Clinical Data Collection - Paper vs. Electronic Data Capture (EDC)

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20 years ago experts predicted that electronic case report forms (CRFs) would replace paper as a natural consequence of the introduction of computers. In 1997, the FDA produced the regulations that would guide the industry through this transition (CFR Title 21 Part 11). Still, 10 years hence, recent analyst research has identified that only 30% of ongoing clinical trials are conducted using EDC. Justification for this slow acceptance has come from many varied sources. Just what are Sponsors looking for in a company that produces clinical trial software (Electronic Data Capture or EDC)? The following are the most paramount issues:

1. Global Scalability - The stage for the majority of clinical trials is global; a vendor company needs the infrastructure to support this, and the EDC application must be adaptable and able to expand to the needs of the protocol.
2. Experience - Because failure is not an option in Medial Research, Sponsors seek vendors that have a proven track record.
3. Robust, Reliable, and proven technology that is complemented by an excellent support processes.

While there are currently as many as 150 companies attempting to fill the void in EDC applications, most do not offer the full package of options that would be required to run all aspects of a clinical protocol from beginning to end. Additionally, the pharmaceutical company needs to consider the demands required of the clinical program, and whether the application can meet those demands. Some important questions to consider are:

- o   Will the stakeholders in the company accept the technology, and are they ready to move ahead with it?
- o   Is the infrastructure stable enough to conduct EDC trials in all of the countries which have the desired patient populations (these may often include Central European or African/Asian countries)?

- How is source data verification managed in this environment?
- How will EDC affect the internal organization?
- What is the opinion of the regulatory authorities of data collected in this way?
- Is there a danger of data being rejected as noncompliant?
- When will the company see a return on its investment?
- How can this be measured when so many of the EDC benefits are qualitative rather than quantitative?

EDC vs. Paper

Pharmaceutical companies have recognized that changing to an EDC trial process involves moving data collection from a series of sequential tasks to a parallel process where live data analysis can be employed to bring about the best results. A primary goal of our own Simplicity© application was to develop the functionality of the EDC system so that it is not only an application that is able to capture clinical data, but can also be used for review and analysis. EDC is able to provide system functionality through the use of high-speed connections using the Internet, eliminating much of the burden that is associated with site management. By comparison, the paper CRF was received in-house and entered by one data clerk and verified by another. The paper clinical trial process was conceived, designed, and refined over scores of years using paper as the medium for collecting clinical data. Since all the procedures and functional roles that make up the clinical data process were structured around paper, it only makes sense that changing it in its entirety will produce some issues and take some time. The primary roadblock to a completely "paperless" study comes from the problem of source documentation. Using the paper method, the investigator records the patient data in the source notes or a pro forma of some kind, and then enters it into the EDC system some time later. "EDC double data entry" is caused by the assumption that a paper source is needed for online EDC systems. In a recent survey conducted by the industry group EDM Forum, 4,840 investigators (both experienced and name in EDC) sited this paradigm as the number one barrier to wide scale use of EDC in their clinical trials. This issue will continue to divide the industry until global health care evolves to the point where all patient data is stored electronically in a validated system. Ergo, today's number one issue to the propagation of EDC for clinical trials becomes the ability to reduce the site burden of EDC and clinical trial conduct in general.

Conducting the Trial

In order to resolve this "final conflict", we need to ask ourselves these two questions:

1: What data do we want to collect for our clinical trials?
2: At what point and from whom do we want to collect it?

Naturally, the protocol and therapeutic area under study primarily drive the first point, but typical clinical data can be roughly divided into two groups:

1. Physiological data such as vital sign readings, laboratory values, and medical history.
2. Patient-reported outcome (PRO) data such as symptom counts, subjective pain analysis, and quality of life assessments.

These two categories historically make up the typical clinical trial, with physiological data accounting for 75% and PRO 25%. In a clinical trial, the interaction between the investigator and patient is limited to the visit, intervals between which can vary from weeks to months. CRF's include questions such as "How have you felt since the last visit?" or "Have you experienced any pain since the last visit?" or "Have you taken your medicine at the correct time?" As we all understand, it is difficult to recall this information over long periods of time, so the patient is asked to record this information in a paper-based patient diary they use at home. The concept is that the information recorded at the medical moment will therefore increase its accuracy. There is legitimate concern that while PRO data clearly contributes important information to the NDA, paper diaries produce data that is notoriously poor (as anyone with a background in clinical trials will tell you). Patients forget to complete the diary at the correct time, and often back or forward fill the diary. Considering that this method is being used to assess primary and secondary endpoints, it's a serious concern that the majority of this data is at best irrelevant and at worst fraudulent.

The Future - Electronic Patient Diaries (EPDs)

One solution, which interfaces well with EDC, is Electronic Patient Diaries. EPD's can contribute well to the overall success of a clinical trial. Instead of using a paper diary, the patient enters data directly into a mobile device. The EPD actively reminds patients to be protocol-compliant regarding when they fill in the diary, instead of filling in the diary data just before seeing the investigator. So how, you may ask, can electronic patient diaries reduce the site burden of EDC? In one ongoing study with over 5000 patients in 23 countries, EPD's will collect over 2,000,000 pages of data. The current level of compliance in the study is a remarkable 97%, and the level of accuracy represents a great improvement over paper. This type of wide scale study is a testament to the ability of EDC to collect and accurately manage data on an enormous scale, and is a perfect

example of how EDC can lead sites to embrace the technology. Imagine having to reconcile and collect all that data using paper? Additional key benefits from EPD's include:

  1. Screening assessment using EPDs - In a bid to recruit the correct patients the first time and reduce dropout, the EPD was used to screen patients. At the screening visit following the preliminary assessment by the investigator, each patient was given an EPD and asked to complete the diary during his or her daily routine. During the screening period the data is transmitted to the central. The Web-based reviewer tool runs a series of algorithms against the data to calculate the eligibility of the patient. At the next visit, the investigator can then move eligible patients to the next phase of the study, or retrieve the EPD from ineligible patients and enroll another round. This dense data sampling is anticipated to reduce the required number of patients, which translates into a great time benefit.

  2. Online protocol amendments. The EPD technology supports the online protocol amendments, which can be sent to the patients' EPDs to allow flexible rule adjustments. It was noticed at the beginning of one study that the level of screening failures was higher than expected. On closer examination, one of the inclusion criteria was inappropriate in this patient population. An amendment was made, and the level of randomized patients increased. This meant that the trial could be proactively, rather than reactively, managed.

  3. Reduced site administration. The trial consisted of several complex phase and dosing transitions, which would have normally placed an additional burden on the site for the duration of the trial. With the intelligent use of EPDs and rules running across the Web-based reviewer tool, the site could use the technology to help administer the patients and their treatment.

  4. Cost-neutral operation. Once a patient had completed the study, the EPD could be recycled and given to the next patient recruited. There was no need for the EPD to be returned to the vendor for configuration, since this was all managed on-site. As a direct result, the investment required to purchase the devices can be amortized across the study to create a cost-neutral operation.

5. EPDs can be used to collect critical PRO data directly from the patient. The patients are allowed to set the alarms and trigger diary reminders, giving them the ability to fit the diaries into their lifestyle. The data transmitted from each patient is sent to a secure server and made available for patient management and administration. Although the sites need to manage the EPDs and keep the batteries charged, the technology reduces the overall levels of site administration and workload for the trial.

Going, Going...

Simplicity© can be combined with EPD's to produce considerable benefits for all factions involved in a clinical trial. For the patient, the primary data capture point is focused upon them. Rather than being a burden, this allows flexibility in the way their data is captured and, in the future, may lead to tailored treatment. For the site, the level of EDC data entry is significantly reduced, and the EPD data is available online. This adds value by allowing the site personnel to fulfill their main objective-individualized and improved patient care. As was seen in the case study earlier in this article, sites can see and feel the benefits of using this technology. As with the adoption and acceptance of any new technology, if the end-users can see the benefits in their daily routine, the level of adoption will increase as a natural consequence. For the sponsor there are many benefits. Use of EPD's and EDC delivers quality data faster. This method of data capture brings the patient in to the center of the trial, thus creating a window into the patients' lives by allowing proactive intervention and trial management based on the real-time access to data. This more effective trial management has demonstrated significant financial benefits by decreasing dropout rates, speeding trial completion, and allowing data-driven decision-making at program, trial, site and patient levels. This will automatically lead to a reduction in the number of monitoring visits and will actually increase the level of proactive trial management. Data collection and management workload will be reduced and productivity will increase with no decline in data quality.

In Summation

At Software Dynamics, our goal is to provide sponsors with the cutting edge technology required to efficiently run clinical trials, from start to finish. Software Dynamics makes it easy for Sponsors to ease into new technology by organizing it in a modular fashion. Simplicity© can be made to fit any study, and can easily migrate data from one phase to another. Sponsors new to EDC can select to have the program include (or exclude) any number of options to fit their need and budget. As new methodology of data collection becomes available, Software Dynamics will continue with whatever R&D is necessary to maintain our technological lead in the industry.

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