VALIDATION MASTER PLANS

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VALIDATION MASTER PLAN

1. Background

1.1 Validation

Validation is an essential part of Good Manufacturing Practice. It is defined as:

"Action of proving, in accordance with the Principles of Good Manufacturing Practice, that any procedure, process, equipment, material, activity or system actually leads to the expected results"
Rules and Guidance for Pharmaceutical Manufacturers and Distributors 2007, Glossary

It extends to any activity which could affect product quality, including computer systems and software. When a facility or equipment is installed or modified, a series of validations should be carried out and documented. This process is summarised in Appendix 1 and a glossary of common terms is given in Appendix 2.

1.2 Validation Master Plan

"All validation activities should be planned"
Rules and Guidance for Pharmaceutical Manufacturers and Distributors 2007, Annex 15, 2.

The Validation Master Plan (VMP) is a summary of the planned validation activities. It lists those activities and essential documents which will be generated and defines staff responsibilities. As it is a summary, it does not repeat information documented in validation protocols or standard operating procedures.

A VMP is expected for all validation activities taking place in Licensed facilities, but it has application also in unlicensed units.

2. Function

Even a relatively simple validation plan, for instance resulting from modifications to an existing cleanroom, will potentially involve equipment suppliers, outside testing contractors, production staff, QA staff and microbiology laboratory staff. Writing the VMP acts as a planning aid for the project managers, and helps them to remain in control as the project progresses.

Participants in the validation will use it to understand both their own roles and the bigger picture.

The VMP is a useful aid for MHRA inspectors and other auditors in understanding what validation activities have been performed and the unit's approach to validation.

Management will use the VMP to ensure they are aware of resource implications and timetables for the validation project.

3. Preparation

The document should be prepared at the outset of the project so it can assist with the project planning process. This means that it is essential the VMP is a controlled document, so only the current version is available to staff.

Preparation is generally a QA responsibility, but production managers provide essential input, for instance in scheduling activities and making staff available where necessary.

Authorisation of the VMP is generally by the person with overall management responsibility for the facility.

4. Contents

The GMP guide gives a list of only seven essential sections of a VMP, and is described as being "brief, concise and clear" *(Rules and Guidance for Pharmaceutical Manufacturers and Distributors 2007, Annex 15, 3-4.)*. Sample Validation Master Plans published by validation contractors seem to contradict this by consisting of extensive and complex documents. The VMP should be as brief as it can be while still containing essential information. If it gets so big that it is not referred to regularly by staff then it is not fulfilling its function.

The following template is suggested for a Validation Master Plan which can be adapted for local use. Items indicated "*" are listed as essential in *Rules and Guidance for Pharmaceutical Manufacturers and Distributors 2007, Annex 15, 4.*

Validation Master Plan Template

Document control details

This will include details such as VMP reference number, version number, date and authorisation signatures.

1. Introduction

1.1. *Purpose of the validation*

- This will usually be to ensure that the facility or equipment being validated conforms to the requirements of current Good Manufacturing Practice, but there may be some additional specific purposes which need highlighting.

1.2. *Validation Policy**

- Comment on how the unit manages validation. Reference to a separate validation policy may be all that is required.

1.3. *Scope of validation**

- List what is to be validated. This should include facilities, equipment and computer systems as appropriate. Peripheral equipment such as label printers will need to be included. The level of validation required should be justified where appropriate. For instance software will require a variable depth of validation depending on its function and source (*Computer Systems Validation 1st edition, NHS Pharmaceutical Quality Assurance Committee, 2007*).
- List what does *not* need to be validated, with a justification. For instance existing equipment within a modified facility.
- Some industrial concerns will record a *Criticality Assessment* to determine which parts of a facility need to be validated because they influence product quality directly (such as process equipment), indirectly (such as monitoring equipment) or do not need to be validated because they have no impact on product quality.

1.4. *Documentation format and control**

- Summarise how validation protocols and reports will be formatted and controlled. Reference to the unit's validation and documentation policies may be all that is needed.

2. Organisational structure of validation activities*

Define the roles of individual categories of staff in the validation activities, for instance making it clear who generates, reviews or authorises the VMP and validation protocols relating to it, and who manages the various activities.

3. Facility Description*

Summarise the facility where the validation takes place. It is helpful to add a room plan but reference to the Site Master File can be made to avoid repetition.

4. Testing and verification requirements

*4.1 Related documents**

List additional documents which relate to the current validation but do not form part of it.

For instance:

- A very large project may require more than one VMP to deal with various stages of construction.
- Some validation activities may already have been completed. For instance Design Qualification and Factory Acceptance Tests may already be finished.
- User Requirement specifications and manufacturers specifications.

*4.2 Validation required under the VMP**

List the Validation Protocols which relate to the current validation. A tabular format may be helpful:

Validation Protocol reference number	Type of validation (IQ/OQ/PQ)	Title of validation protocol	Current status

It is not necessary to provide specific details of the methods or validation.

5. Change control requirements*

State that any changes to the validation master plan or validation protocols have to go through the unit's Change Control process.

6. Standard Operating Procedure requirements

List the Standard Operating Procedures which relate to the current validation. A tabular format may be helpful:

Validation Protocol reference number	SOP reference number	Title of SOP	Current status (available/draft/to be written/to be revised)

This enables review of the adequacy of existing SOPs to be performed during the planning stage and ensures that the resource needed to provide suitable documentation is identified. Provision of new equipment will require SOPs for its operation to be produced and SOPs for monitoring activities may need to be modified.

This section could be combined with Section 4 if convenient.

7. Training requirements

A statement of training requirements. It will be necessary to map the activities to be undertaken against the individual staff members available, to determine gaps in competencies. For instance:

- Operating new equipment
- Carrying our monitoring techniques
- Handwashing and gowning for contractors or QA staff who will need to enter a cleanroom

Training which is then performed should be documented. If no additional training is

required, this should be stated.

8. Maintaining the validated state

Comment on ongoing qualification activities that will be required. There may need to be new qualification activities or modification of existing qualification routines.

9. Validation timetable*

This details when the various validation activities will be performed. A tabular format or Gant Chart may be helpful. An example of validation activities following modifications to a cleanroom is shown:

			Date												
Activity	**Staffing**	**Document reference**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**
Change filter housings	Contractor 1	YYY													
Verify installation documentation	QA	YYY													
Cleanroom testing	Contractor 2	YYY													
Cleaning	Production														
Particle counts	QA	YYY													
Microbiological testing	QA	YYY													
Target date for production authorisation															

Appendix 1

Validation

The validation process

A successfully working facility or item of equipment depends upon its initial design being suitable for the specific purposes required by the unit. To help to ensure this, a User Requirements Specification (URS) is written by the end user to define what the equipment/facility should *achieve*, rather than simply describing its design. It should be written with validation requirements in mind; for instance an isolator will need provision so that particle counting can be carried out. Validation starts with ensuring that the supplier's proposed design is what was originally specified by the end-user (Design Qualification – DQ).

When the facility/equipment is in place, Installation Qualification (IQ) is performed to ensure that the equipment etc. is as ordered, that essential requirements such as operating manuals are available, and that it is ready for operation. For complex equipment, the installers will have completed their own commissioning tests and IQ should confirm that these have been completed satisfactorily.

Operational Qualification (OQ) is then performed to make sure that the equipment/facility works: it switches on, all the features operate, any alarms can be activated and pressures/flow rates etc. are as specified. For a simple piece of equipment, the documentation for Installation and Operational Qualification can be conveniently combined; this is known as Installation/Operational Qualification (IOQ)

The final stage is Performance Qualification (PQ), which is carried out to ensure that the equipment/facility will process product in the required way. Environmental monitoring is important to ensure microbiological quality. For automated processes, it may be useful to test actual product to ensure that it conforms to specifications.

The validation process should be summarised in a Validation Master Plan

Documentation of validation activities

There should be an authorised protocol for each part of the validation to define what is to be validated, how validation is to be carried out and who will perform it. There will also be a validation report which summarises the results and conclusions. Finally, there should be written authorisation to bring the equipment/facility into use.

The validation team

Validation is a team effort. It may involve suppliers, external contractors and Trust Estates departments. Within pharmacy departments, responsibility needs to be allocated for production of documentation, performing testing and review of results.

Revalidation

A modification to a facility, equipment or processes may need validation to be repeated. Revalidation will also be required periodically to ensure that equipment/facilities perform satisfactorily over time.

Linking validation to the unit's quality system

Change control is an essential component of GMP. The change control documentation for the planned introduction/modification of equipment or facilities should outline the validation requirements which will be required.

It may become necessary to modify an aspect of the validation master plan or a validation protocol after they have been authorised. This should be fed back into the change control system to ensure that proper evaluation and communication of the proposed modification is performed.

Validation protocols need to link into the unit's existing quality exception procedures. If a test performed during a revalidation fails, then there may be an implication for products already produced from the facility; this needs to be treated as a quality exception and investigated.

Appendix 2

Glossary

Design Qualification (DQ)	Ensuring that the design of a facility or a piece of equipment matches the defined requirements and is such that it will comply with GMP
Factory Acceptance Test (FAT)	Testing performed on equipment to ensure correct manufacture. Verification of FAT may be part of IQ
Functional Specification (FS)	A document, issued by the supplier/installer, specifying how the new facility or piece of equipment will achieve the objectives detailed in the URS
Installation Qualification (IQ)	Ensuring that a piece of equipment is as specified and is ready to operate
Operational Qualification (OQ)	Ensuring that a facility or piece of equipment operates as specified. In the case of a simple piece of equipment, installation and operational qualification can be combined to use the same documentation (Installation/Operational Qualification – IOQ)
Performance Qualification (PQ)	Ensuring that a facility or piece of equipment can process product in the manner required
Qualification	Validation of equipment (although often used to apply to validation of facilities also)
Site Acceptance Testing (SAT)	Testing of equipment performed on site to ensure compliance with the FDS. Verification of SAT may be part of IQ
User Requirements Specification (URS)	A document, agreed with the supplier/installer, specifying what the end-user expects a proposed new facility or piece of equipment to achieve.
Validation	Proving that processes, facilities, equipment or materials lead to the expected results
Validation Master Plan	A summary of the planned validation activities