



Good Documentation Practice (GDP) Guideline





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1. Preface

The IPA launched its Quality Forum (QF) in April 2015 to help Indian pharmaceutical manufacturers to achieve parity with global benchmarks in quality. The QF made a commitment to a multi-year journey to address key issues facing the industry and develop best practices. McKinsey & Company joined this journey as a knowledge partner.

The QF focused on three priority areas in 2015-16, namely, Data Reliability, Best Practices & Metrics, and Culture & Capability. It took upon itself the challenge of establishing robust and seamless data management and documentation systems and processes and released a comprehensive set of *Data Reliability Guideline* in February 2017. It then took up the task of developing a comprehensive set of *Process Validation Guideline* which will be released in February 2018.

The QF then focused on three more areas in 2016-17, namely Batch Failure Investigation, Complaints – Investigation & Review and Good Documentation Practice. The six participating companies in the QF nominated one senior manager each to study the best practice and frame the Guideline. They are: Anil Arora (Cadila Healthcare), Sanjeev Asgekar (Cipla), Sanjay S Shetgar (Dr Reddy's), Rajiv Desai (Lupin), Panjatcharam M (Sun), and Rakesh Sheth (Torrent). They were assisted in this task by Kartik Reddy and Nikhil Chug of McKinsey. The IPA wishes to acknowledge their concerted effort over the last 12 months. They shared current practices, benchmarked these with the existing regulatory guidances from the USFDA and other regulatory agencies such as UKMHRA, WHO, etc., developed a robust draft document and got it vetted by a leading subject matter expert. The IPA acknowledges their hard work and commitment to quality.

The IPA also wishes to acknowledge the CEOs of six member-companies who have committed their personal time, human resources and provided funding for this initiative.

This document, to be released at the IPA's 3rd India Pharmaceutical Forum 2018 in Mumbai, will be hosted on the IPA website www.ipa-india.org to make it accessible to all manufacturers in India and abroad.

Mumbai
31 January 2018



2. Introduction and Background

This guideline highlights, and in some instances clarifies, the application of data management procedures for all GMP documents. It lays down guidelines for preparation, recording and correction of data and maintenance of records throughout the lifecycle of a document.

It helps to understand who, when, where, why and how to complete the relevant activities and provides evidence to show whether these have been completed as expected.

3. Scope

The principles of good documentation practices are applicable to both paper and electronic data or records filled manually or generated electronically in a GxP environment.

4. Definitions

Accurate: Correct in all aspects or details. Accuracy is assured through equipment/instrument qualification, calibration and maintenance, validation, adherence to policies and procedures, data review, and self-inspection.

ALCOA: A commonly used acronym for ‘Attributable, Legible, Contemporaneous, Original and Accurate.’

ALCOA+: A commonly used acronym for ‘Attributable, Legible, Contemporaneous, Original and Accurate’ which puts additional emphasis on the attributes being ‘Complete, Consistent, Enduring and Available’– qualities which are implicit in the basic ALCOA principles.

Audit trail: The audit trail is a form of metadata that contains information associated with actions that relate to the creation, modification or deletion of GxP records. An audit trail provides for secure recording of lifecycle details such as creation, addition, deletion or alteration of information in an electronic record, without obscuring or overwriting the original record. An audit trail facilitates the reconstruction of the history of such events relating to the record regardless of its media, including the “who, what, when and why” of the action.

Archival: Archiving is the process of protecting records from the possibility of being further altered or deleted, and storing these records under the control of dedicated data management personnel throughout the required records retention period.

Attributable: Traceable to a unique individual. ‘Paper Record’ refers to the initials or hand-written signature of the individual, while ‘Electronic Record’ refers to the log-on user ID or electronic signature of the individual.

Predating/Backdating: Entering an earlier date to a paper document (or electronic record) than the actual one on which a task was performed.

Criterion	Meaning
Attributable	'Attributable' means information is captured in the record such that it is uniquely identified as executed by the originator of the data (e.g., a person and/or a computer system).
Legible	The terms 'legible', 'traceable' and 'permanent' refer to the requirements that data are readable, understandable and allow a clear picture of the sequencing of steps or events in the record.
Contemporaneous	'Contemporaneous' is the process of documentation (on paper or electronically) at the time of the occurrence of an activity.
Original	'Original' data includes the first capture or capture at source of data or information and all subsequent data required to fully reconstruct the conduct of the GxP activity.
Accurate complete	'Accurate' means that data are correct, truthful, valid and reliable. 'Complete' means that all data from analysis, including any data generated before a problem is observed, data generated after repeating part or all of the work, or re-analysis performed on the sample are contained in the data record. For hybrid systems, the paper output must be linked to the underlying electronic records used to produce it.
Consistent	'Consistent' means that all elements of the analysis, such as the sequence of events, follow on and data files are date-stamped (all processes) and time-stamped (when using a hybrid or electronic system) in the expected order and such data are contained in the record.
Enduring	'Enduring' means that all data have been recorded on authorized media which can be preserved for a period of time, e.g., laboratory notebooks, numbered worksheets, for which there is accountability, or electronic media. Data recorded on scrap paper or any other media which can be discarded later, e.g., backs of envelopes, laboratory coat sleeves or Post-It notes, etc. are not considered enduring.
Available	'Available' means that the complete collection of records can be accessed or retrieved for review and audit or inspection over the lifetime of the record.

Backup: A backup means a copy of one or more electronic files created as an alternative in case the original data or system are lost or become unusable.

Computerized System: A computerized system can create, modify, maintain, archive, retrieve or transmit electronic records. A computerized system consists of hardware, software and network components which together fulfill certain functionalities. They can also be defined as a logical entity, partially or entirely controlled by computer but may also include some equipment, utilities, sensors and actuators along with the governing procedures. Examples of such a system are Building Management System (BMS), Automated Manufacturing/Laboratory System, Document Management System, etc.

Contemporaneous: Activities that are recorded at the time when they occur. Entries into GMP records are dated and/or time stamped to document when the activities occur.

Data: Data means all original records and certified true copies of original records, including source data and metadata and all subsequent transformations and reports of this data, which are recorded at the time of the GxP activity and allow full and complete reconstruction and evaluation of the GxP activity. Data may be contained in paper records (such as worksheets and logbooks), electronic records and audit trails, photographs, microfilm or microfiche, audio- or video-files or any other media whereby information related to GxP activities is recorded.

Data Owner: An individual or a team who is responsible for data generation and storage.

Data Governance: The sum total of arrangements to ensure that data, irrespective of the format in which it is generated, is recorded, processed, retained and retrieved in order to ensure a complete, consistent and accurate record throughout the data lifecycle.

Data Integrity: Data integrity is the degree to which a collection of data is complete, consistent and accurate throughout the data lifecycle. The collected data shall be attributable, legible, contemporaneously recorded, be an original or a true copy, and accurate.

Effective Date: It is the date of the document after which it becomes ready for actual use.

Error: A mistake in a document that is observed after a document was printed /executed.

Electronic Records: Any combination of text, graphics, data, audio, pictorial or other information and/or representation in digital form that is created, modified, maintained, archived, retrieved or distributed by a computer system.

Electronic Signature: The technology and controls (automated and/or procedural) established to use electronic signature within a computer system.

Good Documentation Practices (GDP): Such measures that collectively and individually ensure documentation, whether paper or electronic, is attributable, legible, traceable, permanent, contemporaneously recorded, original and accurate.

GxP: Acronym for the group of good practice guides governing the preclinical, clinical, manufacturing and post-market activities for regulated pharmaceuticals, biologics, medical devices, etc., such as good laboratory practices, good clinical practices, good manufacturing practices and good distribution practices.

GMP Documents: All types of documents which have direct or indirect impact on all aspects of the quality of drug substances/products and which are required to demonstrate or provide evidence of adherence to GMP standards and/or any other applicable regulatory requirements, are collectively referred as 'GMP documents.'

Hybrid System/Approach: This refers to the use of a computerized system in which there is a combination of original electronic records and paper records which comprise the total record set that should be reviewed and retained. An example of a hybrid approach is where laboratory analysts use computerized instrument systems that create original electronic records and then print a summary of the results. The hybrid approach requires a secure link between all record types, including paper and electronic, throughout the retention period of the records. Where hybrid approaches are used, appropriate controls for electronic documents, such as templates, forms and master documents, that may be printed, should be in effect.

Legible: Readable by all users of a document. Entries must be permanent and changes should be traceable to a specific individual.

Metadata: Metadata are data about data that provide the contextual information required to understand those data. Typically, these are data that describe the structure, data elements, interrelationships and other characteristics of the data record. They also permit data to be attributable to an individual. For example, in weighing the number 8 is meaningless without metadata, i.e., the unit 'mg'. Other examples of metadata may include the time/date stamp of the activity, the operator ID of the person who performed the activity, the instrument ID used, processing parameters, sequence files, audit trails and other information required to understand the data and reconstruct activities.

Master Controlled Documents: All those approved documents which are usually under the custody of QA documentation cell/designated personnel and from which copies are made and issued for operational use. Examples of such documents include master manufacturing/production records, master packing records, validation/qualification/stability protocols, master SOP, specifications, standard test procedures, master templates/ analytical work sheets, etc.

Original: First capture of the data. Original records (or certified copies of the original records) must be reviewed and retained for future reference.

Paper-based Data: This includes recording formats (such as worksheets and logbooks), batch records, master records, green sheets, apex, but are not limited to these documents alone.

Post-dating: Entering a date for a future activity, i.e., before an activity takes place.

Raw Data: The actual information/data generated either in the form of worksheets/records, computer or instrument printouts, etc., that are result of original tests/observations/measurements/activities and forms the basis of quality decisions are collectively referred as 'Raw Data.'

Records: Records consist of any data that are collected during an operation.

Dynamic Record Format: Records in dynamic format, such as electronic records, that allows for an interactive relationship between the user and the record content. For example, electronic records in database formats allow the ability to track, trend and query data; chromatography records maintained as electronic records allow the user to reprocess the data, view hidden fields with proper access permissions and expand the baseline to view the integration more clearly.

Static Record Format: A static record format, such as a paper or electronic image, is one that is fixed and allows no or very limited interaction between the user and the record content. For example, once printed or converted to static PDF files, chromatography records lose the capabilities of being reprocessed or enabling more detailed viewing of baselines or any hidden fields.

True Copy: A true copy is a copy of an original recording of data that has been certified to confirm that it is an exact and complete copy that preserves the entire content and meaning of the original record, including in the case of electronic data, all metadata and the original record format as appropriate.

Prepared by/Done by/Performed by/Analyzed by/Sampled by/Calculated by: Such a remark records the person who is responsible for an activity by means of preparing, doing or performing the activity.

Verified by/Checked by: Such a remark records the person who is responsible for confirming or checking an activity, based on either:

- Watching or witnessing the activity being performed.
- Verifying that sequential steps were performed based on objective evidence.
- Verifying at end of the specific activity/process to ensure that the activity has been completed satisfactorily as specified in the respective GMP document.

Reviewed by: Such a remark records the person who is responsible for assessing and evaluating the activities performed, recorded, completed in the documents, based on the evaluation of supporting data/documents/references that have been attached.

Review: To look over, study or examine something with the aim of verifying the accuracy of the data.

Approved by/Certified by/Authorized by: Such a remark records the person who is responsible for approving GxP documents based on their evaluation of the conclusion(s).

5. Purpose

The purpose of this Guideline is to:

- Describe the requirements of maintaining complete, accurate, truthful and verifiable data in all cGXP documents that are needed to be maintained as per regulatory requirements and various Governmental regulations, laws, rules and statutes/acts.
- Describe the importance of data generation, maintaining data lifecycle, data governance and data reliability throughout the lifecycle of the document.

6. Responsibilities

Individuals involved in creation and execution of documents:

1. To follow the good documentation practices as defined in this Guideline and in-house policies.
2. To get themselves trained periodically on the principles of Good Documentation Practices.
3. Individuals are responsible for notifying their superiors and file deviations in cases of non-adherence to this Guideline and defined in-house policies.

Quality assurance:

1. Quality Assurance shall be responsible for issuance, storage, retrieval and destruction of controlled documents and records.
2. To ensure that all relevant individuals are trained on the principles of Good Documentation Practices and are following them, the Department Head will ensure refresher training of the persons involved in the GMP activities.

7. Procedure

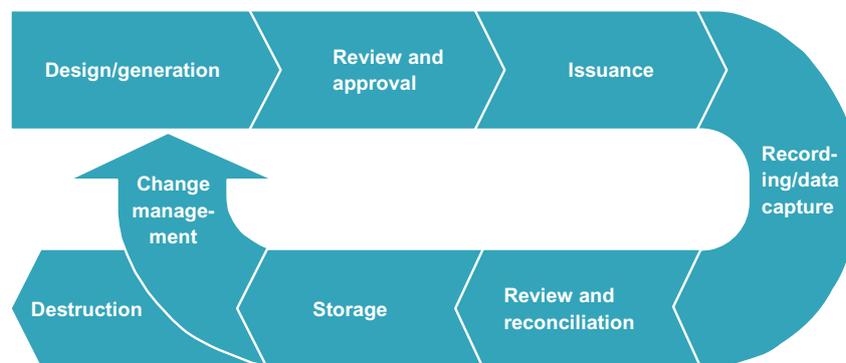
Approach towards record & data management:

The risk-based approach to record and data management shall ensure that adequate control strategies are in place for assurance of the integrity of GxP data. Risk mitigation with respect to record and data integrity risks associated with a process or system or throughout the data lifecycle shall be considered during preparation of risk assessment.

The approach also revolves around managing the entire document lifecycle for paper-based and electronic documentation as per Exhibit 1.

Exhibit 1

A comprehensive deliverable as a guidance for both manual and electronic document is designed



The guideline should articulate that key controls and best practices are captured separately for manual and electronic documents; for a hybrid flow, elements for both flows will be required as may be appropriate

SOURCE: IPA QF sub-group 6

Good documentation practices for manual/paper documentation:

1. Design/generation of manual/paper-based documentation

- 1.1 All documents must be accurate and written in a manner that prevents errors and ensures consistency.
- 1.2 Documents shall have unambiguous contents; the title, nature and purpose shall be clearly stated.
- 1.3 Pages in the master document shall be numbered as X of Y (e.g., Page 2 of 20).
- 1.4 Full text spelling with the abbreviations in brackets shall be used for the first time. Abbreviations may be used in place of full text spelling in the remaining part of the document.
- 1.5 Definitions shall be included in the document for reference. This is most effectively done by including the definitions in a table format, at the start or end of the document.
- 1.6 Reproduced documents shall be clear and legible. The reproduction of working documents from master documents must not allow any error to be introduced through the reproduction

process. A document reproduced from the original should be appropriately identified, e.g., name or identity of the person, date, time and number of copies made.

- 1.7 Records shall be made or completed when any action is taken and in such a way that all significant activities concerning the manufacture of pharmaceutical products are traceable. If documents are to be used together, e.g., a SOP and a form, then each shall reference the other.
- 1.8 All documents shall have the signature and date of the person who prepared, reviewed and approved the document.
- 1.9 All documents shall have an effective date and a review period if applicable.
- 1.10 Master formulae and detailed procedures (SOPs) relating to the system in use shall be available and the accuracy of the records shall be checked. Respective SOPs shall be followed while preparing the documents.
- 1.11 Changes or revisions to documents shall be assessed to check the impact and handled through a review and approval process of change management.
- 1.12 The roles of reviewer and approver shall be defined.
- 1.13 All documents shall have a unique identification number (including the version number).
- 1.14 The use of uncontrolled documents shall be prohibited by local procedures.
- 1.15 The use of temporary recording practices, e.g., scraps of paper, shall be prohibited.

2. Review and approval of documents

2.1 Review of GMP documents

- 2.1.1 Documents within the Quality Management System shall be regularly reviewed and kept up to date.
- 2.1.2 To ensure that the information is correct and accurate, documents and records shall be reviewed by someone who has performed the task and has proper knowledge. A signature and date by the reviewer shall confirm that a review has taken place.
- 2.1.3 When a document has been revised, a system shall exist to prevent inadvertent use of the superseded version.
- 2.1.4 Superseded documents shall be retained for a specific period of time.
- 2.1.5 Unsigned or incomplete documents or records shall not be used to perform any task or considered as evidence of a completed task.

2.2 Approval of GMP documents

- 2.2.1 Documents shall be approved, signed and dated by the appropriate responsible persons. No document shall be changed without authorization and approval.
- 2.2.2 All master documents shall have effective date, approval date and current version number.

2.2.3 Training on the document shall be planned only after approval of document and shall be completed before the effective date.

2.2.4 All GMP documents shall be approved by Quality Assurance.

3. Issuance of GMP documents

- 3.1 The formats or records associated with the activity shall be part of respective SOPs.
- 3.2 Master copies of controlled documents (paper-based and electronic) must be stored in a secure manner and accessible only to authorized individuals.
- 3.3 Records shall be maintained for issuance and retrieval of formats with traceability of the person who issued the document and the date and time when it was issued.
- 3.4 Appropriate procedures shall be in place to ensure that data is recorded in the Controlled Data Sheet or Current formats issued by Quality Assurance.
- 3.5 Appropriate procedures shall be in place to ensure that the system of controlled issuance of bound and paginated notebooks with sequentially numbered pages and blank formats is in place to allow persons to detect missing or skipped pages and help in accountability of issued formats.
- 3.6 Any document printed for review/reference purpose must have suitable watermarks or stamps to have adequate control on the document. This shall be signed and dated by the person who has printed the document.
- 3.7 Appropriate procedures shall be in place to control distribution of documents within the organization.
- 3.8 Reconciliation of issued documents shall be performed and recorded in the respective issuance log.

4. Recording/data capture on GMP documents

4.1 Recording of data on GMP documents

4.1.1 Handwritten entries shall be made in a clear, legible, indelible manner.

Where documents require the entry of data, sufficient space shall be provided for such entries and they shall be laid out in an orderly fashion and be easy to check.

Data overwriting is prohibited.

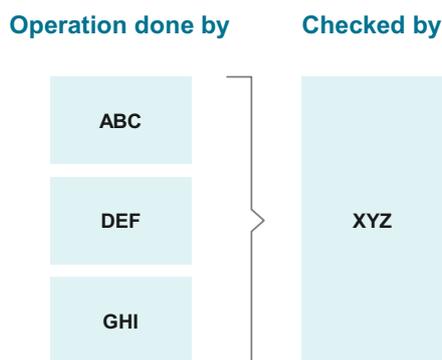
Where the ink fades or smudges during recording of data, the faded or smudged entries shall be struck out and a new entry must be made by giving appropriate justification with signature and date.

If data has been erroneously struck off, appropriate justifications shall be provided along with signature and date.

4.1.2 Indelible ballpoint pen shall be used to record data. Pencil or erasable or water-soluble ink pen shall not be used to complete the GMP documents.

- 4.1.3 Use of white ink, correction fluid or sticky notes (e.g., Post-it notes) to correct the entry in GMP documents shall not be permitted.
- 4.1.4 Entries shall always be recorded at the time of activity in a contemporaneous manner. Date and time of completion of activity shall be recorded in a predefined standard format as found suitable by the firm. The format of date and time should remain consistent throughout all the documentation formats across the firm. In case a printout generated by equipment/instrument/system has a different format, it shall be converted to the standard format while entering in logbooks/GMP documents.
- 4.1.5 It shall be ensured that the time displayed in all the systems, computers and clock of a manufacturing unit is synchronized by an authorized designated person or department.
- 4.1.6 In case operations are continued from one shift to another where the dates are different, the date shall be recorded against the timing in the date column.
- 4.1.7 All numerical/actual values displayed on or observed from the instrument/equipment shall be entered with appropriate units of measure (UOM) as applicable (such as Kg, gm, mg, °C, Psi) in a manner that assures no ambiguity to a second person.
- 4.1.8 Data shall be recorded only in the format duly issued and approved by Quality Assurance.
- 4.1.9 Logbooks shall be kept for major or critical analytical testing, production equipment, areas where product has been processed and other usage logs.
- 4.1.10 Entries in the logbooks shall be made in chronological order including the dates; such entries shall identify the people who carried out these operations. Entries shall never be pre-completed.
- 4.1.11 Data recording shall be done by trained and authorized persons.
- 4.1.12 Data shall be recorded exactly as it is displayed on the respective equipment panels.
- 4.1.13 The numerical value of the data shall be recorded as is (i.e., with all decimals) as it appears in the displays.
- 4.1.14 Numeric rounding practices and recording of significant figures after calculation shall be predefined and followed.
- 4.1.15 Unusual observations during the activity shall be recorded, signed and dated. The same shall be reported to the area person in-charge and QA.
- 4.1.16 If any observation/signature/date is to be repeated, the same shall be rewritten. Markings such as Ditto (-- --), “ as above” or “do” shall not be used.
- 4.1.17 Records should capture the actual and clear observations. Shortcuts such as putting remarks like OK/Not OK, Comply, Done. etc., shall not be acceptable. However, in certain formats like checklists, where the activity is to be conducted and recorded, “Yes” or “No” shall be written indicating whether the activity was performed or not performed. The same shall be signed by the person executing the checklist.

- 4.1.18 Bracketing, such as (), in any form shall not be done to group or to provide the same answer to multiple check points. For example, remarks as shown below are not acceptable:



- 4.1.19 Data recorded in GMP documents shall always be signed and dated.
- 4.1.20 No employee shall be permitted to sign for another member of the staff unless authorized. Signatures shall never be forged.
- 4.1.21 Pre-dating or post-dating of GMP documents is not an acceptable practice.
- 4.1.22 Scratch papers, loose papers or “Post-it” notes shall not be used to record the data.
- 4.1.23 Raw data/print outs or supplements generated during the activity shall be signed, dated and attached with relevant record. Printouts made on thermal paper from an instrument/system shall be photocopied and both the copies shall be secured along with the report. The photocopy shall be marked as “COPY OF ORIGINAL” or “COPY OF TRUE COPY” as appropriate on the photocopy along with initial and date. Information on thermal paper should not be taped over, since the tape will cause the data to fade rapidly.
- 4.1.24 Blank/unused space in the document shall be struck through with a single line with signature and date to ensure that a record cannot be altered on a later date.
- 4.1.25 In case of blank fields wherein striking out is not feasible, “NA” shall be mentioned. This shall indicate that the blank space was not skipped or forgotten while making entry.
- 4.1.26 Where there is a space constraint in making a manual entry in the GMP documents, an additional page can be included as attachment/annexure which shall be numbered with a cross reference in the mother record to which it is attached. The attachment/annexure shall bear paginated with sequential numbering (e.g., Page 1 of 2 or Pg. 1/2 and so on).
- 4.1.27 In the case of modifications to a document before final approval, an additional page can be attached to the original document as attachment /annexure with the changes made, which shall be cross-referred to the original/mother document. The concerned department involved in the approval process shall be informed and involved in the signatory cycle.

4.2 Signing of GMP documents

- 4.2.1 Handwritten signatures must be unique to the individual and listed within the Specimen Signature Register to ensure that the signature is traceable to the concerned employee (or contractor). This register shall have a list of personnel with long and short specimen signature (initials).
- 4.2.2 The meaning of a signature shall be communicated to the personnel involved in signing off GMP documents.
- 4.2.3 Long signatures shall be used for signing of approval page or signing off a master document, report or record.
- 4.2.4 Signing any GMP documents indicates that the person is in agreement with the information provided or conclusions in the record, and is accountable for the documents he/she is signing.
- 4.2.5 The management of the signature record shall be governed by a procedure and routinely reviewed so that it remains current. New employee shall sign the signature register during induction; the signature register must also indicate the date of employee exits.
- 4.2.6 Use of a personal seal to sign documents requires storage of the seal in a secure location with access limited only to the assigned individual, or other means of preventing potential misuse.

4.3 Handling of Missing Entries and Corrections

- 4.3.1 Any alteration/correction of manual entries shall be made in on-line (contemporaneous/concurrent) documentation, and the document shall be signed and dated by the person who made the original entry. If this is not possible, QA shall be notified accordingly. The alteration shall permit the reading of the original information.
- 4.3.2 A single strike-out line must be used always to mark the incorrect entry in such a manner that original entry remains readable. The correct entry shall be written near to the strikeout entry. The reason for alteration, e.g., transcription error, typographical error, recording error, calculation error, etc., shall be recorded. Wherever necessary, detailed reason/justification for such corrections shall be provided for better clarity. For example, in case '01/01/15' is recorded by mistake in place of '01/01/16' and this mistake is observed later during BMR review on 04/01/16, it can be corrected at a later date in the following manner:

~~01/01/15~~ Sign/Date

01/01/16 (Reason)

If changes/corrections have been made to critical data entries, it must be verified that a valid reason for the change has been recorded and supporting evidence for the change is available.

- 4.3.3 Any corrections to a signed-off document shall be routed through error ratification procedure and kept along with original document.
- 4.3.4 Missing entry in the GMP documents for non-retrieval data shall be handled through deviations procedure, for example, an operator has missed the reading of the drying temperature during the operation where there is no automatic data recording mechanism in place.
- 4.3.5 If during review, any entry or signature is found to be missing and if a suitable evidence for execution of that entry or presence of that person in that process is available, then a symbol (*, @, #) shall be done at the place where entry/signature is missed and at the bottom of that page a remark shall be mentioned with the correct entry and reason which shall be initialed as on current date.

Example 1: If a temperature reading was missed out in a record, for which there is supporting electronic data indicating the temperature reading, then the same shall be handled by the above-mentioned procedure. The printout of the temperature reading generated from the system shall be attached with the original record as evidence.

Example 2: If the review reveals missing signature of a person in a record, and there is sufficient evidence that the concerned person was available during the operation, the same shall be handled by above-mentioned procedure with evidence retained with the record.

- 4.3.6 If an error is observed in the master documents, it shall be handled through error ratification procedure or change management, depending on the impact of error.
- 4.3.7 The nature of corrections made shall be reviewed to analyze if they can be incorporated on a permanent basis.
- 4.3.8 In case a data entry error is observed in electronic GMP documents (e.g., transcriptional entry errors), a documented procedure shall be put in place (e.g., having a log to maintain data entry errors).

5. Review and reconciliation of GMP documents

5.1 Error Ratification

- 5.1.1 The errors identified in documents shall be notified to the head of concerned department who owns/is responsible for the document.
- 5.1.2 The error identified shall be verified by the concerned department head to initiate an error ratification form as per Annexure 2.
- 5.1.3 An appropriate numbering system shall be in place for sequential numbering, logging and traceability of error ratification forms.
- 5.1.4 Errors which lead to confusion or complete deviation from the actual meaning of the intended use of the document or have direct impact on product quality shall be routed through deviation procedure.
- 5.1.5 The details of error and the document in which the error was identified shall be recorded as per Annexure 2 and the impact of error shall be assessed.

- 5.1.6 Methodology of rectification of error shall be recorded (e.g., updating the documents, trainings, etc.).
 - 5.1.7 If a correction is required in documents submitted to a regulatory body or a customer, they shall be routed through Regulatory Affairs.
 - 5.1.8 Upon approval and verification by Quality Assurance, the changes shall be made to the document as per the defined methodology for rectification of error.
 - 5.1.9 The original error ratification form shall be maintained by Quality Assurance and a photocopy of the same shall be attached and retained with the respective document.
 - 5.1.10 Quality Assurance shall review and close the error ratification form. Where required, CAPA shall be logged.
 - 5.1.11 Justification for delay in closeout of the error ratification form shall be provided.
 - 5.1.12 A limit should be set on the error ratification forms allowed to be raised for one document. (e.g., not more than 3 Error Ratification Forms shall be allowed for a master document).
 - 5.1.13 Any change in input quantity, numerical value/formula, change in calculation, yield, and addition/deletion of processing step should be routed ONLY through change control procedure.
- 5.2 Cancellation of GMP documents
- 5.2.1 Cancellation of records shall be handled through change management procedure, capturing the reason for cancellation and signed by area person in-charge and Quality Assurance.
 - 5.2.2 The data shall be transcribed with proper justification. The voided data shall be cross referenced in the new document by attaching the original document for traceability.
- 5.3 Missing Documents
- 5.3.1 If any executed record has been lost or is not traceable then it shall be handled through a deviation procedure.
 - 5.3.2 In case of torn/damaged page of document or record, the following procedures should be followed:
 - 5.3.2.1 If any document or record has been torn/damaged during handling, all portions of the relevant pages shall be joined with transparent cello tape and a photocopy of the page shall be taken and signed off with justified reason in the footnote of the document, treating it as original document. It is necessary to retain the original pieces /portions of such pages along with a photocopy of the document.
 - 5.3.2.2 In case of spillage on any document thereby making the entry illegible, this shall be brought to the notice of the department head and further action shall be taken based on decision by Quality Assurance. An incidence report shall be filed and the re-issuance of the format shall be requested to Quality Assurance. The spoiled copy shall be retained along with the new copy.

6. Storage and retrieval of GMP documents

6.1 Retention of Document

- 6.1.1 There shall be pre-defined retention periods for different sets of documents.
- 6.1.2 An inventory of documents within the quality management system should be maintained.
- 6.1.3 It shall be clearly defined as to which record is related to each manufacturing activity and where this record is located.
- 6.1.4 The maintenance of paper records shall be such that it should be easy to archive the records at any time during the record lifecycle.
- 6.1.5 Secure controls must be in place to ensure the integrity of the record throughout the retention period and validated where appropriate.
- 6.1.6 For other types of documentation, the retention period will depend on the business activity which the documentation supports. Critical documentation, including raw data (for example, relating to validation or stability) which supports information in the Marketing Authorization, shall be retained whilst the authorization remains in force.
- 6.1.7 It may be considered acceptable to retire certain documentation (e.g., raw data supporting validation reports or stability reports) where the data has been superseded by a full set of new data.
- 6.1.8 Justification for this shall be documented and shall take into account the requirements for retention of batch documentation; for example, in the case of process validation data, the accompanying raw data shall be retained for a period at least as long as the records for all batches whose release has been supported on the basis of that validation exercise.

7. Revision of GMP documents

- 7.1 All revised documents shall mention its revision history.
- 7.2 Periodic reviews of controlled documents and forms shall be done as per approved procedure and shall be handled through a change approval process.
- 7.3 Only authorized personnel shall revise the documents.
- 7.4 Document revisions shall always be version controlled and only the latest version shall be used at any point in time.
- 7.5 Versions of documents created shall be managed through logbooks.
- 7.6 Revised documents shall have date/time stamped and shall also be signed by respective personnel.
- 7.7 All revisions of GMP documents shall be handled through change approval process.

8. Destruction of GMP documents

- 8.1 A record shall not be destroyed before its stated retention period or validity without appropriate justification and consultation with Quality Assurance.
- 8.2 Any approved or under approval GMP document shall not be discarded or destroyed without the appropriate stamp authorizing cancellation/obsolescence.
- 8.3 Any draft SOP, reference document or record printed for review/reference purpose with a watermark "Draft" can be destroyed. These shall be destroyed by appropriate means like shredding. Documents which are under approval or review shall be stamped appropriately indicating that it is submitted for correction.
- 8.4 Labels used at different process levels shall be destroyed by defacing with a cross "X" mark on it (e.g., status label of equipment, cleaning labels, visual inspection status labels, leak testing status label, product quarantine and release labels, etc.).

Good documentation practices for electronic documentation:

1. Design/generation of electronic documents

- 1.1 Appropriate roles shall be defined with relevant privileges on the electronic system to ensure that there is no overlap of roles.
- 1.2 Access to the master templates shall be controlled.
- 1.3 Access control shall be provided either through biometric or two level controls (unique username and password).
- 1.4 Process controls for creating and updating versions should be clear and practically applied.
- 1.5 Document design should allow entering of data contemporaneously.
- 1.6 Data (and records for storage) may be recorded by electronic data processing systems or by photographic or other reliable means.
- 1.7 Data processing methods should be approved, identifiable and version controlled.
- 1.8 For hybrid systems (part manual and part electronic) a clear white paper shall be produced which is version controlled and describes the systems which are electronically controlled with a roadmap for the future.
- 1.9 For activities where an electronic record is generated in addition to a paper document, it shall be determined in advance whether the electronic record or paper record is used in any decision making process.

2. Review and approval of electronic documents

- 2.1 Review of GMP electronic documents
 - 2.1.1 For data generated from a computerized system, regular review of audit trails shall be conducted to identify incorrect processing of data and prevent incorrect results from being reported. It shall be ensured that both administrative audit trail and business workflow related audit trail are reviewed for each system/application.

2.2 Approval of GMP electronic documents

- 2.2.1 All system based documents shall be approved by Quality Assurance.
- 2.2.2 Review and approval flow of documents shall be designed.
- 2.2.3 Document review and approval should be managed through change control.
- 2.2.4 Approval with electronic signatures should have appropriate date/time stamps.

2.3 Signing of electronic GMP documents

- 2.3.1 The meaning of signature (manual or electronic) shall be communicated to the personnel involved in signing off GMP documents.
- 2.3.2 Signing any GMP documents (manual or electronic) indicates that the person is in agreement with the information provided or conclusions in the record and is accountable for the documents he is signing. (Refer format Annexure 1 for Electronic Signature Accountability Certificate).
- 2.3.3 Equipment/instrument that are access-controlled shall have individual ID and password so as to ensure the capture of attributable records. If individual ID and passwords are not available, all activities associated with those equipment shall be documented for the person who performed the independent activity and when.
- 2.3.4 Use of stored digital images of a person's hand-written signature to sign a document shall not be permissible.
- 2.3.5 Electronic signatures shall be executed to electronically sign off a record, which shall be unique to the individual and shall not be reused by or reassigned to anyone else.
- 2.3.6 An electronic signature must be based on a combination of an identification code (e.g., username) and a password.
- 2.3.7 A signed-off electronic record shall contain information that indicates the following:
 - Printed name of signatory or ID
 - Date and time when signature was executed
 - Meaning of signature (such as review, approval, responsibility)
- 2.3.8 Application of electronic signature to an electronic record must be done at the time the corresponding action or activity is performed and applies to current contents of the record.
- 2.3.9 Non-biometric electronic signature shall employ at least two distinct identification components such as identification code or password.
- 2.3.10 The uniqueness, security, and authenticity of electronic signatures shall be validated during computer system validation.
- 2.3.11 A hybrid approach may be used to sign electronic records when the system lacks features for electronic signatures. For example, a single-page controlled form would

provide fields for the author, reviewer and/or approver of the dataset to apply a hand-written signature. This paper record with the hand-written signatures shall then be securely and traceably linked to the electronic data set, either through procedural means or technical means, such as embedding the scanned image of a certified true copy of the signature page into the electronic dataset.

3. Issuance (control) of electronic documents

3.1 Issuance of GMP electronic documents

- 3.1.1 Automated mail communication should reach the users upon document version changes.
- 3.1.2 Controlled documents shall be issued through document management system.
- 3.1.3 Controlled documents shall have an “issued by” date and time stamp along with name of the person responsible for their dissemination.
- 3.1.4 Authorized personnel shall update the master documents in document distribution system.
- 3.1.5 e-BMR/BPR shall be downloaded with process order.
- 3.1.6 Date and time stamped audit trail records shall be available for document issuance.
- 3.1.7 Periodic audit trail/system audit trail reviews must be conducted.

3.2 Controls on Electronic Data

- 3.2.1 Master documents should be stored in a manner which prevents unauthorized changes.
- 3.2.2 Appropriate controls for electronic documents such as templates, forms, and master documents shall be implemented. Appropriate controls shall be in place to ensure the integrity of the record throughout the retention period.
- 3.2.3 If documentation is handled by electronic data-processing methods, only authorized persons shall be able to enter or modify data in the computer, and there shall be a record of changes and deletions; access shall be restricted by passwords or other means and the entry of critical data shall be independently checked.
- 3.2.4 The use of shared and generic log-on credentials shall not be permissible, since it is essential that personnel actions documented in electronic records can be attributed to a unique individual.
- 3.2.5 Where adequate technical controls are not available or feasible in legacy electronic systems, combinations of paper and electronic records shall be used to meet the requirements to attribute actions to an individual.
- 3.2.6 Users shall not have the ability to amend or switch off the audit trails or have access to alternative means of providing traceability of user actions.

- 3.2.7 Where a computerized system lacks computer-generated audit trails, persons may use alternative means such as procedurally-controlled use of logbooks, change control, record version control or other combinations of paper and electronic records to meet GxP regulatory expectations for traceability to document the what, who, when and why of an action.
- 3.2.8 Business process owners and users shall not be granted system administrator privileges, at any system level (e.g., operating system, application, database), which will enable them to change settings to overwrite, rename, delete, move data, change time/date settings, disable audit trails and perform other system maintenance functions that turn off the GDP controls for legible and traceable electronic data. Such permissions may be given to persons fully independent of the persons responsible for the content (e.g., IT, metrology, records control, engineering, etc.).
- 3.2.9 GMP documents stored electronically shall be protected by backup transfer on magnetic tape, microfilm, paper print-outs or other means. Backup activities shall be conducted according to a predefined schedule and such procedures should be documented.
- 3.2.10 Data saved electronically and respective paper prints shall be checked so as to ensure that the printed data are accurate and identical to the electronic data.
- 3.2.11 The ability to restore and read the backup electronic data should be verified as per a predefined schedule.

4. Recording/data capture on electronic documents

- 4.1 Electronic log must be maintained for document usage. In case of electronic data, the computer systems shall have adequate controls in order to prevent alteration of time/date stamps.
- 4.2 Data shall be entered electronically.
- 4.3 The system shall prompt for error messages for missing data.
- 4.4 Exceptions shall be generated for out-of-limit results.
- 4.5 All entries shall be captured in an audit trail with date and time stamp and name of the personnel.
- 4.6 Executed documents shall be released by Quality Assurance.
- 4.7 It shall be ensured that the time displayed in all the systems, computers and clock of a manufacturing unit is accurate and synchronized.
- 4.8 Equipment/instrument should be connected to electronic system for real time data transfer.
- 4.9 Electronic master production and control record must be validated to run the workflow correctly.
- 4.10 Audit trails that capture changes to critical data should be reviewed with each record before final approval of the record.
- 4.11 E-BMR and LIMS shall be designed to automatically save the data after each separate entry like paper record.

- 4.12 In case of electronic records, the configuration settings or SOPs, as feasible, shall enforce committing of electronic data to durable media at the time of the activity and prior to proceeding to the next step or event in the sequence of steps and events.
- 4.13 When e-logbooks are maintained, an alternative mechanism shall be available to handle situations in case the e-logbook is not working.
- 4.14 Electronic data generated from instruments shall be stored in a defined path of PC/Server. The data storage path shall be defined.
- 4.15 File and project naming conventions are defined by procedure and should be followed accordingly.

5. Review and reconciliation of electronic documents

- 5.1 Cancellation of GMP electronic documents
 - 5.1.1 Cancellation of electronic records shall be allowed only in rare cases supported by suitable justification with the approval of Quality Assurance.

6. Storage and retrieval of electronic documents

- 6.1 Storage of electronic documents
 - 6.1.1 Privileged personnel should have access to the document archival system.
 - 6.1.2 Document shall be stored in suitable media/server, labeled and stored in designated folders for easy retrieval.
 - 6.1.3 Electronic data shall be stored in suitable conditions, free from environmental, vibrations and magnetic fields.
 - 6.1.4 Data modification or deletion shall be tracked through an audit trail.
 - 6.1.5 An electronic log shall be maintained for document archival.
 - 6.1.6 Contingency plans and procedures for disaster management shall be in place for data security.
 - 6.1.7 Data recovery shall be done periodically based on documented procedures.
 - 6.1.8 Reconciliation log shall be maintained for archived data and shall have date/time stamp.
- 6.2 Retention of electronic document
 - 6.2.1 If an electronic record is copied to another system, the metadata including the audit trail and electronic signature is not required to be copied, but must be retained in the original system. If original system is no longer maintained, the metadata and audit trail and electronic signature must be migrated along with the electronic record.
 - 6.2.2 Secure controls must be in place to ensure the integrity of the record throughout the retention period and validated where appropriate.

7. Revision of electronic documents

- 7.1 Revision of electronic documents shall have the revision history on the document.
- 7.2 Revision history shall be periodically reviewed and any changes shall be handled through change control procedure with assessment of impact on validation.
- 7.3 Privileged persons shall revise the documents.
- 7.4 Document revisions shall be version controlled.
- 7.5 Obsolete- versions shall be automatically removed after uploading the latest versions in distribution system.

8. Destruction of electronic documents

- 8.1 Electronic data shall not be destroyed. All electronic data shall be perpetual.

Recommendations for the future

Going forward, documents will be increasingly in electronic formats. However, the following key considerations are critical while (a) deciding which documents should be made electronic (b) designing a robust transition process from manual to electronic.

- Risk based prioritization of manual documents for migration to electronic format
- Risk based selection of computerized system (e.g., Documentum/eBMR) for creation, review and issuance of document in electronic form.
- Comprehensive project plan including actions to be taken during migration to fully electronic state (hybrid documents), investment in resources (infrastructure & people) and capability building (operational and IT).

8. Revision history

Revision no	Effective date	Reason for review	Remark(s)
00		Not Applicable	

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