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Procedure for Documentation, Importance and Relevance for Compliance of Data Integrity in Laboratory Operations of Pharmaceutical Industry

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Abstract: *Data obtained at all stages from laboratory experiments is very significant and its originality is a step further to interpret conclusions based on the findings and to establish the suitability of the tests for the intended purpose. Results obtained from the experimentations lead to selection or rejection of samples based on the acceptance criteria. As the drug products are used for human consumption and compromisation of data at any stage may lead to false results posing risk to human health. Hence, it is necessary to establish and follow the procedures during the entire sequence of experiments from start to end to retain its originality and accuracy to meet the compliance requirements as per the regulatory guidelines.*

Key Words: *Data integrity, Compliance, Laboratory, Documentation, Quality assurance.*

1. INTRODUCTION:

A data in is related to as such facts and it exists in a number of forms such as numbers or text in paper or as bits and bytes in electronic form. Raw data is associated to the original records (e.g., memoranda, notes, worksheets, or exact copies of data) that contains the results of original findings, related activities along with the details stated that are necessary for the reformation and evaluation of a research work, process or study report, etc.

Raw data can be categorized into manual raw data and electronic raw data.

Manual raw data is type of data which is a recorded form and is obtained as a result of an action performed (e.g., pH, temperature).

Electronic raw data is a type of data which is unprocessed raw data i.e., data obtained and is not controlled by user identified parameters such as analog signals, or processed raw data i.e., data obtained and is controlled by user parameters such as integration parameters and can be re-reprocessed data i.e., data obtained and is controlled by user intentionally adjusting identified parameters.

Integrity of the data is the term, related to the quality or condition as a whole/undivided or completeness.

Data Integrity in pharmaceuticals is related to the laboratory data integrity following a good manufacturing practice (GMP) in the organization can be well-defined as “generating, transforming, maintaining and assuring the accuracy, completeness as well as consistency of the data over its whole life cycle as per compliance by following applicable regulations.”

Regulations of FDA, handbook by WHO, MHRA guidelines and guidelines by USFDA were studied for preparation of this article [1-5].

The opinions, views, procedures and its acceptance expressed in this article are based on the literature/documents available and to explain it in simple and a systematic approach however each country specific relevant guidelines or documents from respective regulatory agencies should be referred as applicable.

2. PROCEDURE:

It undermines the safety and efficacy as well gives assurance of the quality of drugs that will be consumed by the consumers, indicating importance of data integrity. If data integrity is avoided and these issues within the organization will lose trust from regulatory point of view and if such issues are tackled and are reported promptly as well as solved then, it builds the trust.

2.1 Documentation and its relevance to data integrity

The following mentioned points are very important to ensure integrity of data within the organization.

2.1.1 The data obtained or generated during the processes/experiments performed should be traceable by all personnel involved in the activity. It should be clear that when the activity was performed and by whom along with its acquisition details', it should be attributable.

2.1.2 The data should be read easily, the handwriting should be clear enough to read easily without overwriting ie., it should be legible.

2.1.3 It is very important to note or document the data at the time of activity.

2.1.4 The data should be documented at the time of activity i.e., it should be contemporaneous. Writing or documenting the data at later stage after performing the activity will lead to incomplete information or will have errors.

2.1.5 It is essential to document the data on a suitable media, should be on written printout or on an issued certified copy thereof and should not be duplicated i.e., it should be original.

2.1.6 It is a part of duty of assigned personnel to perform the documentation activities without errors and with on time, as such performed i.e., documentation activity should be accurate.

2.1.7 There should be inclusion of all the relevant steps or procedures systematically performed as per the suitable procedures followed, to establish new or modification of existing procedures/processes or as the activity performed relevant to specific functions of the organization such as research department, quality control, manufacturing department and documentation should be complete.

2.1.8 All the data obtained or generated from initial stage to final stage should be preserved including for trials or failed activities.

2.1.9 While performing the experiments, the sequence of activities should be documented along with date/time in sequential manner i.e., it should be consistent.

2.1.10 The documented data should not be tampered (e.g., laboratory notebooks, compacts disks, suitable softwares such as LIMS).

2.1.11 There should be set procedures in the organization to use officially issued laboratory note books or the suitable printed papers issued with sign and date from authoritative personnel and post it, loose papers should not be used for documenting the experiments.

2.1.12 The documents should be checked as the activity ends and should be readily available for review and audit or inspection over the lifetime of the record.

2.2 Documentation in laboratory operations and its relevance to data integrity:

Following are the key elements while performing the laboratory operations and have impact on the data integrity,

2.2.1 The processes involved in sampling and sample handling should be performed according to established procedures of the organization specifically made to perform by respective trained personnel in the laboratory.

2.2.2 It is very important to have correct as well as accurate sample labels on respective samples for its identification.

2.2.3 Samples should be stored as per the identified storage conditions and should be protected from contamination, to prevent from obtaining misleading results.

2.2.4 All points mentioned above are related to sample integrity and it should be followed.

2.2.5 To confirm the integrity of materials used during experiments in the laboratory, there should be followed established procedures to list down requirements of standardization, standardization processes, receipt of

documents, calculations, preparations, traceability, assigning expiry or retest dates to prevent from use of expired materials.

2.2.6 Standard procedures should be prepared to perform proper maintenance along with qualification/validation of all laboratory instruments and computerized systems as the data generated depends the accuracy of performance of the instrument.

2.2.7 Analyst should be given proper training for laboratory operations and should be qualified as per the procedure as the ability to perform experiments accurately and proficiently depends on the proper training and successful completion of qualification reflecting the proficiency of the analyst.

2.2.8 It is very important to perform documentation activity in real time for the experiments in the laboratory.

2.2.9 The original recorded documents should be in chronological order, accurate, legible, clearly identifiable (e.g., page numbers, document numbers, laboratory notebook numbers, experiment numbers), traceable as well as readily retrievable at any point of time for review or inspection.

2.2.10 The documentation for the experiments should be recorded as per standardized, preapproved and predefined operating procedures in the laboratory note books, authorized forms or templates as applicable.

2.2.11 Validation or verification of analytical method should be performed as per preapproved protocol in the approved formats for recording of the results of validation experiments to confirm "suitable for its intended use."

2.2.12 If any repeat analysis, re-sampling, complete repetition of experiment requires to be performed then previous results obtained should be invalidated with proper investigation, causes, justification and preapproval.

2.2.13 The handwriting should be clear enough to read easily without overwriting. If in case any of entry is wrong or having error(s) during documentation, overwriting should not be allowed, corrections should clearly written and should be made by the concerned person who has written the original record and if in case the person who has written the original record is unavailable, then another authorized person in charge can do the correction and correctness of the entry should be checked by the reviewer with sign and date of the both persons involved in the correction activity. Figure 1 and 2 shows examples of clear, legible and correctio of entry.

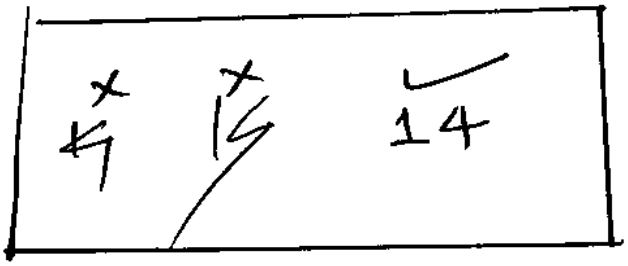

Figure 1: Representation of Clear and Legible entry

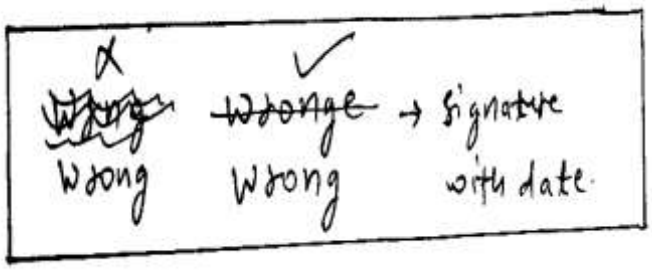

Figure 2: Illustration of correction of entry

All above points mentioned are very important and if compromised will have an impact on data integrity.

2.3 Challenges in compliance of data integrity in laboratory operations:

There are number of ways to compromise the data integrity and following are the probable causes,

2.3.1 Human errors lead to wrong reporting of results and data interpretation may go wrong due to wrong entries by unintentional mistakes.

2.3.2 Improper training, lack of awareness of regulatory requirements and latest updated guidelines.

2.3.3 The intentional willful fraud or falsification of the results when the results failed to meet requirements and are made to appear as per acceptable specification during reporting comprises the data integrity.

2.3.4 If improper practices are followed as it is scientifically unsound and technically unjustified for manipulation, alteration or omission to follow procedures to obtain data that avoids the necessary parameters, generating the results to appear as acceptable and comes under non – fraudulent behavior, however data integrity is compromised in this case.

2.3.5 Repetition of experiments to select good or passing results and exclusion of the results that are failed leads to compromise data integrity.

2.3.6 Data integrity gets compromised if any unauthorized changes are done to the data post acquisition.
2.3.7 There is possibility of errors which may occur while transmitting the data from one system to other system.
2.3.8 It is possible that changes to the data may happen through software malware, bugs for which the operator is not aware.
2.3.9 There is possibility of sudden hardware malfunctions e.g., hard disc crash.
2.3.10 If there are any changes in technology or software compatibility issues then there is possibility of no longer availability of data as due to non-support, making old data records unreadable or inaccessible.

2.4 Essential Requirements for data integrity by regulatory bodies/agencies:

Following are the essential requirements as applicable to maintain the data integrity,
2.4.1 Instruments in the laboratory must be qualified and should be fit for its usage of intended purpose.
2.4.2 All the relevant software which are planned to use should be validated/qualified prior to use.
2.4.3 All the relevant calculations should be done and must be verified.
2.4.4 All the data obtained while performing the experimental analysis should always be backed up.
2.4.5 All the reagents and reference solutions should be prepared as per the procedures and with appropriate records should be kept.
2.4.6 All the methods in use and used prior should be properly documented and approved.
2.4.7 All the procedures or methods should be verified under actual conditions of the use.
2.4.8 Experimentation performed, data generated and transformed should meet the acceptable criterion on the basis of scientific soundness.
2.4.9 The data obtained for the tests should be accurate and complete in all respect.
2.4.10 Experimentation, records, data generated and the reportable value should be checked and verified to ensure its accuracy to completeness and conformance with applicable procedures.

2.5 Identification and controls to prevent data integrity problems:

2.5.1 The organization should implement policies such as to increase the frequency of review of the data to identify and report the issues during the review.
2.5.2 It is necessary to have sudden and surprise spot checks in the laboratory in order to identify and control any issues while performing the activity.
2.5.3 There should be established procedure containing a checklist to review the data for experiments.
2.5.4 It is necessary to identify, check and compare hand writing styles and signatures of each individual.
2.5.5 Established mechanism should be in place to record attendance and it should be verified for individual attendance and presence.
2.5.6 Logbooks should be maintained for each instrument to trace its usage manually and with the record generated electronically, if in case instrument has the facility to track its usage in electronic record such as audit trails.
2.5.7 Organization should prepare procedures to conduct internal check by performing internal audits along with external audits.
2.5.8 Based on the trending the observations, all the analysts should be given training periodically on the relevant activities.
2.5.9 All the policies should be well defined and clear on various activities such as user login and password.
2.5.10 Clear policies and procedures should be in place to have control over the electronic data and software administration.
2.5.11 Each individual user, reviewer and administrator should be assigned with activity specific privileges and should be in accordance with the assigned job responsibilities.
2.5.12 The procedures in place should be cross checked for their adequacy.
2.5.13 Organization should have strategic planning for the laboratory operations.

CONCLUSION: Laboratory data obtained in a regulated and in compliance with the set procedures assures the trust of the organization. The integrity of data obtained in a regulated laboratory is a key feature in determination of the reliability

of that laboratory. If the data integrity is compromised and observation of such a single occurrence poses questions over the reliability and accuracy of the entire data obtained and non-compliance exists.
Hence, it is very important to ensure the data integrity and should be given major importance as the significances of getting it incorrect loses trustworthiness and it may take a very long time to rebuild the trust from regulatory bodies.

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