Table of Contents

1.0 Purpose

This SOP describes the process for printing labels, printed label inspection, and final product label reconciliation.

2.0 Scope

This SOP applies to Biopharmaceutical Development Program (BDP) personnel involved in printing, inspecting, and reconciling printed labels for CGMP and GLP/Toxicology products. The SOP provides for the oversight of GMP labeling operations by Quality Assurance. Oversight of GLP/Toxicology product labeling is provided by Manufacturing Management. This SOP does not apply to labels printed for R&D materials; however, it may be used as a guide for R&D materials.

3.0 Process Overview

3.1 Label Formatting and Approval

Label content is reviewed and approved according to ***SOP 21403 - Origination, Modification, and Control of Labeling for GMP and GLP Products***. This process results in a label proof that has been approved by appropriate BDP and NCI staff.

3.2 Label Printing

Before labels are printed, the label printing area is inspected for the presence of labeling materials that could cause mix-ups. Label-printing equipment is used to produce an appropriate quantity of labels. A representative printed label is inspected against the approved label proof and all labels are inspected for text placement and quality. Label counts for printed labels are reconciled. Produced labels are held in a secure area until use.

3.3 Product Labeling

Before labeling of product, the labeling area is inspected for the presence of other labeling materials and previous products that could cause mix-ups. Designated personnel verify that the correct product will be labeled.

3.4 Label Reconciliation

After product labeling, label counts for label usage are reconciled. After successful reconciliation, unused and damaged labels are destroyed. This procedure provides oversight of GMP labeling operations by Quality Assurance. Oversight of GLP/Toxicology product labeling is provided by Department Management. This is consistent with the requirements of ***SOP 21900 - Expectations for the Production of Product for Toxicology Testing.***

4.0 Authority and Responsibility

4.1 The Manufacturing Department Manager has the authority to define this procedure.

4.2 Manufacturing and Manufacturing Department Management are responsible for general oversight of labeling operations for GLP/Toxicology and GMP products. See specific responsibilities on the Table. Generally, Manufacturing Management performs the functions for GLP/Tox products that are performed by BQA for GMP products.

4.3 BQA is responsible for oversight of labeling operations for GMP products. See specific responsibilities on the Table.

Responsibilities for Labeling Tasks for GMP and GLP/Tox Products

NOTE: In the table below, "Manufacturing" refers to the department that is actually producing the product. (In some cases, this may be a development department.)

Responsibility	GMP Products	GLP/Tox Products
Area inspection before label printing	Label Printing Operator	Label Printing Operator
Printing of labels	Label Printing Operator	Label Printing Operator
Comparison of sample label against the approved label proof	Label Printing Operator and Quality Assurance	Label Printing Operator and Manufacturing Management
Inspection of printed labels for text placement and quality	Quality Assurance	Manufacturing Management
Reconciliation of printed labels	Manufacturing	Manufacturing
Verification of reconciliation of printed labels	Quality Assurance	Manufacturing Management
Holding of unused labels before product labeling	Manufacturing Management or Quality Assurance	Manufacturing Management
Area inspection before product labeling	Quality Assurance	Manufacturing Management

Responsibility	GMP Products	GLP/Tox Products
Inspection of labeling and product before product labeling	Manufacturing Management	Manufacturing Management
Product labeling	Manufacturing	Manufacturing
Reconciliation of label usage	Manufacturing	Manufacturing
Verification of reconciliation of label usage	Quality Assurance	Manufacturing Management
Destruction of unused and damaged labels after reconciliation	Manufacturing Management or Quality Assurance	Manufacturing Management

5.0 Procedure – Label Printing (Form 21411-01)

NOTE: If information required by **Form 21411-01** is also to be documented in a batch record, users may "NA" the redundant section(s) of the batch record (with initials and date). A cross-reference to **Form 21411-01** must be included.

5.1 Area Inspection Before Label Printing

5.1.1 Before label printing begins, the label-printing operator inspects the area to verify that any labeling materials that could cause mix-ups have been removed.

5.2 Label Printing

5.2.1 Follow directions for the operation of the label printer to print labels.

5.2.2 The label file name used to print labels must match the label file name documented on the approved label proof.

5.3 Comparison Against the Approved Label Proof

5.3.1 Inspect the sample label to confirm that the label matches the approved label proof and that the placement and clarity of text is acceptable.

5.3.2 At the beginning of the printing process, apply a sample label to **Form 21411-01**.

5.3.3 This inspection is verified:

5.3.3.1 For GLP/Tox product labels, verification is performed, and documented by Department Management.

5.3.3.2 For GMP product labels, verification is performed and documented by Quality Assurance.

5.4 Printing, Inspection, and Reconciliation of Labels

5.4.1 Print an appropriate number of labels.

NOTE: For GMP label printing on rolls, BQA Auditing is required to be present during label production so that label inspection can occur as labels are being produced.

5.4.1.1 For numbered label stock, after acceptance of the sample label, the number of the first label and the number of the last label are recorded on **Form 21411-01** for each label roll.

5.4.2 Inspection of Labeling for Text Placement and Quality

5.4.2.1 As labels are being printed (roll stock) or after printing (sheet labels), labels are inspected for text placement and quality. For GMP labels, this inspection is performed by BQA; for GLP/Tox labeling, this inspection is performed by Manufacturing Management.

5.4.2.2 During inspection, unacceptable labels either are segregated from acceptable labels (by affixing them to a separate piece of paper to prevent their use) or prominently defaced (use an indelible marker).

NOTE: For rolled labels used on the automatic labelers, do not remove unacceptable labels from the roll. Unacceptable labels may remain on the roll if they are prominently defaced so that they can be recovered after product labeling. Missing labels on a roll miscue the label sensor in the automatic labeling equipment and can cause double or over labeling of a vial.

5.4.2.3 Count the number of labels that are segregated and the number that are defaced and allowed to proceed through the labeling operation. (Vials that are labeled with defaced labels are recovered after labeling and relabeled with acceptable labels, after the defaced labels have been removed.)

5.4.3 Reconciliation of Printed Labels

5.4.3.1 Manufacturing determines the total number of labels printed. The total number of labels printed does not include the sample label affixed to **Form 21411-01**.

5.4.3.1.1 If using numbered label stock on rolls, subtract the first label number from the last label number and add 1 to the number obtained. (This calculation must be performed for each roll of labels produced.)

Total Labels Printed = Last Label Number – First Label Number + 1

5.4.3.2 Manufacturing calculates the total number of labels that will be provided for product labeling.

Total # labels provided for labeling = (# labels printed) – (# unacceptable labels segregated)

5.4.3.3 Verification of Printed Label Reconciliation

5.4.3.3.1 For GLP/Tox product labels, reconciliation is verified by Department Management.

5.4.3.3.2 For GMP product labels, reconciliation is verified by Quality Assurance.

5.5 Holding Labeling Before Use

5.5.1 Place printed labels in a sealable bag with **Form 21411-01** (and any associated documentation).

5.5.2 Hold labels in a secure and locked cabinet/area in either in QA or Manufacturing until the labels are needed.

6.0 Procedure – Product Labeling (Form 21411-02)

NOTE: If information required by **Form 21411-02** is also to be documented in the product's batch record, users may "NA" the redundant section(s) of the batch record (with initials and date). A cross-reference to **Form 21411-02** must be included.

6.1 Area Inspection Before Product Labeling

6.1.1 Before product labeling begins, inspect the area to verify that any labeling materials not relevant to this particular labeling operation have been removed.

6.1.1.1 For GLP/Tox product labeling, this inspection is conducted and documented by Department Management.

6.1.1.2 For GMP product labeling, this inspection is conducted and documented by Quality Assurance.

6.2 Label/Product Verification Before Product Labeling

6.2.1 Before product labeling begins, inspect the label to be used and the product to be labeled to confirm that the correct product will be labeled. This verification is conducted by Manufacturing Management.

6.2.2 Record the total quantity of acceptable labels being provided for labeling (from **Form 21411-01, line a**).

6.2.3 Record the number of defaced labels that are among the labels provided (from **Form 21411-01, line x**).

6.2.4 The accuracy of the transcription of label counts from **Form 21411-01** is verified by Manufacturing Management.

6.3 Product Labeling

6.3.1 Product is labeled by manufacturing personnel.

6.3.2 Remove labels that become unacceptable during the course of the labeling operations and secure them to a separate piece of paper to prevent their use.

6.3.3 Cull any vials with defaced labels from the lot, remove the defaced labels, secure them to a separate piece of paper. Re-label vials with acceptable labels.

6.3.4 Secure defaced labels that have not been used to a separate sheet of paper.

6.3.5 After successful reconciliation, the sheet(s) of unacceptable labels and defaced labels will be destroyed.

6.4 Summary of Label Usage

6.4.1 The summary of label usage is documented by the labeling personnel on **Form 21411-02**.

6.4.2 After product labeling, record the following information:

- Number of labels applied to product containers (b).
- Number of labels on rejected containers (c).
- Number of labels affixed to batch record or production documentation (d).
- Number of labels damaged or found unsuitable during labeling (e).
- Number of labels used for other purposes (f).
- Defaced labels (recovered from vials or the unused labels) (y)

6.4.3 Calculate the number of labels used on line (g).

6.4.4 Number of labels used(g) = b+c+d+e+f.

6.4.5 Indicate the number of unused labels (h).

6.4.6 Review label counts for accuracy and completeness.

6.4.6.1 For GLP/Tox product labeling, this verification is conducted by Department Management.

6.4.6.2 For GMP product labeling, this verification is conducted by Quality Assurance.

6.5 Label Reconciliation

6.5.1 Perform label reconciliation by adding the total number of labels used, plus the total number of labels that were unused. This number must equal the total number of labels received from the holding area.

NOTE: If labels do not reconcile 100%, conduct a search of the labeling area and, if necessary, contact Manufacturing and BQA.

6.5.2 Verify that the number of defaced labels received from holding equals the number of defaced labels recovered from vials or that were unused.

NOTE: If labels do not reconcile 100%, conduct a search of the labeling area and, if necessary, contact Manufacturing and BQA.

6.5.3 Verify calculations for accuracy and completeness.

6.5.3.1 For GLP/Tox product labeling, this verification is conducted and documented by Department Management.

6.5.3.2 For GMP product labeling, this verification is conducted and documented by Quality Assurance.

6.6 Destruction of Unused, Defaced and Damaged Labels

6.6.1 After label reconciliation is complete and successful, record the number of labels for destruction on Form 21411-02 as line (j)

(# Labels segregated(i)) + (# labels unused (h)) + (# defaced labels (y)) + (# damaged labels (e)) = Total # labels for destruction (j)

6.6.2 This calculation is verified by Department Management.

6.6.3 After this verification, labels will be destroyed. Destroy labels in a manner that makes them unavailable and/or unacceptable for use. The destruction is documented and verified.

7.0 References and Related Documents

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

SOP 21900 *Expectations for the Production of Product for Toxicology Testing*

Form 21411-01 *Label Printing*

Form 21411-02 *Product Labeling*

[redacted]