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Qualification Master Plan: Regulatory Requirements

by Thomas Peither

A definition of the term “qualification master plan (QMP)“ is not to be found in the GMP guidelines, only the term “validation master plan (VMP)”, which serves as a parent document. However in practice, depending on the project, it has been shown to be useful to work with a qualification master plan in the same way as with a validation master plan.

From the regulatory perspective there are two documents including references to the content of a VMP/QMP:

- **EU GMP Guidelines, Annex 15**: Qualification and Validation
- **PIC/S-Document PI 006** Recommendations on Validation Master Plan, Installation and Operational Qualification, Non-Sterile Process Validation, Cleaning Validation

In addition, the German GMP inspectorates published an **Aide mémoire on the inspection of qualification/validation** that contains useful advice on the expected content of the QMP.

Annex 15 of the EU GMP Guide, Section 1.4 and 1.5

1.4 The key elements of the site qualification and validation programme should be clearly defined and documented in a validation master plan (VMP) or equivalent document.

1.5 The VMP or equivalent document should define the qualification/validation system and include or reference information on at least the following:

i. Qualification and Validation policy;
ii. The organisational structure including roles and responsibilities for qualification and validation activities;
iii. Summary of the facilities, equipment, systems, processes on site and the qualification and validation status;
iv. Change control and deviation management for qualification and validation;
v. Guidance on developing acceptance criteria;
vi. References to existing documents;
vii. The qualification and validation strategy, including requalification, where applicable.

PIC/S PI 006, Chapter 4 Validation Master Plan

4.1 Principle

4.1.1 Validation in general requires a meticulous preparation and careful planning of the various steps in the process. In addition, all work involved should be carried out in a structured way according to formally authorised standardised working and administrative procedures. In addition validation is characterised by:

- Multidisciplinary approach: A specific characteristic of validation work is that it requires the collaboration of experts of various disciplines such as pharmacists, technologists, metrologists, chemical analysts, microbiologists, engineers, experts on Q.A. validation etc.
- Time constraints: Generally validation work is submitted to rigorous time schedules. These studies are always the last stage prior to taking new processes, facilities into routine operation.
- Costs: Validation studies are costly as they require time of highly specialised personnel and expensive technology.

4.1.2 The above factors require a well organised and structured approach that should be adequately described in a Validation Master Plan (VMP).

4.2 Purpose

4.2.1 The VMP should present an overview of the entire validation operation, its organisational structure, its content and planning. The core of the VMP being the list/inventory of the items to be validated and the planning schedule.

4.2.2 A VMP helps management:

- to know what the validation programme involves with respect to time, people and money, and to
- understand the necessity for the programme.

A VMP helps all members of the validation team:

- to know their tasks and responsibilities.

A VMP helps GMP inspectors:

- to understand the firm's approach to validation and the set up and organisation of all validation activities.

4.3 Definition

4.3.1 A Validation Master Plan is a document that summarises the firm's overall philosophy, intentions and approach to be used for establishing performance adequacy.

4.4 Scope

4.4.1 All validation activities relating to critical technical operations, relevant to product and process controls within a firm should be included in a VMP. This includes qualification of critical manufacturing and control equipment.

4.4.2 It should comprise all Prospective, Concurrent, Retrospective Validations as well as Re-validations.

4.4.3 In case of large projects like the construction of a new facility, often the best approach is to create a separate VMP. (In such situations the VMP should be part of the total project management.)

4.5 Format and Content

4.5.1 The VMP should be a summary document and should therefore be brief, concise and clear. It should not repeat information documented elsewhere but refer to existing documents such as Policy Documents, SOP's and Validation Protocols/Reports.

The VMP should be agreed by management.

4.5.2 A VMP should contain data on the following subjects / proposed chapters.

Introduction

4.5.2.1 Firm's validation policy, general description of the scope of those operations covered by the VMP, location and schedule (including priorities).

Organisational Structure of all Validation Activities

4.5.2.2 Personnel responsibility for

- the VMP,
- protocols of individual validation projects,
- validation work,
- report and document preparation and control,
- approval / authorisation of validation protocols and reports in all stages of validation processes,
- tracking system for reference and review,
- training needs in support of validation

Plant/Process/Product Description

4.5.2.3 Provides a cross reference to other documents. A rationale for the inclusion or exclusion of validations, for the validation approach and the extent of validation should be included.

Note: A common principle in validation studies is to challenge processes, systems etc. The rationale behind any challenge and or ”worst case” situation should be explained. Consideration can be given to the grouping of products/processes for the purpose of validating “worst case” situations. Where “worst case” situations cannot be simulated, the rationale for the groupings made should be defined.

Specific Process Considerations

4.5.2.4 Under this heading specific characteristics/requirements of the plant/ process etc. that are

critical for yielding a quality product and need extra attention may be briefly outlined here.

List of Products/Processes/Systems to be Validated

4.5.2.5 All validation activities comprised in the VMP should be summarised and compiled in a matrix format. Such matrix should provide an overview and contain:

- all items covered by the VMP that are subject to validation describing the extent of validation required [i.e. IQ, OQ and/or PQ]. It should include validation of analytical techniques which are to be used in determining the validation status of other processes or systems,
- the validation approach, i.e. Prospective, Retrospective or Concurrent,
- the Re-validation activities,
- actual status and future planning.

Key Acceptance Criteria:

4.5.2.6 General statement on key acceptance criteria for the items listed under (3.5.2.5) above.

Documentation Format:

4.5.2.7 The format to be used for protocols and reports should be described or referred to.

Required SOPs:

4.5.2.8 List of relevant SOP's should be presented.

Planning & Scheduling:

4.5.2.9 An estimate of staffing (including training needs), equipment and other specific requirements to complete the validation effort should be described in the VMP. A time plan of the project with detailed planning of subprojects. This time plan could be included in the above mentioned matrix (4.5.2.5). A VMP requires regular updating.

Change Control:

4.5.2.10 A statement of the company's commitment to controlling critical changes to materials, facilities, equipment or processes (including analytical techniques), should be included.

German Aide mémoire on the Inspection of Qualification/Validation, Chapter 3.3.2 (in-house translation)

3.3.2 Validation Master Plan (VMP)

The validation master plan contains the qualification and validation projects of the manufacturer. It enables the GMP inspector to understand the company's approach to qualification and validation, the definition and organisation of the required activities. The manufacturer shall individually define the required qualification and validation activities and describe them in a VMP.

Components of the validation master plan shall be:

- Introduction
- Validation policy of the company
- Definitions
- Organisation
- Responsibilities for VMP
- Authorisation of plans and reports at all stages of qualification/validation
- Required training
- Company/process/product description
- Risk assessment principles
- Documentation format for plans and reports
- List of instructions required to carry out qualification and validation
- Inter-departmental planning of personnel requirements, equipment and other requirements
- List of individual validation items and timetable for their completion (This results in the need to update the VMP on a regular basis).
- General obligation to review changes
- Implementation of the obligation for regular revalidation (broad lines)

Cross-references to existing documents are permissible. Although not required by the regulations, some companies distinguish between a Qualification Master Plan (QMP) and a Validation Master Plan (VMP). The requirements for a VMP apply analogously to the QMP; however, the latter only considers qualification projects. Such a division can be quite useful to ensure greater clarity and timeliness of these overarching documents, especially in complex projects. Clear referencing is mandatory.

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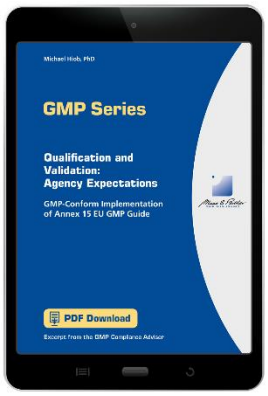
Qualification and Validation: Agency Expectations



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