Guidance Document

Good Documentation Practices

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Introduction

This chapter defines the requirements for good documentation practices which build a basic foundation for a good quality management system. Good documentation practices are those measures that collectively and individually ensure documentation, whether paper or electronic, is secure, attributable, legible, traceable, permanent, contemporaneously recorded, original, and accurate.

Good documentation practices follow to protect the integrity and quality of all documents/records, electronic and handwritten, used in different GMP operations and activities and ensures these records are truthful, readily retrievable and traceable.

General Requirements for GMP Documentation

This chapter covers different levels and types of GMP documentation, including paper and electronic records related to manufacturing, testing, packing of pharmaceutical products, APIs, excipients, dietary supplements, food ingredients and medical devices.

These documents and records consist of raw data, reports, protocols, procedures, deviations, investigations, batch records, formats, and records related to trainings, equipments and retention for manufacturing and analytical controls.

Data integrity should always be given utmost importance which means the extent to which all data is complete, consistent and accurate throughout the data life cycle. Controls should be in place and any data integrity incident, if noticed; an appropriate corrective action should be taken to prevent recurrence of the same. Attempts to cover-up mistakes are considered as 'data integrity' issues and should be prohibited at all levels.

Principles

Personnel should be kept up to date about the application of good documentation practices (GDP) to ensure that the principles of ALCOA and ALCOA-plus are understood and applied to electronic data in the same manner that has historically been applied to paper records. Good documentation requirements for manual and electronic records include the following, as applicable;

- **ALCOA:** A commonly used acronym that all records and data should be attributable, legible,contemporaneous, original and accurate.
- **ALCOA-plus:** A commonly used acronym for "attributable, legible, contemporaneous, original and accurate" data, which puts additional emphasis on the attributes of being complete, consistent, enduring andavailable – implicit basic ALCOA principles.
  - **Attributable:** Attributable means information is captured in the record so that it is uniquely identified as executed bythe originator of the data (e.g. a person or a computer system). Original data and further amendment ifany should be traceable with respect to person, date and time, reason with signatures and in summaryaudit trails.
  - **Legible:** The terms legible refers to the requirements that datais clear, easily understandable, and free fromoverwriting and unauthorized changes, and allow a clear picture of the sequencing of steps or events in the record so that all activities conducted can be fully reconstructed by the people reviewing these records at any point during the records retention period set.
  - **Contemporaneous:** Data should be recorded concurrently at the time of performing the activity and recordings such as in-process, environmental should maintain as and when an activity is carried out alongwith signatures, date and time.

- **Original:** Data should be recorded originally, not entered on a piece of rough paper and then copied, no trial injections. OOS results should be reported immediately and data should not be newly created or rewritten after corrections and cancellations.
- **Accurate:** The term “accurate” means data should be correct, truthful, complete, valid and reliable. Data shouldnot be falsified and fabricated.

Laboratory Records

- System must have a collection of technological & procedural controls to protect data within the system to ensure that all records are authentic, incompatible and (where applicable) confidential. In lab situation this include lab results used to determine quality, safety, strength, efficacy or purity and in manufacturing this includes all decisions related to product release and product quality.
- Controls should be in place, needed for the identification, storage, protection, back-up, archive, retrieval, retention time, and disposal and to protect the integrity of its records. Access to these records should be consistent with confidentiality and records should be readily available.
- All Technical activities should be carried out with valid, correct and current effective versions of instruction documents and recording formats should have an identification number and a version number (where appropriate), allowing the sufficient space to record entries etc.
- Original observations, data, and calculations should be recorded at the time of activity performed, without any bias or prejudice. These records also include the identity of personnel responsible for the performance of activity.
- Automated data capture or printers should be attached and connected to equipment, such as balances, to ensure independent and timely recording of the data.User access rights to automated systems should be restricted to prevent data amendments (or audit trail).
- Ability to change any clock used for recording timed events, for example, system clocks in electronic systems and process instrumentation should be restricted.
- Pre-dating that is, signing for an activity in advance or post-dating (back dating that is, signing for an activity with a back-date) either documents or corrections should be strictly prohibited.
- Impermanent records like data printed on thermal paper, etc. should be copied on to a permanent medium, and the copies should be attached to, or stored along with the original signed records.
- All error rectifications / filling of missed entries should be traceable to the person who made the entry, irrespective of the stage at which the error has been noticed.
- All Documents / records should have page numbers (preferred format: ‘Page X of Y’). All master documents should be typed or pre-printed. Hand-written documents should not be used as master documents.
- Pens with indelible ink / Ball pen(only blue colors)should be used for recording of entries and for signing off any kind of documents. All entries and records should be concise, legible, unambiguous and accurate.

- The following practices should be strictly prohibited: Use of ditto marks (”) or down arrows (↓) or ..do.. to fill in repetitive entries., use of pencil or any removable / water soluble ink, use of eraser or ink remover.

Data Collection and Recording

- Good data and records management practices are critical elements of the quality system and a systematic approach should be implemented to provide a high level of assurance that throughout the product life cycle, all GMP records and data are complete and reliable.
- Laboratory information management system(s) (LIMS) includes the management of data and information contained in both computerized and non-computerized systems should be well defined in quality standard procedures.
- The computerized laboratory information management system used for the collection, processing, reporting, storage, retrieval of data should be validated for functionality before introduction and any subsequent changes should be validated before implementation.
- Technical records of original observations, derived data and enough information to establish an audit trail, calibration records, staff records and a copy of each CoA should be retained for a defined period as applicable.
- Amendments to technical records should be traceable to previous versions or to original observations. Both the original and amended data and files should be retained including the date of alteration, an indication of the altered aspects and the personnel responsible for the alterations.
- Handwritten records should be signed or initialed and dated at the time the information is entered. All entries related to analysis being performed should be done in chronological order. In case continuous pages of a notebook are not being used to record data, continuity should be denoted by mentioning the reference of the notebook number or page numbers at appropriate places. For example, if experiment is recorded in a laboratory notebook on Page 25 and calculations are recorded on Page 35, cross reference of the same should be given on both pages.
- All Instruction documents should have the effective date printed or stamped on them. All dates should be expressed in a format that clearly indicates the day, month and year. Time should be preferably recorded in the 24 hrs format as HH:MM. In case, date and time is printed from a machine or a computer, the date and time format of the instrument/machine should be followed and reviewed periodically for any discrepancy.
- Blank spaces or pages should have a single slanting line from start to end with a signature and date and the reason for the page being blank (e.g. ‘Not Applicable’ or ‘NA’ or N/A).
- If any column or row or cell is Not applicable, “NA” or N/A” should be entered in the space provided in the format.
- Only validated excel sheets should be used for calculations. Wherever such excel sheets are not available, calculations should be re-verified with validated calculators. In case of analysis, step-by-step details of the testing procedure, dilutions, critical test parameters, etc. as required by the standard procedures should be documented concurrently in Analytical Raw data sheet and laboratory Logbooks. All printouts, chromatograms, spectrum, records of analysis, etc. should be duly signed with date by the activity doer person, immediately after the activity is performed.

- All invalidated/disregarded Chromatograms should have a justification written by the 'Doer' with signatures and approved by in- charge.
- Decimals less than one should be preceded by a Zero. Rounding Off' of numerical values during analysis should be followed as under calculation of results in general notices.In case readings or values are to be recorded from digital electronic displays, same values or readings should be transcribed from system to documents**.**
- Processing of chromatograms in chromatographic analysis should be done within 24 hours of completion of analysis sample set, with exception allowed in case of holiday. If the concerned analyst is unable to attend duty on the next working day, the task should be allocated to another analyst for processing of the chromatogram. However, in any rare case after processing of chromatogram the printout is not being taken within 24 hrs it may be taken within next 24 hrs after approval and proper reasoning.

Data Reviewing and Reporting

- Specimen signatures, initials record of each employee involved in GMP documentation should be maintained to use for traceability of signatures for all the records. Signatures essentially mean that the signatory is responsible for the accuracy of data and information for the activity being signed for. Hence, the signatory should confirm the accuracy and completeness of information and data before signing.
- All GMP records should be appropriately reviewed and signature by a second person to confirm the accuracy, compliance and completeness of the work done.
- A single person should not sign for multiple roles for the same activity or entry. e.g. A doer cannot be the 'Verifier' / 'Reviewer' / 'Approver' for the same activity or entry recorded. No employee is authorized to sign for an activity performed by another employee.
- Persons preparing, reviewing or approving documents or persons recording, verifying or approving records should be on the basis of SOPs as accountability steps for different levels of review. All document signatories should be adequately trained for the activity performed by them.
- Attachments to a document should have reference of the parent document, and the parent document should have details of the attachments. In case of electronic records, all child records of a parent document should have an indication of the relationship with the parent document. Data should be recorded directly on only approved and authorized formats (e.g. Logbooks, Raw Data Sheets and other similar records). Analysis data documentation should not be recorded on unauthorized documents e.g. scrap papers, note pads, rough register and other similar items.
- In case a sample has been analyzed by two or more analysts for different tests, each analyst should complete the test & related documentation for respective tests and sign (with date) his or her part. The analyst to whom the sample was issued originally should preferably sign (with date) the CoA; if this is not possible, another suitable analyst or department In charge should prepare & sign the CoA and submit it to a Reviewer. The reviewer should ensure that all tests as per specification have been carried out as per applicable testing procedures and results are documented.
- Analytical results for specific batch of a sample are compiled in the form of 'Certificate of Analysis'(CoA), should be approved by an authorized representative. The test results should be reported accurately, clearly, unambiguously and objectively, and include all the

information necessary for the interpretation of the test results, method used and sections applicable as per regulatory requirements.

Rectification of Errors / Handling of Missed Entries

- **DON'T's:** Entries in documents / records should not be cancelled, erased, obliterated or otherwise rendered illegible,by using correction fluid/tape, overwriting, crossing out with multiple strokes, etc.
- **DO's:** When a correction is necessary, the erroneous entry should be crossed out with a single horizontal line.Enter the correct information as close as possible to original entry that does not obscure the original entry. A brief reason for the correction must be noted as to why the change was made and the correction shouldbe signed and dated. If sufficient space is not available to put the remark, then an annotation mark may be put near the incorrect entry and the annotation mark should be explained on the same page along withsignature & date.
- While stamping on documents for effective date or during review retrospectively, if it is discovered that an incorrect stamp has been used, the scenario should be handled in proper way. The error should be corrected by putting correct stamp imprint adjacent to the incorrect one. The incorrect stamp imprint should be struck off by 'Doer' with single horizontal line in a manner that it should be readable and not obscured. The 'Doer' should sign with date near the struck off, incorrect stamp imprint; this activity should be verified and signed (with date) by reviewer.

Types of Other GMP Documents

- Good data and records management practices are required to establish, implement and maintain an appropriate quality management system, the details of which should be documented in a format, such as a quality manual. The quality manual, or equivalent documentation, should include a quality policy statement of management's commitment to an effective quality management system and to good professional practice. These policies should include a code of ethics and code of proper conduct to assure the reliability and completeness of data.
- All equipments related to manufacturing, testing, and packing of pharmaceutical products, APIs, finish products should be maintained and qualified for its intended use.
- Activities such as equipment qualification, analytical method validation, cleaning validation, stability study manufacturing process validation, analytical method or manufacturing technology transfers etc. should be executed on the basis of predefined , preapproved protocols and results of these activities should be documented in a final report with conclusions.
- Standard operating and test procedures should be clear and concise to provide directions to trained personnel regarding a given set of activities.
- A policy for retention and archiving of all records should be established. The length of time depends on the regulatory requirements or company policies consistent with its contractual obligations; however it should be 1 year after the batch expiration date.

References

1. WHO TRS 996. Annex 05. Guidance on Good Data and Record Management Practices
2. ISO/IEC 17025 - General Requirements for the Competence of Testing and Calibration Laboratories