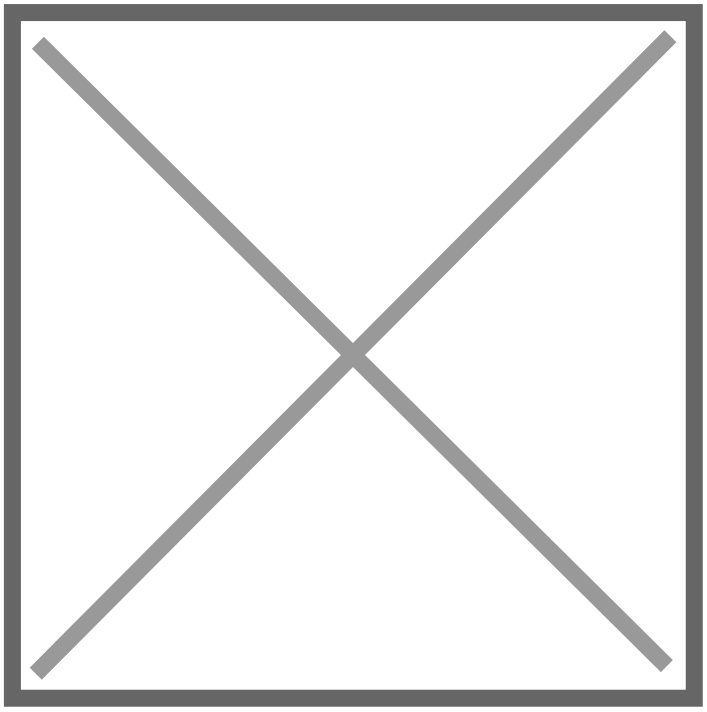
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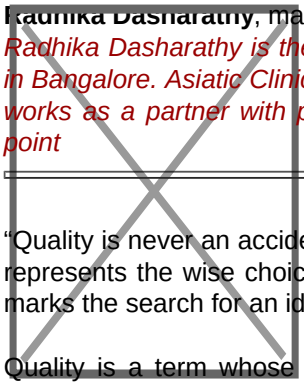
Quality management will improve services

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Radhika Dasharathy is the manager of quality assurance at Asiatic Clinical Research, a clinical research organization based in Bangalore. Asiatic Clinical Research is a full-service contract research organization with a focus on phase II-IV trials. Asiatic works as a partner with pharmaceutical and biotechnology companies to conduct the study ethically, and achieve the end point

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“Quality is never an accident; it is always the result of high intention, sincere effort, intelligent direction and skillful execution; it represents the wise choice of many alternatives, the cumulative experience of many masters of craftsmanship. Quality also marks the search for an ideal, after necessity has been satisfied and mere usefulness achieved.” (Willa A Foster)

Quality is a term whose interpretation has greatly metamorphosed over the years. Even in our day-to-day life, quality is preferred to quantity. Clinical research remains no exception to this, as can be seen by the increased awareness in quality over the last few years.

Quality, in practice, is a relative term and has no absolute definition. To evaluate quality, one needs controls for processes and systems. Some of the references to quality in the pharmaceutical industry highlighting the measurability of quality as a key parameter include:

Quality, as the degree to which a set of inherent properties of a product, system or process fulfills requirements. (International Conference on Harmonization—ICH Q9—Quality Risk Management)

Quality of a medicinal product, is measured by its fitness for purpose. Safety and efficacy are part of it and not separate from it (good manufacturing practice (GMP)).

Pharmaceutical quality, as a product that is free of contamination and reproducibly delivers the therapeutic benefit promised in the product label to the customer.
Quality assurance, as all those planned and systematic actions that are established to ensure that the trial is performed and the data are generated, documented (recorded), and reported in compliance with good clinical practice (GCP) and the applicable regulatory requirement(s) (ICH E6).

Quality control, as the operational techniques and activities undertaken within the quality assurance system to verify that the requirements for quality of the trial-related activities have been fulfilled (ICH E6).

Quality guidelines for clinical research were sketchy initially during the evolution of clinical research. The principles of quality assurance have evolved over a period of time, based on experiences of various pharmaceutical organizations and regulatory

agencies throughout the world and collated in the form of regulatory guidelines and legislations. Although, by function, quality assurance personnel are responsible for the quality in an organization, in practice that's not entirely true. Each individual who is a part of the research activity is responsible to ensure quality in their work

No organization is immune to employee attrition. With change in personnel, practices also tend to change. However, compliance with passion to the high standards set by the organization ensures consistency in practices, and therefore, reproducibility of goods and services rendered. For clinical trials conducted by CROs, adherence to these established quality standards instills confidence in the research sponsors, regulatory authorities, ethical committees and the general public with respect to the trial data. The end result is availability of high-quality medications to combat diseases.

Every organization must thus have a well-established quality management system (QMS). The organization can enforce the objectives of the QMS by having organizational documents like standard operating procedures (SOPs), policies and plans. A document like a manual should describe the organization's mission, vision, quality policy, organizational structure and responsibilities. It should also describe the planned efforts and commitment by the organization to deliver quality products and or services. Implementation of a successful QMS in the organization, involves employee training and awareness, effective communication, document and operational controls, emergency preparedness/disaster recovery procedure, regular monitoring of the QMS, identification of non-conformances, corrective and preventive action (CAPA) and management review.

Current trend

The current trend in the pharmaceutical industry is 'quality by design (QbD)'. QbD means incorporation of quality inputs and use of quality processes to ensure a quality end product. This approach has rationalized the earlier belief that repeated testing of the end product ensured product quality. Instead of waiting for the end product to meet specifications, each input, process and system involved in the manufacture of a product or delivery of a service is controlled against appropriate standards. This approach reduces the time of product or service delivery as well as improves the quality of the product or service delivered, and hence improves efficiency.

The QbD process plays an important role in a highly variable scenario like clinical trials, particularly in phase II and III trials. There are several variables in the clinical trial process, starting from the manufacture of the clinical trial product to inter-patient variability, variability associated with non-compliance that may not be reported, consumption of additional dose and skipping a scheduled dose, consumption of concomitant medication. Further in some trials, the patients are ambulant, that is, not housed in a controlled facility; trial conduct teams are based in hospitals where priority is treatment and not documentation, multi-centric trials which may lead to inconsistency in procedures being followed, global recruitment which may lead to regional variations and procedural non conformances.

Most of the problems can be addressed by adherence to a sound protocol. Each trial activity has to comply with GCP, relevant regulations and the trial-specific protocol evaluated and approved by ethics committee. All non-conformances should be addressed promptly and appropriately. On the quality auditor's part, data monitoring and auditing activities commence at the inception stage of protocol development, proceed during actual trial conduct, CRF compilation and until clinical study report submission. Site management and data management metrics are evaluated; databases and statistical tables are audited. The QA team auditing the clinical trial maintains a well defined quality audit plan that describes, what, when, who will be audited, and the purpose of the audit. The quality auditor's ultimate goal is to ensure compliance of the trial activities and documentation to the protocol, GCP and relevant regulations.

Similarly, in the entire drug development process, each stage has to comply with relevant guidelines and regulations. Thus, functional areas such as drug discovery, drug formulation, manufacturing, preclinical and clinical requires adherence to good laboratory practice (GLP), good manufacturing practice (GMP) and GCP as appropriate. Good automated manufacturing practice (GAMP) and GLP have to be adhered to, during the bioanalytical phase of clinical trials. In the pharmaceutical and medical device industry, validation is defined as the documented act of demonstrating that a procedure, process, and activity will consistently lead to the expected results. The quality guidelines issued by ICH must also be complied with, wherever applicable. In addition, the organizations based on the requirement, can seek certifications (ISO and six sigma) that further prove their commitment to quality.

Overall, assurance of quality is an eternal challenge. Research organizations lacking adequate infrastructure and vision, leading to compromises in quality, is an additional challenge. A well informed, trained and suitably qualified research team will definitely make a difference. Ensuring quality will not be a major concern if each one of us is aware that quality increases efficiency, enhances value of product/service and improves business. Contribution to quality by every individual, in turn, reflects in the quality of the product or service delivered by the organization. Hence make commitment towards quality a habit and compliance a practice.