Advances in Technology that Support Electronic Data Capture (EDC) and Clinical Trial Management Systems

One of the critical elements in clinical trials is capturing data which is accurate and timely. EDC systems – software applications that allow users to enter information into a database over the internet – are used in all phases of clinical trials to collect, manage and report clinical and laboratory data. These systems provide both the tools and the process infrastructure necessary to achieve the required data quality, as well as process scalability.

In this article, Praveen Dass, VP of data management at Quanticate, discusses the challenges associated with data quality during clinical trials and the advantages of centralised data management systems. Dass also looks at the future of data management and analysis, as well as the benefits of outsourcing data requirements for clinical trials.

The Current Landscape

Contract research organisations (CROs) serving the pharmaceutical industry generated a revenue of approximately €4.4 billion in 2010 in Europe and these revenues are expected to exceed €12.9 billion by 2021[1].

The global clinical trial management system (CTMS) market size was valued at over €599 million in 2015, with revenue forecasted to exceed €1.9 billion by 2024. In Europe, the CTMS market size was estimated to be worth over €176million in 2015 and anticipated to witness healthy growth of 12.6% from 2016 to 2024 due to increased emphasis on the development of novel drugs for treatment of chronic diseases and a favourable regulatory environment[2].

CTMSs are an important part of every clinical trial. Selecting the right CTMS can help to address inefficiencies on the operational side of research, such as clinical trial planning, preparation, performance and reporting. In addition, there is a growing need to address the complex process of EDC implementation, as more and more pharma and biopharma sponsors start to recognise the potential opportunities that exist with EDC-CTMS integration[3].

EDC is commonly used to help medical device and pharmaceutical companies achieve maximum efficiency when it comes to entering data, structuring a database and conducting analysis for clinical trials.

Over the last decade, the use of EDC in clinical trials has become more and more prominent, with the global EDC systems market estimated to be worth almost €935million[4] by 2025. And, as EDC technology has evolved over the last decade, previous concerns about data integrity through human error and connectivity issues derived from less reliable IT systems are becoming a thing of the past. Hospitals all over the world are now better equipped, staff are a lot more comfortable with electronic systems than when they were first introduced, and stakeholders are now a lot more aware of the time that can be saved by using EDC. However, as the medical industry embraces new technologies and innovations, including electronic record-keeping, the volume of information collected before, during and after the clinical trials continues to grow. As such, comprehensive data collection and efficient management is now becoming a priority for pharmaceutical companies and CROs.

Addendum E6 Revision 2 (R2) & Risk-based Monitoring (RBM)

Since the development of the International Council for Harmonisation (ICH) Good Clinical Practice (GCP) guideline, the scale, complexity and cost of clinical trials have increased. The E6 R2 addendum came into effect in Europe on 14 June 2017 and includes a number of topical GCP inspection areas.

The guideline was introduced to encourage implementation of improved and more efficient approaches to clinical trial design, conduct, oversight, recording and reporting, while continuing to ensure human subject protection and data integrity. This is likely to lead to the greater adoption of EDC technology from those that still use paper. As the industry embraces new opportunities to increase efficiency during the management of clinical trial data through remote RBM, and the need for sponsor oversight of the systems and data continues to increase.

Risk-based monitoring (RBM), designed to identify incorrect data and predict and mitigate risks before they happen, is also being used more and more frequently during clinical trials, and some argue is the next big change in the industry, like the move from paper to EDC was. RBM is enabled because EDC exists as most of the data analysed comes from the EDC system in real time. This addendum to the ICH GCP incorporates the use of RBM approaches to help companies ensure the safety and quality of clinical trials.

This move will undoubtedly require a shift in mindset for quality assurance (QA) and monitoring teams. It is evident that this new addendum requires a concerted educational effort by many organisations to allow their workforce to adopt a new way of working. Traditional methods rely heavily on human entry and errors can occur when individuals input data, track results and manage databases. The need to reduce risk in clinical trials has led to the increased use of electronic systems for data capture. Human error can have many repercussions in a clinical trial which could ultimately delay product to market, or stop it getting there at all.

Making the Transition to EDC

The advent of EDC technologies is shaping the clinical trials data management landscape, opening up myriad benefits for the industry as a whole. Adoption of EDC in place of paper-based methods was relatively slow due to its associated costs and the time required to implement new systems, as well as the perceived cultural and

technological transformation, which can be too great a leap for some organisations. However, users can do things with EDC that they can't do with paper case report forms (CRFs) or standard databases, creating a strong case for the investment. The last few years have seen a great shift in the uptake of EDC, with paper CRFs now only being considered for very specific requirements.

Firstly, eCRF templates are easily modified to suit each new study, saving time that would be spent on designing and producing paper CRFs. On average it has been proven that EDC cuts 41% of pre-study preparation timev. Using EDC, data is collected and entered into a data collection tool only once, whereas when adopting a paper system, data must be entered firstly into a case report form then into an electronic system by a data entry group. This not only increases processing time but also affects transcription integrity.

In addition, EDC allows data cleaning to take place straight away and doesn't require intensive hands-on work from a data management group for processing. Unlike paper studies, in which the data management group executes the logic checks against data that was collected weeks or months ago, EDC system logic checks are executed when the site enters and submits data, allowing it to be cleaned in real time. This is one of the major efficiencies of an EDC system[6].

Ultimately, following proper system selection and development, as well as good study management, EDC allows users quick access to clean data with low operational costs. It has been reported that switching to EDC saves on average 30% of the time it takes to conduct a clinical trial[7].

But how do users create a comprehensive EDC database design? There is a need for some up-front investment in terms of time and resource to ensure that the database is thorough. If companies do not make this investment, there is a risk that changes or additions will be required at a later date, which will be costly and could have broader implications on operations. In addition, most EDC systems come with a standard suite of reports, however, additional reports may be required for study oversight and management. Most, if not all, EDC vendors provide custom reporting in addition to standard reports. As with database development, the design of reports should be well considered and clearly specified at the beginning of the study[8].

In addition, within the design of an EDC system it is important to consider the format in which data is being collected so that they can be statistically interpreted or programmed in other third-party software once it leaves the EDC system. Implementing a consistent data collection methodology includes standardising the definitions for the data that has been collected across multiple sites.

EDC systems must have an option to follow Clinical Data Interchange Standards Consortium (CDISC) standards and for datasets to be in line with Clinical Data Acquisition Standards Harmonisation (CDASH) guidelines, so that it is ready for statistical analysis in the future. This can save time and efficiencies as non-CDASH data needs to be reworked to meet a CDISC standard upon regulatory submission. The use of greater numbers of standard designs during study builds can not only help with efficiency and quality of reporting, but also significantly reduces the time it takes for databases to be built. While CDASH standards continue to improve, many organisations still find it a challenge to keep to these standards due to differences in requirements between studies and even different clinical study teams within organisations.

The Role of Outsourcing

It's important to provide high-quality data management to support drug development needs and ultimately get drugs to market as quickly as possible. The specialist nature of data management has led to an increase in outsourcing these services within the pharma industry, particularly to niche CROs, with an in-depth

understanding of what is required. This is particularly true of smaller companies that lack the financial resources and internal expertise to effectively implement these capabilities themselves. As the pressure for tighter timeframes continues to grow, big pharma companies are also realising the benefits of functional outsourcing to tackle resourcing while also accessing specialist skills and experience. Contracting out data requirements to niche CROs enables the sponsor to take advantage of the CRO's process knowledge, their standard libraries built over time and the expertise and learning built by working across a number of technologies and protocols. By concentrating exclusively on data, CROs are able to offer efficient and flexible clinical data management solutions, as well as add an extra level of quality governance to the process. By providing end-to-end comprehensive clinical data management solutions from early-phase through to post-marketing trials, the CRO can uphold a standardised and process-driven approach.

Looking to the Future

Cloud-based EDC systems have proven to significantly reduce development cycles and time to approval compared to traditional paper CRF processing, and the industry continues to move towards a wider adoption of EDC methodology. There are a number of EDC options in the market place, however, easy user experience is key and there is a lot of focus from providers to make the user interfaces as easy to use as possible to streamline staff training.

EDC enables high-quality clinical data management, brings efficiencies to the drug development lifecycle and with the growth in technologies such as wireless internet connection and the new generation of e-mobility solutions like smartphones and tablets, entry is no longer restricted to PCs. As we move forward, it is likely that future developments will drive further changes in the EDC paradigmix. It is likely we will see integration across various platforms with EDC to enable data to have one source of truth. We are seeing this today with the use of wearables in clinical trials for data collection, as well as electronic patient-recorded outcomes (ePRO) solutions where patients are able to enter data themselves directly into a tablet or e-mobile device. This negates late patient data entry and allows for reasonably continuous access to patient data via online tools.

Because of these emerging technologies, clinical data managers need to consider how the EDC platform can integrate data from an e-mobile device, and what analysis is required to identify which pieces of data can be trusted and used. Statistics and data modelling are often required to process this raw data; for example, it may be necessary to identify a period when the data capture device was being used by someone else, then exclude values from that time. Understanding protocol and likely error sources is required before processing of this nature can be performed, typically requiring statistical support.

As clinical trials incorporate these additional data and capture sources, the volume and frequency of data being captured has increased dramatically. For example, before you might have had a trial where a patient visit occurs once a week, with a single pulse measurement taken then, now there is the ability to take per-second heart rate readings. Where protocol includes a heart monitoring device (such as in a commercially available sport tracking device) in the clinical trial, there will be a significant increase in data storage requirements.

However, simply having the raw data is not enough; it requires filtering and processing to produce clinically-useful information in reduced volumes. For our heart rate case, every-second values may be unhelpful, but knowing the average resting vs active rates, along with any times of very low or very high readings, can inform efficacy or adverse event reporting. To support this potentially unlimited real-time data, our technology stacks need to be able to handle storing and analysing 'Big Data' in clinical trials.

Final Thought

With the advent of the cloud in clinical trials, as well as the increase in connected devices and technological advancements, the ability to analyse large amounts of data is important. Technology to combat this is continuously evolving and new projects, products and approaches are launched all the time. Some are more about updating existing methodology while others take the latest research to re-visit the core of the current 'big data' offerings and replace them with faster, more flexible and scalable solutions.

Specialist providers offer complete bespoke solutions in clinical data management that can provide real-time, faster access to data, resulting in faster decisions to keep patients as safe as possible. These data visualisations can be generated prior to a database lock as the EDC platform connects with the bespoke technology. It must be communicated to all involved in the trial that the visualisations are an insight into the trial, but not the final data for statistical analysis and interpretation. Outsourcing the data management and analysis of your trial to a CRO with a comprehensive EDC system can mitigate a lot of the challenges for companies looking to adopt these new techniques.

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