voluntary.
    B. The informed consent document tells volunteers that if there is any new information it will be given to them as investigators learn of these.
    C. The informed consent document should clearly state that the study involves research, explain the study's purpose, and describe the procedures that will be done.
    D. All of the above

Answers: 17. (d), 18 (b), 19. (a), 20. (d).