

1. Purpose

The purpose of this guideline is to provide guidance on the preparation of Validation Master Plans (VMP).

2. Scope and Applicability

All functions, departments and manufacturing sites within the sponsor or its contractors operating under GMP regulations or guidelines. This guideline applies to all existing and new drug compounds. It covers the planning of validation activities related to the manufacturing and control of the registered stages of Drug Product or Active Pharmaceutical Ingredient (API) for clinical use, validation or sale.

All manufacturing activities concerned with:

- The receipt and establishment of new Drug Products or APIs.
- Major processing changes to existing Drug Products or APIs.
- The construction of new manufacturing or related facilities.
- Major alterations to existing manufacturing or related activities.

Should be carried out in accordance with approved procedures for validation. Where a project consists of a range of different validation activities then a Validation Master Plan (VMP) should be prepared. Different major projects carried out in one facility may each have its own VMP. Activities should be planned and prepared for by local management who should approve essential documentation prior to starting validation activities.

3 Definitions

3.1 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.

Note: Also known as Bulk drug or Drug Substance.

3.2 Drug Product

The dosage form in the final intermediate packaging intended for marketing.

3.3 Validation

Establishing documented evidence which provides a high degree of assurance that a specific process will consistently produce a product meeting its

3.11 Computerized System

A group of hardware components assembled to perform in conjunction with a set of software programs which are collectively designed to perform a specific function or group of functions in a defined environment (and including peripheral devices, personnel and documentation, e.g. manuals, SOPs).

Computerized Systems can be automated systems or purely information management systems. For GMP they concern systems which can affect product quality, either directly or indirectly.

3.12 Automated System

Includes (but is not limited to) automated manufacturing equipment, process control systems, automated laboratory systems, manufacturing execution systems and, manufacturing and laboratory database systems. The automated system consists of the hardware, software, and if applicable, network components, together with the controlled functions and associated documentation.

Note: Automated systems are a type of computerized system.

3.13 Computerized System Validation

Establishing documented evidence which provides a high degree of assurance that a computerized system will consistently function in accordance with its pre-determined specifications and quality attributes throughout its lifecycle. (It applies to systems which can affect product quality.)

3.4 Process Validation

Establishing documented evidence, which provides a high degree of assurance that a specific process will consistently produce a product meeting its predetermined specifications and quality characteristics.

3.15 Prospective Validation

Establishing documented evidence that systems do what they purport to do prior to the commercial distribution of a new product or an existing product made by a new or modified process.

3.16 Concurrent Validation

The validation carried out during routine production of products for sale. (In exceptional circumstances it may not be acceptable to complete a validation program before routine production starts.)

- 4.6 In the case where third party contractors are used to manufacture an intermediate or API it is the responsibility of the Quality Assurance Agreement Coordination (QAAC) them/ Lead site to ensure that the facilities, equipment and processes at the contractor are qualified/ validated in line with site requirements.

5 Guideline

5.1 When is a VMP required?

- 5.1.1 Significant changes to the facilities, the equipment and processes which may affect the quality of the product, should be validated. A risk assessment approach should be used to determine the scope and extent of validation.
- 5.1.2 A new VMP should be prepared for projects involving major change to existing equipment.
- 5.1.3 A VMP is not required for projects, which involve the installation or alteration of a single item of equipment - these should be documented on separate validation plans and reports.
- 5.1.4 The VMP should be available prior to starting any of the validation activities.
- 5.1.5 For some sites, both a site VMP (for the site's validation requirements) and project specific VMPs may exist. The site validation committee should provide co-ordination as appropriate.

5.2 What should a VMP contain?

- 5.2.1 Each VMP shall describe the scope of the activities and address relevant key elements of validation affected by the change, indicating the actions and documents that will be needed. The key elements are those factors that can have an effect on product quality.
- 5.2.2 The VMP shall identify all the components to be included within a validation project. Flow diagrams or matrixes can be useful to provide an overview and monitoring tool. A high level process map or flowchart of the manufacturing process should be included.
- 5.2.3 Following the issue of the VMP, detailed risk assessments (system and component impact assessments) should be carried out to identify items requiring qualification.
- 5.2.4 The content of the VMP should reflect the complexity of the extent of the validation activities to be undertaken. At minimum the VMP should address the following:
- i. Title, statement of commitment and approval page.
 - ii. Summary description of the project and its scope.
 - iii. A statement of validation policy and the objectives of the validation activity
 - iv. References to other existing validation documents.
 - v. A description of the organization and responsibilities for validation

Appendix 1

