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1.0 Purpose

This SOP describes the procedure used to release Biopharmaceutical products at the Biopharmaceutical Development Program (BDP) by Biopharmaceutical Quality Assurance (BQA).

2.0 Scope

This procedure applies to the release of products manufactured at the BDP or for the BDP (by another institution or contract manufacturer). Products requiring BQA release include:

- Master and Working Cell Banks (eukaryotic, prokaryotic, viral, plasmid, etc.)
- Products for further CGMP manufacturing by other institutions.
- Products to be used in IND directed toxicology studies.
- Product contact reagents for use as FDA (or equivalent) regulated devices.
- Product contact reagents for use in the manufacture of FDA (or equivalent) regulated products.
- Final filled products for clinical use.
- Products from other institutions which have been recertified for human use by the BDP, e.g., expired commercial or investigational products.
- Any material generated at, or for, the BDP which may be administered, directly or indirectly, to humans.

This procedure does not apply to:

- Accession banks and end of production cell banks.
- Activities that occur prior to the generation of the accession bank.
- Materials used solely as Quality Control assay reagents.

- Reference standards for in-house use.
- Research and development materials.
- In-house manufactured reagents/solutions for in-house manufacturing.

Products may not be shipped without written approval from BQA.

3.0 Authority and Responsibility

3.1 The Director of Regulatory Compliance (RC) has the authority to define this procedure. The Director of RCBQA, or designee, is responsible for release of products from the BDP. Only the Director of RC, or QA/RA designee, may release products from the BDP for direct or indirect use in humans.

3.2 The Director of Biopharmaceutical Process Analytic\Quality Control (PA\QC), or designee, is responsible for testing of products per the requirements of the Master Specification (MS) and generation of the Certificate of Analysis (COA).

3.3 The Regulatory Affairs Associate Director, or designee, is responsible for the generation of CMC and related documentation.

3.4 The BQA Compliance Manager, or designee, is responsible for assuring batch records are complete and correct, test specifications have been met, and for the generation of the Release letter, Product Release Checklist, and compiling any supporting documentation required.

3.5 BQA is responsible for quality oversight of this procedure.

4.0 Procedure

4.1 Upon notification of the completion of the review of the Batch Production Records (BPRs) by BQA that are associated with a product, a Release of Product document package is created by the BQA Compliance Manager, or designee, for that product. The document package consists of the following.

4.1.1 BPR List: BQA reviewed and approved BPRs are listed by their Production phase (e.g., Master Cell Bank (MCB), Working Cell Bank (WCB), Harvest, Purification (HP), Final Product (VFP), etc., as defined by the project), the name of the BQA individual performing the review and the date the record was reviewed. The closure of the BPRs are verified by BQA (refer to Attachment IV).

4.1.2 Certificates of Analysis: The completed COAs are obtained from BQA for the product and attached with the document. The COA(s) will cover the Cell Banks (MCB, WCB, EOP) the Sterile filtered Purified Bulk, and Final Vialed Product as defined by a project. The review/approval of the COA(s) will be verified by BQA on the Product Release document.

4.1.3 Stability Protocol: A copy of the signed approved stability protocol is obtained from BQA and attached to the document, if required for the project. The review/approval of this document is verified by BQA.

4.1.4 Quality Event Closure/Resolution: The logs for Deviations, Product Holds, Product Quarantine, Material Review Board, Out-of-Specification Notices, Engineering Events and EM Excursion Notices are reviewed to verify that any events related to the product being released have been closed or the event has been determined to have no significant product impact prior to the release of the product.

4.1.5 Product Label: A copy of the final container label (from the BPR) is attached to the document. The copy will be signed (by using the Document Review Stamp) by BQA to signify that the label information was compared to the product information contained in the Release Memorandum and was correct.

Upon the completion of the Release of Product document package, a Release Memorandum is created by the BQA Compliance Manager, or designee, for that product (Attachments 1, 2, and 3).

The Release Memorandum will include the following information in paragraph or list style.

- Statement of Use (Phase I, Phase II, etc.).
- Statement of GMP, GLP, or non-regulated.
- Product hazards statement and known risks disclosure (if applicable).
- Listing of product information including (as applicable to product).
  - NSC number, (if applicable)
  - Project number
  - Description
  - Part number
  - Lot number
  - Date of Manufacture (or Freeze Date for cell banks)
  - Volume
  - Concentration (or Cells/Vial for cell banks)
  - Caution Statement
  - Inventory count (or Quantity for cell banks)
  - Leidos Biomedical Research, Inc.
  - Storage Location (for cell banks)

4.2 The Product Release Memorandum and Release of Product document are combined with a copy of the signed COA(s), the stability protocol (if appropriate), and a copy of the label(s) applied to the product.

4.3 The documentation compiled in Sections 4.1 and 4.2 may be reviewed by a second BQA individual to verify completeness and correctness of the compiled documentation. Any changes/corrections to the documentation are made at this time. These compiled documents are now referred to as the Release Package.

4.4 The Release Package for Investigational Use Product is submitted to the Director of RC, or designee, for final review and approval. Approval to release a product for "Use in Humans" requires the signature of the Director of RC, or QA/RA designee, who has been given temporary authority, in writing, for product release. The BQA Compliance Manager has the authority to release product in the Director's absence.

4.5 The release of Toxicological Use products or products for Further Manufacturing Use (e.g., cell banks) may be completed by the BQA Compliance Manager, or QA/RA designee.

4.6 The Release Package is forwarded to the BDP Program and Technical Director, or designee.

5.0 Documentation

5.1 Document the review of the required information on the Release of Product document (see Attachment 4 for an example). The information recorded on the document can be modified based on the type of product (clinical or toxicology) being released.

5.2 Document the release information on the Product Release Memorandum (see Attachments 1, 2, and 3 for examples). The memorandum can be modified based on the type of product (clinical or toxicology) being released.

5.3 The product release package is scanned electronically. The scan file is maintained in the appropriate electronic project information file.

5.4 The original of the Approved Release Package is sent to the BDP Program and Technical Director, or designee. Scanned copies of the approved release package are sent to the distribution listing on the Release Memorandum and to the approvers of the document.

5.5 The BQA copy is maintained as part of the project files in a secured storage room for as long as the project files are retained.

6.0 Attachments

Attachment 1 Example Release Memorandum for Master Cell Banks

Attachment 2 Example Release Memorandum for Final Product

Attachment 3 Example Release Memorandum for Toxicology Product

Attachment 4 Example Product Release Document

Attachment 5 Product Release Flow Chart

Attachment 1

Example: Release Memorandum for Master Cell Banks

DATE: XX/XX/XX

TO: [Current Director Name]
BDP Program and Technical Director
Biopharmaceutical Development Program

FROM: [Current Manager Name]
Compliance Manager, Biopharmaceutical Quality Assurance
Biopharmaceutical Development Program

SUBJECT: QA RELEASE OF THE [product name] MASTER CELL BANK, [lot number]

The BDP Quality Assurance Department has completed the review of the manufacture and testing of the [product name] Master Cell Bank, Lot [lot number]. The batch record has been reviewed and conforms to CGMP requirements as are applicable to the generation of cell banks. The Certificate of Analysis has been reviewed. Test results conform to specifications.

The BDP has completed the production of the product in conformance to the following specifications that NCI has reviewed and approved.

(List Master Specifications and COAs)

[Include statement if product manufacture was subcontracted to another organization]

This lot is released for CGMP manufacturing use.

Lot Information:

Project number:
Description:
Part Number:
Lot number:
Freeze date:
Volume:
Cell/Vial:
Caution Statement:
Quantity:
Storage Location:

pc:
BRB Project Manager / NCI - BRB (if applicable)
MMIC / Leidos Biomedical Research, Inc. / BDP
Director PA/QC / Leidos Biomedical Research, Inc. / BDP
BDP Project Scientist / Leidos Biomedical Research, Inc. / BDP
Director Regulatory Compliance / Leidos Biomedical Research, Inc. / BDP
BQA Project Files

Attachments: Product Release, Copy of Certificate of Analysis and Product Label

Attachment 2
Example

Release Memorandum for Final Product

Date: XX/XX/XX

To: [Current Director Name]
BDP Program and Technical Director
Biopharmaceutical Development Program

Through: [Current Director Name]
Director of Regulatory Compliance
Biopharmaceutical Development Program

From: [Current Manager Name]
Compliance Manager Biopharmaceutical Quality Assurance
Biopharmaceutical Development Program

Subject: QA RELEASE OF [product name] Final Vialed Product, [lot number]

The BDP Quality Assurance Department has completed the review of [product name] Final Product, [lot number]. The batch production records have been reviewed and conform to CGMP requirements as are applicable to the manufacture of product for Phase 1 and 2 investigational use. The Certificate of Analysis for the final product has been reviewed. Test results conform to specifications.

The BDP has completed the production of the product in conformance to the following specifications that NCI has reviewed and approved.

(List Master Specifications and COAs)

[Include statement if product manufacture was subcontracted to another organization]

Notification of known and possible risks [Example of risk statement]:
It is Leidos Biomedical Research, Inc. policy to disclose known and possible risks that may be associated with biologic products manufactured for the NCI. [State: There are no known risks currently associated with this lot of product, or list the known risks, if any.] However, there is a remote chance that adventitious agents may be present that are currently unknown or for which tests were not conducted. Additionally, tests may not be available yet or the level of adventitious agent, if present, may be below the sensitivity of an assay. This product may only be used in FDA approved clinical studies. This product is not for commercial distribution or use.

This lot is hereby released for investigational use and may be shipped as directed by the NCI.

Lot Information:

NSC Number:
Project Number:
Description:
Part Number:
Lot number:
Manufacturing date:
Volume:
Concentration:
Caution Statement:
Number of Vials Released:
Leidos Biomedical Research, Inc. Retain Count:

pc: BRB Project Manager / NCI - BRB
MMIC / Leidos Biomedical Research, Inc. / BDP
Director of PA/QC Leidos Biomedical Research, Inc. / BDP
Project Scientist / Leidos Biomedical Research, Inc. / BDP
BQA Project Files

Attachments: Product Release Document, Copy of Certificate of Analysis, Stability Protocol, and Product Label

Attachment 3

Example

Release Memorandum for Toxicology Product

Date: XX/XX/XX

To: [Current Director Name]
BDP Program and Technical Director
Biopharmaceutical Development Program

From: [Current Manager Name]
Compliance Manager, Biopharmaceutical Quality Assurance
Biopharmaceutical Development Program

Subject: **BQA RELEASE OF [product name] Toxicology Lot, [lot number]**

The BDP Quality Assurance Department has completed the review of [product name], Toxicology Lot [lot number]. The batch production record has been reviewed and conforms to FDA requirements as are applicable to the manufacture of product for Toxicology use. The Certificate of Analysis has been reviewed. Test results conform to specifications.

[Include statement if product manufacture was subcontracted to another organization]

The BDP has completed the production of the product in conformance to the following specifications that NCI has reviewed and approved.

(List Master Specifications and COAs)

This lot is hereby released for toxicology use and may be shipped as directed by the NCI.

Lot Information

NSC Number:
Project number:
Description:
Part Number:
Lot number:
Manufacturing Date:
Volume:
Concentration:
Caution Statement:
Number of vials Released:

pc:
BRB Project Manager / NCI - BRB
MMIC / Leidos Biomedical Research, Inc. / BDP
Director of Regulatory Compliance / Leidos Biomedical Research, Inc. / BDP
Director of PA/QC / /BDP
BDP Project Scientist / /BDP
BQA Project Files

Attachments: Product Release Document, Copy of Certificate of Analysis and Product Label

Attachment 4

"Example"

Product Release Document

Product:	NSC Number:	Project Number:
Part Number:	Lot Number:	Manufacturing Date:

Number of Vials Released to Approve Goods Inventory:

Batch Record Review

The following batch records have been reviewed by BQA. These batch records are complete and correct.

	Lot Number	Review Initials	Review Date
Master/Working Cell Bank			
End of Production Cell Bank			
Bioreactor / Harvest			
Sterile Filtered Purified Bulk			
Final Vialed Product			

Verified By_____ Date_____

Quality Events

Quality Event logs have been reviewed for closure or determination of no significant product impact (list event tracking numbers).

Verified By_____ Date_____

Certificates of Analysis

The COAs have been reviewed by BQA. This product conforms to specifications. Copies attached

Verified By_____ Date_____

Stability Protocol

The Stability Protocol [xxxxxx] has been reviewed. A copy is attached.

Verified By_____ Date_____

Product Disposition

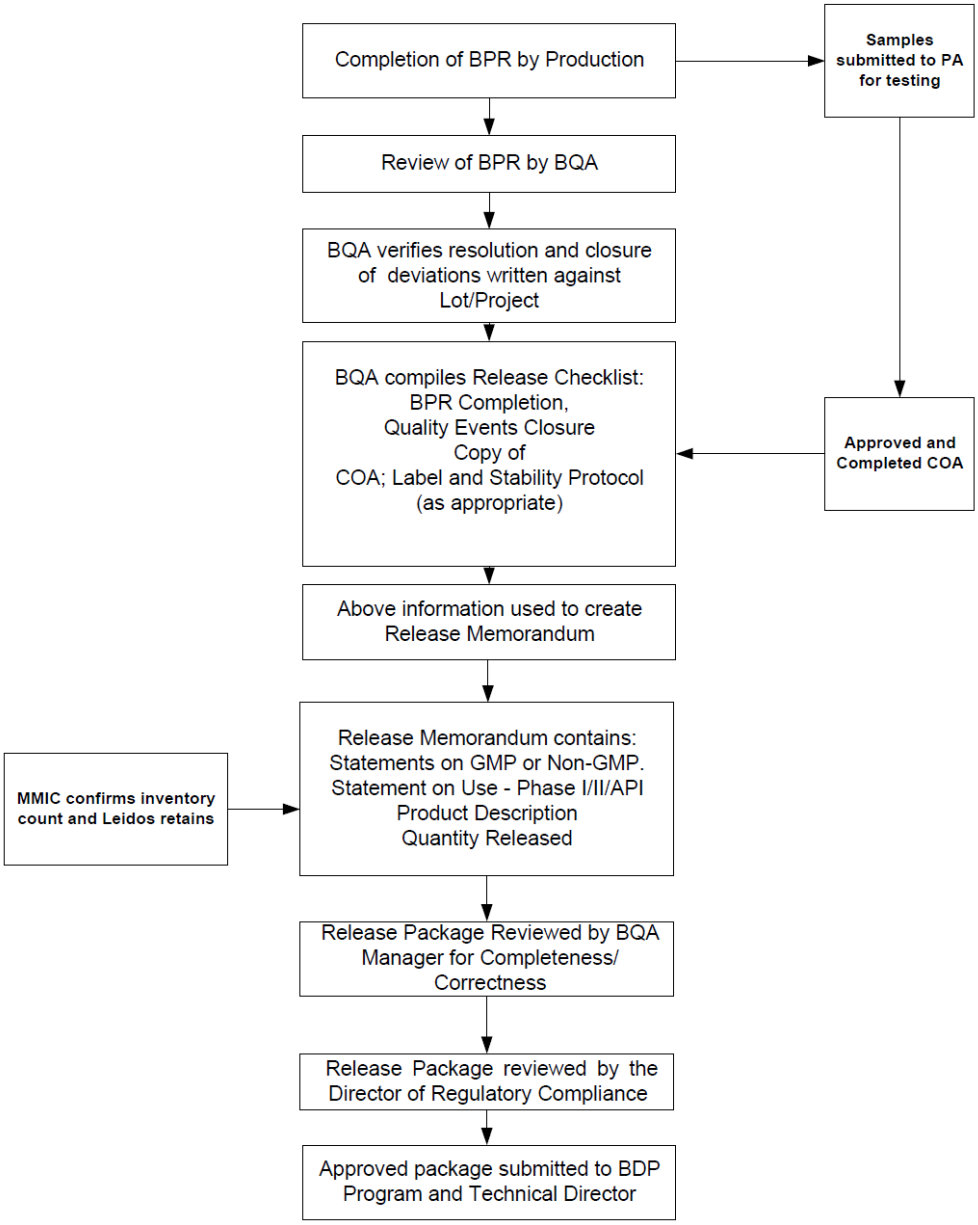
This product conforms to FNLCR and Leidos Biomedical Research, Inc. specifications. It is hereby released for [insert intended use] only.

_____ Date_____

Director, Regulatory Compliance [or designee]

Attachment 5

Product Release Flow Chart



API = Active Pharmaceutical Ingredient
BQA = Biopharmaceutical Quality Assurance
BQC = Biopharmaceutical Quality Control
MMIC = Materials Management Inventory Control
RA = Regulatory Affairs