Frederick National Laboratory for Cancer Research, Frederick, MD

Biopharmaceutical Development Program

Standard Operating Procedure

Title: Good Documentation Practices

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1.0 Purpose

This SOP defines the requirements for Good Laboratory Practices (GLP) and/or Good Manufacturing Practices (GMP) documentation to ensure that documents are legible, understandable, reproducible, permanent, and traceable.

2.0 Scope

This procedure applies to Biopharmaceutical Development Program (BDP) personnel completing documentation subject to regulatory review. BDP documentation includes, but is not limited to, batch production records, forms, logbooks, and laboratory notebooks.

3.0 Authority and Responsibility

3.1 The Director, Biopharmaceutical Quality Assurance (BQA) has the authority to define this procedure.

3.2 BDP employees are responsible for complying with this procedure.

This procedure is made available through federal funds from the National Cancer Institute, NIH, under contract [redacted].

3.3 Supervisors/Managers of the Biopharmaceutical Development Program are responsible for ensuring adherence to this procedure.

3.4 BQA is responsible for quality oversight of this operation.

4.0 Characteristics of Good Documentation

4.1 Accurate – documents must contain accurate data and an accurate account of events.

4.2 Complete – required information must be included in the document.

4.3 Permanent – information cannot be erasable nor be obscured in any way.

4.4 Legible – documentation must be easy to read.

4.5 Timely – Manufacturing, testing, and support activities must be documented at the time the work is performed.

4.6 Clear – the documentation must be clear to limit misinterpretation of what was performed and recorded.

4.7 Traceable - documentation must provide information on:

4.7.1 The activity being documented.

4.7.2 The individual(s) performing the activities.

4.7.3 The materials and equipment used in the activity.

4.7.4 The activities preceding and following the process.

4.7.5 The location and proper identification of raw data.

4.8 Appropriate corrections and handling of deviations.

5.0 Good Documentation Practices

5.1 Accurate

5.1.1 Entries must accurately represent the data or activity. Data entries may require either a "Performed By" or "Recorded By" signature/initials to indicate the type of information being recorded.

5.1.1.1 "Performed By" indicates that the step was performed by the individual signing/initialing the record.

Example: An operation requiring an operator to weight items and record the readings of the weight in a table would require an entry to record the individual's initials and date that the operation was performed as stated.

5.1.1.2 "Recorded By" indicates that the entry or series of entries were written by the individual signing/initialing the record.

Example: Recording Quantity Issued, BDP Part Number, Lot Number, and Expiration Date in a table format would require an entry to record the individual's initials and date that information was written.

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5.1.2 Operations/Steps requiring a second person's independent review of the operations conducted (checker) must be signed/initialed and dated as the operation is performed.

5.1.2.1 Critical steps or operations that require this type of "Verification" include calculations, measurements, addition of components, and other critical actions as defined in the Master Production Record (MPR).

5.1.2.2 The second person’s signature/initials indicates that he/she has personally observed/witnessed the entire step being performed and has accepted the responsibility for assuring that the entire step was performed completely and correctly.

5.1.2.3 Verifications of calculations attest that the calculation has been checked and the same result obtained. Calculations must be verified prior to proceeding with the next step that uses the results of the calculation.

5.1.3 If an operation requires a “Reviewed By” signature, it must be signed/initialed and dated at the time the review is performed. The reviewer’s signature/initials indicates that the data recorded has been checked for accuracy, completeness, clarity, and the need for any comments or explanations to the record have been made.

5.2 Complete

5.2.1 Activities must be completely documented so that events can be reconstructed at a later time (for example, for troubleshooting, trending, etc.)

5.2.2 Do not leave blank or unused spaces on documentation or records.

5.2.2.1 If data is not going to be entered, mark the space with N/A or other appropriate code (refer to Section 5.10) and initial and date this entry.

5.2.2.2 A sequential group of unused spaces or data entry lines may be marked with a single line through all of the spaces and N/A written across this line (including initials and date).

5.2.3 The use of extra pages to record additional information is acceptable and encouraged as long as the pages are properly identified (see Section 5.8).

5.2.3.1 Raw data that is being attached to an additional page or to a page from a BPR or similar document must be attached firmly enough to preclude it from getting separated from the documents. Taping of the data to the page or placing it into a plastic sleeve is examples of acceptable methods.

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5.3 Permanent

5.3.1 Do not use pencil or colored ink other than black or blue permanent ink to record data. Red ink is reserved to suggest changes to the revision of an approved document. The recorded data must be dark enough to be legible and to be copied by machines.

5.3.2 Do not use correction fluid or tape, or cross out entries so that the original entry becomes unreadable.

5.4 Legible

5.4.1 Entries in records must be legible to reviewers of the document.

5.4.2 Signatures and initials must be clear enough to identify an individual who signed a record and must match the signature and initials on file with BQA.

5.4.3 Do not "overwrite." Overwriting creates confusion about the entry making it difficult to identify the intended data.

5.5 Timely

5.5.1 Date records with the date on which the data is entered.

5.5.2 Entries into documentation and records must be made as each step is completed, not after the entire process is performed.

5.5.2.1 Contiguous operations (performing aseptic processing in a hood) that may jeopardize the work being performed should the operator repeatedly stop to sign entries into a BPR, may be signed at the end of the operation by the operator. In such cases, verifiers, if any, shall initial and date each step as the written entry is completed.

5.6 Clear

5.6.1 Documentation must be written so that anyone versed in the general field can follow the document and reach the intended outcome. Avoid the use of terms, symbols, phrases, etc., that may not be understandable to other potential reviewers of the document.

5.6.2 Calculations must be documented and easy to follow. Use formulas or equations to show how results were obtained. Calculations must include units of measure, conversion factors, and equivalency factors.

5.7 Traceable to the individual(s) performing the activity

5.7.1 For GMP activities, use the approved form to document an activity. This allows the activity to be traceable to the process approved by BQA. Forms that are authorized for use will display information at the top left corner of the form that includes the form number, associated SOP number, revision level, and effective date.

5.7.2 Sign/Initial and date each notebook page, record, data form, etc., as required.

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5.7.3 Signatures and Initials

5.7.3.1 Signatures and/or initials on a record or document identify who was responsible for performing the work and who was responsible for checking or verifying the work.

5.7.3.2 Signatures and initials must be unique and legible. There must be a document available that correlates the person's initials with his/her signature and printed name (signature and initial log). This log is maintained in BQA. See ***SOP 21406 - Personnel Signature and Initial Verification System***.

5.7.4 Signatures are required for the final approval of master documents such as Master Production Records (MPR), Master Specifications (MS) (previously known as Assay Profiles - AP), Certificates of Analysis (COA), Standard Operating Procedures (SOP), and Installation/Operation/Performance Qualification Protocols (IQ/OQ/PQ).

5.7.5 Do not sign for someone else's work without authorization.

5.7.5.1 In rare circumstances (Vacation/Absence) and with prior approval, a knowledgeable individual may sign as a substitute for another person by acknowledging this action with their initials and date of signature. ***See SOP 21007 - Alternate Signature Authority***.

5.7.5.2 When a document must be signed and the individual designated to sign the document is unavailable, an approved alternate may sign the document. The designation of approved alternates is described in ***See SOP 21007 - Alternate Signature Authority***. The approved alternate would sign/initial the document, date it, and indicate the name of the person who was originally designated to sign the document.

For example, Tom Johnson was designated to sign Document A on November 20, 2013; he is unavailable, and Lori Jones is his approved alternate. She would sign Document A "Lori Jones, 11/20/13 for Tom Johnson."

5.8 Protection and Traceability of Raw Data

5.8.1 Record data directly into the Batch Production Record (BPR), logbook and/or laboratory notebook, form, or other data collection record.

5.8.2 If procedures require transcription of the data to a paper record or data entry into a computer, reference the original raw data, if possible, and keep the original raw data as part of the batch record package.

5.8.3 Information that is attached to another record (data printout, charts, raw data) must be linked to that record by including (as appropriate) the document number, project/part number, lot number, and section number (as applicable) on each page of the attachment. Data printouts, charts, or other data attached to another record must also be initialed and dated by the person attaching this information.

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5.8.4 For data that is spliced or taped-in to the record, the initials and date of the person adding the data should be written across the splice of pasted/taped-in data.

5.8.5 Should a photocopy of a record be needed (e.g., oven or autoclave chart), the individual making the copy will confirm that the copy is a true and exact reproduction of the original document. The copy will be stamped or labeled as “True and Exact Copy,” and the individual making this confirmation will initial and date the copy near the "True and Exact" stamp.

5.8.6 Do not use “sticky” notes, paper towels, etc., to record data. However, if they were used and they contain raw data, they must become part of the permanent record and be identified properly.

5.9 Forward and Backward Traceability

5.9.1 Logbooks, laboratory notebooks, and data sheets have consecutively numbered pages for accountability. Do not remove pages from bound notebooks or logbooks.

5.9.2 Records must contain sufficient identifying information so that it is possible to trace the activity forward and backward in time to associated documentation. Record sample names, part numbers, lot numbers, and QC test request numbers.

5.10 Appropriate Corrections (Explanation and Error Codes)

5.10.1 Correction of an entry must allow the original entry to be readable and provides information on the date of the change, the person making the change and the explanation of the change. Therefore, if a mistake is made, do not correct it with whiteout or anything else that would hide or obliterate the original entry. Erasures and overwriting of data are not allowed.

5.10.2 To correct an entry, the individual who made the mistake must line out the mistake by putting a single line through the entry, write the correct information next to the entry, initial and date the correction, and provide an explanation for the change. All corrections must be clear and legible.

5.10.2.1 If there is insufficient room to write the correction next to the entry, then place a numbered asterisk next to the entry and record the correct information elsewhere on the page or use the comments section of a BPR or similar document.

5.10.2.2 Indicate the reason for the correction and/or use the codes below. Circle the codes to distinguish them from the initials of the individual making the correction.

NOTE: If the reason for a change is not apparent, a written explanation must be included.

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5.10.2.2.1 LE (Late Entry) – This code is used to reflect the fact that a required entry was not made at the time the step was being completed and that data is being added at some point later. This code is not used to correct previously-recorded data.

NOTE: Backdating of information is not allowed. The entry must clearly show that information is being added currently and must not be signed with the date the work was performed.

5.10.2.2.2 CE (Calculation Error) – This code is used to explain that recorded data is being revised as a result of a calculation or math error.

5.10.2.2.3 UR (Upon Review) – This code is used by reviewers of documentation (either by the Project Scientist, BQA, or within the department itself) to indicate that a change or addition is being entered as a result of their review.

5.10.2.2.4 RE (Recording Error) – This code is used to indicate that a result is being corrected at the time of entry by the recorder (e.g., entering data into the wrong space or recording the wrong date, etc.).

5.10.2.2.5 SE (Sample Error) – This code is used to indicate that data is being changed because the sample used to generate data was improperly collected, handled, etc.

NOTE: This code would not be used if the assay was completed and generated an Out-Of-Specification result (OOS). Refer to ***SOP 22004 - Managing Out-of-Specification Test Results or Unexpected Test Results***.

5.10.2.2.6 AE (Assay Error) – This code is used to indicate that data is being changed because an assay was determined to have been improperly conducted.

NOTE: This code would not be used if the assay were completed and generated an OOS. In that case an OOS investigation would be needed. Refer to ***SOP 22004 - Managing Out-of-Specification Test Results or Unexpected Test Results***.

5.10.2.2.7 TE (Typographical Error) – Used for spelling errors and changes in sentence structure, etc.

5.10.2.2.8 N/A (Not Applicable) – This code is used to indicate that a data record section will not be filled out or completed because the information is not applicable to the activity being conducted.

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5.10.2.2.9 ES (Equivalent Substitution) – Used when an equivalent substitution is being made for a requirement (e.g., raw material substitution, using a higher resolution balance to conduct weighing, etc.).

5.10.2.2.10 VD (Verbal Data) – used to indicate that data was recorded based on a verbal communication of information. The entry must include the names of the individual who provided the verbal data and who recorded it.

5.10.3 If any of the changes have a significant impact on the documentation or process they are used in, or result in (or cause) a deviation from specified requirements, bring it to the Supervisor's/Manager's attention.

5.11 Handling of Deviations

5.11.1 Data that represents a deviation from specified requirements must be registered as a deviation following ***SOP 21301 - Deviations from Written Documents and Corrective and Preventative Actions*** or ***SOP 21526 - Engineering Event Management.***

5.11.2 Data associated with a deviation must be identified in the record by cross-referencing the deviation number. This allows traceability to the record that documents the review, assessment of product impact, corrective/preventive action, and approval of the deviation.

6.0 Records Retention

6.1 Documentation and records must be stored in a manner that ensures integrity, security, and accessibility. Documents completed in accordance with GMPs and GLPs must be forwarded to BQA for storage (see ***SOP 21402 – Document Storage and Archival Process***).

6.2 Documentation will be retained as per the requirements specified in ***SOP 21407 – Record Retention***.

7.0 References and Related Documents

7.1 **SOP 21007** *Alternate Signature Authority*

7.2 **SOP 21301** *Deviations from Written Documents and Corrective and Preventative Actions*

7.3 **SOP 21402** *Document Storage and Archival Process*

7.4 **SOP 21406** *Personnel Signature and Initial Verification System*

7.5 **SOP 21407** *Record Retention*

7.6 **SOP 21526** *Engineering Event Management*

7.7 **SOP 22004** *Managing Out-Of-Specification Test Results or Unexpected Test Results*

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