First Class Pharmaceuticals

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VALIDATION MASTER PLAN

Version No 3
June 2006

Approval of the Validation Master Plan

Sign here after reviewing and approving the document, standards and schedules

Title	Name	Signature	Date
Written By:			
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Quality Assurance Manager	**Original**
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Validation Master Plan - Change History Record

Ver No.	Section Amended	Amendment Details	Approved By	Date of Approval
01	N/A	Original		

Table of Contents

1. Introduction

The key document in an organisation's validation program is its Validation Master Plan (VMP). It is divided into three parts:

Part A Validation philosophy, scope, responsibilities, guidance documents, training requirements, validation phases, plans and documentation overview.

Part B Guidelines for validation plans and protocol preparation

Part C Schedules of Work.

This Validation Master Plan (VMP) summarises the overall intentions and approach to the validation of the FCP site.

It is intended to be a working document and should be periodically updated by site management responsible for the execution of validation.

The Validation Master Plan:

- Identifies which items are subject to validation, periodic review or routine validation.
- Provides schedules of validation.
- Identifies appropriate standards and guidelines to be referenced.
- Describes functional responsibilities.
- Defines protocol preparation, execution and reporting responsibilities.
- Provides general guidance for validation document format.

2. Purpose and Scope

2.1 Scope

The validation master plan covers services installation and commissioning, equipment qualification, computer systems validation and process validation for a range of existing processes. This includes:

- critical (product contact) equipment qualification
- critical computer systems validation
- critical utility and services qualification
- facility qualification
- capital works projects (prospective validation)
- validation of new, or changed, products and processes
- QC laboratory equipment qualification

- QC laboratory test method validation
- retrospective (annual) review of critical systems and processes
- routine revalidation of critical systems

The validation master plan does not include specific methods, laboratory test programs or specific acceptance criteria. These items should be covered in individual protocols.

2.2 Regulatory Standards

Validation and operations should be capable of meeting the following regulatory GMP standards.

- Australian Therapeutic Goods Administration (TGA) cGMP – The PIC/S Guide to Good Manufacturing Practices and associated Annexes.

GMP Guidelines and cGMPs

- PICS – Recommendations on Preparation of Validation Master Plans, Installation and Operational Qualification, Non Sterile Process Validation and Cleaning Validation – 2001
- PIC/S Guidance Good Practices for Computerised Systems in Regulated "GXP" Environments
- Annex 15 EU cGMP - Qualification and Validation
- ISPE baseline Guide Pharmaceutical Water and Steam Guide
- ISPE GAMP (Good Automated Manufacturing Practices) Guidelines Edition 4

Other Industry Standards and Guides

- British Pharmacopoeia - current,
- European Pharmacopoeia - current,
- United States Pharmacopoeia - current,
- FDA Guideline on General Principles of Process Validation
- FDA Guide - Inspection of High Quality Water Systems
- FDA Guide - Inspections of Validation of Cleaning Processes
- FDA Guide - Inspection of Quality Control Laboratories
- PDA Guide to the Validation of Computerised Systems

2.3 Organisation, Authority and Responsibility

2.3.1 Validation Organisation

Validation is managed by the Quality Management Group. Validation schedules and performance to validation plan(s) are presented at the Quality Meetings for review and action as appropriate.

The personnel shaded in the Organisational Chart shown in Attachment 1 take primary responsibility for management of the validation. Validation teams are established as required to carry out specific validation projects.

2.3.2 Authority and Responsibility

The Quality Assurance Manager takes overall responsibility for the validation program in consultation with the Production Manager.

The following table details the authority and responsibility for each phase of the plan.

Table 1 Authorisations List

Activity	Protocol & Document Prep'n	Protocol & Document Approval	IQ Reports	OQ Reports	PQ Reports	Final Report Approval & Certificat'n
Design Qualification	Project Team	Project Team QA Manager Prod'n Mgr	-	-	-	Project Team QA Manager Prod'n Mgr
Facility, Services, Equipment Qualification	Project Team	Project Team QA Manager Prod'n Mgr	Project Team Contractor QA Mgr	Project Team Contractor QA Mgr	-	Project Team QA Manager Prod'n Mgr
Process Validation	Project Team	Project Team QA Manager Prod'n Mgr	-	-	Project Team Contractor QA Mgr	Project Team Contractor QA Manager
GMP Computer Systems	User Group PC & LAN Administrator	QA Manager User Group PC & LAN Administrator	PC & LAN Administrator Contractor QA Manager	User Group PC & LAN Administrator Contractor QA Mgr	User Group PC & LAN Administrator Contractor QA Mgr	User Group PC & LAN Administrator QA Manager
Cleaning & Sanitation Programs	Project Team QA Manager	Project Team QA Manager Prod'n Mgr	-	-	Project Team QA Manager Prod'n Mgr	Project Team QA Manager Prod'n Mgr
Laboratory Equipment Qualification	QA Sup'r	QA Sup'r QA Manager	QA Sup'r Contractor QA Mgr	QA Sup'r QA Manager	-	QA Sup'r QA Manager
Test Method Validation	QA Sup'r	QA Sup'r QA Manager	-	-	QA Sup'r QA Mgr	QA Sup'r QA Manager

2.3.3 Validation Training

Validation Principles Training

Validation training will be undertaken on an as needs basis but prior to the commencement of validation activities such as executing protocol. The training will cover the following:

- content, intent and scope of the VMP (this document)
- preparing protocols - layout and content
- executing protocols
- recording and maintenance of raw data
- making changes during validation projects
- preparing validation reports - content and standards

Validation training will be given to all people involved in the above activities. It will also ensure that personnel are familiar with the operation of plant and equipment.

GMP Training

Staff will be trained in the principles of GMP and on the job application of GMP as part of orderly start up of process lines. Specialist training in the operation of equipment and performance of test methods will be conducted as required.

The training will include, where applicable:

- Regulatory Standards
- Principles of Cleaning and Sanitation
- Personnel Hygiene
- Good Laboratory Practices
- Good Manufacturing Practices
- Company Documentation (SOPs and Batch Records)

Specific instructions on equipment operation and safety shall be conducted as part of Operational Qualification.

Standard Procedures Training

Training in the application of specific Standard Operating Procedures (SOP) will occur as part of the start up of operations. Training will be verified as part of equipment qualification, cleaning validation and process validation.

3. Risk Management and Establishment of Validation Priorities

The scope of the validation activities relates directly to the risk assessment. The following definitions are used to identify priorities in the Validation Schedules (Part C):

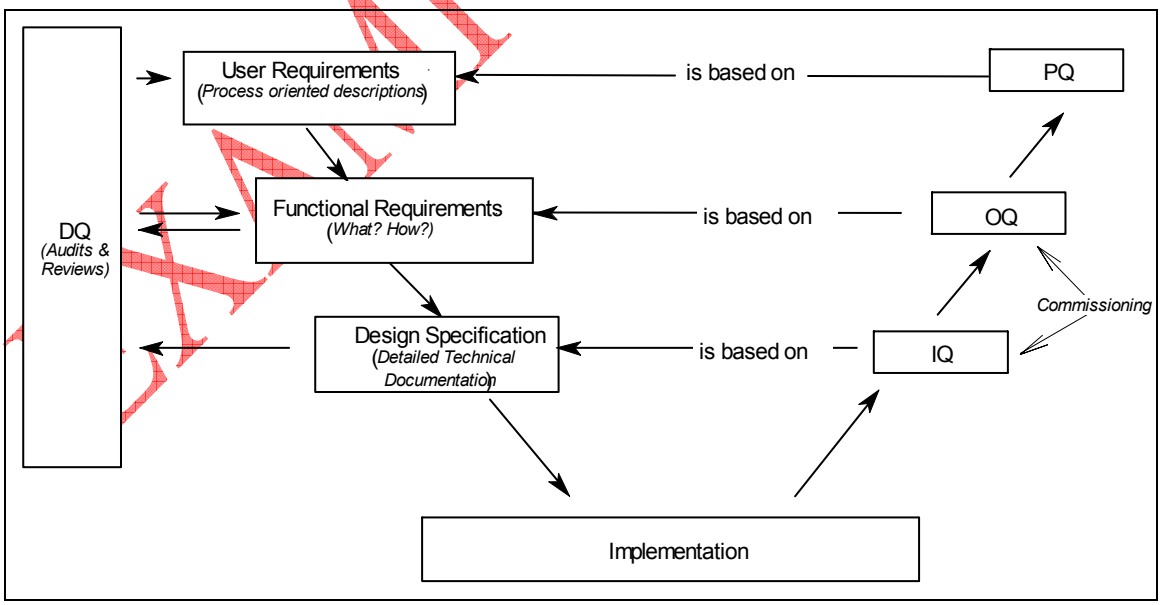
- Validated
- Validation Not Required or Not Applicable.
- To Be Assessed in the next 12 months (TBA)
- Requires Validation in the current planning period (RV)

These decisions, and all assumptions upon which they were made, should be documented and filed by Quality Assurance.

4. Validation Phases

Validation is an activity that involves establishing documented evidence that a process does what it purports to do based on a plan. Prospective Validation usually takes place in five distinct phases:

1. **Design Qualification** (DQ)
2. **Installation Qualification** (IQ)
3. **Operation Qualification** (OQ)
4. **Performance Qualification** (PQ)
5. **Certification**



4.1 Design Qualification (DQ)

4.2 Installation Qualification (IQ)

IQ ***(Installation Qualification)*** ensures that what has actually been provided complies with the Design Specification. IQ establishes that:

- operational and maintenance documents are present and registered,
- product contact surfaces are finished to pharmaceutical standards and clean
- support utilities and lubricants are reviewed and compliant,
- installation, hookup is complete and satisfactory (as determined by a physical inspection),
- safety and inspection are complete and satisfactory (as determined by a physical inspection),,
- software interfaces and controllers are documented and connected,
- instrument calibration is complete,
- preventative maintenance requirements are documented and complete,
- training on equipment and safety is complete,
- deficiency reports are reviewed and closed out

Installation Qualification (IQ) protocols are customised from a general template **(refer Attachment 2).** Specific IQ protocols should be prepared for major utilities, computerised systems and for individual items of equipment. Guidelines are included in Section B of this document.

A report summarising the results of IQ should be written, reviewed and approved.

4.3 Operation Qualification (OQ)

OQ ***(Operation Qualification)*** verifies that the equipment or process does operate as described in the Functional Requirements. It may commence before IQ reports are written but should not commence before the IQ is substantially completed. Allowance for what minimum checks are required before OQ can commence shall be stipulated in the Validation Plan and/or IQ Protocol.

OQ establishes that:

- utilities and services have been installed and qualified,
- critical instruments have been calibrated,
- equipment control function tests have been qualified,
- control over critical operating variables have been established and all tests have passed,
- final commissioning trials under operational conditions are satisfactory and all tests have passed,
- standard operating procedures have been published,
- safety conditions, alarms and controls have been qualified,
- deficiency reports have been reviewed and closed out,
- IQ report has been prepared and completed.

Operational Qualification (OQ) protocols are customised from a general template **(refer Attachment 3).** The test case/test plans must be specific for the item under qualification. Specific OQ protocols should be prepared for major utilities, computerised systems and for individual items of equipment. Guidelines are included in Section B of this document.

IQ and OQ may be combined into the one document. This is suitable when the work is being carried out by the same people and immediately following IQ.

A report summarising the results of IOQ should be written, reviewed and approved.

4.4 Performance Qualification (PQ)

4.5 Certification

Before the facility, equipment or process can be handed over to Production for routine operations, a formal report must be written summarising the results of all validation activities, and a validation status assigned and a Certificate issued.

It may be that not all results are available, or that some deficiencies or other issues are still outstanding when production requirements necessitate using the facility, equipment or process. These situations must be foreseen and allowed for within the Validation Plan or Protocol, an Interim Report prepared and an Interim Certificate Released.

5. Validation Documentation

5.1 Preparation of Protocols and Specifications.

5.2 Support Documentation

5.2.1 Protocol Supplement or Variation (refer Attachment 5)

During the course of validation there may be a need to update or amend protocols. This shall be done via protocol supplements, rather than re-issue of new protocols.

5.2.2 Deficiency Report (refer Attachment 6)

During the course of validation activity deficiencies may arise. These should be documented according to a deficiency report.

6. Validation Plans for New Projects, Products or Processes

6.1 Introduction

6.2 Publication and Control of Validation Schedules

7. GMP Systems Expected to be Validated

Area or GMP System	List of GMP Critical Systems Expected to be Validated
Facility Qualification (GMP Room Commissioning)	As required by new project plans. The following rooms should be qualified: • Raw materials and finished products storage • Dispensaries and sampling areas • Equipment washing, preparation and storage rooms • Component (bottles, caps etc) preparation areas • Manufacturing areas • Filling areas • Packaging area
Services Qualification	•
Process Equipment Qualification	•
Process Validation	•
GMP Computer Systems	•
Cleaning & Sanitation Programmes	•
Laboratory Equipment Qualification	•
Test Methods	•

15. Validation Guidelines List

Part B of this document provides validation guidelines to assist protocol writers in the preparation of protocols. The guidelines are **NOT** mandatory standards but represent the current expectations of Quality Assurance. Alternative approaches are acceptable. The guidelines should be updated as experience is gained or industry expectations change. The list of validation guidelines include the following:

Guideline #	Title
1	Design Qualification – GMP Design Review and Qualification of Specifications
2	Construction Documentation and Quality Assurance – New Facilities
3	Installation Qualification and GMP Room Finishes – New Facilities
4	Operational Qualification of GMP Manufacturing Rooms
5	Critical Utilities - Heating, Ventilation and Air Conditioning (HVAC)
6	Qualification of Process and Purified Water Systems
7	Qualification of Compressed Gases Systems (Air and CO_2)
8	Qualification of New Manufacturing Equipment – General Approach
9	(Re) Qualification of Existing Manufacturing Equipment – General Approach
10	Computer Validation
11	Guidelines for Process Validation
12	Guidelines for Conducting Retrospective Process/Product Review and Verifications
13	Guidelines for the Content of Process Validation Protocols
14	Guidelines for the Content of Process Validation Reports/Executive Summaries
15	Support Systems - Calibration and Preventative Maintenance Programs
16	Guidelines for Equipment Cleaning Programs - CIP and Manual
17	Validation of Quality Control Testing Procedures

17. List of Attachments

1 Organisational Chart
2 IQ Template
3 OQ Template
4 PQ Template
5 Validation Supplement/Change
6 Validation Deviation