

1 Purpose

This document provides guidelines for the way in which the commercial manufacture and packaging of Active Pharmaceutical Ingredients (API) and formulated drug products should be documented.

2 Scope and Applicability

This Guideline describes documentation systems comprising:

- Master Formula
- Batch Production Record
- Batch Packaging Record
- Check-lists
- Computerized Systems

This Guideline applies to all APIs, formulated and packed drug products Manufactured.

3 Definitions

3.1 Starting Materials

Any material used in the production of an API, intermediate or a formulated product, but excluding packaging material. Starting material can be further defined as follows:

- Excipient – material used in the production of a formulated product (excluding APIs)
- Raw Material – material used in the production of an API or Intermediate. A raw material may be further classified as either a CRM (Contributory Raw Material) or an NCRM (Non contributory raw material) dependant on it's role in the synthesis

3.2 Packaging Materials

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.

3.3 Master Formula

A Master Formula is a compendium of information that describes all aspects of the manufacture, packaging and control of an Active Pharmaceutical Ingredient (API) or formulated drug product. It may exist as a single document or, more likely, as a series of separate documents maintained by functional groups within a manufacturing site.

requirements reflecting market requirements. Contract giver should provide similar documentation to site contractors that are responsible for making their product(s).

5.1.2 Identification of Documents

All documents to be distributed must have a title describing the purpose of the document and documents must contain:

- Product name or material name
- Date of issue
- Edition/version reference

Information on markets for which the documents are applicable must be available.

The document(s) must be paginated and have identifiers (e.g. product name, code number and edition/version number) on each page.

Documents will be distributed electronically.

Documents provided within a secure, internationally accessible information management system should contain the above identifiers either within the document or available as data associated with the document and accessible to any viewer of the document.

5.2 Manufacturing Documentation issued by Manufacturing/Packaging Sites

5.2.1 Master Formulae

Each site manufacturing and/or packaging its commercial products must create Master Formulae based on the CMC documents. The Master Formulae must be consistent with the relevant parts of the CMC documentation for the product, taking into account the requirements of the markets that the site supplies.

5.2.2 Master Batch Production Record

Site manufacturing a commercial API or formulated drug product must prepare product specific Master Batch Production Records relevant to manufacturing activities conducted at the site, based on the Master Formulae created by the site. The Master Batch Production Record must have a logical layout and be easy to follow. Documents must be identified with the company name as described in Section 5.1.2. They must be approved/issued through a controlled system.

Master Production Batch Records may be prepared in local language. Contents and layout of the Master Batch Production Record should be as follows.

5.2.2.1 Starting Materials

Starting materials should be identified by their standard names and code numbers.

The quantities for the specific batch size should be given with sufficient

The Master Batch Packaging Record must have a logical layout and be easy to read and follow. Documents must be identified with the company name as described in Section 5.1.2. They must be approved/issued through a controlled system.

The contents and layout of the Master Batch Packaging Record should be as follows.

5.2.3.1 Materials

Bulk materials and packaging materials should be identified by their standard names and code numbers.

The standard quantities of bulk material and packaging materials, including labels, required per unit should be given.

5.2.3.2 Instructions

The equipment to be used must be identified and any necessary settings specified. Appropriate environmental requirements for processing must be specified where necessary (e.g. temperature, humidity, air classification, etc).

References to Standard Operating Procedures and check-lists should be given when applicable.

Appropriate details of each packaging step should be given.

Reconciliation* of printed packaging materials and yield calculations of the finished product should be requested and acceptance limits should be given. (* This may not be necessary when label verification is performed on line.)

In-process control instructions should be included.

5.2.3.3 Format and Layout

Sufficient space should be provided where data are to be entered, e.g. starting and finishing times, material control numbers, equipment settings, calculations and confirming initials.

Space should be provided for documenting the name and batch number of the preceding product packed to be entered, and for documenting verification of equipment cleaning and line clearance. Alternatively, this information can be recorded in equipment/line logs, providing that the retention and disposal of such logs satisfy the requirements given in Section 5.3 - Retention and Disposal.

5.2.4 Checklists/Generic cGMP Documents

5.2.4.1 Preparation

Batch Production Record is given to the production department.

5.2.5.2 Use in Production

Upon receipt the production department should check that the received Batch Production Record is the one intended.

During production all recordings required in the Batch Production Record should be entered concurrently, as the operations are performed.

Data entries, calculations and checks performed should be confirmed as correct by signing or double signing as specified. Double-checking is required at least for charging-in, calculations and line clearance.

If an erroneous entry is made, it should be crossed out but left legible. The corrected entry should be signed and dated. If the reason for the error is not immediately evident, a brief explanation should be documented at the time of the correction.

Any temporary, unplanned deviation from the instructions should be documented at the time of occurrence and the reasons for the deviation investigated according to local procedures. Release of the batch(es) will be dependent on the outcome of these investigations.

Planned, but temporary, deviations from approved instructions should be handled through local change control procedures. Permanent changes to approved instructions should be handled by local change procedures.

Records created during processing, e.g. completed checklists, generic cGMP documents, diagrams, charts and graphs, should be identified by product name, batch number, date and signature and be attached to the batch documentation.

After completion of each major stage in the production process the Batch Production Record should be checked by responsible or other appointed person.

The check should verify that the Batch Production Record has been correctly filled in and that the process parameters are within specified limits.

The completed Batch Production Record, including any associated documentation (e.g. deviation reports), should be sent to Quality Assurance/Quality Control for evaluation and approval.

5.2.6 Batch Specific Copies of Master Batch Packaging Records

5.2.6.1 Preparation

For each specific batch or part of a batch to be packaged, one copy of the Master Batch Packaging Record must be produced by e.g. photocopying or

- 5.4.5 The computerized documentation system must be validated according to established procedures. This must also include computerized systems inter-linked with the documentation system.
- 5.4.6 Retention of documentation must be secured by back-up systems of sufficient durability or otherwise by print-outs.
- 5.4.7 Previous versions of software used must be supported to assure that documentation conforms with the requirements of Section 5.3 - Retention and Disposal.