Data Integrity in Pharmaceutical Industry

Editorial

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Data collected, observed or created enable researchers to answer complex questions, test hypotheses, and evaluate outcomes of research. Research data can be generated for different purposes and by using different processes and techniques; however, the components of data are the same regardless of the field of study, including physical, chemical, medical etc. Timely, accurate, and complete data generation, recording, and maintenance are essential for the integrity of research. The requirements that assure validity of robust data apply equally to data recorded on paper, electronic or combination of both.

The primary goal for preserving data integrity is to detect and prevent human or accidental and intentional or deliberate errors during collection and protecting original data from intentional modifications, falsifications, or even deletion during life cycle management of data. Research misconduct, unethical research practices, poor mentoring or training in handling data, lack of proper guidance and attention to details, and poor data collection practices can risk data quality and integrity. Some of the examples of research misconduct and unethical research practices are fabricating, falsifying, collecting or selecting data for getting desired results, and testing until the desired results are obtained.

The degree of impact from faulty data may vary by the discipline and the nature of investigation; consequently, ensuring accurate and honest data collection is essential for maintaining the integrity of research. Improperly collected or faulty data may affect the researcher's ability to answer questions accurately and repeat or validate studies, mislead other researchers and influence decision making, and leading to wasted resources etc. Data integrity is essential in every area of scientific research in the academic and in the industrial environments; however, it is even more important in the healthcare industry. There is a potential to cause harm to patients when these data are used to support research, development, registrations, and commercialization of pharmaceutical products for human and animal health use. This is due to the fact that the compromised data may impact the product quality of the final product, i.e. medicine, as laboratory data assure the quality of the raw materials, in process materials, and the finished products. Subsequently, inferior quality products may be unsafe for patients.

In the pharmaceutical industry, ensuring data integrity involves generating and documenting data accurately, protecting data from accidental or intentional modifications, falsification deletion or destroying data. The US-FDA uses the term ALCOA which refers to complete, consistent and accurate data that should be Attributable, Legible, Contemporaneous, Original or a true copy, and Accurate. Some examples of the data integrity issues that have been observed during FDA inspections are: alteration of raw and original data and records, repeat analysis of assay with the same sample without justification or out of specification analysis investigation, manipulation of a poorly defined analytical procedure and associated data analysis in order to obtain passing results, back dating test results to meet the protocol requirements, creating acceptable test results without performing tests and using test results from previous batches to substitute testing for another batch.

Recent data integrity issues related to non-cGMP compliance in the world, specifically in India and China, has led to issuance of numerous warning letters, import alerts, and consent decrees by the FDA, WHO Notices of Concerns (NOC), and EU Statements of Non Compliance. For example, in the past five years 29 warning letters citing data integrity issues were sent to companies around the world which included 18 to the facilities in India [1,2]. Many examples of non-compliance were poor system related rather than a proven intention to mislead. However, there were some warning letters that included citations related to data manipulation, data tampering, incomplete data, undocumented results and manufacturing steps, poor safeguards against data tampering, destruction of data, incomplete data entry, substitution of failing results with passing results, fabricating injection sequences etc.

These concerns over data integrity prompted US-FDA to announce new draft guidance [3] in April 2016 for pharmaceutical industry to ensure data are consistent and accurate. The guidance includes 18 questions and answers and well defined terms related to current Good Manufacturing Practices (GMPs). Additionally, these questions and answers provide a detailed outline for ensuring data integrity. The FDA's expectation from the pharma industry is data supporting pharmaceutical product registrations are reliable and accurate. A quote from the guidance is "cGMP regulations and guidance allow for flexible and risk-based strategies to prevent and detect data integrity issues. Firms should implement meaningful and effective strategies to manage their data integrity risks based upon their process understanding and knowledge management technologies and business models." In addition to United States of Pharmacopeia (USP) issuing a general chapter <1029>related to Good Documentation Practices, other world-wide regulatory authorities (e.g. MHRA ICH, European Council, and WHO) have put much emphasis on the data integrity in recent years as they have found serious cases of data integrity beachesalso [4-8].

Data integrity can be assured by the Quality Assurance (QA) and the Quality Control (QC) approaches. These approaches are applied at different stages of studies. For example, the QA activities take place prior to data collection by establishing quality systems, standardization of protocols, Standard Operating Procedures (SOPs), and training of personnel, engaged in data collection, that prevent any data integrity issues prior to data collection. A well-defined and rigorous training program that effectively communicates the value of accurate data collection, recording, and maintenance to new recruitments and an ongoing basis to the existing scientific/laboratory staff is essential. Additionally, a Quality System with Standard Operating Procedures (SOPs) and protocols must be developed to ensure that personnel do not make unintentional mistakes related to data integrity. On the other hand the QC activities, monitoring, detection, and corrective action, related to data take place after data collection. Based on appropriate internal protocols and SOPs the data should be reviewed in a timely manner by the appropriate coworkers, line supervisors or study directors for unintentional or intentional data issues. A clearly defined communication procedure between the personnel and the supervisor or the study director will minimize possibility of faulty data generation. Appropriate laboratory investigations followed by Corrective and Preventive Action or Corrective Action Preventive Action (CAPA) plans are needed in case of detection of any data integrity issues. A defined internal audit program should be established which may detect deficiencies in data collection process that may impact data integrity. Internal auditors must understand what to look for while investigating potential data integrity deficiencies. Independent third party auditors or consultants may help to enhance the programs related to data integrity.

In summary, the development and registration of medicines for commercialization involves multiple activities, one of them is linked to the robustness and accuracy of the data submitted by the sponsor in the dossiers to the national regulatory authority for supporting an application for a drug product. These data must be comprehensive, complete, reliable, accurate and true to assure the quality of studies supporting applications and must comply with a number of standards, i.e., Good Manufacturing Practices (GMP), Good Clinical Practices (GCP), and Good Laboratory Practices (GLP). Establishing robust Quality Assurance and Control systems a quality culture that encourages personnel to be transparent about failures can minimize data risks and improve the situations where data reliability may be compromised. This enables to investigate and address root causes when data integrity issues arise. However, deliberate data integrity issues require major cultural changes in an organization.

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