Table of Contents

1.0 Purpose

This SOP describes the procedure for any additional manipulation performed on a product that is either a drug substance or final drug product. The goal of the additional processing for the non-conforming material is to bring it into specifications while minimizing the introduction of new quality concerns.

2.0 Scope

This SOP applies to BDP personnel involved in reprocessing, reformulation, reworking, and/or relabeling of CGMP drug substance or final drug product.

3.0 Authority and Responsibility

3.1 The Director, Regulatory Compliance (BQA) has the authority to define this procedure.

3.2 The Project Scientist, or designee, is responsible for requesting approval to perform additional processing of CGMP materials and obtaining permission from the Material Review Board including BQA and the NCI Project Director/ Manager.

3.3 Biopharmaceutical Quality Assurance (BQA) is responsible for:

- The routing of the request for approval.
- The final approval or disapproval of the request.
- Reviewing documentation pertaining to this procedure.
- The approval of the material or for placing the material on QA Hold or Quarantine.
- Maintaining the processing records in the project files.
- Quality oversight of this procedure.

4.0 Definitions

4.1 **Reprocessing**: Introducing an intermediate or API, including one that does not conform to standards or specifications, back into the process and repeating an MPR listed step(s) or other appropriate chemical or physical manipulation step(s) (e.g., distillation, filtration, chromatography, and milling) that are part of the established manufacturing process. Continuation of a process step after an in-process control test has shown that the step is incomplete, is considered to be part of the normal process, and is not reprocessing (ICH Q7A definition).

4.2 **Reworking**: Subjecting an intermediate or API that does not conform to standards or specifications to one or more processing steps that are different from the established manufacturing process to obtain an acceptable quality intermediate or API (ICH Q7A definition). Reworked material must be shown to be of equivalent quality to material produced by the original process.

4.3 **Reformulation**: A change in excipients or buffers.

4.4 **Relabeling**: Removal, alteration, replacement, or over-labeling of the original container label without opening of the immediate product container closure.

5.0 Procedure

5.1 Request for additional processing

5.1.1 The Project Scientist, or designee, requests permission to perform additional processing of material by using Form 21705-01. Requests must be submitted and approved prior to performing work.

5.1.2 The completed form is submitted to BQA for logging and tracking.

5.1.2.1 This form captures the:

- Product description.
- Reason for the additional processing.
- Steps/Details involved with the additional processing and the MPR title/number to be followed or written (if required). Details of the process must be sufficiently descriptive so it can be used to define the production requirements, and includes details on how to document the activity.
- Possible impact on the product undergoing additional processing, including stability, bioavailability, safety, purity, and quality.
- Process Analytics/Quality Control (PA/QC) testing of the additionally processed material. Processed material must meet release specifications and any additional testing requirements necessary to demonstrate that negative product impact is unlikely.

5.1.3 BQA reviews the document and ensures that it is complete. Documents may be returned to the requestor at this point for more information or clarification.

5.1.4 A simultaneous review or alternate review method may be requested to facilitate the review process. BQA will circulate the completed document for review and approval.

5.2 Approval Process

5.2.1 Recommended actions are reviewed by the Program and Technical Director, BDP, the Director of PA/QC, and the Director of Regulatory Compliance (BQA), or their designees.

5.2.2 Additional processing may only occur with the final approval from BQA and the NCI/BRB.

5.3 Records

5.3.1 Materials are processed following approved MPRs or performed in conjunction with an approved deviation, Material Review Board (MRB), or out-of-specification plan.

5.3.2 Manufacturing and BQA review the completed Batch Production Records (BPRs) for the process.

5.3.3 Based on the results of the BPR review, and acceptable PA/QC testing, material will be judged as acceptable, placed on QA Hold/Quarantine, or rejected by BQA.

6.0 Documentation

6.1 The original of Form 21705-01 will be maintained in the BQA project files.

6.2 A true and exact copy of the approval, Form 21705-01, will be placed with the completed batch production records.

7.0 Regulatory Reference

21 CFR 211.115 Reprocessing (a) Written procedures shall be established and followed prescribing a system for reprocessing batches that do not conform to standards or specifications and the steps to be taken to ensure that the reprocessed batches will conform with all established standards, specifications, and characteristics. (b) Reprocessing shall not be performed without the review and approval of the quality control unit.

SOP 21301 Deviations from Written Documents

SOP 22004 Managing Out-of-Specification Test Results or Unexpected Test Results

SOP 21008 BDP Material Review Board

Form 21705-1 Request for Additional Processing of Material

8.0 Change Summary