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1.0 Purpose

This Standard Operating Procedure (SOP) defines the procedures for initiation, review, and approval of Certificates of Analysis (COA) for projects/products and any revisions of those documents. This includes COA Templates that are controlled and used for products that are produced multiple times for the same clinical trial.

2.0 Scope

This SOP applies to Biopharmaceutical Development Program (BDP) staff that are responsible for initiating the Certificates of Analysis that indicate the results of the testing. In the event a Certificate of Testing is required (e.g. for starting material), this procedure also applies.

3.0 Overview / Process Flow

Attachment 1 describes the overall workflow in the eDMS that includes the actions and actors at each step.

4.0 Authority and Responsibility

4.1 Director, Process Analytics/Quality Control (PA/QC)

- Defines this procedure.

4.2 PA/QC Management

- Reviews the data, records, and documentation associated with the results associated with a project Master Specification (MS).

- Updates the COAs with testing results.
- Reviews and approves final COA.

4.3 **Development/Project Scientist**

- Reviews and approves the data records, and documentation associated with the results associated with a project MS. This excludes any COAs that contain PII/PHI.
- Reviews and approves final COA as appropriate.

4.4 **Quality Assurance (QA)**

- Reviews the data and records associated results with a project MS.
- Initiates new COAs during testing review.
- Updates with testing results.
- Distributes COAs for Cell Therapy projects.
- Reviews and approves final COA.

4.5 **Biological Resources Branch (BRB)**

- Reviews and approves the documents and has the final approval for release of the document(s) and product.

4.6 **Biopharmaceutical Quality Assurance Documentation (BQAD)**

- Completes change request prior to COA creation.
- Reviews the COA for final formatting and routes the document(s) for approval.

5.0 General Information

The BDP manufactures a variety of products for NIH / NCI and other government programs. The various phases of production vary based on the type of product and may include a Master Cell Bank (MCB), a Working Cell Bank (WCB), a Reference Standard (Ref. Std), Toxicology Lot (Tox Lot), Harvest Pool (HP), Final Vialed Product (FVP), End of Production (EOP) Cells/Cell Bank, and Sterile Filtered Bulk (SFB).

A MS is the list of assays/tests, associated SOPs, and the specifications that are required to test the material for the project. A COA provides the results of that testing.

6.0 Control of Certificate of Analysis and COA Templates

6.1 The document number for the COA are assigned as follows: (Refer to ***SOP 21405 - Assigning and Requesting Lot Numbers for Product***) COAs are numbered as:

COA-####-NN LZZZZZZZZ

COA = Certificate of Analysis

= Project number

NN = Sequential Number assigned by the eDMS

LZZZZZZZ = The assigned lot number

6.2 The eDMS attaches the COA Template to the infocard for the requestor to complete.

Templates that are project specific are reviewed and approved. These are used in the case of multiple lots (cell therapy products) for the same clinical trial. These templates are numbered as follows:

COA-TEMP-####-NN

COA= COA

TEMP = Template

= Project number

NN = Sequential numbering, assigned by the eDMS

6.3 The Infocard for the COA is titled in the following manner:

General COAs:

LZZZZZZZ**,** Product Name, Phase of Production

L2205002 hAnnA1 Sterile Filtered Bulk Drug Substance

COAs with PII:

LZZZZZZZ, COA Type, Product

For Example: L2204001 Final COA; CD33CART Final Product

Additional information added to the title should be limited and must be added after the information noted above.

7.0 Creation of the Certificate of Analysis (New)

7.1 Once the MS has been approved, a COA can be drafted.

7.1.1 When a Master Specification is approved, they will include the Author - who initiates the COA, Owner - who is responsible for the project, and reviewers for the document to the infocard. The reviewers will include BDP and BRB Staff and the customer/PI staff when appropriate. The review and approval for COAs is controlled and tracked through the eDMS.

7.1.2 COAs for products that include PII/PHI are initiated by QA when the lot number is assigned. Some COAs for some products have specific Personal Identifiable Information (PII) which is confidential and must be kept secure. These are maintained in a limited access vault, separate from all other COAs.

7.1.3 COAs for Research and Development (R&D) products are not reviewed by BQA. They are reviewed and approved by the project scientist, QC, and BRB.

7.2 The COA includes the results of the testing as defined by the MS. This includes a tracking number (QC Test Request Number). This is the number assigned to the sample when submitted for testing. The COA is generated with the information from the MS and updated as the test results are obtained and must be saved as a .docx file in the eDMS system. Tests have different turnaround times depending on the type of test. Therefore, all the test results cannot be added to the COA at the same time, but when each test is completed, and the test report is completed and reviewed/approved by QC and QA. QC and/or BQA adds the tests results to the COA.

7.3 When all tests have been completed and added to the COA, it is routed through the eDMS to all reviewers in BDP and BRB.

7.4 Once all tests results have been reviewed and all comments addressed, the COA is routed for approval based on the following type of COA. See Matrix below.

Approval Matrix for COAs	Biopharm Products	Cell Therapy COAs General (e.g. virus / vector)	Cell Therapy COAs with PII/PHI	Research and Development COAs
Project Scientist Lead	X	X		X
QC Lead	X	X	X	X
QA Lead	X	X	X	
BRB	X	X	X	X

8.0 Approval Signatures

Approval signatures are appended to the documents when they are published the in the eDMS. Therefore, only pdf published COAs are available in the Release Vaults. COAs with PII/PHI are limited in access.

9.0 Revision to Certificates of Analysis

9.1 If revisions to COAs are required, open the infocard in the eDMS and select the revision icon. The draft infocard is now in a one-step collaborate route. In the collaboration, use the edit icon to make changes. The Track Changes function in Microsoft Word is used to show the changes being made and use the Comments functionality to collaborate with the reviewers. Save your changes with a .docx file extension.

9.2 When launching the document on a workflow, the packet includes sections to document the changes being made and justifications for those revisions.

9.3 The revised document is launched from the task packet and sent for review and approval to the same functional groups.

10.0 References and Related Documents

21010 *User Manual for MasterControl Documents*

21405 *Assigning and Requesting Lot Numbers for Product*

Attachment 1 - COA Workflow