BIOPHARMACEUTICAL DEVELOPMENT PROGRAM

SOP Title: **Preparation of Manufacturing Reports**
SOP Number: **24407**
Revision: **08**

TABLE OF CONTENTS

1. PURPOSE

This SOP defines the content and format of Manufacturing Reports and describes the preparation, review, and approval process within the Biopharmaceutical Development Program (BDP).

2. SCOPE

This procedure applies to Biopharmaceutical Development Program and Regulatory Affairs (RA) personnel (or designees) who are involved in the preparation, review, and approval of Manufacturing Reports for the Frederick National Laboratory for Cancer Research (FNLCR)/ NCI at Frederick.

3. RESPONSIBILITIES

3.1 The Associate Director of Regulatory Affairs (or designee).

- Defines the procedure.
- Reviews and approves Manufacturing Reports

3.2 BQA Regulatory Affairs (or designee).

- Prepares, reviews, submits, and archives Manufacturing Reports in accordance with this procedure.

3.3 The Project Scientist, Manufacturing Director, the BDP Program and Technical Director, the NCI/BRB Project Director, and the NCI/BRB Chief (or their designees)

- Reviews and approves manufacturing reports.

3.4 Process Analytics/Quality Control (PA/QC) Director (or designee).

- Reviews Manufacturing Reports that contain analytical specifications, data, and/or assay descriptions upon request.

4. GENERAL FORMAT OF MANUFACTURING REPORTS

4.1 A description of general formatting requirements applicable to the preparation of Manufacturing Reports is included in SOP **24408 – Preparation of Regulatory Documents.** The document template specific to manufacturing reports should be prepared as below:

The header should include the document title, project or product name, the page number, and lot number as applicable.

Example Header:

BDP/FNLCR/Leidos Biomedical Research Inc.
Manufacturing Report for ATI-1013 Master Cell Bank Lot L2104006
Page 2 of 32

The footer contains a confidentiality statement and project contract information. The name of the institution requiring written permission in the footer can be changed depending on who the document is written for. The contract number can be obtained by consulting Program Management. The contract information should be stated as below:

"The data contained in this report are confidential and the property of U.S. Government. It is not to be disclosed to a third party, used in an IND, or used in any other publications without the written permission of the Biological Resources Branch, DTP, DCTD, NCI. This document is made available through federal funds from the National Cancer Institute, NIH, under contract (Insert contract number here)."

The word “Confidential” is included on the last line of the footer in bold.

The month and year of the document approval is also included in the footer. If needed, a placeholder can be added for the date, which should be updated when the final pdf is created.

Example Footer:

The data contained in this report are confidential and the property of U.S. Government. It is not to be disclosed to a third party, used in an IND, or used in any other publications without the written permission of the Biological Resources Branch, DTP, DCTD, NCI. This document is made available through federal funds from the National Cancer Institute, NIH, under contract (Insert contract number here)

Confidential **June 2022**

5. CONTENT OF MANUFACTURING REPORTS

5.1 A Manufacturing Report document is a summary of the manufacturing processes and testing for a particular lot. This report discusses the composition, manufacture, and control of the drug/biologic substance and/or the drug/biologic product, or a cell bank. Sufficient information is required in these reports to ensure the proper identification, quality, purity, and strength of the product.

5.2 The amount of information required in the report will vary depending upon the stage of the product development and the intent of the Manufacturing Report.

5.3 The requirements of the sponsor will impact the content of the Manufacturing Report. For example, a sponsor may not provide adequate information to complete a Chemistry, Manufacturing, and Controls section (CMC). In this case, a Manufacturing Report would be provided to the sponsor including all the information that a CMC would contain except the information that is not available. Refer to SOP **24411 - Preparation of Chemistry, Manufacturing and Control Section (Module 3-Quality) in Common Technical Document (CTD) Format.**

5.4 The cover page of the Manufacturing Report contains the following information: “Manufacturing Summary Report “, Product Name, Lot Number, date, name of manufacturer, and approval signatures. Refer to Attachment 1 for an example Cover Page.

5.5 The Table of Contents should be developed in consultation with the Associate Director of Regulatory Affairs or designee. A recently completed Manufacturing Report of the same product type or cell bank type may be used as a template. Use of an eCTD heading format is recommended, refer to Guidance for Industry: Chemistry, Manufacturing, and Control (CMC) Information for Human Gene Therapy Investigational New Drug Applications (INDs), January 2020 for examples of eCTD headings. Refer to Attachment 2 for Table of Contents for a

Manufacturing Report for a product, and Attachment 3 for an example Table of Contents for Manufacturing Report for a cell bank.

5.6 The description of the manufacturing should be obtained from batch production records or laboratory notebooks as source documents.

5.7 Include drug substance (bulk) and drug product (final vialed product) Certificates of Analysis (COA) in the appropriate sections or as Appendices.

5.8 PA/QC Report Summaries may be included in the Appendices on a case-by-case basis. (For example, if an assay is problematic, an unusual result occurs, or a request is made by the client or a regulatory agency.) If PA/QC reports are included, ensure that molecular weight markers and band(s) or interest (product bands, dimer, etc.) are labeled for all SDS-PAGE, IEF, and Western Blots. Clearly identify reference standards.

5.9 A table of the raw materials used, including the manufacturer/vendor, catalog number, lot number, and source/origin should be included in the manufacturing report. For any raw materials made using materials of animal origin, a certificate of origin or BSE/TSE statement from the manufacturer should be included.

5.10 Include sequencing data for the biological substance or vector in the biological substance manufacturing section, if applicable.

5.11 Include assay descriptions if the Manufacturing Report is to be used in an Investigational New Drug Application (IND) to support the manufacture of a clinical product or as requested by a client.

5.12 Include a description of the container closure system used and an example of final product labeling.

5.13 If stability is conducted include either a copy of the stability protocol or a study design table. Data available from stability timepoints should be included.

5.14 Specifics for Manufacturing Reports that Contain Cell Bank Information

Master Cell Banks (MCB) and Working Cell Banks (WCB) should be well characterized and a description of how the bank is manufactured and tested should documented. Information on where the cell bank originated should be described. For further guidance see Q5D Derivation and Characterization of Cell Substrates Used for Production of Biotechnological/Biological Products, 16 July 1997. An example of an E. coli plasmid cell bank Table of Contents is included as Attachment 3.

5.15 Certificate of Analysis

5.16.1 If the cell bank is manufactured using another cell bank, include the certificate of analysis of the starting cell bank.

5.16.2 Include the certificate of analysis for the final cell bank as an attachment.

6. DRAFT REVIEW AND FINALIZATION OF A MANUFACTURING REPORT

6.1 The Microsoft word files should be provided for review electronically. An email is sent to the following personnel to review the documents. The NCI/BRB chief should be copied on the review email. Additional personnel may review the report at the request of the Associate Director of Regulatory Affairs (e.g., depending on the content of the manufacturing report, PA/QC Director or staff may also review).

- Project Scientist(s) or designee
- Manufacturing Director or designee
- Associate Director of Regulatory Affairs or designee
- BDP Program and Technical Director
- NCI/BRB Project Director or designee

6.2 After revisions from the reviewer comments and recommended edits are completed, the final documents are sent with a link to the shared folder for approval. Approvals are completed when signatures below are obtained:

- Project Scientist(s) or designee
- Manufacturing Director or designee
- Associate Director of Regulatory Affairs or designee
- BDP Program and Technical Director
- NCI/BRB Project Director or designee
- NCI/BRB Chief or designee

Approvers can be changed or other approvals (e.g., PA/QC Director) can be added at the discretion of the RA Associate Director.

6.3 Requirements for the review, approval, making an electronic copy, and distribution of regulatory documents including Manufacturing Reports can be found in **SOP 24408 – Preparation of Regulatory Documents**.

7. REFERENCES AND RELATED DOCUMENTS

Document Number	Title
24408	Preparation of Regulatory Documents
24411	Preparation of Chemistry, Manufacturing, and Controls Section (Module 3-Quality) in Common Technical Document (CTD) Format
21 CFR 610	General Biological Products Standards
FDA Guidance Documents	• Guidance for Industry for the Submission of Chemistry, Manufacturing and Controls Information for a Therapeutic Recombinant DNA-Derived Product or A Monoclonal Antibody Product for In Vivo Use, August 1996. • Guidance for Industry: Content and Format of Chemistry Manufacturing and Controls Information and Establishment Description Information for Vaccine or Related Product, January 1999. • Guidance for Industry: Content and Format of Investigational New Drug Applications (IND's) for Phase I Studies of Drugs, Including Well-Characterized, Therapeutic, Biotechnology-derived Products, November 1995. • Points to Consider in the Manufacture and Testing of Monoclonal Antibody Products for Human Use, February 1997. • Guidance for Industry: Container Closure Systems for Packaging Human Drugs and Biologics; Chemistry, Manufacturing, and Controls Documentation, May 1999. • Guidance for Industry: Guidance for Human Somatic Cell Therapy and Gene Therapy, March 1998. • Guidance for Industry: Chemistry, Manufacturing, and Control (CMC) Information for Human Gene Therapy Investigational New Drug Applications (INDs), January 2020. • Guidance Document: Portable document Format (PDF) specifications, September 2016
ICH Guidelines	• International Conference on Harmonization (ICH) Guideline Q3A(R2): Impurities in New Drug Substances, October 2006.

Document Number	Title
	• ICH Guideline Q3B(R2): Impurities in New Drug Products, June 2006. • ICH Guideline Q1A(R2): Stability Testing of New Drug Substances and Products, November 2003. • ICH Guideline Q6B: Specifications: Test Procedures and Acceptance Criteria for Biotechnological/Biological Products, September 1999. • ICH Guideline Q5A(R1): Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin, September 1999. • ICH Guideline Q5D: Derivation and Characterization of Cell Substrates used for Production of Biotechnological/Biological Products, July 1997.

8. ATTCHMENTS

Attachment 1: Sample Cover Page

Attachment 2: Example Product Manufacturing Summary Report Table of Contents

Attachment 3: Example E. coli Plasmid Cell Bank Manufacturing Summary Report Table of Contents.

Attachment 1: Sample Cover Page

MANUFACTURING SUMMARY REPORT

TITLE
LOT NUMBER
DATE

Biopharmaceutical Development Program
Frederick National Laboratory for Cancer Research (FNLCR)
Leidos Biomedical Research, Inc.
[redacted]

Approved By/Date: _____
Project Scientist:

Approved By/Date: _____
Manufacturing Director:

Approved By/Date: _____
Associate Director of Regulatory Affairs:

Approved By/Date: _____
BDP Program and Technical Director:

Approved By/Date: _____
NCI/BRB Project Director:

Approved By/Date: _____
NCI/BRB Chief:

Attachment 2 : Example Product Manufacturing Summary Report Table of Contents

Table of Contents

Attachment 2: Continued

BDP/FNLCR
[redacted]
Page 3 of [redacted]

Attachment 2: Continued

Figures

Tables

Appendices

SOP Title: Preparation of Manufacturing Reports
SOP Number: 24407
Revision: 08

Attachment 3: Example E. coli Plasmid Cell Bank Manufacturing Summary Report Table of Contents

Table of Contents

Attachment 3: Continued