Frederick National Laboratory for Cancer Research, Frederick, MD

BIDD

Blophannaceuitcal Development Program

Standard Operating Procedure

Title: Laboratory Notebooks Control and Use

SOP Number: 21408

Revision Number: 04

Supersed es: Revision 03

Effective Date: JUL 08 2019

Originator/Date: [redacted]

Approval/Date:

Approval/Date:

Table of Contents

1.0 Purpose

This SOP defines the conventions for obtaining, controlling and capturing data in laboratory notebooks.

2.0 Scope

This procedure applies to BOP employees who use laboratory notebooks, their Managers/ Supervisors and BOA personnel (or their designee). Laboratory notebooks are the property of the NCI.

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

3.0 Authority and Responsibility

3.1 Biopharmaceutical Development Program (BDP) personnel are responsible for:

3.1.1 Obtaining laboratory notebooks from BQA (or their designee).

3.1.2 Controlling the laboratory notebooks in their possession to protect them from physical damage and to maintain security.

3.1.3 Documenting laboratory work (including research and development work) in a laboratory notebook unless the work is recorded in a batch record.

3.1.4 Documenting work in a laboratory notebook using conventions established by this SOP.

3.1.5 Preparing notebooks for archiving when they are complete or no longer active.

3.1.6 Returning completed notebooks to BQA (or their designee) for archiving.

3.1.7 Surrendering notebooks upon request and when employment is voluntarily or involuntarily terminated. (Laboratory notebooks are the property of the NCI).

3.2 Managers/Supervisors of BDP personnel who use laboratory notebooks are responsible for:

3.2.1 Oversight of the laboratory notebooks for the employees who report to them and assuring that completed notebook pages are reviewed in a timely manner.

3.2.2 Final technical review of the notebook and preparing the notebook for archiving before it is submitted to BQA for archiving.

3.2.3 Ensuring that terminating employees turn over their laboratory notebooks to supervisory or BDP BQAD personnel.

3.3 Biopharmaceutical Quality Assurance (BQA) is responsible for quality oversight of this procedure.

3.4 The BQA (or their designee) department is responsible for:

3.4.1 Stocking and assigning laboratory notebooks.

3.4.2 Assisting laboratory notebook users to customize their notebooks to meet the needs of the user and the requirements of this SOP.

3.4.3 Producing or obtaining laboratory notebooks for users.

3.4.4 Archiving laboratory notebooks.

3.4.5 Accessing Laboratory Notebooks from archives when requested for reference.

3.4.6 Maintaining the traceability of all issued and archived Laboratory Notebooks.

4.0 System Overview

4.1 Laboratory notebooks used at the BDP are the property of the NCI and are legal documents that provide a mechanism to capture critical information about experiments or processes that may be needed to reconstruct events at a later time (for example, as part of a CMC section in an IND), to serve as a foundation for future work, to transfer information from development to other departments or institutions, or to protect intellectual property.

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Research and development laboratory activities must be captured in a laboratory notebook. Conventions for the management of these data are defined to ensure that appropriate data are captured, are accurate and reliable, and are retrievable. Additionally, a properly kept laboratory notebook is the scientist's proof of his/her discovery or invention and is frequently used as the source of information that will be needed in pursuit of a patent.

Laboratory notebooks are used to document laboratory activities that are not being documented on a Master Production and Control Record (MPR) or on approved forms from SOPs. Whenever feasible, GMP and GLP activities should be documented on the approved form(s) that is associated with the SOP that provides the instructions for the performance of the activity.

Laboratory notebooks are requested from BQA. The user and BQA work together to customize a laboratory notebook that will meet the needs of the user and will comply with the requirements of this SOP. Notebooks are assigned a tracking number and are issued to the user. The user enters data into the laboratory notebook using the conventions in this SOP. Managers/Supervisors assure that completed laboratory notebook pages are reviewed in a timely manner. When the notebook is completed, or is no longer active, the user and his/her Manager/Supervisor review the laboratory notebook, prepare it for archiving and submit it to BQA.

Laboratory Notebooks (active and archived) are tracked by BQA.

5.0 Obtaining and Configuring Laboratory Notebook

5.1 Laboratory notebooks are permanently bound, pre-numbered notebooks obtained from the BQA Department using the Request for Laboratory Notebook(s), Form 21408-01, (Attachment 1).

5.1.1 Laboratory notebooks are issued to a specific "owner" who has the responsibility to maintain, use and store the laboratory notebook appropriately.

5.1.2 When an employee terminates employment, or moves to another department, the laboratory notebook(s) assigned to that employee must be returned to BQA where they will be reassigned (if appropriate) to another person responsible for the project or must be prepared for archive (as per section 9.0 of this procedure).

5.2 Laboratory notebooks are configured by the notebook manufacturer or by the BQA Department to contain pre-printed blank Table of Contents pages.

5.3 For each new laboratory notebook, the following pages must be established (by the initial notebook user) and maintained. Exceptions are allowed with the approval of supervisory personnel and BQA.

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5.3.1 Tracking Information (Notebook Cover Page)

5.3.1.1 Notebooks are imprinted (or configured) on the first inside page with the following information:

Notebook No.:

Issued To:

On (Date Issued):

Department:

Returned (Date):

BQA will not accept laboratory notebooks for archiving if the following information is not completed:

Prepared for archiving by (signature/date):

Reviewed/approved for archiving by (signature/date):

5.3.1.2 All information (except the return date and archiving information) is complete when the notebook is issued. Notebook numbers are assigned using consecutive numbers from the laboratory notebook database in BQA.

5.3.2 Signature Cross-reference Log (Page 1)

5.3.2.1 Page 1 of the notebook must be labeled “SIGNATURE CROSS-REFERENCE LOG” and be configured to contain columns for “PRINTED NAME”, “SIGNATURE” and “INITIALS.”

5.3.2.2 Individuals entering data (or verifying data) for the first time in the laboratory notebook must register their name, signature and initials on the signature page at the front of the laboratory notebook. This allows work to be associated with specific, defined individuals.

5.3.3 Document Cross-reference Log (Page 2, more pages as anticipated)

5.3.3.1 Page 2 must be labeled “DOCUMENT CROSS-REFERENCE LOG” and be configured to contain columns for “DOCUMENT ID,” “LOCATION,” and “NOTEBOOK PAGE NUMBER REFERENCE.”

NOTE: Document locations need to be descriptive enough that your supervisor could locate documents in your absence.

5.3.3.2 Documentation that is associated with notebook activities but cannot be affixed into the notebook (due to size, etc.), is maintained separately from the notebook. The location of these documents and the pages in the notebook that they are associated with are listed on this page(s). In addition to maintaining hard copies of original data, record original data from analytical instruments, captured on software and computer files that may be stored in network files or by other appropriate mechanism in the notebook along with the path and filename.

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5.3.4 Table of Abbreviations (optional)

5.3.4.1 Page 3 can be labeled “COMMON ABBREVIATIONS” and be configured to contain columns for “ABBREVIATION” and “MEANING.”

5.3.4.2 Commonly-used abbreviations, symbols, code numbers, or other information that is used throughout the book are listed on this page to clarify the meaning of the abbreviation. Also, see **SOP 21404, *Abbreviations Used in the BDP***.

5.3.5 Customized Pages (optional)

5.3.5.1 For laboratory notebooks that document repeated execution of the same assay or activity, worksheets may be prepared to capture appropriate data and bound into a notebook. Users should work with BQA to design and produce these customized logbooks.

5.3.6 For laboratory notebooks assigned for training purposes only, a label will be placed in the inside front cover with the following statement: “This laboratory notebook is to be used for training purposes only and not used for experiments for MGP, GLP, or BDP-project directed R & D work.”

6.0 General Conventions for the Use of Laboratory Notebooks

6.1 Obtaining and Storing Lab Notebooks

6.1.1 The initial user will obtain a notebook from BQA and will configure it before use, according to Section 5.0, above.

6.1.2 Issued laboratory notebooks will be maintained in a manner to protect them from physical damage and to maintain security.

Store notebooks in a secure area – preferably not on the lab bench.

The notebook must remain on site unless there is an approval to take it off site. Approval to take laboratory notebooks off site must be made at the Director level and be in writing.

NOTE: This restriction does not apply to off-site archiving under the control of a designated BQA archivist.

6.2 Maintaining Signature Logs, Table of Contents, and Document Cross-Reference Logs

6.2.1 Signature Log

As individuals enter data (or verify data) for the first time in the laboratory notebook, they must register their name, signature and initials on the signature page at the front of the laboratory notebook (page 1).

The signature page is updated continually, throughout the use of the notebook, to add new individuals that are adding or verifying data in the notebook.

6.2.2 Table of Contents

The Table of Contents must be updated continually to add new experiment titles and page numbers as they are completed.

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6.2.3 Document Cross Reference Log

Documentation that is associated with notebook activities but cannot be affixed into the notebook (due to size, etc.), is maintained separately from the notebook. The location of these documents and the pages in the notebook that they are associated with are listed on this page(s). In addition to maintaining hard copies of original data, record original data from analytical instruments, captured on software and computer files that may be stored in network files or by other appropriate mechanism in the notebook along with the path and filename.

6.3 Using Pages

6.3.1 Consecutive Use

Pages of the notebook must be used consecutively. “Saving” pages to input data for an experiment to be conducted at a later time is prohibited. Ripping out pages is prohibited.

6.3.2 Conventions for documenting simultaneous experiments

For periods of time when simultaneous experiments are on-going, it is acceptable to reserve sufficient pages to complete the documentation of an experiment. Pages reserved must be titled with the experiment name. As each simultaneous experiment is completed, any reserved but unused pages must be “N/A’d” (and include the analyst’s signature and date).

6.3.3 New Pages

New experiments, procedures etc. must be documented starting with a new page.

6.3.4 Descriptive Titles for Experiments

A descriptive title for the work must be provided (for example, “Preparation of Reagent A”, or “Purification of X using Resin B”).

6.3.5 Experiment Page Numbering

It must be clear what pages are included in a specific experiment. For the first page of an experiment, indicate “*start*” for the “From Page No._____” prompt (at the top left of the page). For the last page of an experiment, indicate “*end*” for the “to Page No._____” prompt (at the bottom right of the page). For intermediate pages, complete the “From” and “To” page number prompts so this it is clear what pages document a specific experiment.

6.4 Use of Worksheets

6.4.1 Developing and using worksheets to guide the organization and documentation of activities can be helpful. Worksheets enhance the consistent presentation of information and prompt for appropriate experiment data.

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6.4.2 Worksheets can be developed for commonly performed processes (for example, cell splitting or reagent preparation) and designed to prompt for required information (for example, equipment numbers, reagent lot numbers, incubation times, etc.). Worksheets are permanently affixed into the laboratory notebook in the same manner as raw data.

6.5 English

6.5.1 All entries in the lab notebook must be in English (except commonly used abbreviations and symbols).

6.6 Documentation at Time of Performance

6.6.1 Experiments must be documented on the day work is performed, as soon as it is practicable to record entries into the lab notebook. As experiments or procedures are completed, the Table of Contents will be updated to reflect this new information.

6.7 Good Documentation Practices

6.7.1 Good Documentation Practices must be followed at all times (see also **SOP 21409, *Good Documentation Practices***) including:

- Use of blue or black ink.
- Legibility of all entries.
- Real time recording of data.
- Proper practices for corrections
- Accurate signatures and dates for work.
- Use of lines and/or “NA” (with initials and date) to justify blank spaces in the notebook.

6.8 Data Integrity

6.8.1 Data contained in BDP laboratory notebooks should be attributable (to identify individuals who performed/recorded the work), legible, contemporaneously recorded, original (first capture of information), and accurate. Data must be reliable and credible (refer to the SOP 21910 Integrity of BDP Data).

7.0 Documenting Experiments

Work must be recorded in laboratory notebooks in sufficient detail so that the experiment or procedure can be reconstructed at a later time and to provide traceability of materials, reagents and equipment that was used. Information that must be captured includes:

7.1 Purpose of the experiment

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7.2 Method or procedures used

7.2.1 If desired, for procedures that are performed routinely, the routine procedure may be described in an earlier page of the laboratory notebook and then cross-referenced when used to conduct later experiments. Experiment-specific information (equipment used, materials, process information, etc.) must be provided for each specific experiment.

7.3 Equipment, materials, and reagent traceability

7.3.1 Document raw material/reagent identification including brand, catalog number, lot number and expiration date. Record the BDP raw material release number (R number) if provided.

7.3.2 Document reagent preparation data.

7.3.3 Document equipment used, including any standardization of the equipment that was performed to prepare the unit for use (if not documented elsewhere).

NOTE: The use of equipment "MEF" (Master Equipment File) number is encouraged in addition to the equipment description since this number allows traceability back to the specific piece of equipment. Use of an MEF number or an equipment serial number is required for GLP/GMP activities.

7.4 Location

7.4.1 Document the area in which the procedure was performed. If the area is not under a routine environmental monitoring schedule, include any environmental monitoring that was performed during the time period of the experiment (if applicable).

7.5 Process Information

7.5.1 Document process information that will be needed to reproduce the experiment exactly at another time, for example:

- Times (for incubation, mixing, holding, etc)
- Temperatures (for incubation, mixing, holding, etc)
- Flow rates
- Sampling points
- Etc.

7.6 Raw Data

Raw data must be adequately identified and maintained.

7.6.1 Raw data include data such as HPLC tracings, testing results, reports, etc.

7.6.2 Raw data must be appropriately labeled to indicate sample number (or ID), date, technician name, notebook page cross reference, etc., and be SIGNED and DATED by the analyst or scientist. Also include any explanations of the data that would be helpful to another person reviewing the data at a later date.

7.6.3 Affix raw data into the notebook using permanent tape or glue. The analyst must initial and date across the splice between data sheet and notebook page.

7.6.4 Alternately, raw data may be maintained separately from the lab notebook (for example, if the data is too large to fit into the notebook). The location of this data must be indicated on the notebook page pertaining to the experiment and must be indicated on the Document Cross-Reference Log.

7.6.5 Electronic files must be protected by saving the files to a network server or other appropriate means. Locations storing electronic raw data must be backed up to protect inadvertent loss of data. This is in addition to maintaining a hard copy of the raw data, when possible. The location of this data must be indicated on the notebook page pertaining to the experiment and must be indicated on the Document Cross-Reference Log.

7.6.6 The location of the data not being stored within the laboratory notebook must be indicated on the “Document Cross-Reference Log” at the front of the notebook.

7.7 Calculations

7.7.1 Calculations must be shown and include units and conversion factors.

7.8 Conclusions

7.8.1 Conclusions that might be drawn from the data should be documented. Any explanations for the observed results should be discussed. Additional activities planned should also be documented.

7.9 Analyst Signature

7.9.1 The analyst/scientist must sign and date the bottom of each page at the time the page is completed.

8.0 Reviewer Responsibilities for Laboratory Notebooks (Managers/Supervisors)

Reviewer responsibilities (refer to Section 3.2) for laboratory notebooks are dependent on the status of the activities being reviewed. GMP/GLP activities require a different type of review than development activities. Therefore, for laboratory notebooks that contain mixed activities, each experiment needs to be identified as “GMP/GLP” or “development”. Notebooks that contain only GMP/GLP activities or only development activities can be labeled on the laboratory notebook cover page as “GMP/GLP” or “development”.

8.1 For routine development activities, the reviewer should assure that:

8.1.1 Sufficient information has been captured so that the experiment conducted can be repeated exactly at another time.

8.1.2 Good documentation practices were used.

8.1.3 The review is timely (within 30 days).

Reviewers would NOT be required to re-check calculations or to evaluate the science or conclusions of the experiment.

8.2 For GMP or GLP activities, the reviewer should assure that:

8.2.1 Sufficient information has been captured so that the experiment conducted can be repeated exactly at another time.

8.2.2 That good documentation practices were used.

8.2.3 That all data captured are confirmed as accurate, complete, and comply with established procedures (for example, equipment numbers, lot numbers, expiration dates, calculations, etc).

8.2.4 That conclusions drawn from the activity are appropriate (especially for test results).

8.2.5 The review is timely (**within 30 days AND** before any final result is formally reported).

8.3 For a potentially patentable development:

The initial review should be the same as for routine development activities, but the employee and/or reviewer should alert BDP Management who may decide to require additional review/evaluation to protect the invention.

8.4 BQA will provide each manager with a list of active lab notebooks (or inactive notebooks held within their department) on a periodic basis. The reminder will include a note that the quality of the laboratory notebooks is the ultimate responsibility of the department manager.

9.0 Archiving

Any notebook that is completed, or one having no entries made for two years, is considered inactive. Unless the original notebook is needed within the department, inactive notebooks should be archived.

Laboratory notebooks used for training purposes only and that do not document any GMP, GLP, or BDP project directed research and development work are not required to be reviewed by Quality Assurance prior to archival. Therefore, any training laboratory notebooks may be archived as soon as they are received in BQA.

NOTE: Completed laboratory notebooks may be kept in the department for reference purposes, but they must be prepared for archiving according to the requirements below. BQAD must be updated on the status of the Laboratory notebook (inactive) and the person that is responsible for the notebook. It is highly recommended that departments needing access to inactive notebooks consider maintaining a copy of the notebook in the department and archiving the original.

9.1 Preparing Laboratory Notebooks for Archiving (Notebook Owner)

The notebook “owner” will prepare the laboratory notebooks for archiving by:

9.1.1 Completing a Notebook Overview Statement (Notebook Cover Page)

In addition to the tracking information on the cover page, the notebook owner will add a short statement or paragraph on the general topic of the activities included in the lab notebook, and whether the notebook is a continuation of work captured in other notebooks.

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- If this notebook is a continuation of work, the notebook number(s) for the previous work must be identified.

9.1.2 Additional information, if available, may be included in this overview statement such as information related to the goal of the activities, project number, stage of the project, where other related information may be found, etc.

9.1.3 Marking any empty or unmarked notebook pages with an "X" and "NO INFORMATION ON THIS PAGE," and signing and dating the bottom of the page.

9.1.3.1 Alternately, for notebooks with large portions of empty or unmarked pages.

- Mark the first and last blank page of the lab notebook prominently in the body of the page with *"Page # (first blank page #) through page # (last blank page #) have been intentionally left blank* as *of (current date)".* The person making this statement will sign and date these pages.
- Following the last entry in the Table of Contents, indicate *"Page # (first blank page #) through page # (last blank page #) have been intentionally left blank* as *of (current date).*

9.1.4 Ensuring that the Table of Contents is up-to-date (See note).

9.1.5 Ensuring that the Signature Log is up-to-date (See note).

9.1.6 Ensuring that the Document Cross-Reference is up-to-date (See note).

9.1.7 Retrieving any documents or raw data that are stored outside of the notebook (and add to the notebook per section 7.6). Referenced documentation that is part of other official BOP records may remain in the original, official file.

NOTE: Laboratory notebooks, initiated before the establishment of revision O of this procedure (January 13, 2003), may not contain a Table of Contents, Signature Log, or Document Cross-Reference Log.

9.1.8 Signing the inside front cover of the laboratory notebook: "Prepared for Archiving by: (signature / date)".

9.2 Preparing Laboratory Notebooks for Archiving (Supervisors)

9.2.1 After preparing the laboratory notebook for archiving, the notebook (and any associated raw data that was filed separately) must be examined by the scientist's supervisor to ensure that all data is available and has been reviewed and signed. The Supervisor will document review by signing the inside front cover of the Laboratory notebook: "Reviewed / Approved for Archiving by: (signature / date)".

9.2.2 After review by the Supervisor, the Cover Page will be amended with the statement "This Notebook Completed By [Name]. No Marked Entries After [Date]."

9.2.3 Entries into the laboratory notebook after this date are prohibited.

9.3 Laboratory notebooks and associated raw data to be archived are submitted to BQA.

9.4 Archiving of Laboratory Notebooks by BQA (or their designees)

Inactive laboratory notebooks no longer required within the department must be archived. An inactive laboratory notebook is one that is completed (all pages used, or the work that the notebook is dedicated to is complete) or one where no entries have been made for two years. After being prepared for archiving by the laboratory notebook owner and supervisor, the lab notebook is physically stored under the control of BQA.

9.4.1 The user of the laboratory notebook and/or his/her Manager / Supervisor must prepare the notebook for archiving (see Section 9.1 and 9.2) and submit it to BQA.

9.4.2 BQA will confirm that the laboratory notebook owner and the owner's Manager / Supervisor have verified that the laboratory notebook has been properly prepared for archiving (as per section 5.3). The owner and their manager indicate their verification of proper preparation for archiving by signing and dating the notebook's inside cover page.

9.4.3 BQA will store laboratory notebooks. Generally, laboratory notebooks for projects that are still active will be stored on-site as space permits. As needed, commercial archival services may be used.

9.4.4 BQA maintains traceability information for all laboratory notebooks.

10.0 Obtaining Archived Laboratory Notebooks for Reference

10.1 Archived notebooks may only be used for reference. No data may be entered into an archived notebook. Any data entered after the completion date shall be considered void.

10.2 To retrieve an archived notebook for reference, contact BQA to request the notebook (by email to the BQAD Outlook In-box). The requestor is responsible for the care of the archived notebook from the time the notebook leaves the archives until the time it is returned to BQA.

11.0 References and Related Documents

11.1 **SOP 21404** *Abbreviations Used in the BDP*

11.2 **SOP 21409** *Good Documentation Practices*

11.3 **SOP 21910** *Integrity of BDP Data*

11.4 "Guide for Keeping Laboratory Records," National Institutes of Health, August 2001.

12.0 Attachments

12.1 Attachment 1 Form 21408-01, Request for Laboratory Notebook

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

Attachment 1

FNLCR, BDP
Form No.: 21408-01
SOP No.: 21408
Revision 04 JUL 07 2019

Request for Laboratory Notebook(s)

To Be Completed by Notebook Requester:	Department: *
Requested By:	Date:
Product Name:	Project Number:
Location of Notebook(s): Building:	Room:

Notebook Area Manager Approval:	
Manager Approval:	Date:

To Be Completed by BQA:	
Number Assigned:	Assigned By:

To Be Completed by Notebook recipient:	
Received By (Print and Sign Name):	Date:

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