

## **1 Purpose**

The purpose of this Guideline is to provide guidance in the GMP requirements for the labeling and packaging of investigational materials at all stages of manufacturing and packaging.

## **2 Scope and Applicability**

This guideline can be applicable to the labeling and packaging of Active Pharmaceutical Ingredients (API) and API intermediates; and intermediate, bulk, and packaged Investigational Medicinal Product (IMP) for clinical use. The Guideline applies to pre-printed materials used for packaging and labeling operations.

## **3 Definitions**

### **3.1 Packaging Material**

Any material employed in the packaging of an API, intermediate or formulated product, excluding any packaging material used for transportation or shipment. Packaging materials are referred to as primary or secondary according to whether or not they are intended to be in direct contact with the product.

### **3.2 Active Pharmaceutical Ingredient (API)**

Any substance or mixture of substances intended to be used in the manufacture of a drug (medicinal) product that when used in the production of a drug becomes an active ingredient of the drug product. Such substances are intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment or prevention of disease or to affect the structure and function of the body.

### **3.3 Bulk IMP**

Product that has completed all manufacturing stages up to, but not including, primary packaging. For example, tablets not yet packaged into bottles/blisters.

### **3.4 Bulk Packaged IMP**

Any Investigational Medicinal Product that is within its primary container-closure but has not been labeled or assembled in accordance with the clinical study protocol, e.g., tablets in blisters, solutions in vials.

### **3.5 Intermediate API**

A material produced during the steps of processing of an API that undergoes further molecular change or purification before it becomes an API.

### **3.6 Intermediate IMP**

Partly processed materials that will undergo further manufacturing steps before it becomes a bulk product e.g., tablet blends.

### **5.3 Label Issuance and Control for IMP**

- 5.3.1 Access to pre-printed label storage areas must be limited to authorized personnel.
- 5.3.2 Labels indicating a “released” status, where used, must be stored securely and access restricted.
- 5.3.3 Where applicable, the number of units to be packaged or labeled should be specified prior to starting the operation. Reconciliation must be made at the end of the process, and any discrepancies investigated.
- 5.3.4 Obsolete labels and packaging material must be destroyed.
- 5.3.5 The use of printing devices used to print labels must be controlled through standard operating procedures to ensure that imprinting conforms to the print specified in the production record.
- 5.3.6 Printed labels must be carefully examined for proper identity and conformance to the specifications in the master label record. Results of the examination must be documented.
- 5.3.7 A copy of each type of pre-printed label used must be kept in the production record.

### **5.4 Packaging and labeling Operations for IMP - General**

- 5.4.1 Material status must be clear. It can be written/printed on the label or, when a validated computerized inventory system is used, can be in encrypted form on the label. The description and batch number should always be present in human readable form, except in the case of blinded materials where different controls apply (see Section 5.4.8).
- 5.4.2 There must be documented procedures to ensure that correct packaging materials and labels are used, including specific procedures for the generation, handling and approval of master labels.
- 5.4.3 Label operations must be designed to prevent mix-ups. There must be physical or spatial separation from other unlabelled materials/batches.
- 5.4.4 Within the EU, or where required elsewhere by local regulations, material with an expiration or retest date should include this information on the label. In the US, the expiry date is not required to be on the label, and can be supplied on the certificate of analysis.
- 5.4.5 Packaging and labeling facilities must be inspected immediately before use to ensure that materials not needed for the next operation have been cleared from the area. This examination must be documented in a logbook and/or the production record.