The Monitor’s Changing Role, Considerations for Electronic Data Capture (EDC) Implementation in Clinical Trials – Part 2

Electronic data capture (EDC) for clinical trials often follows a paper processing model. Following such a model is straightforward and can ease adoption of what may be new technology for an organisation. This approach, however, misses opportunities to leverage the technology to achieve further benefits in reduced time to market, improved data quality, reduced site visits, immediate feedback to queries, mid-study monitoring and analysis, and cost savings. In order to take full advantage of the EDC, and using it as a true comprehensive trial management system, operational processes must shift from the paper-based paradigm and embrace the additional power of automation. When this is done, project managers and monitors can take advantage of features the EDC provides, such as real-time monitoring, invoicing, user activity logging, inventory management and reconciliation, just-in-time randomisation, serious adverse event (SAE) trending, automated reporting and notifications, and site query analysis, to name a few. This article provides practical information on shifting operational practices to the new trial management EDC system paradigm.

Some of the most utilitarian features that EDC can provide are field constraints that provide automatic feedback to the user if a mandatory field is missing, has values that are out of range, has values in the wrong order (e.g., systolic/diastolic) or contains the wrong type of data. Careful consideration of constraint parameters during setup results in cleaner data requiring fewer corrections. Cross-form and field-matching constraints further ensure consistent data and eliminate contradicting data throughout the study. Additionally, EDC reduces human error by executing automated calculations for a number of functions, such as eligibility status, indicating what data needs to be collected based on a set of circumstances, and actual dose amounts. The challenge for these features is to ensure they are well thought out and set up correctly. When using paper, the focus is on training the sites to collect the data. With EDC, the focus is the definition and consideration of the factors that will take full advantage of the EDC’s capacity to help clean data in real time. While simple constraints might be straightforward, identification of cross-form and field-matching constraints may require input from a data manager, statistician, or experienced EDC project manager.

Another consideration when setting up the EDC is the operational logic and decision trees that will improve the study flow. For example, some EDCs keep future visits or scales hidden until the data is required to be populated; others deactivate forms if the case is a screen failure; and others display additional questions depending on prior answers. Such advanced functionality is available within some EDC systems and contributes to streamlined workflow and reduced errors in data. Initially, it can be difficult for those new to EDC adopt the shift in thinking to foresee and implement these features from the start. It is vital to embrace the easy-to-understand features and then build upon that with additional features that improve the flow of the study and provide the cleanest data. Collaboration between the project manager, data manager and EDC provider can help identify additional opportunities to implement advanced EDC functionality to produce a successful study. With each future study and more experience, the complexity of the logic employed will increase while errors and queries of data will decrease.

As an example, one of the top five global animal health companies is quoted as saying the following about their EDC provider: “The quality of the data exported from VISION™ allowed our team the ability to focus on writing the submission reports, rather than cleaning the data, which enabled us to submit the study report eleven (11) months ahead of schedule.”

In addition to data collection, most EDC systems can also provide study administration tools, such as notes to file, protocol deviations, communication logs and visits, and handle adverse events and concomitant medication coding. Functionalities such as these within the system are advantageous as they keep important study documentation in a single place and allow for real-time monitoring.

Beyond the basic data collection setup, some EDC systems also have tools available that can support other critical functions, such as inventory management, invoicing, and randomisation. Inventory management tools include such features as drug status tracking, automatic notification to project managers and monitors when inventory becomes low, automatic orders of inventory, notifications of inventory orders, and notification of site receipt of inventory orders, shipment tracking, and automatic inventory reconciliation. These capabilities reduce stress for the project manager by reducing dependence on site personnel to manually track inventory and ensure inventory availability throughout the study duration.

Site event invoicing can be a time-consuming and tedious activity for a study monitor to successfully manage. Some EDCs have integrated invoicing functionality that can be customised to study-specific triggers to support tracking and making payments. During setup, it is important to use appropriate triggers for payment. As examples, a payment may be triggered as visits unfold, with amounts depending on whether the case is a screen failure or enrolled; when specific procedures (such as labs) have been performed; when a case has been completed; and/or forms are signed and reviewed. With EDC, the complexity of the payment scheme can incorporate additional details without it burdening the
monitoring staff. Invoices are generated automatically, reviewed and submitted for payment. Once received, monitoring staff just have to approve them.

Proper control of the randomisation function is imperative to maintaining masking integrity for the study. Use of a paper-based table could result in a masked user inadvertently seeing randomisation details, or a user could misread the table and give out the wrong treatment. An EDC-integrated randomisation feature that generates the treatment group, in a just-in-time fashion, eliminates potential issues associated with inevitable human error. EDC just-in-time randomisation utilises algorithms similar to what statisticians use to develop paper-based randomisation tables, but instead of generating a whole table all at once, the system will do so at the moment a treatment assignment is requested. Some EDCs can handle both site- and study-based randomisation as well as additional stratification criteria (e.g., gender). Some even can mitigate dosing mistakes by randomly reassigning the correct treatments to ensure balanced blocks at the end of the study.

To effectively utilise an EDC’s custom notification feature, it is essential to consider which notifications will be critical for which roles. Too many notifications means more than just overloaded emails; it means important information will be lost or overlooked. Common custom notifications for monitors may include serious adverse event, new case enrolled or randomised, case terminated, query resolved, invoice received, and inventory ordered or low. Custom notifications for sites might include lab received, query generated, inventory ordered, and payment made. These types of notifications serve to alert the recipient about important study milestones that may require attention. From a monitoring standpoint, automatic notifications allow confidence that events requiring action will come straight to their inbox. This reduces some of the stress of monitoring, decreases time lost checking for each piece of information, and helps focus the monitor’s work to areas that actually require action.

In addition to the data collection and administrative features available with EDC, summaries and mid-study reporting features can be defined and set up prior to the start of the study. Some EDCs provide wide-ranging and common summaries to show enrolment data over time, open/resolved queries, adverse events, document status, parameter trending, site and patient status reports, and population distributions (e.g., gender). It is advisable to review the standard EDC-provided summaries with the statistician and study sponsor to determine what additional summaries or ad-hoc reports will best benefit the study team while monitoring study progress, and note whether the EDC automatically updates reports with the latest data each time they are accessed (preferable). Some of the most commonly used mid-study monitoring reports include summaries (adverse events, notes to file, deviations, form states, and query status); ad-hoc reports that display field values and/or initial values, previous values, when entered, by whom entered, error status; and other metrics such as per-site or per-case query rates, query category or type, change rate for fields, per-site or per-case deviation, and note to file rates. These reports can be used to identify areas which may require more training or trends (for example, in deviations or notes to file) that can be addressed in future protocols or immediately.

In summary, planning appropriately to leverage the advantages of the EDC over a paper-based system results in many efficiencies that should result in cleaner data, fewer cases lost to data issues, and ultimately decreased time to market. Careful consideration to basic constraints, logic, and calculations is required to ensure clean data is collected from the outset. Form functionality must be well thought out and conceptualised as a decision tree to facilitate logical and functional workflow of the study. Additional integrated components such as just-in-time randomisation, inventory management, automatic reordering, notifications, invoicing and budgeting should be implemented whenever possible to streamline study management. To facilitate mid-study monitoring, consider which summaries, reports and metrics will be useful.

Monitoring during the study is also more efficient when an EDC is used. Although more attention and time must be dedicated to study setup details, the data will be cleaner and more reliable at end of the study, and during the study, the monitor can focus on those areas which specifically require more clinical and data trending attention. The basic functions
of the EDC automatically ensure this can be achieved as the constraints fire, and site personnel can notice and correct in real time data issues such as blank fields, out-of-range entries, and incorrect formats.

Monitors can quickly view the data any time because the EDC is accessible via the internet. There is no need for the monitor to wait for a site visit to review the data. This allows the review to occur closer to data collection, and queries are entered and responded to when information is still fresh. If data is entered off a paper source document, such as an owner survey, the paper source document can be scanned and uploaded, and the monitor can review the source document in comparison to the data entered.

Tracking mid-study metrics allows the monitor to develop strategic plans with sites to improve retention and recruitment. Because the data used to create these plans is real-time data, monitors can quickly help sites that are finding it difficult to recruit early in the study, and help avoid a delayed study due to slow recruitment. Other monitoring-related issues, such as training needs, can be identified by tracking queries per case or site. When similar queries occur repeatedly, monitors can spot trends early on that require additional site training.

In EDCs that have accessible pre-set summaries or ad-hoc reports that can be shared with different users, more accurate communication can occur between users about the progress of the study. Users can view the same latest report simply by logging into the system. This reduces the time to create reports on a regular weekly/monthly basis to send to the sponsor, and frees the monitor’s time to focus on higher order monitoring tasks.

Site visits are more focused and streamlined because most of the source data files have already been reviewed within the EDC. Only those that have a source outside of the EDC need to be compared to the electronic entries. More time can be spent talking to the site personnel about broader study-related issues and logistics, as well as obtaining feedback on workflow that would make future studies easier to implement. Monitors who are using EDC report that site visits are shorter and more focused, and allow them to have richer conversations with the site personnel.

There is also a shift in the number of studies that can be handled simultaneously by a monitor from one to two studies when conducted on paper versus four to six when using an EDC. It is evident that the time spent setting up and planning the EDC and taking advantage of its functionality reduces errors, improves efficiency and quality of data collection, reduces time from data collection to data analysis, and ultimately results in shorter times to market.

“Taking advantage of the power of EDC decreases the time to market and impacts the bottom line,” said Jim Pedzinski, VP Business Development, Prelude Dynamics – a company focused on solutions for clinical trial management. “Planning prior to go-live allows you to take full advantage of this tool.

It is a shift in paradigm, but one that I believe is moving the industry in a positive direction and is critical for our clients’ successes.”

In conclusion, when using an EDC over a paper-based system, the role of monitors shifts from detailed oversight to helping coordinate and plan the most efficient workflow and cleanest data collection strategy. Instead of reviewing and comparing the source data to the database, time is spent working with site coordinators and investigators on key issues like subject recruitment and retention. In addition, sponsors can have access to real-time mid-study reports and summaries instantaneously and can quickly provide the monitors with additional guidance. This leverages the monitor’s abilities to focus on the most important tasks and less on the time-consuming tasks of data-cleaning, thus as our clients have shared, they can do more with less, faster and under budget.

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