BEST PRACTICE: GOOD DOCUMENTATION PRACTICES IN THE QUALITY CONTROL LABORATORY

OVERVIEW

Purpose

This Standard Operating Procedure (SOP) defines the procedures for the use of laboratory notebooks / Test Sheets / Forms in the Quality Control (QC) laboratories.

Scope

This procedure applies to all QC laboratories that use laboratory notebooks / Test Sheets / Forms to record cGMP testing activities at the _____ site.

Reference Documents

The following table lists the documents referenced in this procedure:

Document #	Title
tbd	

Roles and Responsibilities
The following table lists the roles and responsibilities for this procedure.

Role	Responsibility
Analyst	Responsible for: ▪ Documenting and recording all GMP laboratory analyses in accordance with the Good Documentation Practices (GDPs) outlined in this procedure
Document Administrator	Responsible for: ▪ Ensuring that unique codes/numbers are assigned to each laboratory notebook / Test Sheet / Form ▪ Ensuring that each page is marked with the unique number and is sequentially numbered ▪ Maintaining a log of issuance and completion ▪ Storing completed laboratory notebooks / Test Sheets / Forms
Lab Management	Responsible for: ▪ Ensuring compliance to this procedure ▪ Ensuring that Analysts are trained on this procedure ▪ Ensuring that the issuance and archival of laboratory notebooks / Test Sheets / Forms is properly administered
QA	Responsible for: ▪ Ensuring compliance to this procedure

Definitions

Term or Phrase	Definition
Controlled Form	A controlled document (e.g., analytical test sheet, etc.) derived from, verified against, and related to an approved SOP or test method. Controlled forms are governed by Change Control. The form is suitably formatted to allow efficient recording of a series of actions listed in the associated test procedure. Controlled forms must be issued/assigned a unique control issue number, be dated at the time of issue, and reference the associated controlling SOP or test method to allow for verification. The disposition of all controlled forms must be tracked, and they cannot be discarded once issued. Controlled forms created as analytical test sheets to replace the use of lab notebooks should be used as the primary means to document the analysis if equivalent (or better) controls are in place to manage their use.
Documentation Shorthand and Abbreviations	▪ Shorthand descriptions of materials, glassware use, solution preparations, etc, are acceptable but must be meaningful and denote the correct accuracy. Any abbreviations must be more than an assigned number or letter and should be able to describe the item or action without cross-referencing to a previous section of the analysis. ▪ Shorthand symbols of common lab actions are acceptable for recording solution preparations, etc. when approved by Lab Management, including: o slash (/) or arrow (→) symbols used to denote a material was "transferred into" a container NOTE: The type of container and units of measure are still required to adequately describe the action. o colon (:) symbol used to denote a ratio, where one quantity of material (e.g. solvent) is "added to" a second quantity of material o "QS" or "qs" abbreviation, meaning "diluted to volume" or "quantity sufficient" ▪ Common clerical, scientific, or numerical symbols are acceptable, including: o & (and), # (number), ~ (approximate), ✓(checked)
Laboratory Notebook	A bound, hardcover book whose cover and/or binder is permanently and uniquely marked. Each page includes the unique lab notebook identifier and is sequentially numbered to ensure data traceability at the site. Once executed, notebook entries become a legal record. As such, the notebook should be of high quality, formatted, and pre-printed with a table of contents and pages having: ▪ A header section to record the title and/or project ▪ A lined, bordered area for recording raw data

Term or Phrase	Definition
	▪ A footer section to allow for signatures and dates of the user (i.e., analyst) and witness/reviewer ▪ Pre-printed with "Continued From" and "Continued To" (or equivalent) to facilitate data traceability
Raw Data	Any data generated or captured during the execution of a test method or protocol or in support of a GMP related activity constitutes raw data. Raw data that has undergone a change, transformation, or rendering is considered processed data. Some examples of (raw) data include: ▪ Observations ▪ Memoranda ▪ Notes ▪ Physical measurements ▪ Photographs ▪ Information from lab reagents and materials (e.g., lot number of a solvent or filter, etc.) ▪ Calculations ▪ Results ▪ Transcriptions ▪ Signatures and dates ▪ Instrument output (displayed value or analog printout) ▪ Executed worksheets or forms ▪ Recorded actions and test conditions ▪ Electronic (digitized) data files, including all processed data files ▪ Exact copies of original data ▪ Standard, sample, and solution preparations ▪ Equipment/metrology information The proper capture and recording of raw data is necessary for the evaluation and potential reconstruction of a test or analysis. In the event that exact transcriptions of raw data have been prepared and independently verified, the exact copy or exact transcript may be substituted for the original source as raw data.
Supplemental Data Packet (SDP)	A grouping of original data or hard copies of data, including instrument output that result from a singular analysis. Data that is typically too large or has too many pages to be properly affixed to the pages of a laboratory notebook / test sheet / form is considered supplemental or ancillary data.
Uncontrolled Form	A template created to facilitate recording of raw test data. Uncontrolled forms (e.g., empty tables to summarize data) are affixed to the laboratory notebook / test sheet / form and should be treated as supplemental data to the analysis. Uncontrolled forms are not issued or tracked and do not require a unique control issue number.

Issuance of Laboratory Notebooks and Test Sheets

1. Laboratory Notebooks and Test Sheets must be uniquely coded and assigned sequentially within the QA/QC Department.
2. The coding format minimally consists of a unique 5 digit sequentially numbered code. Alpha-numeric codes may also be created (e.g., 00129, or A00129).
3. If not pre-printed, each page must be clearly stamped with the unique code and page number.
4. Designated QA/QC resources will administer (e.g. Document Administrator) the issuance process by maintaining a log to record and track usage.
5. The analyst requests a laboratory notebook or test sheet from the administrator (if not supplied with the test sample). The laboratory notebook or test sheet will be used to record all raw data generated during GMP activities.

   Note: Laboratory notebooks can also be designated to log/track specific lab tasks, such as sample handling, training, and record other laboratory data, such as reference standard usage and shared standard/solution preparations, etc.

6. At time of issue, the analyst will sign and date the Issuance Log indicating the receipt of a new laboratory notebook or test sheet. The responsible analyst will also record their printed name and start date into their notebook.
   a) No more than 3 notebooks can be issued to an analyst and can be in use at the same time.
   b) Multiple notebooks may be issued to lab supervisors or lab managers when designated as logbooks (e.g., for sample tracking or logs).
7. The administrator will sign and date the Issuance Log at the time the completed laboratory notebook or Test Sheet is returned.

   Note: Test sheets may also be stored with the batch record.

8. QA/QC will store the laboratory notebook or Test Sheet until final archival.
9. Loss of a laboratory notebook or Test Sheets will require the issuance of an exception report, and an assessment into the loss of any analytical work and an evaluation of any possible impact on materials or product will be required.

General Format and Use

Documenting in Real-Time

1. Information/data must be entered into the notebook or test sheet as it is collected and in chronological order. All entries must be consecutive and chronological. Do not pre-record sections of the analysis.
2. Do not leave space for later entry.
3. Do not record any observations on separate pieces of paper or copies of the test method for subsequent transfer to the laboratory notebook or test sheet.
4. Only use the laboratory notebook or test sheet to record raw data, such as calculations showing solution scale up.
5. If applicable, start a new page each day and record the date. Additionally, if the analysis is still in-progress, fill in the page numbers using the "Continued To" and "Continued From" sections.
6. Laboratory notebook pages and test sheets should be signed each day analytical work is performed. At the end of each full page, the analyst must sign and date the bottom of the page.
7. Void any unused portion of the page using a diagonal line and then sign and date to establish that no additional data will be entered onto the page at a later time.

General Documentation Practices

1. All entries must be legible.
2. Clearly list and separate each major section of the analysis (e.g., using uppercase, STANDARD PREP, or underlining, Standard Prep).
3. Record data directly into the laboratory notebook or test sheet with permanent, indelible dark (e.g., black) ink. The written record must be suitable for photocopy (medium point pen is preferred). Penciled entries and colored markers (e.g., highlighters) are not permitted.
4. All blank portions of a page that are more than 3 consecutive lines must be properly voided (lined out) using a single diagonal line. Sign and date next to this line, using "Not Applicable or "NA" as the reason.

5. The removal of any data or pages from a notebook/test sheet or the obliteration of any data within a notebook/test sheet, document, or template that has been affixed is strictly prohibited.
6. Record within the printed boundary of the page. Post-analysis remarks can be added beyond the boundary as a result of the data review process, and must be signed and dated with accompanying reason.
7. Cross out errors with a single line and sign and date. Corrections made must include a reason. Footnoting, indicating multiple corrections for the same reason, is allowed.
8. The use of correction fluid or correction tape or the use of anything that obliterates data is specifically prohibited.
9. Document a complete description of anything that is unusual, unexpected, or out of the ordinary.
10. If exceptions or deviations from the test method are expected (e.g., extending the chromatographic run time, scaling down a dilution, etc.), the analyst must first document the intended change. The supervisor should review and approve the entry and justification prior to the analyst proceeding. The analyst and supervisor must both provide a signature and date next to the entry.

    NOTE: Scale-up of reagent preparations does not require pre-approval, but must be recorded in the notebook.
11. Laboratory notebooks must have a table of contents, which should be updated by the analyst upon the completion of the notebook.
12. Laboratory data are recorded by analysis type or technique for a specific material or product. The analysis shall be initiated and traceable to a work request, manufacturing lot number, test method, protocol, investigation, etc.
13. Each analysis is started on a separate notebook page or test sheet. Do not record different techniques or objectives with the initial analysis. Multiple lots of the same product can be recorded under the same notebook reference or test sheet number if the analysis and measurement for all preparations is performed at the same time or is a continuation of an ongoing analysis.
14. Include all units of measure and conversion or equivalency factors, where applicable.
15. Show calculations and record all results. All raw data must be included. Include an example calculation for each different type of calculation used.

16. Shorthand descriptions of materials, solutions, or preparations, etc, are acceptable, but must be meaningful. Any abbreviations must be more than an assigned number or letter and should be able to describe the item or action without cross-referencing to a previous section of the analysis.

Cross-Referencing

1. If data from another document or notebook or test sheet is used, it must be cross-referenced.
2. If data from another notebook or logbook is cross-referenced, ensure that the information is reviewed prior to, but no later than, the date when the data in the referencing notebook is reviewed and signed off.
3. If the analysis will be continued by another analyst, the first analyst should:
    a) Note the handoff by signing and dating in the page where they left off.
    b) State the status of the work as they left it and the name of the analyst who will continue the work. For example, "HPLC set-up completed. Transferred to John Doe – NB 00020-12".
    c) Add the second analyst's notebook and page number in the "Continued To" section at the bottom of the page. Void any unused portion of the page using a diagonal line across the page.

    The second analyst should record their work in a similar way by cross-referencing the first analyst's notebook reference.
4. If an analysis continues onto another page, at the bottom of the page, the analyst should clearly state
    a) "Continued on page" and list the page number where the write-up continues.
    b) On the continuation page, the analyst should write "Continued from page" and list the page number that the analysis is continuing from.
5. If this information is pre-printed in the notebook or test sheet, the analyst just fills in the page numbers, if applicable.

Using Inserts and Attachments

1. Sign, date, and add the notebook number & starting page or unique test sheet number to each insert or attachment. Attach inserts with tape or acid-free glue to fit flat on the notebook page. Sign and date across the edge of the insert and onto the original page to establish that the insert was attached when stated. Stapling an attachment to the page is not considered a permanent action.
2. If permanently attaching a chart or printout into the notebook is not feasible, summarize the output in the notebook and cross-reference the original output. The

original output is added to the Supplemental Data Packet (see later section describing the use of Supplemental Data Packets).

3. Any uncontrolled templates affixed into the notebook must be blank prior to adding them to the notebook. As verification, the insert must be signed and dated across the page by a second analyst or data reviewer before using.
4. If separate standardized, controlled forms are used to collect data during an analysis, reference their use in the notebook and add the completed form to the SDP. A minimized copy of the controlled form can be affixed in the notebook if the original is included in the SDP.

Specific Requirements to Ensure Good Documentation of Test Data

Specific Requirements

1. Each write-up should contain some or all of the following sections and information, as appropriate, clearly listed and sufficiently separated on the page.
    a) Header – title and project
    b) Method and Specification Reference
    c) Sample Information
    d) Reagents and Solutions
    e) Equipment and Materials
    f) Standard Preparation
    g) Sample Preparation
    h) Instrument Setup
    i) System Suitability
    j) Calculations
    k) Results
    l) Conclusion
2. **Header – Title:** Include the type of analysis, analyte name, and technique (e.g., "Impurities of XXX by HPLC").
3. **Method Reference:** Record the method name, number/code, version (and/or current effective date).
    a) Reference the test method, procedure number, protocol, or compendial method (e.g., USP <general chapters>) used

    NOTE: The analyst should not record the preparation steps verbatim from the test method, but does need to record the actions necessary to demonstrate that the test was fully executed as intended, including steps affecting integrity of the data and data traceability.
4. **Specification:** Record the current specification number provided with the test request (or as listed in the batch record) and confirm the information is current by comparing to the specification maintained by Document Control. Record the effective date of the specification to be used.
5. **Sample Information:** List the sample information in table format (for multiple lots) and clearly describe and indicate the exact nature of what is being done with the samples. At a minimum, list the following:
    a) List number/drug code, etc.

b) Lot number
c) Unique ID (i.e., a meaningful abbreviation), if needed
d) LIMS ID (if applicable)
e) Strength (theory)
f) Description/stage
g) Number of dosage units utilized, if more than a composite or more than 1 container used

6. **Reagents and Solutions:** Record all reagents and solutions that are used to prepare the test sample(s), reference standards, and other analytical solutions. Prepare standard solutions and solutions of reagents (e.g. test solutions, volumetric solutions, mobile phases, etc.) in a common logbook, if applicable. If a common logbook is not available, record the preparation in the lab notebook or test sheet used for the analysis.

   For reagents include:

   a) Reagent name and grade
   b) Manufacturer
   c) Manufacturer's lot number
   d) Any assigned lot numbers (if available)
   e) Expiration date

   For solutions of reagents include:

   a) Solution name
   b) Date of preparation – include corresponding reference to the original preparation if applicable
   c) Final solution expiration dates
   d) Final concentrations, if applicable (e.g., normality, etc.)
   e) Preparation steps, including weights and volumes for all preparations (e.g., of mobile phases, buffer solution, test solution, etc.)
   f) Reagent references (if previously prepared)

7. **Equipment and Materials:** List the equipment and materials used to test the samples and standards. Identify all instruments, including calibration ID and due date. Record the supplier name, lot numbers, and expiry (if applicable) for any materials that come in contact with the standard or sample during preparation.

   a) If more than 1 piece of the same equipment is used during the analysis (e.g., balances), then include the calibration ID in the section of the write-up where it is used.

8. **Standard Preparation:** List all reference standards used to test the samples. List all steps used to prepare the standards for the analysis. Record the standard preparation in step-wise format using past tense verbiage. Do not record in paragraph form. The steps should indicate any standard manipulation, or an action on the standard, with adequate accuracy and significant figures. The preparation should not be transcribed (i.e., re-written verbatim) from the test method. For each standard, record the following information:
    a) Reference material name
    b) Reference material vendor or manufacturer
    c) Vendor or manufacturer lot number
    d) LIMS ID (if applicable)
    e) Reference standard purity factor (%)

       All reference standards have a purity factor. Confirm and record the purity of USP and other compendial standards if not labeled.
    f) Expiration dates/solution stability dates
    g) Any other pertinent information (e.g., pre-treatments, like drying steps, etc.)
    h) Standard weights (required by the method) and dilution schemes for all preps of standards

       Any abbreviations recorded and labeled should be meaningful and unique and should be carried throughout the analysis (e.g., STD1, WSTD for working standard, STKSTD for stock solution, etc. Do not use "A, B, C" or "1, 2, 3").
    i) Calculation showing final standard concentration (for quantitative purposes)
    j) Logbook or system references, if previously prepared solutions are used
9. **Sample Preparation:** All steps used to prepare the samples for the analysis are listed. Record the sample preparation in step-wise format. Do not record in paragraph form. The actions recorded should indicate any sample manipulation and be written in past tense (e.g., use "mixed", not "mix") with adequate accuracy and significant figures. The preparation should not be transcribed from the test method into the notebook or test sheet (i.e., rewritten verbatim). Include the following:
    a) Sample weights and units
    b) Sample dilutions, with units and type of glassware used
    c) Treatment steps, such as mixing, filtration, sonication, etc., recorded with enough detail to clearly explain the action

       NOTE: Any abbreviation recorded and labeled should be meaningful and unique and should be carried throughout the analysis (e.g., SPL1, WSPL for working sample, STK SPL for stock sample solution, etc. Do not use "A, B, C" or "1, 2, 3").
    d) Preparation date

e) Expiration date/solution stability date

10. **Instrument Setup:** List the instrument and settings used for the analysis of samples and standards. All instrument conditions and settings used for the analysis are listed, including:
    a) Instrument name
    b) Equipment/instrument ID number
    c) Instrument calibration due date
    d) Accessories used, including serial number
    e) Parameters, settings, and conditions needed to reproduce the analysis
    f) For electronic systems, any references to electronic files needed to reproduce the analysis
11. **System Suitability:** List the system suitability criteria or standardization criteria from the test method and summarize the results.
12. **Calculations:** Record the calculations as follows:
    a) If any data is hand calculated, then a record of all equations used in connection with the analysis, including units of measure, conversion factors, and equivalency factors, must be listed in the laboratory notebook or test sheet.
    b) Calculations performed by validated software applications do not need to be fully reproduced in the notebook. However, an example calculation should be recorded in the notebook and any factors used in the application clearly explained in the notebook.
    c) Ensure adequate significant figures to calculate the final result based on the specification.
13. **Results:** Record all observations. Record all raw data without a printout in the notebook.
    a) Summarize final test results for the compound(s) analyzed, including results calculated automatically.
    b) Report results with correct number of decimals. Refer to the specification and any department SOPs on rounding requirements, if needed.
    c) For qualitative tests, record any observations that support the Pass/Fail statement listed in the procedure.
    d) Transcribe results into LIMS (if applicable).
    e) A summary of results may be copied and affixed to a notebook page or test sheet.
14. **Conclusion:** Record the scientific conclusion deduced from the data obtained during the analysis.

a) Clearly state the Pass/Fail outcome from the results and compare the specification.
b) For qualitative Pass/Fail tests, record the Pass/Fail criteria from the test method and then report “Pass” or “Fail”.

   For example,

   - Lot 12345: 95.6% meets specification of 90.0-110.0%
   - Lot 23456: White precipitate formed – Pass

Processing Supplemental Data

Requirements

1. Create a Supplemental Data Packet (SDP) by attaching a cover sheet for the supplemental data generated during the analysis. The cover sheet must be labeled with:
    a) Title of the analysis
    b) Associated laboratory notebook number or test sheet code and starting page number of the analysis.
    c) Total number of pages containing data in the packet (including cover sheet). This is not meant to represent the number of physical pages.
    d) Lot number(s) tested. For multiple lots, the first lot tested will include the original SDP.
    e) Signature and date of analyst and reviewer
2. If an SDP is needed, only one packet is created for the analysis. Each page of supplemental data must include:
    a) The notebook number and starting page of the analysis
    b) The signature and date of the analyst
    c) The signature and date of the reviewer
    d) The page number within the packet. Number each side of the page if data is present. Renumber printouts containing page numbers if additional pages are present in the SDP.
3. The SDP cover sheet and associated supplemental data must be attached, bound, or filed together in a secure way to facilitate transport, data integrity, and traceability.
4. The SDP will be submitted with the notebook or test sheet for review.
5. The original, reviewed SDP will be stored per department procedures (e.g. with the laboratory notebook, or test sheet, or included with the batch record). Exact copies can be made for inclusion with multiple batch records.
6. Information from instrument printouts may be photocopied and affixed to the notebook page or test sheet, with a reference to the SDP as the location of the original documentation.
7. Instrument output generated on thermal paper, or similar, which is susceptible to fading, must be photocopied. The photocopy can be affixed to the notebook or added to the SDP.

8. If an instrument printout cannot be affixed into the notebook or test sheet, the pertinent information can be copied into a table on the notebook page/test sheet and the instrument printout treated as supplemental data.
9. Ancillary files or reports containing HPLC chromatograms, GC chromatograms, and other printouts are added to the SDP and treated as above.
    a) Any chromatograms not used must be clearly voided with one diagonal line, labeled as "Data not used" and signed and dated. A reference and explanation must be recorded in the "Results" section of the notebook write-up
    b) Test injections of blanks or reference standards must be documented and traceable
10. If, after data review is complete, the analysis needs to be extended under the same notebook reference for some reason (e.g., due to an ongoing investigation), a second SDP should be created with its own cover sheet, if needed. In this case, the title and dates will indicate the different data sets.

Notebook and Analytical Worksheet Data Review

Review General Requirements

1. Completed laboratory notebook pages and test sheets should be reviewed and signed by a Peer/Data Reviewer (or designee) in a timely manner.
2. Each completed page is to be reviewed (counter-signed) by another individual in a timely manner.
3. If, during testing, a witness or verification is needed, the witness will sign and date next to the action reviewed (e.g., for a pre-run chromatographic checklist, etc.)
4. The SDP and its contents must be reviewed and counter-signed.