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1.0 Purpose

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

2.0 Scope

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

- Cell therapy products for clinical use.

Products may not be shipped without written approval from BQA (See **Attachment 4**).

3.0 Authority and Responsibility

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

3.2 Manufacturing is responsible for assuring the batch production and control records (BPR) and supporting documents are complete and correct.

3.3 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).

3.4 Quality Assurance is responsible for verifying batch records are complete and correct, test specifications have been met, and for the generation of the Release letter, Record Review Checklist, and compiling any supporting documentation required.

3.5 BQA is responsible for quality oversight of this procedure.

4.0 Procedure

4.1 Upon 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 finalized by the BQA for that product. The document package consists of the following.

4.1.1 Cell Therapy Product Record Review Summary: A summary of BQA reviewed and approved BPRs and PA (QC) tests results. These are listed by their Production phase (e.g., Apheresis Preparation, Cultivation and Transduction, Cell Therapy Product Harvest etc., as defined by the project). The initials of the reviewer and the date the record was reviewed is included in this record. (Refer to Form 21909-01. Each Cell Therapy project requires the generation of a specific checklist.).

4.1.2 Certificates of Analysis: The completed COAs are obtained from BQA for the product and included in the interim product release package. The interim COA(s) covers testing of the drug substance and the drug product as defined by project specifications. Minimally this includes results of day 3 sterility testing. The final COA includes the same testing and the final day 14 sterility testing. The review/approval of the COA(s) is verified by BQA on the document.

4.1.3 Quality Events: Deviations, Product Holds, Product Quarantine, Material Review Board, and Out-of-Specification Notices are reviewed and documented prior to the interim release of the product. Any excursion with product impact (e.g., , Out-of-Spec Notices, deviations, engineering events) that require investigation and disposition materials are verified and closed prior to interim release and final release.

4.1.4 Product Label: A copy of the final container label (from the BPR) is attached to the document. Identifiable information such as name and date of birth is redacted on the file copy.

4.1.5 Interim Release: Interim release of the Product is based on a review of the batch records and conformance to final product specifications. All testing reports are received with the exception of sterility. Minimally a passing day 3 sterility report is required prior to interim release.

Final Release: Upon the completion of the Release of Product Document package, a Release Memorandum is created for the product.

4.1.6 Release Memorandum: Both interim and final release include the following information in paragraph or list style.

- Statement of Use
- 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).
  - Study Subject ID
  - DIN number, (if applicable)

- Project number
- Description
- Part number
- Lot number
- Date of Harvest / Manufacture
- Volume
- Content
- Caution Statement
- Quantity Released

4.2 The Product Release Memorandum and Release of Product Document are combined with a copy of the signed COA(s), and a copy of the label(s) applied to the product (Interim Release only). Patient Name and date of birth are redacted on the label copy.

4.3 The documentation compiled in Sections 4.1 and 4.2 should 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 Regulatory Compliance, or designee, for interim release review and approval. Approval to release a product for "Use in Humans" requires the signature of the Director of BQA, or QA/RA designee, who has been given temporary authority, in writing, for product release. The BQA Manager has the authority to release product in the Director's absence.

4.5 The **final** Release Package for Investigational Use Product is submitted to the Director of Regulatory Compliance, or designee, for final release review and approval after the final testing results are received.

5.0 Documentation

5.1 Document the review of the required information on the Release of Product document (see **Attachments 2 and 3** for an example). Project specific release forms are generated as part of the project documentation and included in this procedure

5.2 Document the release information on the Product Release Memorandum (see **Attachment 1** for example).

5.3 The original of the Approved Release Package is transferred to the secure cell therapy batch record file cabinet in the document storage room. Scanned copies of the approved release package, minus patient name and other identifying information, may be sent to the distribution listing on the Release Memorandum and to the approvers of the document via Secure Email and File Transfer Service or other secured document transfer methods.

5.4 The original BQA copy is maintained as part of the project files in the secure cell therapy batch record file cabinet in the document storage room for as long as the project files are retained. Patient Information included on documents are redacted prior to distribution electronically or in hard copy.

5.5 After final product release, the product release package is scanned electronically. The scan file is maintained in the appropriate secure electronic project information file.

6.0 References and Related Documents

Form 21909-01 *CD33 Cell Therapy Record Review Summary*

Form 21909-02 *GD2 Cell Therapy Record Review Summary*

Attachment 1 Example Release Memorandum for Cell Therapy Product

Attachment 2 Example Interim Product Release Document

Attachment 3 Example Final Product Release Document

Attachment 4 Cell Therapy Release Process

7.0 Change Summary

Attachment 1
Example
Release Memorandum of Cell Therapy Product

☐ Interim COA ☐ Final COA

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]
Manager of Quality Assurance Compliance
Biopharmaceutical Development Program

Subject: QA RELEASE OF [product name] Final 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 for the release of product with interim COA for Phase 1 and 2 investigational use. The Certificate of Analysis for the 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 cell therapy products manufactured for the NCI. There are no known risks that have been added by the manufacturing process currently associated with this lot of autologous product. 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 for autologous use. 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:

Study ID
DIN Number:
Project Number:
Description:
Part Number:
Lot number:
Manufacture date:
Volume:
Concentration:
Caution Statement:
Quantity Released:

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

BQA Project Files

Attachments: Release of Product Document; Copy of Certificate (s) of Analysis and Product Label

Attachment 2
"Example"

Product Interim Release Document

Product: DIN Number: Project Number:

Part Number: Lot Number: Harvest / Manufacture Date:

Number of Units Released to Approved Goods Inventory:

Record Review

Batch Records and testing have been reviewed by BQA per CAR-T Cell Record Review Checklist Form 21909-01 as required by the specifications for release with interim COA. Critical steps have been reviewed per Cell Therapy Critical Step QA Record Review, Form 21911-01.The record meets the requirements for expedited review and release with interim COA.

Verified By_____

Quality Events

List below all applicable Quality Events.

Quality Event logs have been reviewed. Quality Events with product impact have been reviewed and closed. All other Quality Events with no product impact have been investigated.

QUALITY EVENT	CLASSIFICATION	STATUS

Verified By_____

Pending EM

Below are pending EM to be completed prior to the issuance of the final COA.

QCTR	EM Description	STATUS

Verified By_____

Certificates of Analysis

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

Verified By_____

Labels

DIN, patient name, and lot number traceability has been verified from receipt to product labels.

Verified By_____

Product Disposition

This product conforms to FNLCR and Leidos Biomedical Research, Inc. specifications. It is hereby **interim** released for autologous use only.

_____

Director, Regulatory Compliance [or designee]

Attachment 3
"Example"

Product Final Release Document

Product: DIN Number: Project Number:

Part Number: Lot Number: Harvest / Manufacture Date:

Number of Units Released to Approve Goods Inventory:

Record Review

Batch Records and testing have been reviewed by BQA per CAR-T Cell Record Review Checklist Form 21911-02 as required by the final specifications for release.

Verified By_____

Quality Events

Quality Events with product impact have been reviewed and closed. All other Quality Events with no product impact have been investigated.

QUALITY EVENT	CLASSIFICATION	STATUS

Verified By_____

Pending EM

All pending Environmental and Personnel monitoring required prior to final release are completed and reviewed. EM investigations noted above are completed and closed.

QCTR	EM Description	STATUS

Verified By_____

Certificates of Analysis

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

Verified By_____

Labels

DIN, patient name, and lot number traceability has been verified from receipt to product labels.

Verified By_____

Product Disposition

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

_____

Director, Regulatory Compliance [or designee]

Attachment 4
Cell Therapy Release Process