

## Monitoring Change Among CRAs

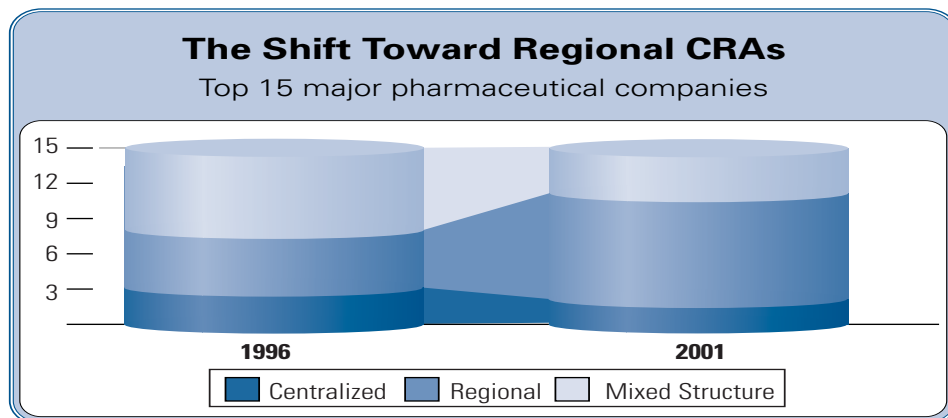
► Regionalization, improved compensation and the growth in freelance opportunities have all contributed to establishing the CRA function as a more permanent career.

► Under regulatory, economic and technological change, the CRA role continues to change and evolve suggesting a shift in CRA specialization, workload and responsibilities.

Long considered one of the toughest and critically important jobs in clinical research, the role of the study monitor—otherwise known as the clinical research associate (CRA)—has been steadily changing.

A majority of sponsor companies now support a regional CRA structure and primarily look to fill the monitoring function with individuals who have general skills rather than therapeutic area specialization. CRA salaries and employment incentives have improved significantly, at the same time that their roles and responsibilities have expanded. New communication and eClinical technologies are changing the ways that CRAs monitor investigative sites. And the FDA now views CRAs as an important mechanism to identify noncompliance and misconduct. Since 1996, for example, the number of CRA audits conducted by the FDA has nearly quadrupled from six in 1996, to more than 20 in 2002.

Historically, turnover among CRAs has been higher than any other clinical research function due to grueling travel schedules, poor pay and lack of respect. Changes in company practices, regionalization and the rapid growth in freelance monitoring have



Source: CenterWatch

contributed to improved job satisfaction among CRAs. Investigative sites have consistently rated the quality of CRAs as one of the top five most essential factors contributing to study success. Yet sites give most sponsors and CROs low marks for CRA quality and turnover. Several sponsors—Lilly, Merck and Pfizer—have improved CRA quality as evidenced by positive feedback from their sites. These top sponsors report that their CRAs are better organized and that they now offer improved training programs for them.

“As their role and responsibility continues to grow, the CRA becomes even more indispensable. For the sponsor or CRO, the CRA is really the person who makes or breaks a study,” said Karen Woodin, Ph.D., a former CRA and CRA manager, now working as a consultant. “And that has to do not only with their monitoring of the data, but also the many intangible aspects of knowing how the site is doing. The CRA is truly on the front line looking for problems at the site.”

### Growing Responsibilities

The CRA’s primary responsibilities in a clinical trial are to ensure that good clinical practices are followed, that the site complies with

regulations and that the study’s objectives are met. They monitor data and conduct thorough source document verification, carefully checking case report forms (CRFs) and physician records to see that patients are appropriately enrolled and studied, and to ensure that the data they’re given matches the data on the patient’s chart. The CRA also checks to see that sites are complying with increasingly complex regulations.

That job is not getting any easier. Technologies—such as laptops, hand-held devices, cell phones, pagers and the Internet—have helped CRAs become more efficient. But like most other jobs, the technology has also led to additional responsibility. “They’re not just going out to the site and comparing source documents and case report forms,” explained Susan Gould, director of clinical operations at drug delivery firm Control Delivery Systems. “They’re actually now able to filter the data, look for trends and generate queries back at their home office.”

Louis Kirby, M.D., a principal investigator at a site in Arizona, believes that CRA job complexity has increased due to a tightening regulatory climate. “It used to be just the FDA

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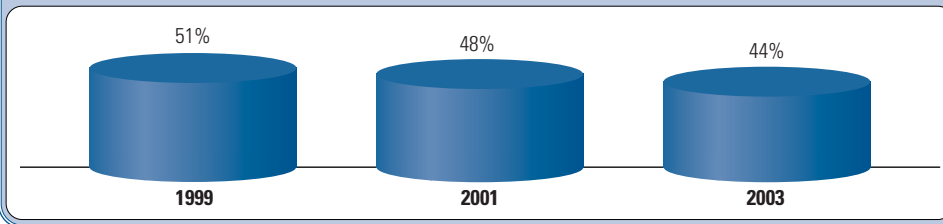
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**Quality of CRA Staff**

Percent of sites rating CRA quality "Excellent"



Source: CenterWatch, U.S. Investigative Site Surveys

guidelines. Now it's ICH and FDA guidelines with HIPAA on top. As the regulatory environment has become more complex, monitors have had to respond," he said. As a result, said Kirby, CRAs are spending 20%-30% more time at the sites.

Being on the front lines, the CRA is uniquely positioned to be the interface between the project team and investigative site personnel. As such, sponsors and CROs increasingly look to their study monitors to perform additional duties on a trial. At the outset, CRAs may find investigators for a study, evaluate sites and weigh in on their selection. CRAs are involved with negotiating grants and contracts. Pre-study visits and initial investigator meetings are frequently coordinated and run by CRAs. After the study is completed, the CRA will likely be the person the sponsor expects to wrap up any final details.

Study monitors are also at the hub of multi-site projects, acting as a direct link among sites that might otherwise not communicate. Sites routinely refer to the CRA for updates and information about the protocol and experiences with it, as well as other ongoing study-related matters. Under competitive enrollment, CRAs are often asked to share aggregate multi-site project enrollment information and tips on successful recruitment.

Attending to these diverse duties means a CRA first and foremost needs to be flexible. Equally important, the CRA must be efficient, organized and detail oriented. Good

CRAs also have solid interpersonal skills—they're comfortable with people, so that they can consult with the site and with the sponsor to keep the study running smoothly, and negotiate the twists and turns that can come up during the course of a trial. Finally, though CRAs must ensure good practices are followed, a top CRA is not so strict as to not know when to bend the rules.

"You really are the eyes and the ears of the study and that requires the ability to make observations while wearing multiple lenses," said Jessica Donahue, an independent CRA and project manager. Woodin added, "CRAs have to be the enforcer on studies to be sure things are done right. But at the same time they have to be able to coach people and make them feel good about what they're doing. It takes a special kind of person."

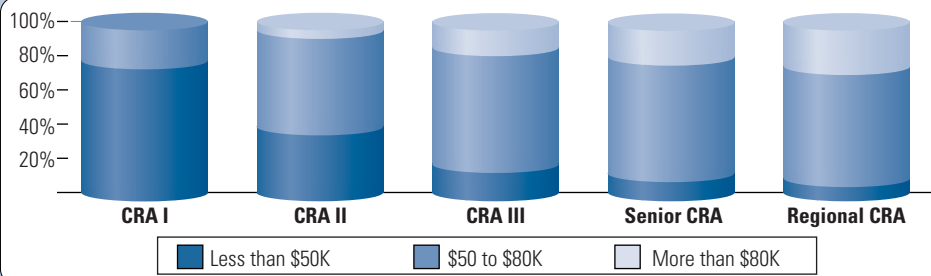
**An Improving Career Path**

Study monitors typically work long hours and travel extensively. For CRAs operating out of a central office, travel schedules can be particularly onerous. And historically, CRAs have been paid relatively modest salaries for demanding and intense work. All of this has been a recipe for burnout and high turnover.

The CRA's job has traditionally been seen as a stepping stone instead of a career path. Until recently, as many as 80% of working CRAs did not make it past the five-year mark. Typically, young, largely female study monitors cut their teeth at CRO companies, which have long served as a rigorous and reliable

### CRA Salary Ranges

Percent earning annual gross salaries



Source: CenterWatch Analysis, 2003

launching pad into the pharmaceutical industry. CROs offered an entry-level job at entry-level pay and a chance to receive immediate direct experience before moving on to a new position. Many study monitors progressed to corporate management positions, including CRA managers and clinical project managers.

Though still in the minority, the number of people who view field monitoring as a permanent career is increasing, in part due to economic changes.

“In the past there wasn’t as much of a premium placed on CRAs with many years’ experience. You just needed a warm body essentially to go out, collect the data and bring it in. So you didn’t look for the person who had five years’ experience and probably wouldn’t have found them anyway. But now there’s a recognition that somebody who is particularly experienced in a single therapeutic area could really provide a lot of sophistication to running a trial. And they are being paid accordingly,” Gould said. Monitors are now commanding far more competitive salaries. Many field-based CRAs now earn salaries approaching six figures. Freelance monitors can earn \$100 to \$125 per hour.

A recent CenterWatch survey of careers in clinical research finds that CRA salaries are growing faster than almost all other job functions as demand for experienced study monitors has increased. Competition for experienced CRAs, as a result, has intensified. At the same time, market consolidation (e.g., mergers and a down economy) has contributed to declining tenure rates. Whereas in 2001, 50% of CRAs reported less than three years with a company, in 2003, nearly 60% fall into this group.

The industry is doing its part to maintain a higher level of overall CRA experience through much improved and expanded training programs. Ron Montgomery, a former Upjohn CRA who is now a consultant, observed that while years ago few companies offered training, “Now you have any number of training courses put on by trade associations, conference planners and other private institutions. Corporations are much more intentional about training CRAs than they were 15 years ago,” he said. Donahue agreed. “Today’s training programs are light years away from the paltry training I received at a CRO in the mid-90s. At that time, your training was really baptism by hellfire.”

“It is very clear that sponsors and CROs now recognize the huge importance of CRA experience,” noted Kirby. “We’re now reaching a point, particularly with CROs hiring monitors, that there’s a much higher overall level of experience shared by monitors in the industry. Ten years ago this was not the case.”

### The Power of Regionalization

Though the pendulum of centrally based and regionally based field monitors has swung back and forth during the past two decades, regionalization is now the primary structure embraced by nearly all major pharmaceutical companies. In a review of the top 15 largest sponsor companies, for example, nearly 80% utilize a regional approach.

The prevalence of regional CRAs is the result of cost controls and a desire to improve job satisfaction and investigative site relationships quality. Regionalization has helped companies lower travel costs and measurably improve CRA quality of life. The advantages

for both employer and employee are significant.

A centralized CRA can travel as much as 80% to 90% of the time. These CRAs regularly leave Sunday nights and return home late in the week. While still traveling to multiple sites, regional CRAs cover a tighter geographic area and are often home in time for dinner each night. Because there are no security checkpoints, no delayed flights, no airport traffic, or other problems, a regionally placed CRA might spend 50%, or as little as 30%, of the time away from home.

Most CRAs like working regionally and feel it gives them the best of both worlds—the work they enjoy and a more balanced lifestyle. Given the demographics of the typical CRAs—who tend to be younger women of childbearing age—regionalization offers the ability to manage work and family life.

“Companies are maximizing their dollars and putting people in strategic areas where they need coverage,” said Donahue, who claims that she used to travel 100% of the time. “They can’t afford to spend a whole heck of a lot of money on travel, and they are trying to make sure that they cover those areas where sites are located.”

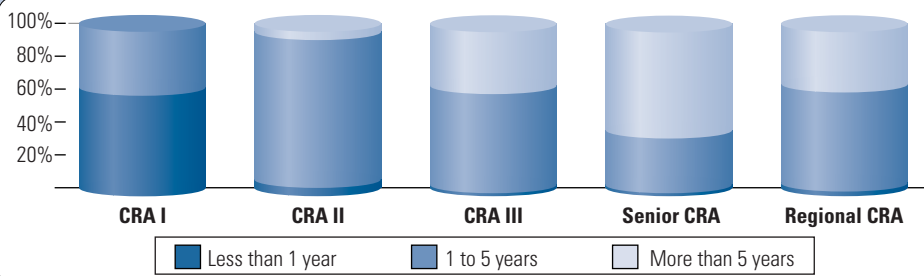
More experienced CRAs typically receive regional positions. A new CRA needs the support system an office can provide, even if he or she is traveling most of the time.

Sponsors also find that their regional CRAs build better rapport with their investigative sites. This is particularly pronounced in Europe where regional CRAs best understand local culture and nuance. “People at sites become the CRA’s support network because you’re out there together,” said Woodin. “It’s a lot different than people who are in a large corporation and who establish their support network among company employees.”

Whereas centralized monitors are seen as visitors, regional CRAs become a more inte-

## CRA Experience

Percent of total



Source: CenterWatch, 2003

gral part of the site. Observed Montgomery: “Any time you can build a relationship with a site—you still have to be professional in order to ensure that you’re objective and critical. But as a regional CRA, you are more available and aware of what’s really happening with your sites.”

Within a regional system, CRA employers are challenged to create a strong connection between the employee and the home office. Though many companies put regional monitors through intensive training, it’s difficult to foster loyalty and commitment with the organization whose name appears on a paycheck.

“There is an issue monitors face when they’re working remotely or on a regional basis and feeling a little bit alienated from their company,” said Rod Saponjic, vice president at Monitorforhire.com, a CRA matching service. “That becomes a real challenge for those organizations. How do we get these people to feel like they’re part of the company when they’re operating remotely? I see a real danger here in that regional CRAs begin to feel autonomous.”

Under regionalization, sponsors are finding that they need fewer CRAs who are specialized in one therapeutic area. Although there are exceptions, most regional monitors working for major biopharmaceutical companies are generalists today. Some sponsor companies report having specialized CRAs stationed in very large metropolitan areas. Although many CRAs believe that therapeutic area specialization might make them more marketable to a diverse group of biotechnology and pharmaceutical companies, many are happy to be generalists.

“We find that most CRAs appreciate

working on different types of studies as opposed to staying with the same type of study. And for an independent it makes even more sense because the breadth of experience in different therapeutic areas makes them more attractive to sponsors,” said Saponjic.

For all of the benefits that regionalization may offer, there are some emerging practices that may challenge it. Many employers, for example, believe that regional CRAs have more time than their centralized counterparts. As such, many sponsors are increasing regional CRA workload. And in a down economy, sponsor and CRO companies may expand regional territories and operate using a leaner CRA infrastructure.

### On Being Independent

In 2001, right around the time that Jessica Donahue was having her first child, she had the opportunity to leave a CRO company and become a freelance monitor. Some political changes were taking place within her company, and a friend had just offered to give her freelance work. Like many CRAs, Donahue took the chance and never looked back. Working independently as a CRA and project manager has allowed her to spend more time with her family and enjoy her job far more.

Though independent CRAs are not new to the clinical trials industry, their ranks are growing. “There are a lot more independent CRAs out there now. As they become more experienced and get a little older, the more they want to try freelancing,” said Woodin.

“The added flexibility—and better pay—are the attractions. There is a lot of financial gain and personal rewards of being your own boss,” said Donahue. Added Woodin: “Their family situations will be such that freelancing is easier. Or their companies will be merging

and they’ll be out of a job. Or they want more control over the projects that they work on and their travel schedules.”

Whatever the motivations, freelancing almost always seems to lead to better job satisfaction. Still, working independently isn’t for everyone—some like the security and the benefits a full-time employer can offer.

“One downside of being an independent CRA is that you’ve got to manage your own small business,” said Woodin. “You have to worry about your tax situation and you have to worry about your own benefits—like health and life insurance—because they don’t come with the job.” For independents who want to find work between jobs, freelancing can sometimes lead to a full-time position, but not always.

Most independents though are happy going it alone. “I’ve found a lot of independents who do this because they just want to call their own shots. And it doesn’t matter what stage they are in their careers,” said Donahue. “I think a lot of it is the financial gains and personal rewards of being truly independent.”

Competition for freelance work has intensified. As a result, over time it may become more difficult for freelance CRAs to command higher fees. Still, as budgets continue to tighten in the current operating environment, sponsor companies will likely be gun-shy about hiring full-time staff.

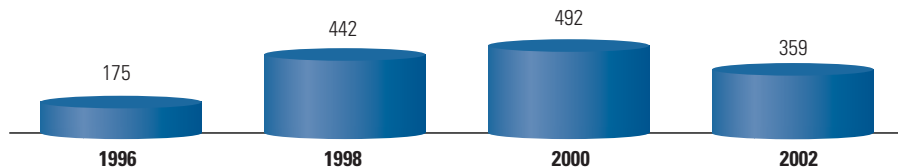
Many CRAs—full-time and independent—consider certification programs an important way of differentiating their experience level. The Association of Clinical Research Professionals (ACRP) reports that it has now certified more than 4,500 study monitors since first offering its program. Each year, ACRP certifies about 400 CRAs.

### The Impact of Technology

Since the mid-1990s, industry thought leaders and observers have speculated that tech-

## Annual CRA Certifications

Number of CRAs receiving ACRP certification



Source: Association for Clinical Research Professionals, Total Certified CRAs since 1995=3,811

nology will ultimately replace the role of the study monitor. That has hardly happened. Instead, to date, technology has largely facilitated change in the CRA's role.

"What we see is tremendous pressure for CRAs to be more efficient," said Scott Freedman of Monitorforhire.com. "CRA workload has become much more diverse. They're working on multiple protocols across multiple therapeutic areas. Those who have been in the job longer are figuring out better and faster ways of doing things. Technological advances have quickened the pace of everything. Cell phones, laptops, hand-helds, emails, instant messaging and the Internet. These are all the tools available to CRAs to help them do things faster with fewer errors."

Though certain advances, such as more sophisticated systems for tracking patient enrollment, have made the CRA's job easier, clinical trials continue to be paper-intensive. CRAs are highly receptive to using electronic data capture (EDC) technologies, but their influence on these decisions is limited. EDC is gaining acceptance, but most expect adoption to be gradual.

Though EDC may deliver clinical research data to the sponsor faster, it won't eliminate source document verification. Some see source document verification becoming more difficult for CRAs under an EDC environment. Though investigative sites will enter the data directly, it's still the study monitor's responsibility to verify that the source document actually exists. "If the companies are sending data directly in after the first capture," said Woodin, "then that's going to change the whole way we look at source document review and data collection cycles. There's going to be a lot of change in the ways that things are done in the future."

This year, there have been some reports from major pharmaceutical companies indicating that traditional study monitoring activity may decline as projects consistently utilize complete electronic data capture solutions. Last February, for example, Novartis reported that it had used a proprietary EDC system on 130 individual clinical studies in 2002. The company stated that it had saved \$65 million on these projects through lower study monitoring and data management

costs—much of this due to reductions in the use of CRO services. Novartis also claims that the company was able to lock the data for 70% of completed EDC-based trials in less than five days and 15% in less than one day.

The jury is still out as to where and how electronic clinical trial technologies will impact the role of study monitors. Still, Novartis' report—and those now coming from other companies—are beginning to catch industry attention.

### Looking Ahead

The rate of change in the clinical research enterprise is fast and dynamic. Changes in the CRA's role and responsibility is equally so.

"If the past is any indication," said Montgomery, "it's going to become more intense and there's going to be more demand for efficiency and more effective practices. Every corporation wants to get their drugs developed safely and quickly. Time is indeed money and the study monitor is an essential player in this complex and demanding process."

—Susanna Space

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