Title: The GMP Banking Process

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1.0 Purpose

This Standard Operating Procedure (SOP) describes the procedures, documentation, and controls necessary for establishing and preserving Good Manufacturing Practices (GMP) Accession Cell Banks (ACB), Master Cell Banks (MCB), Working Cell Banks (WCB), and End of Production Banks (EPB) (if required) at the Biopharmaceutical Development Program (BDP.)

2.0 Scope

This SOP applies to BOP staff and outsource contractors making GMP mammalian cell banks, bacterial cell banks, and virus banks.

3.0 Authority and Responsibility

3.1 The Managers of the GMP Cell and Virus Bank Production Laboratories, Biopharmaceutical Development Program (BOP) have the authority to define this procedure.

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3.2 BDP Production personnel are responsible for the implementation of this procedure. The BDP Contracting Officer Technical Representative (COTR) is responsible for oversight of this procedure if outsourced.

3.3 Biopharmaceutical Quality Assurance (BQA) is responsible for quality oversight of this operation, release of GMP banks, and stability testing oversight of the banks.

4.0 Bank Production Procedure at the BDP

The banking process starts with an Accession Bank or seed stock created from cells (mammalian or bacterial) or viruses that have been optimized for growth and/or production received from the investigator. Documentation of the Accession Bank may be made in a laboratory notebook for the project or an issued Master Production Record (MPR).

A Master Bank is created from one or more vials of the Accession Bank or seed stock (for viruses). One or more vials of the Master Bank may be expanded to produce a Working Bank (optional).

If eukaryotic or prokaryotic cells are used in a protein production process at the end of the manufacturing stage, cells are taken from the production vessel and grown into an End of Production (EOP) Cell Bank. Any product collected after the EOP cells are taken must not be used. Any further productions utilizing the same bank must end at the time point that the EOP cells were pulled.

4.1 Before initiation of a MCB, WCB, or EOP bank, a Master Specification for that bank is created and approved (Refer to ***SOP 13200 - Qualification of Cells and cGMP Banks***) to determine what testing will be required. For virus banks, the Project Scientist will work with Process Analytics/Quality Control (PA/QC) Department to determine what testing is required.

4.2 Once a schedule has been determined to produce a bank, request a Batch Production Record (BPR), and Lot Number (Form 21405-01, ***SOP 21405 - Assigning and Requesting Lot Numbers for Products***), and Part Number (***SOP 21903 - Using the Part Number/Master Specification Program to Establish Raw Material Part Numbers and Master Specifications***) from BQA.

4.3 When the raw materials have been released, and the area has been prepared for GMP production, submit a request for an area clearance (Form 21104-01, ***SOP 21104 - Pre-Production Clearance***) to BQA. BQA personnel will arrange to perform an area clearance with Production personnel. When clearance has been granted, BQA personnel will give a copy of the completed Form 21104-01 to the Production staff to be posted on the door to the released area(s). When production has been completed, the form is included in the batch record.

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4.4 Prepare the cell bank according to the instructions contained in the BPR. As soon as labeling information is determined, submit Form 21403-01 (***SOP 21403 - Origination, Modification, and Control of Labeling for GMP and GLP Products***) to BQA for label approval. All GMP banks must be stored in BQA approved controlled temperature equipment in a qualified storage facility (Refer to Section 4.0).

4.5 When the production is complete and it has been determined that the bank has been successfully frozen, return the completed BPR to the department supervisor for review. After the Supervisor has reviewed it, the signed BPR is returned to BQA in an orange folder for review (***SOP 21103 - Quality Assurance Review of Completed Batch Production Records and Other Manufacturing Production Records***).

4.6 Submit the required number of samples of the bank to PA/QC for the tests listed on the Master Specification. The PA/QC project monitor tracks the status of testing and when all testing is complete, PA/QC and BQA complete a Certificate of Analysis.

4.7 When the batch production record and test results have been reviewed and accepted, BQA will release the bank by issuing a release letter. If the bank is a product, the information on the bank will go to the Product Review Board (***SOP 10001 - Project Acceptance and Completion of Projects for Clinical Use***) for a final review before releasing it to the investigator.

4.8 Banks used for production must be released before use. Should a bank need to be used prior to full testing per the Master Specification, the bank may be conditionally released if certain baseline tests meet the specified acceptance criteria. However, release of any product manufactured using a conditionally- released bank is contingent on successful completion of full testing per the Master Specification. Baseline testing for each type of bank is as follows.

4.8.1 Eukaryotic banks - sterility, mycoplasma

4.8.2 Prokaryotic banks - purity/morphology, gram stain

4.8.3 Viral Banks - Sterility, viral content

NOTE: A Working Bank may be produced from the Master Bank before the Master Bank is released.

4.9 If a lot fails to meet any of its in-process or release criteria, the lot is placed on BQA Hold or Quarantine per ***SOP 21704 - Biopharmaceutical Quality Assurance Hold/Quarantine Policy for Materials and Products***, an investigation is conducted and the disposition of lot will be determined as per ***SOP 21008 – BDP Material Review Board***.

4.10 Should a bank be held at a contract storage facility that needs to be destroyed it may be performed by the facility. The request to the storage facility must be in writing and a written confirmation that the bank was destroyed must be received from the facility. This document will be maintained in the project file and the BPR.

4.11 Submit a copy of the request and the memo to the Project File on BDP Public in the Correspondence folder.

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5.0 Procedures for Banks made by Outsource Contractors in the BDP

5.1 An approved contract must be in place between the contractor and the BDP before work can begin by the contractor.

5.2 A Quality Agreement (***SOP 21108 - Establishing a BDP Quality Agreement with Subcontractors***) must be in place between the BDP and the Contractor. The Quality Agreement will outline what is required to comply with GMPs for the manufacture, storage, and shipment of banks.

6.0 Storage, Stability and Distribution

6.1 General policies and procedures for handling of banks are addressed in ***SOP 21709 - Handling and Storage of CGMP Mammalian, Bacterial, and Viral Cell Bank Materials***.

6.2 Master Banks may be placed on a stability program, if required, upon release, following an approved stability protocol. If applicable, inform PA/QC in writing that the bank was released and needs to be entered into the stability program. Include the name of the bank, lot number, part number, date of manufacture, quantity per vial (example: cells/vial), volume per vial, and tests to be performed at 5-year intervals. PA/QC will then enter the information required into a stability program. At the required time interval, PA/QC will notify the Production staff that the bank needs to be tested for the required stability tests. It is up to Production personnel to perform the tests. If a bank has been destroyed, notify PA/QC to take it off of the stability schedule.

6.3 Test reports from each stability test are reviewed by the department Supervisor, PA/QC, and BQA, and a copy is placed into the batch record.

6.4 In order to transfer any cell line to a third party such as an Outsource Contractor or Principle Investigator, any issues such as licensing rights or intellectual property rights must be addressed with the Intellectual Property personnel working with the BDP and permission must be granted in writing by the BRB. A joint decision will be made by the BDP Project Scientist and the BRB Project Scientist on how many vials will be distributed.

6.5 The contact person at the BDP must fill out a distribution form and Safety Request for Shipment form (see ***SOP 20201 - Distribution of Products and Materials to External Recipients***). The shipment is made through Materials Management and Inventory Control (MMIC.)

7.0 Documentation

7.1 Documentation for a bank will remain under BQA control as defined in ***SOP 21103 - Quality Assurance Review of Completed Batch Production Records and Other Manufacturing Production Records***.

7.2 The production of GMP banks is documented in an approved Batch Production Record.

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8.0 References and Related Documents

8.1 **SOP 10001** *Project Acceptance and Completion of Projects for Clinical Use*

8.2 **SOP 13200** *Qualification of Cells and CGMP Cell Banks*

8.3 **SOP 20201** *Distribution of Products and Materials to External Recipients*

8.4 **SOP 21008** *BDP Material Review Board*

8.5 **SOP 21103** *Quality Assurance Review of Completed Batch Production Records and Other Manufacturing Production Records*

8.6 **SOP 21104** *Pre-Production Clearance*

8.7 **SOP 21108** *Establishing a BDP Quality Agreement with Subcontractors*

8.8 **SOP 21403** *Origination, Modification, and Control of Labeling for GMP and GLP Products*

8.9 **SOP 21405** *Assigning and Requesting Lot Numbers for Products*

8.10 **SOP 21704** *Biopharmaceutical Quality Assurance Hold/Quarantine Policy for Materials and Products*

8.11 **SOP 21709** *Handling and Storage of CGMP Mammalian, Bacterial, and Viral Cell Bank Materials*

8.12 **SOP 21903** *Using the Part Number/Master Specification Program to Establish Raw Material Part Numbers and Master Specifications*

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