Evolving Clinical Trial Landscape Requires Quality Focus

The strive to deliver the very best outcomes sits at the heart of clinical research. Arguably the mechanism for delivering that "perfect" outcome rests squarely on the shoulder of a single key principle – quality. Quality permeates all areas from study design, to data collection, to successful publication, and many more.

The idea of quality includes a vast array of perspectives gained from the evolution of trends in the development of quality management practices. For example, Good Clinical Practice (GCP) is regarded as the ethical and scientific quality standard for conducting a trial and applies to all steps in the process that combine for a successful trial conclusion. The GCP role is to ensure that the clinical trial data and reported results are credible and accurate and that the rights, integrity, and confidentiality of the trial subjects are protected.

Clinical research has become increasingly complex with even small nuances potentially having a big impact on outcomes. Globalisation, outsourcing and increasing regulatory demands are all affecting clinical trials and their quality. Artificial Intelligence (AI) and machine learning (ML) are contributing new ways of discovering and acting on data management in clinical trials, particularly discovering any anomalies in the data.

Concurrently, wearables and mobile technologies, along with cloud technology and related platforms, enable the collection of frequent, specific, and multidimensional data but can pose new challenges to collecting and distributing quality clinical trial information. Clinical trial participants are often using these devices in a remote way that requires diligent work on the part of the clinician to ensure data is properly classified and disseminated throughout the appropriate channels. Social media is a rapidly increasing data source for clinical research, but the quality and ultimate validity of the information reported continues to be a concern for many.

Investigator sites and Institutional Review Boards (IRBs) have been under increasing scrutiny by the European Medicines Agency (EMA), the UK's Medicine and Healthcare products Regulatory agency (MHRA), and the U.S. Food and Drug Administration (FDA) when it comes to quality. To meet the regulatory expectations, sponsors and CROs (Clinical Research Organizations) need to improve quality by developing systems with specific and exacting standards for each clinical trial process.

This article will review best practices for achieving quality by addressing challenges focused on the all-important but rapidly growing complexity of managing the distribution of critical safety documents and the processing of Individual Case Study Reports (ICSRs) and aggregate reports to sites, Ethic Committees (ECs), IRBs, and others in the reporting chain.

Quality Systems Require Many Touch Points

Quality systems have many touch points including personnel roles and responsibilities, training, policies and procedures, quality assurance and auditing, document management, record retention, and reporting and corrective and preventive action. With an objective to improve quality, newer inspection approaches such as risk-based inspections, surveillance inspections, real-time oversight, and audit of sponsor quality systems have become a focal point.

As one example, the FDA has partnered with Duke University to implement the Clinical Trials Transformation Initiative[1] in order to conduct research projects on design principles, data quality and quantity including monitoring, study start-up, and adverse event reporting. This public-private partnership is intended to drive adoption of practices that will increase the quality and efficiency of clinical trials.

Minimising the Potential for Human Error

Rejection of clinical trial data after an inspection is ineffective and even worse, wasteful in time and cost. A better approach to avoid post-inspection waste is to change the process from focusing on inspection-based quality improvement to focusing on

proactively determining and finally deploying specific, automated, and documented processes for quality management. Once these business processes have been defined and potentially redesigned, the often error-prone human element is greatly reduced.

For example, when key processes for safety document distribution require multiple steps that involve constant manual intervention, often using systems and tools that were not designed for that purpose, undetected small errors can combine into large scale problems. An automated process provides structure and a degree of rigidity which means that the documents are getting to the right people at the right time, every time. By monitoring with a central dashboard, the process is transparent and controlled.

Globalisation of clinical trials has put added pressure on quality measures. When, for example, six sites with thousands of participants are running in multiple geographic areas and time zones, it is almost impossible for manual intervention processes to assure the vigilance necessary to meet rigid – and varying – regulations for delivering error-free and on-time safety information.

Quality in Roles and Responsibilities

Quality also permeates the development of specific roles and responsibilities of the teams managing and monitoring the trial sites – and there can be various people involved – including but not limited to, the principal investigator (PI), Study Manager, Site Mangers, Clinical Research Associates (CRAs), *et al.*

Again, globalisation causes challenges in maintaining clear oversight of processes

when working with a variety of people often with different skill levels or experience in clinical trial management. The methods and degrees of monitoring vary from one clinical trial to another depending on the degree of risk involved and the size and complexity of the trial. While sponsors and CROs want to make sure that the teams in charge are well-qualified, it's not always possible to recruit the levels of expertise needed to assure the most clear and transparent outcomes. Some team participants may be contract workers/freelancers and Site Managers may be simultaneously working on several different trials. This can present the Study Manager with that uncomfortable question "how confident are you in the validity of data from ALL your sites?" Let's not forget that it is the study manager who is ultimately responsible for safety document distribution. Manual assembly of this information is labour intensive, costly, offers opportunity for errors and often lacks documented audit trails.

Automating the safety document distribution process clearly delivers a significant advantage. Utilising a central 'hub' into which documentation is delivered from each site can provide a clear and transparent advantage. Such automated systems to date have provided a portal into which documents are entered which, while a significant step forward, creates the issue of access and password retention for sites. However, the latest applications have solved this issue and allow secured, validated and auditable access for all authorised users without the need for passwords. The result is an easy-to-use single view which is shared across all the trial sites. Depending on different roles identified at each site, there is tiered access to appropriate information. For example, a local investigator may only have access to local sites while Study Managers have access to all sites, no matter the geographic area. This empowers study team members and simplifies access to a real-time overview, significantly reducing the workload across the team and enhancing collaborative communication. For example, in a recent case, a trial team which applied the automated interactive hub approach, in just one month, moved from struggling to deliver 20 safety documents a day with its manual system to easily delivering more than 50 documents daily via automation of the process.

Quality of Delivery and Oversight

Depending on their local infrastructure and regulations, sites expect to be able to receive information according to their preferred method and the information must be blinded or unblinded depending on specific regulations. This means recipients expect to have courier deliveries, email with attachment, email with secure link, even Fax. Any automated systems that are supporting recipients must have this flexibility, not only to ensure strong adoption, but also to deliver a unified view of compliance for the sponsor. Regardless of the distribution method the transparent oversight of the activity must remain.

With a single view, on a dashboard, the hub approach illuminates all the distinct actions and rates of progress behind each specific process, which means faster and more-informed decision-making and certainty of outcome. For example, country rules that drive the safety document distribution are audit-proof. That means that the people on the team responsible are able to see to whom a document was sent, why it was sent on a specific date, and confirmation of receipt. Supporting this effort are automated compliance reports which can identify anomalies at a site, i.e., if perhaps more training is needed to assure better adherence to policies and procedures.

Quality in Execution

Seeking an automated approach can often seem daunting. Will a new system fit easily into the existing infrastructure, will it easily connect to an existing safety database and CTMS and will it be intuitive enough not to cause interruptions in human adoption? These are all significant questions. Perhaps the simplest answer is that full automation leads to a more streamlined process which

naturally enhances the availability of critical information, provides flexibility and clarity in reporting. It also reduces manual efforts, human errors, and operational costs associated with audit trails and compliance documentation. Where solutions have been successfully implemented, they have seen significant reduction in cost and resource requirements and seen much improved compliance from sites.

In short, focusing on quality in all aspects of a clinical trial is the foundation for delivering valid and compliant outcomes. With a simple, easily implemented, automated, interactive, and central database, a commitment to maintaining data integrity and participant safety through quality guidelines provides a systematic approach to continuous process improvement.

REFERENCES

1. https://ctti-clinicaltrials.org

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