Procedure: Reprocessing of Drug Product and API

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# Purpose

To define the procedure for reprocessing intermediates or finished product and to confirm that these procedures are in compliance with the principles of Good Manufacturing Practice (GMP) and other regulatory requirements.

# Scope

The scope of this procedure includes all pharmaceutical products manufactured by [Company].

# Responsibilities

Amend to reflect the organisational structure.

|  |  |
| --- | --- |
| Role | Responsibility |
| Quality Manager | Ensures this procedure is implemented and followed.  Authorises all reprocessing activities. |
| Production Manager | Ensures this procedure is implemented and followed. |
| All personnel | Ensures this procedure is followed. |

# Procedure

Amend and edit to reflect the product the company manufactures.

## Reprocessing of API and intermediates

### Reprocessing by repeating a chemical reaction

As there is a potential for formation of by-products, reprocessing an API (Active Pharmaceutical Ingredient) or intermediate by repeating a chemical reaction (adding fresh reagents or solvents to unreacted or base material and starting over) should be preceded by a careful evaluation to ensure that the quality of the final API is not adversely impacted.

Where such reprocessing occurs, written process change procedures must be approved by Production and Quality Control that clearly specify the conditions and limitations of repeating chemical reactions.

In addition, the procedures should establish how this type of reprocessing will be evaluated, and what additional tests will be conducted on the reprocessed material to show that the resulting material is of a purity and quality comparable to that normally produced by the process. These tests should include, as appropriate, purity, impurity profiles, stability testing on initial reprocessed lots, and testing for physical attributes.

### Reprocessing by physical manipulations

Intermediates and API batches that occasionally do not conform to specifications for percent transmittance/colour, or critical attributes (e.g., purity, impurities, particle size) can be reprocessed by repeating a phase washing or redistillation step or other physical manipulation steps (e.g., dissolution, filtration, crystallization, milling, blending) that are part of an established process.

If it becomes necessary to more than occasionally reprocess batches by physical manipulation, a thorough investigation must be conducted and documented to determine the adequacy of the original process. Appropriate actions must be taken to minimize the risk of recurrence. For example, if investigation of the non-conformance and/or review of the process reveals an abnormally high rate of batches that need redistillation, it would be reasonable to incorporate the redistillation as part of the normal process.

All reprocessing procedures must be reviewed and approved by the Quality Manager. These procedures should specify the conditions and limitations for reprocessing by physical manipulations and require an evaluation of each non-conforming batch to determine its suitability for reprocessing. For example, one or more redistillation of the final product might be justified, but continuous reprocessing of batches until they meet a given quality specification would indicate a problem with the original process. A specific record should be generated to document reprocessing steps and subsequent handling and incorporated into the original batch record.

Appropriate tests should be conducted on reprocessed batches to ensure that reprocessing does not adversely affect the quality or purity of the API or intermediate. These tests should include, as appropriate, purity, physical attributes, and impurity profiles. In all cases, the significance of the non-conformance and its impact on the critical quality attributes of the API or intermediate should determine how much analytical data is sufficient to justify the reprocessing. Reprocessing operations should be subjected to appropriate evaluation to show that these steps consistently perform the expected functions and result in batches that comply with all established standards, specifications, and characteristics.

## Reprocessing of Finished Product

Steps must be taken to ensure that reprocessed batches conform to all validated standards, specifications and processing criteria established for the product.

Reprocessing can be performed only after review and approval of the Quality Manager.

## Reprocessing / reworking rationale

Reprocessing can only proceed after:

* careful consideration of the implications to the quality of the intermediate product or API by the Quality and Production Managers, including consideration of the formation of by-products and over-reacted materials,
* the reprocessing protocol is documented before reprocessing commences and is approved for use by the Production and Quality Managers,
* confirmation that the process method to be used is an established and validated manufacturing stage for the API or intermediate, and
* careful consideration of the need for additional testing requirements to demonstrate that no undesirable by-products have been generated and that impurities are within acceptable defined limits.

After reprocessing is complete, the Quality and Production Managers carefully scrutinize the results of testing, the method of manufacture and reprocessing and all associated activities to determine the suitability of this product for sale. In particular, assessment of the results of In-process and Bulk Product assays are to be carefully reviewed and compared to results of previous batches to confirm the suitability of the product.

If reprocessing were to occur routinely then the process is to be revalidated and the reprocessing stage included as part of the standard manufacturing process

## Returned product

The written procedure for the receipt, holding, testing, and disposition of returned product must followed. All returned material must be destroyed, as appropriate. If the reason for the return implicates associated batches, an appropriate investigation should be conducted. Records of returned product should be maintained and should include the name, batch or lot number, reason for the return, quantity returned, date of disposition, and ultimate disposition.

## Product salvaging

Product that have been subjected to improper storage conditions, including extremes in temperature and humidity, smoke, fumes, pressure, age, or radiation due to natural disasters, fires, accidents, or equipment failures should not be salvaged. Whenever there are doubts that the material have been subjected to adverse conditions described above, salvaging operations should only be conducted if there is both:

1. evidence from inspection of the premises that the material and their associated packaging were not subjected to improper storage condition, and
2. evidence from laboratory tests and assays that the material meet all applicable standards of quality and purity.

Appendices

Amend as required or delete.

Definitions

Amend as required or delete.

| Term | Definition |
| --- | --- |
|  | Insert terms/abbreviations and definitions for those used within the procedure. Do not include any terms or abbreviations not used within the procedure. |
| API | Active Pharmaceutical Ingredient |
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Document Information

| Revision History | | | |
| --- | --- | --- | --- |
| Revision | Modified by | Change Control No. | Description of Change |
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| Associated forms and procedures | |
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| Associated records | |
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