



Keeping Trials on Track

Portable software helps monitors manage site visits, validate protocol compliance, and assess the integrity of trial data, insists John Humphreys of Perceptive Informatics, a PAREXEL International company



In today's highly competitive biopharmaceutical marketplace, companies conducting clinical trials cannot afford delays in achieving critical study milestones – delays that can add millions of dollars to the cost of a trial. The intense pressure to bring innovative compounds to market as quickly and efficiently as possible makes it more important than ever for trial sponsors to keep clinical trials on track by closely monitoring site performance and data quality issues that could jeopardise study deadlines.

At the same time, biopharmaceutical trials are growing in complexity and scope. A typical Phase III trial might encompass thousands of patients at dozens of sites in multiple countries around the world. In addition, sponsors must supervise their trials diligently in order to meet growing demands from regulatory agencies to improve patient and drug safety. All of these challenges make it essential for sponsors to maintain the highest levels of scientific and ethical performance at trial sites.

Much of the day-to-day responsibility for meeting those challenges falls squarely on the shoulders of site monitors. They play a vital role in keeping the full range of site-based trial activities on schedule. Equally important, monitors ensure that Good Clinical Practices (GCP) are in place at every site, trial protocols are strictly observed, study data is fully and accurately collected, and adverse events are appropriately reported. These tasks also put them on the front line of risk management. Because they are in regular contact with site personnel, monitors serve as a sponsor's 'early warning system' – detecting performance, data and safety issues, and working to resolve them before they grow into larger problems that could delay or derail the trial.

Whilst the job of site monitor has changed dramatically in recent years as a result of these greater responsibilities, new tools have emerged to help them deal with the changes and perform those tasks better. Specifically, site monitoring tools that operate independently of sponsor- or site-based computer systems are now available that allow monitors to perform their duties more thoroughly and efficiently. Whether accessed on the web, on a laptop, or, in the latest advance, on a simple USB 'thumb' drive, advanced monitoring software has the power to improve the view of the data monitors need to keep the trial on track and meet the requirements of the protocol, sponsor and patients. To take advantage of these capabilities, however, sponsors and monitors must select a system with the right capabilities and flexibility to fit the needs of this demanding job.

MONITORING KEY SITE ACTIVITIES

Through a combination of remote monitoring and on-site visits, site monitors seek to answer important questions about the tasks being performed at the trial sites to ascertain that they are being performed thoroughly, ethically, and in compliance with the trial protocols and schedules. Their key activities include:

- ◆ Monitoring GCP compliance – is the site following all applicable regulatory guidelines and operating in a manner that protects the safety of patients and the integrity of the trial process and data?
- ◆ Ensuring trial protocol compliance – are all tasks being performed in strict accordance with the regulatory applications, ethics committee/review board filings
- ◆ Affirming the accuracy and reliability of trial data – have all the required tests been performed? Is all the data gathered from patient visits and lab tests complete and consistent?
- ◆ Keeping the site on schedule – is the site satisfying its required milestones and deadlines?

Determining the answers to these questions is essential to keeping clinical trials on track and performing at a high level of quality and efficiency. To get those answers, monitors must be in close, regular contact with site personnel. They must also review a large volume of trial documentation – such as case report forms (CRFs), physician notes, lab results, and pharmacy reports – to ensure that the required tasks have taken place and the information is accurate. All of these functions require the gathering and analysis of huge quantities of data from multiple sources at each site.

SOFTWARE TOOLS IMPROVE MONITOR EFFICIENCY

Given the data-intensive nature of site monitoring, it is no surprise that computer technology and advances in software can significantly increase the efficiency of site monitoring. Whilst many clinical trials still use paper-based CRFs, sponsors that have switched to computerised clinical trial management systems (CTMS) and other electronic tools gain substantial improvements in productivity and data reliability. For monitors, the advent of portable site management and monitoring software has revolutionised the way they carry out their duties, allowing them to gather the data they need to meet the expanding requirements of their position more quickly and accurately.

The trend today is for monitors to utilise self-contained monitoring software that can be carried to trial sites on a laptop computer or other device and used to gather data without a

connection to a mainframe computer or the internet. This independent, 'offline' capability allows monitors to gather and review data anywhere, at any time, without having to rely on other systems or technologies – flexibility that is tremendously important for a job that requires constant travel to multiple locations in different states or even different countries. The data gathered by the monitors using this type of software is synchronised as necessary with other trial software/databases at a time that is convenient for the monitors.

Trial monitoring tools typically support both monitoring and site management functions, including monitoring tasks and data gathering, milestone planning, issue resolution and recruitment performance. With information on all of their sites available at their fingertips, monitors can easily review site status and plan their workload intelligently. For example, the software can allow them to rank their sites according to those with the most open issues, or those that have enrolled the most new patients since the last site visit, and schedule visits for those sites sooner than those with lower activity levels. At the site, the monitor can typically view patient task lists that highlight new patient visits, review tests still to be performed for current patients, or create task lists for each site visit.

To deliver the greatest benefits, monitoring software must allow monitors to record and view essential data easily, such as:

- ◆ General comments on site status and GCP compliance, based on trial-specific or sponsor-specific criteria
- ◆ Site visit details, such as the people with whom the monitor met, and what was discussed
- ◆ Patient details, such as CRF and randomisation number, patient history, and adverse events reported
- ◆ CRF page queries and source data verification comments

Equally importantly, all data entered during a site visit should automatically flow to the site visit report, which should have the flexibility to be customised by trial, by country, or other criteria to accommodate regional or regulatory differences. In addition, a portable system must support easy data synchronisation with a trial's main data repository to ensure that sponsors and monitors have access to the latest trial information.

The latest technological development for monitors is site management software that runs on USB thumb drive, which provides even greater flexibility and portability. All of the necessary software and data – with proper encryption – is loaded on the drive. To use it, the monitor needs only to access a computer with a USB port. No additional software or hardware is required; the monitor simply plugs into the drive, and the monitoring application automatically opens. With this approach, there is no need for any lengthy or costly deployment of information technology resources to set up the monitoring system or validate a laptop configuration. Once the software itself is validated, it can be used without further technical or validation issues.

At trial sites, monitors must often visit numerous venues to gather data and talk to site personnel, such as the pharmacy, the lab, and physicians' offices. With the USB-based software, monitors do not need to carry and reboot their laptops at every location; all they need is the thumb drive. As a result, monitors save time – their most precious commodity. And with less time

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spent on computer issues, they have more time to perform their monitoring duties. Security is also improved, to the extent that a thumb drive is much less likely to be stolen than a laptop during a monitor's travels.

BENEFITS FOR SITE MONITORS AND SPONSORS

Although improved efficiency is a significant benefit of portable site monitoring tools, their biggest advantage is the higher level of consistency and harmonisation of activities and data among the monitors. The technology allows all of the monitors in a particular trial to use the same monitoring approach, following the same checklists and asking the same questions. This means that the data collected by the monitors will be more consistent and reliable – between monitors, and between all the sites in that trial, no matter where they are located.

An independent, software-based monitoring system is also much easier to update as the trial goes on. If a particular data issue or adverse event manifests itself during a trial, the monitoring system can be easily revised to reflect this new information. The software also allows the monitor to better focus on the site visit. All the pertinent information they need to do their jobs is available at their fingertips, including specific issues and tasks to be addressed. Other important benefits include:

- ◆ Standardisation of a single monitoring tool across various monitoring providers (such as in-house and outsourced)
- ◆ Ease of creating a common 'network' of monitors without systems integration requirement or other computer issues
- ◆ Elimination of duplicate or redundant data entry and reformatting of reports for different software applications or hardware platforms
- ◆ Consistency of tools and forms that improves data accuracy and reliability
- ◆ With its ease of access to a full range of site data, a monitoring system can serve as a powerful 'early warning' tool, alerting monitors to sites that need additional attention or resources

CONCLUSION

As clinical trials continue to grow in scope, complexity and risk, the pressure on site monitors to keep those trials on track will increase as well. By providing monitors with the right site management tools, trial sponsors can relieve some of that pressure and allow monitors to perform their vital functions with greater efficiency and consistency, while avoiding the expense and risk of trial delays. The result will be reduced costs and faster time to market – improvements that are essential in a competitive global marketplace. ◆