The CRA

A Key to Site Effectiveness

BY DENISE MYSHKO

The responsibilities of the clinical research associate are evolving beyond simply monitoring. Technological advances mean CRAs are becoming more involved in site management — helping sites get the study started, as well as assisting with the enrollment of patients.

ELECTRONIC DATA CAPTURE AND OTHER CLINICAL-RESEARCH TECHNOLOGIES ARE HAVING A FAR-REACHING IMPACT THAT EXTENDS BEYOND JUST THE QUICK AND EFFICIENT GATHERING OF DATA. Clinical research associates — employed by the sponsor or CRO to review study records to ensure that a trial is being conducted according to the protocol — are finding that their responsibilities are shifting toward data management.

"Forward-thinking companies are now using their monitors for more critical activities," says Ken Light, management executive at BusinessEdge Inc. "They are leveraging CRAs to help drive investigator knowledge transfer and training, with the more administrative monitoring tasks being done electronically."

As technology becomes a larger part of trials, CRAs will find their roles expanding, making it possible for them to monitor more sites while the technology handles the routine tasks.

Scott Freedman, president of monitorforhire.com, agrees that while CRAs are still responsible for ensuring that the sites are following clinical practice and SOPs, as well as the protocol, they are taking on more in the way of data management.

"We conducted a survey a couple of years ago on the adoption of technology; it revealed that monitors have become very sophisticated and that with the emergence of technologies in a number of trials, their role is changing in

Some of the newer technologies have removed the tedious and repetitive tasks traditionally performed by monitors, but they are still required to check source documents against case report forms.

With EDC and other technologies, **by the time a CRA gets to a site, many of the queries have already been identified**; therefore the monitor is free to handle other site-management responsibilities.

Truly superior CRAs have training in "soft skills," such as how to motivate sites, how to deal with difficult people, expertise with patient access methods, and good time-management skills.

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terms of data management and assisting on the data management side," he says.

Some experts predict that the CRA of the future will be more of a site manager, helping with patient recruitment and facilitating rapid study start up.

According to Sandra Garrett, Ph.D., president and CEO of Medifacts International, the CRAs involved with remote data capture are moving from data "verifiers" to site managers.

"I would say 75% of their time is focused on patient recruitment, and the rest of their time is spent reviewing regulatory documents and other source documents that cannot be verified through remote data capture," she says. "In the future, I believe they will be responsible for training clinical coordinators in the field to make sure the remote data-entry process is facilitated in the most efficacious way."

According to Kim Oliver, director of clinical operations at Kforce Clinical Research Staffing, EDC and other technologies have meant that by the time a CRA gets to a site many of the queries have already been identified, therefore the monitor is free to handle other responsibilities.

"Monitors are becoming less of a box checker/data verifier," she says. "Traditionally, a monitor verifies source documents against the CRF, such as a blood pressure. With advancing technology and a movement away from 100% source document verification, the monitor can focus more on site management, such as training site personnel and helping to develop patient-enrollment plans."

John C. Huber, VP of clinical operations at ClinPro Inc., says the role of the monitor has become more complex, and CRAs have a widening sphere of influence.

"Monitors have to be careful not to introduce bias into their monitoring practices," he says. "Maintaining objectivity and observational integrity are critical to investigational drug profiling. I can imagine a future for monitoring that entails further separation between the monitor and the sponsor's interests."

Demand for CRAs is Strong

The CRA typically is required to oversee the initiation, progress, and conduct of the clinical trial to ensure the scientific integrity of the data collected and the protection of the rights, safety, and well-being of human study subjects.

Training in good clinical practices and ICH guidelines is important since CRAs need to verify the documentation of the informed-consent process for each study subject. In addition, they must ensure that adverse experiences are properly documented and reported, review the case report form against the subject's medical record for completeness and accuracy, and ensure the required regulatory documents are filed and maintained.

"If CRAs are using technology properly, they won't necessarily have to go to a clinical site until the site has answered all of their queries," says Edward Ikeguchi, M.D., chief medical officer at Medidata Solutions Worldwide. "CRAs now are able to view the problem spots occurring in clinical trials. They can focus their attention on the sites that aren't accruing patients as they should, that have numerous or longstanding queries, or that have inordinate numbers of adverse events and other problems."

According to Mr. Huber, the majority of clients' requests are for monitors with specific therapeutic experience, whereas in the past a generalist was easier to place.

"Advances in specialized therapeutic areas have led to a demand for CRAs who have specialized knowledge and skills," he says. "There is still a demand for the CRA who can learn and adapt quickly. It is becoming more challenging to meet some of the demands of the industry in terms of CRA skill sets in specific therapeutic areas."

Ensuring CRAs receive appropriate training is important.

Medifacts starts its CRA training with a comprehensive corporate orientation to help them develop better relationships with other departments, such as data management, regulatory, QA, and safety.

"After that, we focus on giving CRAs additional therapeutic training as well as training on the individual protocol," says Amy McNeeley, senior director of human resources worldwide at Medifacts.

Dr. Garrett notes that one of the best training opportunities that Medifacts offers CRAs is

A Day in the Life of CRA Sally: An Independent Monitor

THERE'S NO QUESTION THAT BEING AN INDEPENDENT CLINICAL MONITOR IS DEMANDING. SO WHY IS THIS ONE OF THE FASTEST-GROWING JOBS IN THE CLINICAL-RESEARCH FIELD? THIS IS AN ACCOUNT OF A "TYPICAL" DAY IN THE LIFE OF AN INDEPENDENT MONITOR.

Sally is working on three trials: two oncology trials and one for a new pain medication. She monitors a total of 23 sites, visiting most of these once a month to check patient charts and case report forms, reconcile the study drug log and review regulatory binders, and discuss the overall trial progress and changes with the site. In between, she stays in touch with the investigator and clinical research coordinator (CRC) to stay up to date on enrollment, protocol questions, and site supplies. She also checks in with the sponsor to make sure there are no updates she may have missed while she was traveling.

6 a.m. — MONDAY

The alarm rings. It's time to get a jump on the morning's e-mail; there are 25 to answer before Sally leaves to catch a plane for the scheduled site visit.

Like most days, Sally's morning began the night before: filing reports, checking enrollment forms, and reviewing site files for the week. Her sponsors want expense reports on Mondays, so she was up late.

Today's visit is something new. The patients in this trial are using hand-held devices to enter their data, so there are no source documents to verify rating scales. They sync the Palm with the computer nightly to upload the data, and Sally checks this online. For some reason, the data from Friday are missing for 15 patients. Sally leaves a message for the CRC to look into this and e-mails the sponsor that she will follow-up on the problem.

E-mails answered, Sally checks her supplies — case report forms (CRF), drug return envelopes, FedEx labels — all the things a monitor needs to set up a mobile office. It's a travel-intensive job. Even though most of her sites are within 200 miles, she's on the road about 50% of the time. This is better than when she first started as a full-time monitor and had a much wider territory. Then, she was on the road at least 80% of the time. She checks the weather report, prints her boarding pass, reviews her auto rental reservation, and grabs her travel bag before dashing off.

8:01 a.m. — IN THE CAB

Time to check voice mail. The office is already calling: "We sent 75 queries yesterday to the investigator site at 4 p.m. that need a 24-hour turnaround. Make sure they get them done. Also, where is the diary data from Friday!? Thanks."

The phone rings. It's another site with a question about site responsibilities. Who does the sponsor need updated financial disclosures from, and what is the start date for site personnel on the signature log? Also, who should the site submit the invoice to for the latest newspaper ad for recruitment? Sally spends 10 minutes talking them through their questions.

10:13 a.m. — ON THE PLANE

E- mails have started rolling in — 17 in the last hour. She answers these and takes five minutes to balance her checkbook. Sally calls the site and finds out they haven't received the queries. She calls the in-house team again to resend them.

11:07 a.m. — TOUCHDOWN

Sally goes to the car rental. As she's getting in, she receives a call from the project manager about the queries. The office now needs them by 3:30 p.m. Sally checks her PDA; there's a message from a sponsor. Can she do a prestudy visit next week? Sally checks the schedule. Yes, she can do it. But it will mean pushing back vacation at least a month. She sends a note back. "Yes, I can do it. Send me the site contact information." She makes another call to the travel office to book her flight and auto.

12:30 p.m. — AT THE INVESTIGATOR SITE

Sally arrives and signs in. She spends a few moments talking to the CRC, asking how things are going and if she needs anything. They talk about the trial subjects. One has withdrawn from the study over the weekend. There are 12 more who have been screened. The CRC had forgotten to add those to the enrollment log.

As a former CRC, Sally understands their pressures, and she tries to get to know the site staff. It

to spend time doing in-house data review before a database lock.

At Kendle, a specialized group, staffed by dedicated training professionals, coordinates the training of new associates, says Christopher C. Bergen, the company's president and chief operating officer.

"This training is typically delivered in a classroom setting for basic therapeutic knowledge and soft skills," he says. "Training also is done at the project team level by the project leader and lead CRA for areas such as protocol-specific training and functional expertise training. Finally, there is a good deal of on-the-job training that is provided by the CRA's senior managers, who have accumulated a breadth of drug-development experience."

But training can only go so far. There is a high demand for qualified CRAs who have specific experience in some specialty categories.

"Many of the large pharmaceutical companies, as well as many CROs, have moved away from hiring entry-level people and training them; their preference is to bring in qualified people who can hit the ground running," Mr. Freedman says. "On the other hand, there are still some CROs that bring in study coordinators or people who have worked in other clinical R&D roles and train them as monitors."

One area where there is particular demand is oncology.

"There is a perception, be it real or not, in the industry that oncology studies are different," Ms. Oliver says. "Sponsors want people with an oncology monitoring background or who are trained in oncology nursing. Most of

helps to get things off on the right foot and puts a human face to the sponsor. It's still a people business underneath the forms. Anticipating the site's needs and communicating these to the sponsor can avoid 50% of the problems.

12:47 p.m. — AN AIRLESS CONFERENCE ROOM

Needing space to work, and with all the exam rooms occupied, the CRC clears the table in a renovated storage space now used as a conference room. First up: check the CRF and review the 12 newly screened subjects. Nine met inclusion/exclusion criteria. Two were slightly over the allowable weight, but there are documented waivers from the sponsor for them. One of the subjects was six months over the allowable age of 65, and the sponsor was not informed. Sally informs the site that it will have to forward a protocol violation form to the sponsor and inform the IRB of the oversight.

It's 1:30 p.m., and she's still reviewing case report forms. This site has 34 patients so far and counting.

Sally checks her e-mail. "We sent those queries more than two hours ago and haven't received any answers yet."

Normally, she could talk the site through this on the phone. But since she is onsite, she sits with the CRC and answers them one by one.

Her cell phone rings; another site has questions. These will have to wait until she leaves for the day.

2:23 p.m.

Sally tackles the problem of the missing data. Eight patients forgot to sync their handhelds the night before. Problems with PDAs prevented the other six from uploading the information, and the data are lost. The site has to add source notes to all of the charts and call tech support to inform them of the issue. They must also e-mail the sponsor with specifics on each subject and which data were lost.

3:00 p.m.

Back to the queries: Sally checks more charts and helps the coordinator request more study medication from the vendor. She pulls the CRC aside to finish the queries. Thirty-two done so far…

3:30 p.m.

Queries done, and Sally returns to verify the study drug. The coordinator has to leave to see a subject who is currently in the study. While she is troubleshooting the subject's PDA, it starts smoking. The CRC dashes off to grab the fire extinguisher! Errant equipment extinguished, the coordinator gives the patient a new PDA and puts the old one aside to ship back. The remainder of the afternoon is spent counting pills and reconciling the drug dispensation log.

6 p.m.— A BRIEF BREAK

Sally goes to the hotel, checks in, changes, and heads to the hotel fitness center. Then she goes back to the room to check e-mails and head out for a walk and some dinner.

8 p.m. to 11 p.m. — IN THE ROOM

Time to follow up on the day's work: four reports and three follow-up letters to write, review, and send. Sally saves itineraries from the travel department and checks the weather for the next week.

She reminds herself to call her husband and give him the bad news about their vacation. She checks tomorrow's travel arrangements, and the day is done. The late e-mails can wait until morning.

ALL IN A DAY'S WORK …

Being a monitor can be a trial in-and-of itself. In the past, few would make it through the five-year mark. Today, monitors are staying in the field longer and often are making it their life's work.

That is because of a number of factors, including a deeper appreciation of the monitor's central role in running a trial, efforts on the part of employers to provide improved salary opportunities, and more options to work locally.

Additionally, more monitors are becoming independents to take advantage of greater flexibility and opportunities for work/life balance. Ultimately, most experienced monitors will say they are happy with their chosen field and regard it as their long-term career option.

DR. SANDRA GARRETT

our requests are for monitors who have at least five years of oncology training."

In trials where remote data capture is being used, **CRAs are less focused on the review of data and instead can focus on other aspects of the trial**, such as patient recruitment.

She says sponsors are asking for monitors who have experience with specific technologies or who are located in nontraditional site hubs.

"Because there is so much competition for patients, sponsor companies are going into secondary markets, for example, Little Rock, Arkansas," Ms. Oliver says. "They want locally based CRAs, which is a difficult request to fill at times because there may not be an adequate pool of highly trained professionals to draw from in these secondary markets."

Some experts say it's not just the secondary markets where the talent is lacking; there also is a shortage of good, available people because of increasing demand and rising expectations.

"There is pressure to try to do more with less," says Suzanne Ives, a senior strategic pharmaceutical business resource at BusinessEdge. "This is resulting in new challenges that sponsors didn't have to deal with before."

DR. EDWARD IKEGUCHI

If CRAs are using technology properly, they can focus their attention on the sites that aren't accruing patients as they should, that have outstanding queries, or that have adverse events and other problems.

Managing the CRA Workforce

Dr. Garrett says of all the staff groups within an organization, it is probably most difficult to recruit, train, manage, and retain CRAs.

The more qualified CRAs are in high demand and typically have multiple opportunities from which to choose, Mr. Bergen says.

"For this reason, prospective employers need to have something that makes them stand out from the competition, such as a supportive culture, interesting assignments, training and career development opportunities, and other compelling reasons to join their company," he says.

Experts say a staff that is organized regionally — instead of remotely — can address some

CROs and Monitors

CROS ARE LEARNING THAT THEY CAN GAIN FROM A BROADER VIEW OF OUTSOURCING AND THE TACTICAL AND STRATEGIC BENEFITS IT OFFERS.

Cosourcing of contract monitoring can offer significant margin advantages to CROs, even large ones, seeking to optimize total financial performance under variable demand scenarios. High costs of recruiting and training are avoided, offsetting margin declines from using contract monitors in place of in-house staff. It is estimated that two-thirds of CROs' use of outsourced monitoring is tactical.

Increasingly, CROs are finding that outsourcing monitoring can confer strategic advantages, particularly for companies pursuing aggressive business plans. For these CROs, outsourced monitors offer a ready source of experienced, therapeutically specialized, geographically localized talent that complements in-house monitors. Because they are farther along in their careers by the time they enter the outsourced monitor market, these monitors tend to have more years on the job, with higher educational attainment than the typical corps of in-house monitors.

Thus CROs can use outsourced monitoring to leverage their core competencies, expand market share, and offer a broader scope of services than they could without the benefit of outsourced monitoring. Through tactical and strategic outsourcing, CROs are achieving higher revenue, better margins, and the opportunity to win business that was previously unwinnable.

Clinical monitoring is a major line item in most CRO contracts, and therefore a major source of CRO revenue. Clinical monitoring provides more than 30% of the Phase II to Phase III revenue of the top five public CROs (Covance, Kendle, PPD, ICON, and Parexel). An intelligent strategy for outsourcing this activity requires CRO management to decide which of its activities are differentiating and which are not, retain what is, and consider outsourcing the rest.

Internet-based providers of contract monitoring services offer a rationalized business process that eliminates several steps common to insourced (from the CRO's perspective) provision of monitoring. Specifically, recruiting, interviewing, and preemployment background checking are automated on the Internet. Severance, human resources, and payroll functions are absorbed by the employee or eliminated.

As the Internet approach has gained favor, providers in this highly competitive market have begun to move beyond pure Web-based applications, integrating more and more into the back-office operations of their customers. The result is faster delivery of monitors to projects, improved quality of monitors brought to the team, consistent customer management reporting, and measurable cost reduction versus an expensive and culturally damaging hire-and-fire approach to managing variable demand for monitors.

Source: Hovde Associates LLC, Kennett Square, Pa. For more information, visit hovdeassociates.com.

We've looked at what frustrates CRAs and why they choose to leave. Many of them have a difficult time with remote IT support.

So we built an internal IT department that works with them to make sure that they can be productive.

of the travel concerns inherent with the role of a monitor.

"We work very hard with our sponsors to match the right person in the right regional location with each study so that people do not have as many overnight travel demands," says Judy Swilley, VP of clinical monitoring at Charles River Laboratories Inc. "Today, there is more focus on the expansion of regional CRA teams than there has been historically."

For a CRO, managing staff workflows can be even more of a challenge. Medifacts shifts CRAs into the data-review arena when work slows.

"We like to have additional CRAs employed by the company who may not be 100% dedicated to a project," Dr. Garrett says. "They can use their time for other related activities, for example, in-house data review. This real-world experience gives them the opportunity to look at the consequences of the quality of their monitoring, of the data query, and of the data resolution. This can be a sobering experience. Monitors see first hand the impact that inefficiencies in the field have on the overall data-management team. There is a powerful domino effect."

She says there are also other benefits.

"First, this allows us to retain employees," she says. "Second, it reduces the likelihood of burnout. Third, it gives us the support staff in the data management, data review, and data-query process during peak times when we're getting ready to close databases. And fourth, when we are at peak volume, we don't have to hire data reviewers on a contract basis." ✦

PharmaVOICE welcomes comments about this article. E-mail us at feedback@pharmavoice.com.

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