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1.0 Purpose

This SOP establishes a procedure for the required content, format, and approval of Master Production Records (MPR) in accordance with cGMP guidelines.

2.0 Scope

This SOP is to be followed by Biopharmaceutical Development Program (BDP) personnel involved in the cGMP production, purification, and processing of clinical grade material. Fill/Finish, Mammalian Cell Culture, Fermentation and Recovery, etc., may have specific sections pertaining to those specific areas only.

3.0 Authority and Responsibility

3.1 The Director, Regulatory Compliance, BDP has the authority to define this procedure.

3.2 BDP personnel are responsible for preparation of Master Production Records.

3.3 The Director, Late Process Sciences, Production Managers and/or Project Scientists is responsible for assuring the technical accuracy of the Master Production Record.

3.4 Biopharmaceutical Quality Assurance (BQA) is responsible for review and approval of Master Production Records.

3.5 BQA is responsible for quality oversight of this operation.

4.0 Definitions

4.1 **Master Production Record (MPR):** An original document containing detailed instructions for performance of a specific process. The document is used to record critical steps, parameters, raw data, etc., as events occur during the production of a product. The MPR also contains materials, supplies, equipment, and supporting testing data or documentation required to make the production record complete.

4.2 **Critical Operation:** A step or phase in the manufacture of a product where a deviation from the process specified in the MPR may have a significant impact on product identity, purity, safety, potency, stability, or quality.

4.3 **Batch Production Record:** An exact copy of the Master Production Record issued to the Production Group by BQA. It contains specific information, such as product lot numbers, project number, location (building) which are associated with the manufacture of a specific batch of product.

5.0 Format of Master Production Records (MPR)

5.1 Master Production Records are created in Microsoft Word® using Arial Font in landscape format.

5.2 Each page of the MPR contains a header containing the following information.

5.2.1 A unique MPR document number is assigned by the eDMS (electronic Document Management System). Section 7.0 defines the numbering convention. Each documents includes a revision level. A unique title is defined by the originator of the document.

5.2.2 If appropriate. the project number, space for lot number and location (building), are also included.

5.3 The footer of each document includes pagination.

5.4 Signature of the person issuing the record.

5.5 Post-Manufacturing Document Review.

- Checked By/Date.
- BQA Approval/Date.

5.6 Contents Page (See Attachment 2).

5.7 References and General Instructions (Attachment 3). This provides a list of project-related Standard Operating Procedures (SOPs) and other BPRs.

5.7.1 Documents referenced in the MPR must be included in the document reference list.

5.8 Use the appropriate Safety statement for the product and the procedures involved in manufacture of the product.

5.9 Personnel (Attachment 5). This section documents the personnel involved in the production process in a table with spaces for the names of the operators, signatures, and initials.

5.10 A table is provided to record raw materials used in the procedure, BQA release numbers, and expiration dates, if applicable (Attachment 6).

5.11 A list of equipment used in the procedure is provided to capture associated BDP numbers, and/or NIH numbers, and calibration / certification expiration dates (Attachment 6). Cleaning expiration dates of equipment may also be included when appropriate.

5.12 A process flow chart (Attachment 4) is provided.

5.13 Detailed instructions of how to perform the specific process (Attachment 7). The instructions must be clear, complete, and must include sufficient detail to enable accurate repetition of the process. This section must include **Performed by** for discrete steps and **Verified by** initials or signatures, and dates for all critical steps. This section shall also include records of critical steps and parameters such as volumes, weights, start/stop times, temperatures, pressures, flow rates, et cetra.

5.14 Comments section: Include a page at the end of each MPR (or section if applicable) on which to record comments. All Batch Production Record (BPR) entries must be initialed and dated by the operator and the Supervisor or Project Scientist.

5.15 Include a list of any attachments required to complete the document (Attachment 8). These attachments are on individual pages at the end of the document.

5.16 Examples of modules and templates can be downloaded from the BDP intranet.

6.0 Organization and Preparation of Master Production Records

6.1 The MPR may organize production records as a series of linked individual, approved, and freestanding process templates (modules). Each module represents a distinct phase of the process, i.e., Staging, Protein A, purification, low-pH virus inactivation, et cetra. An alternative organization is assigning each defined portion of a production process a separate MPR, i.e., Seed, Production, and Centrifugation.

6.2 Staging Module of the Master Production Record

6.2.1 If a separate staging module is utilized, it will constitute the first approved module in the process Master Production Record. It may be issued in advance of the process modules to allow setup and staging activities to begin.

6.2.2 If a separate staging module is not used, the staging of materials is captured in the beginning of each MPR as dictated by Steps 5.8 and 5.10 of this SOP**.**

6.3 Preparation of Master Production Records

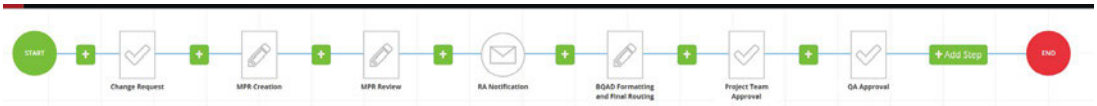
6.3.1 BDP personnel prepare a final draft of the new MPR and submit an electronic copy in the eDMS prior to initiation of production.

6.3.2 BQAD incorporates tables and items required and ensures that the document is formatted properly.

6.3.3 The draft is routed through the eDMS for review and approval. The area Supervisor and/or Project Scientist reviews for technical completeness and accuracy. At the same time, QA is reviewing for cGMP compliance. Comments and questions by the reviewers are addressed by the author and area supervisor.

Upon approval and signature by BQA, the MPR is ready for issue. See Figure 1 for the MPR Review and Approval Workflow.

Figure 1 MPR Review and Approval Workflow



7.0 Initiating a New Master Production Record

7.1 If a previous MPR is being used, an editable e-copy can be requested from BQAD, or, if previously approved though the eDMS, can be obtained from the eDMS.

7.2 Follow the instructions in SOP 21010 Section 6.2. The infocard type is MPR.

7.3 **Assignment of Numbers to Master Production Records**

7.3.1 MPR identification codes begin with MPR designated letters and are then assigned a unique number by the eDMS as follows.

MPR-C-1XXXX = Mammalian Cell Culture

MPR-F- 3XXXX = Fermentation (Bacterial and Mammalian Cell Productions)

MPR-P-5XXXX Section XX - XX = Preparation, Purification, Production (If, in the event there are no sections assigned, the number will read Section NA – NA.)

MPR-SC-7XXXX= Sterile Core

7.4 **Non-GMP, Toxicology, and GLP or R&D** runs using MPRs issued by BQA (including draft MPRs) are issued with a lot number. This information is logged into the batch record database maintained by BQA.

7.5 If forms are included in the production record, the forms are assigned a number in the same way as the production record. Any forms used with the MPR that are part of other GMP documents (SOP's, Validation Protocol's, etc.) should be used as attachments only.

8.0 Approvals

8.1 The eDMS audit trail includes the approvals of the MPR. MPRs are approved by

- Author
- Director, Late Process Sciences, or Production Manager and/or Project Scientist
- BQA

8.2 Documents approved prior to the implementation of the MPR creation in the eDMS includes the approval signatures on the first page of the document.

8.3 Effective date is the date of the last signature.

9.0 Revision of Master Production Records

9.1 Revisions to MPRs are done through the eDMS.

9.2 Follow ***SOP 21010 - User Manual for MasterControl*** for revising documents in the eDMS.

9.3 A list of the revision(s) made and reasons for the revision(s) must be submitted with the revised batch record. These are included in the document task packet. The revisions and justifications are reviewed and approved by all the reviewers.

9.4 Global changes to step format or content in an MPR must be approved by both Production and Quality Assurance in advance of the MPR revision.

10.0 Storage of Master Production Records

10.1 For Master Records approved before the implementation of this procedure, BQAD maintains all current approved Master Production Records in the Document Control Room.

10.1.1 The master version of each Master Production Record is stored in the eDMS.

10.1.2 BQAD maintains Master Production Records for a minimum of ten (10) years.

11.0 Issuance of a Master Production Record as a Batch Production Record

Batch production records are controlled and issued to manufacturing per ***SOP 21923 - Control and Issuance of Batch Production Records for Use in Manufacturing.***

12.0 References and Related Documents

Attachment 1 *MPR Cover Page Example*

Attachment 2 *Contents Page Example*

Attachment 3 *Reference and General Instructions Example*

Attachment 4 *Process Flow Chart Example*

Attachment 5 *Personnel Example*

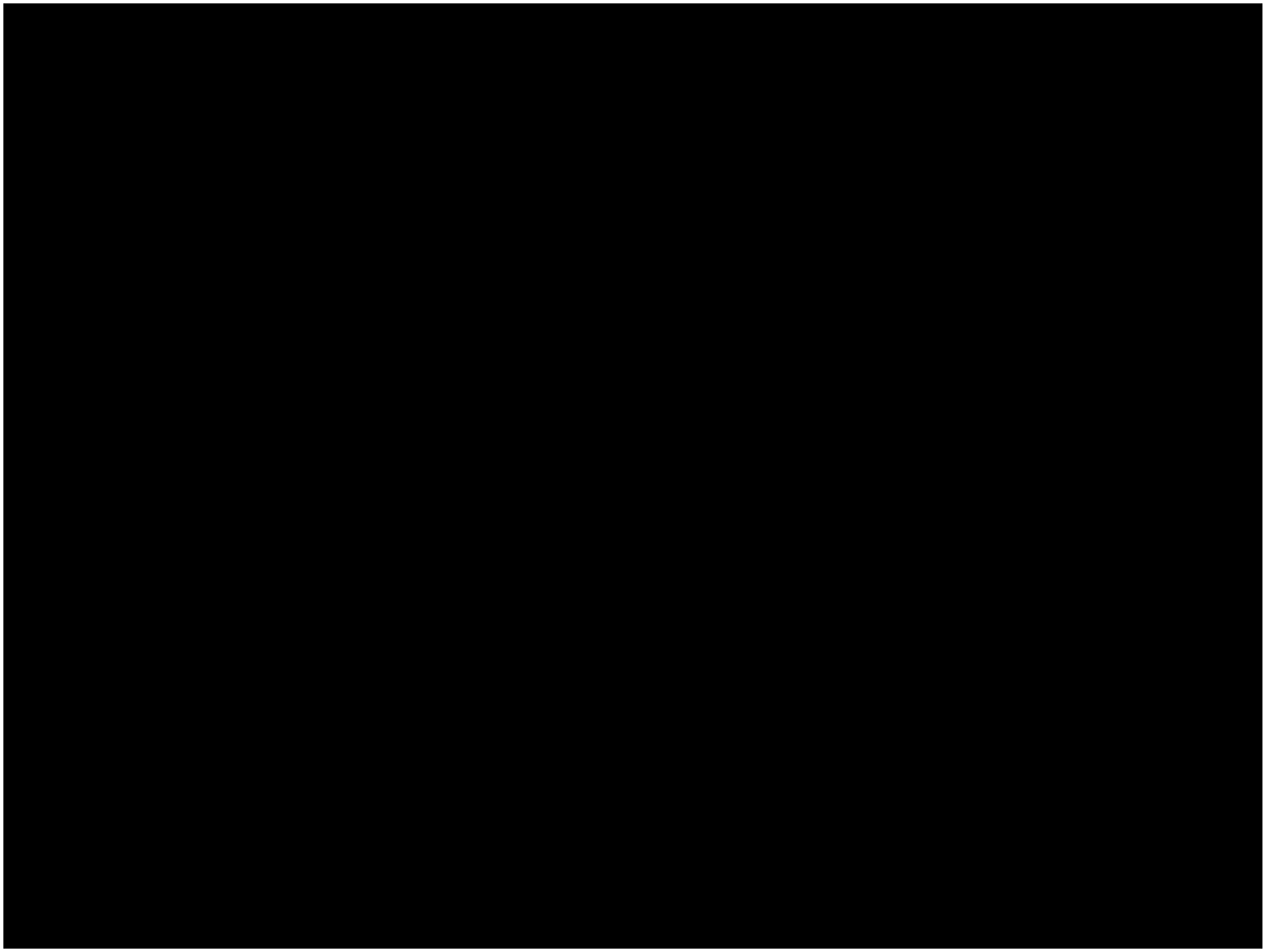
Attachment 6 *Equipment List / Non-Product Contact Consumables / Product-Contact Consumables Example*

Attachment 7 *Processing Example*

Attachment 8 *Attachment Page Example*

SOP 21923 *Control and Issuance of Batch Production Records for Use in Manufacturing*

SOP 21010 *User Manual for MasterControl*



Attachment 1: MPR Cover Page

Biopharmaceutical Development Program Frederick, MD

EXAMPLE
Master Production Record (MPR)
TITLE on each page

Document No.	Project No.	Lot No.	Location	Revision	Effective	Page
MPR-X-XXXX	**XXXX**		**ATRF**	**XX**	**MM DD YYYY**	**X of XX**

Biopharmaceutical Development Program
Frederick National Laboratory for Cancer Research
Leidos Biomedical Research, Inc., P.O. Box B
Frederick, MD 21702-1201

MPR Approval

Author Approval: _____

Project Scientist Approval: _____

Biopharmaceutical Quality Assurance (BQA) Approval: _____

Comparison of Copy to Master Document

This document is an accurate reproduction of MPR-X-XXXX Rev XX as found in the Master Document File.

Checked by: _____ Date: _____

Post-Manufacturing Document Review

This completed production record has been reviewed and found to be complete, correct, and in conformance with relevant standard operating procedures (SOPs) and other documents.

Checked by: _____ Date: _____

BQA Approval: _____ Date: _____

ATTACHMENT 2: Contents Page

Biopharmaceutical Development Program Frederick, MD

EXAMPLE
Master Production Record (MPR)
TITLE on each page

Document No.	Project No.	Lot No.	Location	Revision	Effective	Page
MPR-X-XXXX	**XXXX**		**ATRF**	**XX**	**MM DD YYYY**	**X of XX**

Contents

ATTACHMENT 3: References and General Instructions

Biopharmaceutical Development Program Frederick, MD

EXAMPLE
Master Production Record (MPR)
TITLE on each page

Document No.	Project No.	Lot No.	Location	Revision	Effective	Page
MPR-X-XXXX	**XXXX**		**ATRF**	**XX**	**MM DD YYYY**	**X of XX**

1.0 References and General Instructions

1.1. Related SOPs

SOP XXXXXX: Title
SOP XXXXXX: Title
SOP XXXXXX: Title

1.2. Follow SOP 21409, General Documentation Practices, for documenting in the MPR.

1.2.1 Water for Injection (WFI) drawn on-site (not purchased from a vendor and released by MMIC) must be used within one day from the day the water is withdrawn. If water from a validated WFI system is used in lieu of pre-packaged WFI, record the building and point of use # in the space provided for the BDP Part#/Lot#.

1.2.2 Graphs. Printouts, chromatograms, and other attachments should be labeled with the lot number, date and operator's initials, MPR number, project number, and section number (as applicable).

1.2.3 When recording the calibration due dates for a piece of equipment that has multiple calibration points, use the earliest calibration due date.

1.2.4 For items and materials recorded and having assigned expiration dates, the expiration date should be greater than 30 days from the date the items are staged unless there is no substitute item.

ATTACHMENT 4: Process Flow Chart

Biopharmaceutical Development Program Frederick, MD

EXAMPLE
Master Production Record (MPR)
TITLE on each page

Document No.	Project No.	Lot No.	Location	Revision	Effective	Page
MPR-X-XXXX	XXXX		ATRF	XX	MM DD YYYY	X of XX

2.0 Process Flow Chart

ATTACHMENT 5: Personnel

Biopharmaceutical Development Program Frederick, MD

EXAMPLE
Master Production Record (MPR)
TITLE on each page

Document No.	Project No.	Lot No.	Location	Revision	Effective	Page
MPR-X-XXXX	**XXXX**		**ATRF**	**XX**	**MM DD YYYY**	**X of XX**

3.0 Personnel

3.1. Document the personnel involved in the staging process in the table below.

Operator (Print Name)	Signature	Initials

ATTACHMMENT 6: Equipment/Product-Contact Consumables/ Non-Product Contact Consumables

Biopharmaceutical Development Program Frederick, MD

EXAMPLE
Master Production Record (MPR)
TITLE on each page

Document No.	Project No.	Lot No.	Location	Revision	Effective	Page
MPR-X-XXXX	**XXXX**		**ATRF**	**XX**	**MM DD YYYY**	**X of XX**

4.0 Equipment List

4.1. Document that the equipment is clean, ready for use, and will be within its calibration expiry at time of use. Record calibration expiration dates, and any additional equipment used in the extra spaces provided.

Non-Product Contact Equipment:

Item	ID	Calibration/Certification Exp. (If Applicable)
Item 1		
Item 2		
Item 3		
Item 4		NA
Item 5		NA

Pipet Aid	Filter Replacement Date

Recorded by/Date:

ATTACHMMENT 6: Equipment/Product-Contact Consumables/ Non-Product Contact Consumables (Continued)

Biopharmaceutical Development Program Frederick, MD

EXAMPLE
Master Production Record (MPR)
TITLE on each page

Document No.	Project No.	Lot No.	Location	Revision	Effective	Page
MPR-X-XXXX	**XXXX**		**ATRF**	**XX**	**MM DD YYYY**	**X of XX**

Item 1
Item 2
Item 3

5.0 Materials and Supplies

Confirm that the following materials have been released by BQA or approved by MMIC, are available in the quantities specified and will be within their expiry at the time of use. Record any additional materials and supplies used in the extra spaces provided.

5.1 Materials

Item	BDP Part #	BDP Lot#	Quantity Required	Quantity Stocked	Exp. Date
Item 1					
Item 2					
Item 3					

Recorded by/Date:

Biopharmaceutical Development Program Frederick, MD

EXAMPLE
Master Production Record (MPR)
TITLE on each page

Document No.	Project No.	Lot No.	Location	Revision	Effective	Page
MPR-X-XXXX	**XXXX**		**ATRF**	**XX**	**MM DD YYYY**	**X of XX**

5.2 Consumables

Item	BDP Part #	BDP Lot#	Quantity Required	Quantity Stocked	Exp. Date
Item 1					
Item 2					
Item 3					

Recorded by/Date:

ATTACHMENT 7: Processing Instructions

Biopharmaceutical Development Program Frederick, MD

EXAMPLE
Master Production Record (MPR)
TITLE on each page

Document No.	Project No.	Lot No.	Location	Revision	Effective	Page
MPR-X-XXXX	**XXXX**		**ATRF**	**XX**	**MM DD YYYY**	**X of XX**

6.0 Processing

6.1 Process step description
6.1.1 Sub-processing step description
6.1.1 Sub-processing step description

6.2 Process step description

6.3 Process step description

6.xx Comments

_____

_____

_____

Reviewed By Manager/Date:

ATTACHMENT 8: Attachments Page

Biopharmaceutical Development Program Frederick, MD

EXAMPLE
Master Production Record (MPR)
TITLE on each page

Document No.	Project No.	Lot No.	Location	Revision	Effective	Page
MPR-X-XXXX	**XXXX**		**ATRF**	**XX**	**MM DD YYYY**	**X of XX**

7.0 Attachments

Attachment 1: Title of Attachment