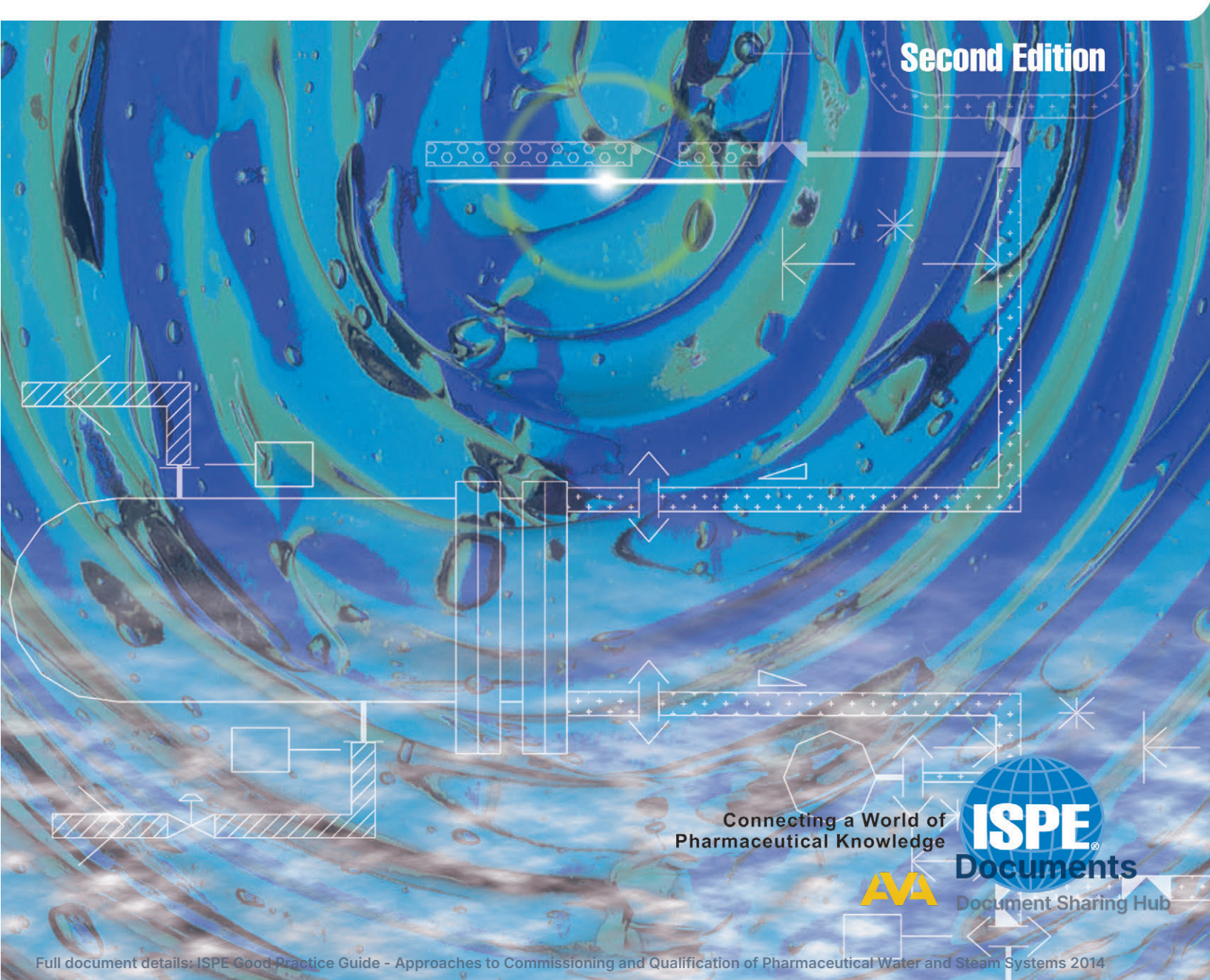
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Approaches to Commissioning and Qualification of Pharmaceutical Water and Steam Systems



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Approaches to Commissioning and Qualification of Pharmaceutical Water and Steam Systems

Second Edition

Disclaimer:
This Guide is meant to assist pharmaceutical companies in managing the commissioning and qualification of pharmaceutical GMP water and steam systems. ISPE cannot ensure and does not warrant that a system managed in accordance with this Guide will be acceptable to regulatory authorities. Further, this Guide does not replace the need for hiring professional engineers or technicians.

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Preface

The ISPE Good Practice Guide: Approaches to Commissioning and Qualification of Pharmaceutical Water and Steam Systems focuses on the engineering approaches and practices involved in providing cost effective water and steam systems in a timely manner that are specified, designed, installed and operated to meet their intended purpose. Specifically, this Guide addresses the lifecycle process of designing, constructing, commissioning, and qualifying water and steam systems regulated by international healthcare authorities.

This Guide describes how a capital project delivers process, commissioning and qualification (verification) activities, and on-going monitoring work together through the validation lifecycle for GMP water and steam systems.

The main benefit of this Guide is that it describes a project execution, commissioning and qualification (verification) approach for GMP water and steam systems based on process understanding. The required quality of water or steam is achieved without unnecessary project expense due to duplication of effort and non-value adding activities.

This Guide describes current, established, good practice, and references other guidance documents published by ISPE, where applicable. The focus is on achieving cost-effective compliance with existing regulations and associated guidance.

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Acknowledgements

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1 Introduction

1.1 Overview

Water and steam may be used in cleaning operations, laboratory activities, and the manufacture of pharmaceutical or biopharmaceutical products. Water and steam may come into contact with product or process contact surfaces, or may be used in the testing of products.

Good Manufacturing Practice (GMP) processes may produce drug substances or drug products. Water also may be used as a final product, e.g., as US Pharmacopeia (USP) packaged waters or other pharmacopeial equivalent, or as a combination drug product, including:

- Sterile Water for Injection
- Sterile Water for Irrigation
- Sterile Water for Inhalation
- Sterile Purified Water
- Bacteriostatic Water for Injection
- Water for Hemodialysis

Systems that generate and distribute pharmaceutical water and steam are subject to commissioning and qualification or verification practices.

Commissioning and qualification or verification is intended to bring a pharmaceutical water or steam system into operation, as part of design and construction. The water or steam systems (i.e., equipment and controls) are subject to GMPs. Commissioning and qualification or verification should verify that these systems create water and steam (i.e., product) of a consistent and repeatable quality. Qualification also should verify that supporting quality systems have been integrated into the validation lifecycle in order to maintain the validated state of the system.

Historically, the qualification model has consisted of an independent confirmation of the entire system installation and operation after the engineering commissioning has been completed.

The ISPE Good Practice Guide: Approaches to Commissioning and Qualification of Pharmaceutical Water and Steam Systems, along with the ISPE Good Practice Guide: Applied Risk Management for Commissioning and Qualification [1], changes this focus based on the use of a risk assessment to determine the process steps and controls that ensure the system output meets the quality requirements.

1.2 Purpose

This Guide addresses both a traditional commissioning and qualification and a science and risk-based approach to the commissioning and qualification of pharmaceutical water and steam systems.[1] This Guide aims to assist in the integration of the capital project management process, the commissioning and qualification process, and the on-going operation into the Quality Risk Management (QRM) validation lifecycle.

[1] Note: other approaches also may be used for commissioning and qualification.

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The purpose of this Guide is to describe how a traditional approach or the principles discussed in the ISPE Guide: Science and Risk-Based Approach for the Delivery of Facilities, Systems and Equipment [2] and the ISPE Good Practice Guide: Applied Risk Management for Commissioning and Qualification [1] can be applied to GMP water and steam systems. Ultimately, the goal is to increase understanding of GMP water and steam systems in the pharmaceutical and biopharmaceutical industries. It should be recognized that there are a number of ways of achieving this goal; this Guide describes examples of how to implement a traditional approach or a science and risk-based approach.

The main emphasis of this Guide is on high purity water and pure (clean) steam. Discussion and information on other pharmaceutical waters and steam are also provided. The United States Pharmacopeia (USP) [3], European Pharmacopeia (EP) [4], and Japanese Pharmacopeia (JP) [5] define different types of compendial high purity water, including:

- Water for Injection (WFI)
- Purified Water
- Highly Purified Water
- Pure Water (purification train water feed to a pure (clean) steam generator)

The type of water used for a specific pharmaceutical and biopharmaceutical process is dependent on a technical evaluation of which water is appropriate for that process.

Different compendial pharmaceutical waters have different specifications. The commissioning and qualification practices to create and preserve water quality, in generation, storage, and distribution systems, may vary according to the type of compendial water. Harmonization of pharmacoepial mandates for WFI and purified water classifications between the USP [3], EP [4], Chinese Pharmacopeia (ChP) [6], Brazilian Pharmacopeia [7], and JP [5] is an ongoing endeavor. At the time of publication of this Guide, there are still differences between these pharmacopeias.

The intended audience for this guidance is both corporate and local within an organization and in the following disciplines:

- Critical Utilities
- Facilities
- Engineering, Process and Project Management
- Business Process Owners
- Process Analytical Technology (PAT) and Validation Team
- Quality Control
- Quality Assurance

1.3 Objectives for this Guidance

This Guide has seven principle objectives:

1. Provide understanding on the importance of Commissioning and Qualification (C&Q) (verification) and how it fits into both a validation lifecycle and a project lifecycle

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2. Explain and demonstrate an example of a science and risk-based risk management process for water and steam systems and what are typical system boundaries and critical aspects

3. Discuss Critical Aspects (CAs), Critical Quality Attributes (CQAs), and Critical Process Parameter (CPPs)

4. Discuss business essential parameters – key business considerations for design, construction, commissioning, and qualification. Some of these relate to non-product quality items like Health, Safety, Environmental (HSE) considerations, Information Technology (IT), or other "commissioning only" project scope items

5. Provide identification of and discussion on project scope activities included in the qualification of water and steam systems in the context of full project delivery

6. Provide information on the User Requirements (URs), Functional Specification (FS), and how a Quality by Design (QbD) approach may be implemented

7. Ultimately, provide an alternative "science and risk-based" method that can be applied to the qualification of GMP water and steam systems

1.4 Scope

The scope of this Guide is to cover practices and activities associated with the commissioning and qualification or verification of pharmaceutical water and steam systems. Discussion is centered on those items which directly affect water or steam CQAs during production, storage, and distribution.

This Guide can be used as a standalone document as well as in conjunction with the ISPE Baseline® Guide: Water and Steam Systems (Second Edition) [8], the ISPE Good Practice Guide: Applied Risk Management for Commissioning and Qualification [1], and the ISPE Guide: Science and Risk-Based Approach for the Delivery of Facilities, Systems and Equipment [2].

This Guide aims to provide an example of how risk assessment can be used to determine the critical aspects, the definition of CQAs and CPPs, and the identification/appropriate execution of quality indicating verification activities applied throughout the validation lifecycle.

This Guide provides an approach for commissioning and qualification and how they correspond to:

- The validation lifecycle
- Risk management
- Process analytical technology
- Quality by Design (QbD) concepts

Those critical aspects that assure water or steam quality over the life of a system should be identified and documented. These items should be subject to both commissioning and qualification processes. Other Good Engineering Practice (GEP) related requirements (H/S/E/Business), which have impact on water or steam system performance, should be commissioned only. Appropriate system lifecycle operating and maintenance programs should be identified and implemented.

The risk assessment and risk mitigation processes used during design and qualification is fundamental to ensuring product quality, and in allowing system designers and operators to gain process understanding of those product CQAs and process CPPs which affect water or steam quality.

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GEP commissioning is intended to provide documented evidence confirming that a system is installed and operates to meet the specifications traceable to user requirements.

The approach to commissioning and qualification described in this Guide uses the following process to complete qualification:

- The system requirements, CQAs and CPPs are defined.
- The risks to the CQAs are identified, and the associated controls/critical aspects are defined (these may be design controls or procedural controls).
- The means of detection if the risk occurs are defined.

These are then scored considering:

- Severity of the risk – if it occurs.
- Likelihood of occurrence – with the controls defined in place.
- Probability of detection – this has to be effective prior to release of any product associated with the system output.

Installation Qualification (IQ) and Operational Qualification (OQ) should confirm that:

- The design qualification was satisfactorily completed.
- The system commissioning was completed confirming that the installation and operation complied with the design specification.
- Engineering change management was done with quality engagement - the installation is still considered “design qualified” with the installation and operation meeting the final revision of the specifications.
- The risk controls identified in the risk assessment are in place and operating as specified.
- The commissioning is completed following agreed GEPs (see the ISPE Good Practice Guide: Good Engineering Practice [9]), with defined deliverables; qualification can now focus on those critical aspects that can directly affect the quality of system output.
- The scope of the engineering testing and inspection covers requirements for business, safety, and compliance with specifications (from a contractual and quality perspective).

  Typical documents delivered would include:

  - Installation Verification
  - Operational Verification
  - Commissioning/Verification Summary Report
  - Turnover Package

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1.4.1 Regulatory Aspects

This Guide addresses compliance with international regulations and guidelines for water and steam systems, and considers:

- New systems and extensions to existing ones
- Existing validated systems

A wide range of healthcare requirements related to water and steam system compliance have been taken into account, including:

- GMPs
- ICH Q7A [10], ICH Q8(R2) [11], ICH Q9 [12], and ICH Q10 [13]
- ASTM E-2500 [14]

The following regulations and guidelines have been specifically considered in developing this document:

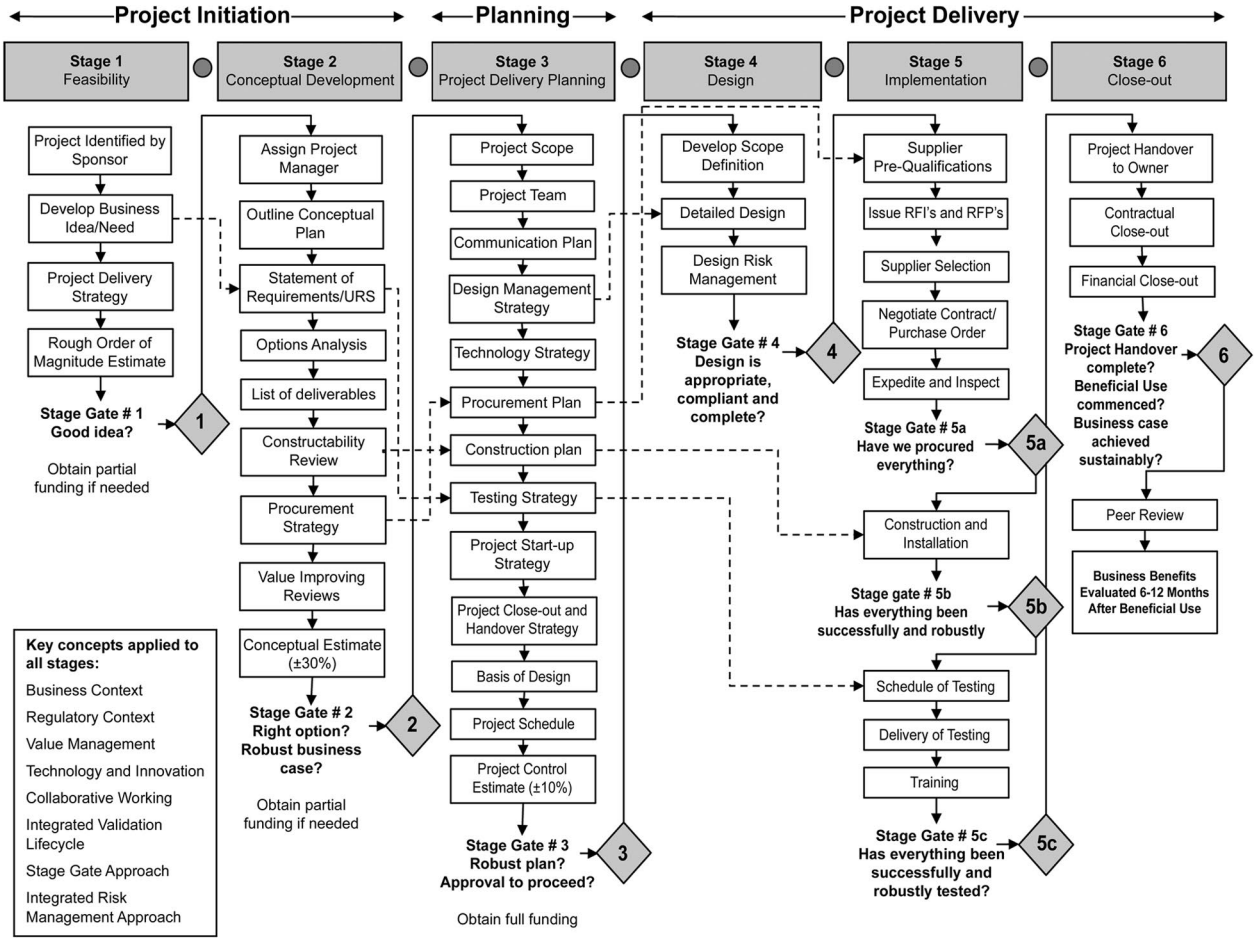
- FDA regulations, Compliance Policy Guides, and “21st Century Initiatives” [15]
- Relevant sections of EU GMPs, e.g., Annexes [16]
- USP [3]
- EP [4]
- JP [5]
- ChP [6]

The commissioning and qualification of such a system would typically be considered a part of an overall project to provide this system.

A typical project lifecycle is shown in ISPE Good Practice Guide: Project Management for the Pharmaceutical Industry – Figure 1.7 [17]; aligned terminology is used in this Guide.

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Figure 1.1: Project Management Flowchart



1.5 Benefits

This Guide provides alternative approaches to commissioning and qualification (verification) practices and activities associated with GMP water and steam systems. Benefits and attributes of this approach include:

- Risk assessment to identify aspects that are “critical to quality.” This provides a focus for the quality related activities during design, construction and qualification with a supporting rationale.
- A streamlined delivery model minimizing duplicate testing, utilizing engineering documentation to provide the documented record that the installation and operation meets the specification. This approach utilizes the Subject Matter Experts (SMEs) in the most effective manner.
- Risk-based approach to the qualification of GMP systems is employed as compared to the traditional approach that repeats the engineering work, delivering separate, often voluminous IQ and OQ documents.
- The risk assessment provides a useful tool to reference when considering the potential impact of proposed changes.
- The approach described impacts IQ and OQ; Performance Qualification (PQ) follows the traditional approach, providing operational data on the system that will support long term operation.
- Integration of project management good practices

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This Guide can be used by industry professionals involved in the design, construction, commissioning, and qualification of new or newly renovated water and steam systems, which are regulated by the international healthcare authorities.

Other benefits of a quality centric qualification approach include:

- Efficient and cost effective use of resources and minimum overlap in either commissioning and traditional validation or the use of PAT in lieu of traditional validation
- Effective focus on objectives and deliverables through the entire lifecycle
- Minimal duplication and overlap in documentation
- Efficient handling of audits, inspections and assessments

1.6 Structure of this Guide

This Guide is presented in three main sections:

1. Introduction
2. Validation Lifecycle
3. Appendices

The main section of the Guide, the validation lifecycle, focuses on high purity water systems.

The Guide describes two approaches to the commissioning and qualification of pharmaceutical water and steam systems. The two approaches share common activities until the completion of the C&Q stage, where the validation lifecycle is divided into two tracks:

- Track 1 describes a traditional qualification approach
- Track 2 described a QRM approach

The two tracks recombine at the sampling stage of the validation lifecycle, from which commissioning and qualification activities are again common to both approaches.

Information and references are given (mainly in Appendices) on lower grade process water and types of pharmaceutical steam.

The Appendices provide additional material and guidance in order to assist in the identification of regulations, issues, and topics that should be considered.

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1.7 Key Concepts

Key concepts and principles of a global implementation as used within this Guide include:

Critical Aspects

Critical aspects of manufacturing systems are typically functions, features, abilities, and performance or characteristics necessary for the manufacturing process and systems to ensure consistent product quality and patient safety.

Critical Quality Attribute (CQA) (ICH Q8(R2))

A physical, chemical, biological or microbiological property or characteristic that should be within an appropriate limit, range, or distribution to ensure product quality.

Attribute of the water or steam product which usually relates to the identity, purity, or quality of the water or steam product. Some attributes for water and steam are contained levels of Total Organic Carbon (TOC), conductivity, microbial activity, etc.

Critical Process Parameter (CPP) (ICH Q8(R2))

A process parameter whose variability has an impact on a critical quality attribute and therefore should be monitored or controlled to ensure the process produces desired quality.

Qualification (ISO)

The process to demonstrate the ability to fulfill specified requirements.

Verification (ISO) (1) (ASTM) (2)

(1) Confirmation, through the provision of objective evidence that specified requirements have been fulfilled. (2) A systematic approach to verify that manufacturing systems, acting singly or in combination, are fit for intended use, have been properly installed, and are operating correctly. This is an umbrella term that encompasses all types of approaches to assuring systems are fit for use such as qualification, commissioning and qualification, verification, system validation, or other.

Quality (ICH Q6A)

The suitability of either a drug substance or drug product for its intended use. This term includes such attributes as the identity, strength, and purity (from ICH Q6A Specifications: Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances) [18].

Quality by Design (QbD) (ICH Q8(R2))

A systematic approach to development that begins with predefined objectives and emphasizes product and process understanding and process control, based on sound science and quality risk management.

Quality Risk Management (QRM) (ICH Q9)

A systematic process for the assessment, control, communication, and review of risks to the quality of the drug (medicinal) product across the product lifecycle.

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System

An organization of engineering components, which have a defined operational function, e.g., piping, instrumentation, equipment, facilities, computer hardware, computer software.

Commissioning

Commissioning is a well-planned, documented, and managed engineering approach to the start-up and turnover of facilities, systems, and equipment to the owner/user that results in a safe and functional environment that meets established design requirements and stakeholder expectations.

The term commissioning is used within this Guide to describe the GEP activity used to provide documented evidence that a system is installed and operates to meet the specifications.

Validation Lifecycle

Listing of a series of events within the life of a direct impact manufacturing system which are identified as important to create or maintain product quality over the life of the direct impact system when using traditional C&Q methodology.

User Requirements Specification (URS)

A description of the requirements of the facility in terms of product to be manufactured required throughput and conditions in which the product should be made.

Critical Component

A component within a system where the operation, contact, data, control, alarm, or failure may have a direct impact on the quality of the product.

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2 The Validation Lifecycle

Water and steam systems usually start off as capital construction projects.

Many tasks in a validation lifecycle and a project lifecycle are similar in timing and scope. The phases within a project lifecycle and the interdependencies and interrelationships between lifecycle components need to be understood in order to understand the concept of a validation lifecycle.

Both cycles are optimized when activities are appropriately coordinated in an approved manner to eliminate unnecessary duplication of testing efforts and reporting.

One of the key elements of science and risk-based management is the determination of CQAs and CPPs. This also has been proposed for traditional C&Q.

The primary focus of this Guide is on commissioning and qualification, or verification with discussion of the major phases, including:

- Project Initiation (Feasibility and Conceptual Development)
- Requirements Definition
- Project Delivery Planning
- Initial Risk Assessment
- Specification and Design
- Procurement and Construction
- Commissioning and Qualification, or Verification
- On-Going Operations
- Maintaining the Qualified State over the System Lifecycle

Further details of these phases are given in Table 2.1. In general, the following sections are arranged in order of the validation lifecycle elements for direct impact water and steam systems.

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Table 2.1: Typical Validation Lifecycle for Water or Steam Systems

Engineering and Validation Project Requirements Defined Tasks	Project Initiation (Feasibility and Conceptual Development)	Design (Basis of Design and Detailed)	Procurement and Construction	Commissioning, Qualification and Project Closeout	On-Going Operations
Project Delivery Planning • Project Team Organization • Responsibilities • Cost Controls and Schedule • Design Management, Procurement, Construction and Testing Plans • Project Validation Plan	X Preliminary planning	X Full project delivery plan by end of basis of design	X Procurement and construction plans tracked and managed	X C&Q and close-out plans tracked and managed	
Process User Requirements Definition • Initial Critical Quality Attributes and Critical Process Parameters	X				
Design Phase Items • URs • Design (conceptual and detail) FDS • DDS • Safety Review • System Level Impact Assessment • Component Level Impact Assessment • Final CQAs and CPPs • Quality Risk Assessment/Critical Aspects List • Design Review (DR) (DQ for Q7A Facilities or as defined in Annex 15 to the EU Guide to Good Manufacturing Practice)	X Feasibility and conceptual design	X Basis of design and detailed design	X Early procurement activities linked to detailed design completion		
Commissioning and Qualification Plan • Project Commissioning and Qualifications Plan Development (Verification Plan)		X			
Procurement and Construction • System Fabrication and Construction • Supplier Documentation/ Generation of Turnover Packages (TOPs) • Supplier Documentation and Material Certificate Review			X Procurement and construction plans delivered		
Commissioning • Factory Acceptance Test (FAT) • Start-Up Activities • Commissioning Activities (IV/OV) • Standard Operating Procedure (SOP) and Maintenance Development • Sampling • Training				X C&Q plan delivered	

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Table 2.1: Typical Validation Lifecycle for Water or Steam Systems (continued)

Engineering and Validation Project Requirements Defined Tasks	Project Initiation (Feasibility and Conceptual Development)	Design (Basis of Design and Detailed)	Procurement and Construction	Commissioning, Qualification and Project Closeout	On-Going Operations
Qualification • Qualification Protocol Development (IQ, OQ, PQ) • IQ Execution • OQ Execution • PQ Execution (may be negated by PAT) • Qualification Final Reports • Verification Testing and Performance Testing Replace C&Q for QRM				X C&Q plan delivered	
Project Completion and Document Delivery • Project Handover and Closeout • Project Learning Review				X Project close-out plan delivered	
On-Going Quality Monitoring • Water Chemistry • Micro • Endotoxin • Facility Specific Quality and Business Parameters • Continuous Improvement					X
Periodic Performance Evaluations					X
Maintaining the Qualified State over the System Lifecycle • Determine Need Based on Project Change Level or Periodic Performance Evaluation • Depending on Situation; may go back to URs					X

2.1 Project Delivery Planning

Project delivery planning activities incorporate initial key tasks which can affect the success of a project to install a pharmaceutical water or steam system. These key tasks include:

- Project team definition
- Responsibilities of project team members, including Engineering and the Quality Unit (QU)
- Engineering and QU change controls
- Planning of each part of the project lifecycle
- Schedule development and project cost controls
- Documentation requirements

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- Approvals both within and external to the project team
- Project risk assessment and management

For pharmaceutical water and steam systems, project teams may include:

- In-house engineers and system operators
- Contracted Architect and Engineer (A&E (the design authority))
- Equipment suppliers
- Third-party inspection personnel
- QU personnel
- Construction contractors
- Commissioning and qualification consultants
- Maintenance personnel

The project delivery strategy should define the need for active participation by project team members throughout the project lifecycle, typically through the use of Responsible, Accountable, Consulted, Informed (RACI) Charts or a similar responsibility matrix. The roles, responsibilities, and effective communication of project team members should be understood.

Change management programs should be established at the start of a project. Elements of conceptual design and the basis of design (also called front end design), may be managed under change control. Detailed design engineering activities are, typically, under engineering change management. Although Design Review (DR) can occur throughout the design process with compliance to QbD, approval of Enhanced Design Review (EDR) usually signifies the transition from Engineering Change Management (ECM) to QU change management.

The ISPE Good Practice Guide: Project Management for the Pharmaceutical Industry [17] describes the typical activities during project delivery planning and typical tasks in each of the stages of the project lifecycle.

The ISPE Baseline® Guide: Commissioning and Qualification [19] and the ISPE Good Practice Guide: Applied Risk Management for Commissioning and Qualification [1] describe typical commissioning and qualification documents, roles, and responsibilities that may be appropriate for many systems. Information provided in this Guide is based on these ISPE documents, but adds additional information that relates more specifically to water and steam systems.

The role of the QU is to ensure that an organization's quality system is established and appropriately utilized in the management of GMP activities. The role of the QU includes ensuring that staff is qualified for their roles, and that the appropriate reviews are used. The QU should review and approve, as a minimum:

- Requirements that influence product quality, and/or the assurance of product quality, and acceptance criteria
- Plans to demonstrate the above requirements have been achieved.
- Results that demonstrate the above requirements have been achieved and a conclusion that systems are fit for intended purpose and ready for next steps (e.g., process validation)

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2.1.1 Documentation

This Guide provides guidance on the types of documents normally created during a water or steam project. The possible role of QU approvals on specific documentation during the commissioning and qualification portions of the project is also discussed. When referencing documentation from one project phase to another (e.g., commissioning work being referenced in qualification), the QU's approval may be sought for the specific test case being referenced.

There also should be QU involvement whenever any document that the QU previously approved should be changed. For all other changes, the project team should have an established project document change management procedure.

Turnover Packages (TOPs)

A risk analysis should be completed early in a project to determine the documentation requirements for equipment, components, or systems. Based on this risk analysis, facility owners should approve the turnover requirements. The turnover requirements document should detail the TOP requirements and responsible personnel. Each project may have unique requirements for TOP documentation.

A sample turnover package is in Appendix 7.

TOP requirements should be included with the equipment or system procurement documentation. Equipment or system suppliers should submit a plan for execution of a TOP for approval by the facility owner.

Information TOPs are typically created for facility owners by project personnel; these documents contain information generated during project execution, which will be used to commission, qualify, validate, and maintain the facility. Projects may consist of multiple systems, which could be commissioned and qualified at separate times.

2.2 Design Phase Items

The design phase of either a water or steam project should follow a project information development process and be appropriately documented. These documents may include the URs, the Functional Design Specifications (FDSs), and the Detailed Design Specifications (DDSs). Depending on the proposed project execution strategy and size of project, these documents may be combined.

Technical requirements which are identified by users, but which are not related to water/steam quality generation or maintenance should be tested as needed. HSE considerations, IT, or other non-product quality related items should be documented to meet local requirements. This may occur as part of the turnover packages, commissioning test plans, or reports.

2.2.1 User Requirements (URs) or User Requirement Specification (URS)

URs should describe requirements of the pharmaceutical water or steam system in terms of product to be manufactured and distributed. The URs should describe the source of the feed water, the output quality and quantities required, and operating and maintenance requirements.

URs should specify what the GMP water or steam system is required to do. Items recorded in the URs should be verified.

URs are usually brief documents; revisions to the URs should be made through a formal change management system to help to ensure that the project team is aware of any changes.

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URs should provide a briefing document[2] to the system designer. The URs should be maintained as lifecycle documents. The URs should be approved by appropriate parties to ensure agreement on project needs. Where possible, URs should be finalized prior to the start of detailed design. Revisions to the URs should be avoided once the detail design has started to avoid costly and time-consuming changes.

URs should be used as a reference during the design review/design qualification process to ensure that the design satisfies user expectations. The results of the design review/design qualification process should be summarized in a DR (design qualification) summary report.

2.2.2 Functional Design Specification

The FDS should specify **how** the GMP water or steam system will perform required functions. The FDS may be one or more documents. Typically, the FDS is preceded by procurement and installation. The FDS should be tested or verified during commissioning.

The FDS should include requirements such as:

- Specific capacity and flow of the water or steam system
- High purity water generation system feed water quality
- Alarms and messages
- Point of use: water flow, temperature, and pressure
- Sanitization techniques to be used in the storage and distribution system
- General Human-Machine Interface (HMI) layout
- Process control system strategy including input/output and interlock configurations
- Electronic data storage and system security

(For further information, see GAMP® 5 (Appendix D2) [20]).

2.2.3 Detailed Design Specification (DDS)

The DDS is a set of documents that specify a system, and includes the component and construction specifications and associated drawings for the GMP water or steam system.

It is considered good practice to define which drawing will be used as the compliance reference document – usually a Process Flow Diagram (PFD) or Process and Instrumentation Diagram (P&ID); other drawings may then be categorized as engineering reference drawings, e.g.:

- If sloping of pipework is defined as critical to quality, the isometric drawing also may be considered a compliance reference drawing.
- The mechanical floor layout drawing may be considered a compliance reference drawing.

The DDS should describe the construction and required control logic to ensure that the design can produce a system that will provide a reliable delivery of water or steam to end-users. The DDS may include:

[2] i.e., a "brief" description of the proposed water system enabling discussion of the future system.

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- Materials used to build the water or steam system that will ensure continuous quality water or steam[3]
- Pump, heat exchanger, storage vessel, and other field component/device specifications, including critical instruments
- The definition of the installation requirements for equipment[4]
- Documentation requirements for the system:
  - Materials/construction specifications
  - Construction inspection requirements
  - TOPs requirements
  - Documentation requirements
  - System commissioning requirements
- Storage vessel vent filter operation (e.g., electrically heat traced versus steam heat traced)
- Treatment system description (i.e., process flow sheet, etc.) in relation to source water quality and seasonal variations
- Electrical drawings; these drawings should allow both a construction check and fault diagnosis throughout the system
- Hardware specification; architecture and hardware of the control system (see GAMP® 5 [20])
- Redlined P&IDs

Depending on the quality of the system feed water, water generation systems usually require unique items to meet the user requirements completely.

2.2.4 Quality by Design (QbD) Considerations

The FDA has encouraged QbD based on using PAT as the means to control the production of a product. TOC and conductivity measurements can be used for online monitoring, but are not typically used on control loops. Online microbial detection instruments are available. These instruments can count the microbial colony forming units, but cannot capture and save the microbial colony forming units. USP Standards for pharmaceutical grades of water require that the colony forming units found in the water sampled are incubated and that the colony forming units are identified. Therefore, pharmaceutical water systems cannot constitute a fully PAT system at time of publication.

Water systems should be designed by specialist designers, as the quality of a water system design is critical. The designs should include only items that are known and developed by system users, such as types of instruments, methods of microbial control, or methods of chlorine removal.

Through design qualification, quality has agreed that the proposed design is fit for its intended use. Quality has approved the commissioning and qualification plan, confirming agreement with the process, personnel, and documentation standards expected results and acceptance criteria. The work is conducted following GEP, associated documentation standards, and change management processes.

[3] Were alternative materials to be used, problems with contamination, corrosion, or leachables could occur.
[4] Incorrect installation of equipment, such as reverse osmosis units or other de-ionization equipment, could lead to damage or problems with equipment performance.

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At the completion of the operation verification a brief commissioning summary report should be produced by an independent engineer (i.e., not the engineer responsible for the commissioning) to confirm that the documentation is acceptable and demonstrates that the system is installed and operates to meet the specifications; any changes from the agreed design should be managed through the management system. Approval of this document by quality releases the system to have the qualification summary report completed.

2.3 Commissioning and Qualification Plan

The C&Q plan may be generated at the conclusion of (or concurrent with) the project design phase.
There may be benefits in defining the commissioning and system validation strategy prior to the start of detail design.

The approach used may influence the content and structure of the detail design documents – for example, the specifications may incorporate the supply, construction, as well as the commissioning and qualification requirements for the system.

The C&Q plan should define the activities and responsibilities that make up the commissioning and qualification of a system (or components of a system) within its operating environment. It should include the:

- Project scope definition and/or system boundaries
- The approach to be used and the document deliverables
- Minimum required documentation deliverables and personnel/SME responsibilities
- TOP requirements
- Identification of the group which should receive documentation (validation, facilities, engineering, manufacturing, etc.)

The C&Q plan should focus on the transition from commissioning to Performance Qualification (PQ) in order to maintain the system in a satisfactory state for qualification, e.g., maintenance and sampling. The C&Q plan may be divided into two separate documents.

Frequently, an overall validation master plan describes the validation strategy for a complete process facility. The C&Q plan is generated and used to describe commissioning and qualification for a specific system (i.e., WFI system, process nitrogen system, etc.)

C&Q plans should be cost effective. The development of C&Q plans for pharmaceutical water or steam systems should be considered to ensure that responsibilities are clearly defined and activities, which impact final water or steam quality, are included and commissioning activities are not unnecessarily repeated during qualification.

The QU should be involved with development of the commissioning and qualification plan.

The design of pharmaceutical water systems is usually based on the average and instantaneous quantity and quality (or different qualities) of water required by an end-user. Sampling (whether on-line using PAT or off-line) of the generation and distribution system should be dictated by the design and address any risks identified through applied risk management for C&Q and also address any regulatory expectations. It is considered good practice to sample the system as soon as it is made operational in order to obtain an understanding of its operating characteristics.

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2.4 Procurement and Construction

Procurement activities should ensure that purchased equipment complies with the specifications created during the project design phase with any variations from the specifications reviewed and accepted or rejected by the design authority[5] and organization.

A user/an owner/user that has a lot of experience with local installations can add a lot of value during the procurement and construction stage – suggesting changes/improvements based on that detailed experience.

The most efficient process will not repeat tests, unless there is a logical reason to do so – e.g., reconfirming control wiring is correct after it has been disconnected for shipping purpose, then reconnected.

In addition to the traditional approach of purchasing, installing and operating a water and steam system, organizations also can contract for the supply of water from a third party that installs, operates, and maintains the system, generally charging based on the utility consumption. The utility consumption should be discussed prior to the Project Delivery Strategy Phase which is is the first stage in procurement planning. This is a risk based decision function. Refer to the ISPE Good Practice Guide: Project Management for the Pharmaceutical Industry [17] for general procurement principles, if needed.

A generation system can be purchased from a specialist supplier and the procurement, installation, and quality control of the storage and distribution system project managed within an organization. Alternatively, a complete installation of the storage and distribution system can be purchased from a specialist contractor.

An assessment of supplier Quality Management System (QMS) can allow organizations to use appropriate supplier data to support commissioning and verification, potentially reducing the scope of FATs/Site Acceptance Tests (SATs).

The commissioning strategy should incorporate the results of any supplier assessments, and define both the receipt and installation verification approaches, and the calibration strategy to be used within a project.

Procurement specifications should define:

- Roles and responsibilities for a construction
- Related quality control activities during construction
- Performance and/or timeline based payment schedule

Installed systems should have documentation that is acceptable to the owner or the owner's representative.

Installation verification should provide documented evidence that installed equipment complies with design specifications and incorporates agreed engineering changes.

The completion of procurement and construction is usually identified through the review and acceptance of construction TOPs.

2.5 Commissioning and Qualification

This section of the Guide is intended to indicate project activities or items typically included in the commissioning of compendial water and steam systems.

[5] For example, the project designer's representative and the organization's representative.

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The process of commissioning should provide documented evidence that will ensure that the system owners or systems users receive a system that can produce or deliver a supply of water or steam in a manner that is consistent with the system owner's requirements.

Once the commissioning process has started, an approved change management system should be established in order to control, capture, and document changes to compendial water and steam systems.

2.5.1 Start-Up Activity

A system release memo should be prepared and submitted before beginning start-up, commissioning, or validation. The memo should include the pre-start-up safety report.

Before starting the main activities for commissioning, a walk down inspection (possibly via a check list) of a system should be performed. Responsible personnel should be notified of any problems observed in:

- General cleanliness
- Visibly sagging or unsecured piping/tubing especially of indirect impact system utilities
- Disconnected piping/tubing
- Improper air breaks to floor drains
- Disconnected wiring/pneumatic lines
- Disconnected/broken instruments
- Disconnected/broken valves
- Disconnected/broken pumps
- Leaks
- Threaded fittings in hygienic piping/tubing systems
- Lack of identification for process piping or system components
- Dead legs

2.5.1.1 Safety Reviews and Checks

Prior to system start-up, several safety reviews and checks should be performed on the compendial water or steam system, including:

1. A safety review of ports to be sampled to ensure that sampling technicians have the appropriate Personal Protective Equipment (PPE) needed to safely take samples.
2. A safety review of the equipment to ensure that the mechanical associates have the appropriate PPE needed for the safe operation of the equipment. The owner and/or owner's representative should provide authorization before turning on the utility supplies to the system (electricity, water, compressed air).

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3. A documented check that the system is in a safe condition. The procedures and scope of this check usually depends on the project, but would typically include a safety focused document check, e.g.,

    - Hydraulic or pneumatic pressure testing completed satisfactorily
    - System valves in the specified condition, i.e., open or closed
    - Warning labels and signage is in place
    - Insulation review
    - Relief devices check

A walk down of the electrical connections should be performed by an SME or authorized person to ensure that they are acceptable to the owner or the owner's representative and that fuses/overload ratings are as specified.

2.5.2 Commissioning Activities

The commissioning process usually begins when construction of a water or steam system nears completion. System components are put into operation through a series of engineering activities. This work is usually defined in a documented commissioning plan.

Throughout the commissioning process, the principles of GEP (see the ISPE Good Practice Guide: Good: Good Engineering Practice [9]) should be applied when putting system components into operation. GEP principles include:

- Compliance with pressure vessel codes
- Electrical codes
- Plumbing codes
- Other local building codes and practices

Pharmaceutical water and steam systems require commissioning prior to operation.

The following is a representative list of typical commissioning activities that bring pharmaceutical high purity water systems into operation:

- Walking down and checking that P&IDs, general arrangement, and isometric drawings are representative of the installed system.
- Checking system for maintainability, e.g.,
    - Verifying that components (such as pumps, vent filters, gasket replacement, gauges, and sensors, etc.) that will require maintenance and/or calibration have sufficient room for mechanics to safely service components.
    - Checking that all the parts to be replaced during preventative maintenance are clearly identified.
- Checking that installation records (i.e., construction turnover packages, etc.) for the system equipment and components have been created. In addition, check vessel internals for items such as sprayballs and vortex breakers.
- Checking that the water system has been installed in accordance with the design, installation drawings, and that planned backflow prevention (including air breaks for drains) equipment has been adequately installed.

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- Checking that the pipe flushing with soft or de-ionized water to remove construction debris, or use of mechanical cleaning methods, as necessary, and have been verified as complete and documented properly. **Note:** in-line filters and/or strainers that had been installed during the flushing phase, but are not part of the permanent installation should have been removed after the flushing phase and this should have been documented.

- Checking that the pipe system pressure (i.e., hydrostatic or pneumatic) tests and have been verified as complete and documented.

- Checking that the cleaning and passivation of stainless steel equipment and piping systems and have been verified as complete and documented.

- Checking that a documented and approved material joining program (e.g., welders certificates, procedures, isometric drawings, and non-destructive tests including joining of metals used on "product/process contact surfaces") has been used during construction of the system and that appropriate joints have been examined/ inspected (e.g., per ASME BPE [21]).

- Checking that specified piping/tubing material was received and installed, as specified.

- Checking heat numbers of materials (if applicable). Polymer materials, such as PVDF and PP, should be documented by conformity declarations, which would be joined by welding.

- Checking received materials of construction versus materials specifications for components (e.g., instruments), which will be in direct contact with the compendial water or steam.

- Checking that the piping/tubing system specified to be sloped and drained was constructed to achieve drainage to low points. High purity water systems should be sloped to aid in drainage of the systems. It may not be possible to slope some sections of piping/tubing. These sections should be identified on the drawings. Alternative methods (i.e., blowing with air or removable spool pieces) may be used in these areas of piping to achieve required drainage.

- Checking that instrumentation loop checks have been performed.

- Checking that instrument inspection and calibration was performed per the specification and according to the manufacturer's recommendations.

- Testing "usability" of each sample point, by use of correct sample bottles (size and volume).

- Confirming that area ergonomic conditions (i.e., acceptable ventilation, sample point access, etc.) are suitable to conduct sampling. Inadequate area ventilation can lead to water sample contamination. Samples should be taken in the same way that the port is going to be used.

- Checking that a master list was created between non-critical and critical instrument components, see elsewhere in this section of the Guide or the ISPE GAMP® Good Practice Guide: A Risk Based Approach to Calibration Management (Second Edition) [22].

- Performing start-up and checks of support utilities, electric power, pump motor run, and pump hot alignment and lubrication checks.

- Checking for adequate pressure and fluid flow per design within the system, including sprayballs operation.

- Checking the high purity water generation system feed water flow, quality, pressure, and temperature.

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- Performing tests to confirm specified operation of the unit operations in pretreatment and final treatment, including shutdown, start-up and alarming. Included in these tests are specific automation system tests, e.g., valve sequencing, interlocks, loop tuning, and connections between water systems and process systems (i.e., connection to glass washer or other processing pieces of equipment). This data can be compared to the FAT to determine system performance.

- Performing tests to confirm the operation of heating and/or cooling exchangers that may exist within the water or steam system (i.e., run hot water sanitization cycle and cool down for operation after sanitization).

- Performing system safety tests (i.e., relief, emergency shutdown, continuity, etc.)

- Checking that applicable construction codes (pressurized equipment, electrical, mechanical codes, etc.) and building permit conditions have been followed including seismic and electrical/electromagnetic fields (EMF) requirements.

A TOP should be created so that initial system operating and maintenance tasks may be performed.

TOPs may be created on a "by system" basis to allow systems to be commissioned in an organized fashion within a larger facility construction project. **Note:** in Europe, a technical dossier, describing the system/equipment, is required to cover the same items recommended in this chapter of this Guide. If the technical dossier is not present, the system is of "less" use.

Typical items, which contribute to product quality are confirmed during commissioning or qualification may be:

2.5.2.1 "As-Built" Drawings

Drawings can depict flow of materials, critical features, or sampling locations. Drawings issued for construction may include submittal drawings (for approval), P&IDs, equipment drawings, and PFDs.

Approved "as-built" drawings should verify features which may be relevant to product quality or maintenance. Components shown on the drawings should be physically inspected (field verified) to confirm that the drawings accurately reflect features such as:

- Appropriate installation

- Tagging

- Location

- Direction of flow

- Sample Point of Use (POU) location

- On-line quality monitoring devices or other instrumentation in the process flow

Typically, an organized set of "as-built" drawings which include isometric drawings is created for high purity water or steam systems. Where modifications are planned for a system, "as-built" isometric drawings can be used to determine the correct technique to drain the system. "As-built" designated drawings should be signed-off by the owner or owner's representative and made available to the owner or owner's representative.

Example 1: Sample POU Drawing

A drawing should show sample points and all POUs in a system. It should show all sampling points and their designation/identification for the purpose of commissioning the system and so that the chemists or microbiologists know where to collect the samples.

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Example 2: P&ID Drawing

A P&ID drawing should show the sequence of equipment, which can directly impact product (water) quality, and key piping and instrument characteristics, such as:

- Materials of construction
- Line sizes
- Valve types
- Nozzle orientations
- Piping “unique identifier” labeling
- Materials of construction
- Insulation
- Flow direction

2.5.2.2 Equipment or Piping Component Installation

Water and steam generation and distribution equipment should be installed so that the equipment functions per design. Checks should be performed to confirm whether equipment (e.g., reverse osmosis units, stills, pure (clean) steam generators, and continuous de-ionizers) is installed per design. The installation should be compared to construction drawings and specifications. Any discrepancies between the design and the installation of water and steam generation and distribution equipment should have a documented assessment to determine the impact on the water or steam quality and/or the need for modifications based on the assessment.

For equipment and piping components, as-found conditions should comply with installation drawings and specifications.

2.5.2.3 Welding and Other Material Joining Procedures and Documentation

Welding or other material joining techniques, such as (ASME BPE [21] section on material joining) and documentation is required. The weld procedure should be pre-approved by the system owner or the owner’s representative (e.g., the third party inspector) before execution of the weld procedure.

Appropriate welding or other material joining methods and procedures and documentation practices should be established and used for all applicable piping/tubing components.

Many high purity water and pure (clean) steam systems are largely constructed of 316L stainless steels (DIN 1.4435 and/or DIN 1.4404). Where appropriate, plastics and other metals may have been used for these systems.

An appropriate welding or material joining program should be defined prior to construction activities and as a minimum, include:

- Routine inspections by qualified or certified SMEs throughout installation to verify that requirements are being met.
- A defined weld or material joint inspection program. This should be performed for all applicable piping and tubing in the high purity water or pure (clean) steam system.

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For example, for high purity water distribution systems constructed of 316L SS, weld joint quality is typically determined based on internal and external features of completed welds. (See Section MJ of the ASME BPE [21], or the EN ISO 3834 standard [23], to determine documentation requirements. See BS EN ISO 9712 standard [24] to determine third party requirements).

Examination of all external welds (both manual and automatic machine) is normally performed by the installer of the piping/tubing system. Examination reports should be completed by the installer on weld log sheets. Internal welds may be inspected by indirect visual methods (i.e., borescopic or using mirrors) by the system owner or the owner's representative at a typical minimum of 20% of total daily completed welds for automatic machine welds and 100% of daily completed manual welds. For welds produced by an automatic machine, the number (or percentage) of daily internal welds inspected may be increased based on the number of rejected welds. See the European Pressure and Machinery Guidelines (EU PG) [25] for pressure and x-raying of welds for pure (clean) steam lines which may require special safety requirements.

- Labeling of welds or other connections and appropriate inspections during construction. Inspection reports should be included with supplier documentation.

- A weld map drawing showing weld locations. The heat numbers of metals joined on either side of a weld should be included in weld logs. The heat numbers should be traceable to material certificates of analyses. (The "heat number" corresponds to the chemical composition of the material (i.e., 316L SS or similar grade such as DIN 1.4435 or DIN 1.4404) used to construct the system. The "heat number" map should include product/process contact surfaces of tubing, valves, fittings, etc.)

- Review of the qualification records of welders. The qualification records of a welder should be adequate prior to the welder performing any work. The qualification records should be included in TOPs. EN 287-1 [26] and EN 1418 [27] can be used as a guide to determine welder certification requirements.

- Verification should be obtained that approval signatures (including installation contractors, owner, or owner's representative) have been provided on weld documentation, including the weld maps.

2.5.2.4 Materials Certification

Materials used to construct water systems should preserve the quality of the water or steam product. Materials should be used that are "not reactive, additive, or adsorptive" to the water or steam product. Engineers that design systems may specify materials, e.g., metals, plastics, or elastomers, which should ensure the quality of water or steam products.

316L stainless steels and non-leaching plastics/elastomers are typically specified for high purity water and pure (clean) steam systems. Other materials also may be used. Although the surface of these materials is usually included in a piping component material specification, material surface finish is not, typically, critical to water quality maintenance.

2.5.2.5 Line Slope

Line slope in water and steam systems is a GEP activity. (See Section SD of the ASME BPE).

The usefulness of line slope can vary depending on the type of system, e.g.,

- In pure (clean) steam distribution systems, sloping of distribution lines is intended to prevent "cold spots" (where condensate may collect) or preserve the physical properties of pure (clean) steam delivered to a point of use.

- In one-way high purity water distribution systems where pure (clean) steam is used for sanitizations, sloping is intended to achieve adequate system sanitizations.

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- In re-circulating high purity water distribution systems, slope verification documentation may be "non-value added," because the system is continuously recirculated.

Line sloping is usually intended to:

- Ad in system drainage to low points for future system shutdowns
- Assist in the removal of passivation chemicals

Re-circulating high purity water distribution systems are not usually drained, but if they are, air can be used to supplement the system drainage procedure. Where re-circulating high purity water distribution systems are shut down and drained, they are usually flushed and sanitized before being put back into service.

For the Detailed Design Specification (DDS) development, engineers should make a determination whether line slope verification should be included in the project, based upon requirements and risk assessment. The line slope verification can be verified using a calibrated level device and documented on the isometric drawings. Slope verifications should be performed prior to the addition of any insulation.

For systems where commissioning has been deemed necessary, the acceptance criteria are that "as-built" isometric drawings that indicate the slope are available and that an approved slope measurement procedure has been used. Suppliers and engineering departments should produce slope information.

If line sloping is for GEPs, commissioning should be performed to verify the extent of line sloping included in a project. Organizations may choose to install piping/tubing level and plumb, e.g., where line sloping has been determined to be non-value added in relation to water quality.

2.5.2.6 Hydrostatic Pressure Test

Water or steam systems should be free of leaks, which can lead to contamination of the water or steam. From a system operating consideration, hydrostatic pressure tests should be performed and documented. Water (e.g., softened water) used for hydrostatic testing of high purity water systems should be of appropriate quality to avoid the introduction of contamination, which could cause problems during construction or start-up.

Hydrostatic pressure tests may be conducted in selected sections of the system, such as sections of piping that can be isolated and pressurized at varying times during construction. Tests can be performed by making reference to a particular section of the system P&ID. For further information on the requirements for hydrostatic pressure tests, see ASME B31.3 [28].

2.5.2.7 Cleaning and Passivation

Product contact surfaces should be maintained in a passive condition (by passivation) in high purity water and pure (clean) steam systems to help to maintain the quality of water or steam.

Passivation usually involves introducing an acid solution into the system to remove elemental iron and to maintain or enhance the chromium to iron ratio of a weld and produce a passive layer on the surface of the metal. Completed welds should undergo passivation procedures. The first step of a passivation procedure is usually a chemical cleaning process to prepare the metal of the completed weld for passivation. Specified cleaning and passivation procedures should be followed and documented. Documentation usually includes:

- Cleaning and passivation procedures
- Cleaning agents used
- Cleaning temperature and times

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- Passivating chemical solutions used
- Temperature and contact times
- Identification of line sections
- Components passivated
- Approval signatures

Cleaning and passivation activities may be delayed to:

- Prevent the need to repeat cleaning and passivation steps if piping or tubing modifications are needed during start-up and commissioning
- Provide a chemical sanitization just prior to the start of water quality testing

The project team should plan when to perform the system cleaning and passivation, which may be performed sequentially on specific segments of equipment or piping/tubing sections.

Cleaning and passivation of a system should be performed only on an as need basis.

For further information on passivation, see ASME BPE [21] and ASTM A380 [29].

2.5.2.8 Vent Filters

Vent filters are used on high purity water storage vessels as a particulate and microbial barrier between the surrounding environment and the water. Pressure safety devices (i.e., rupture discs, etc.) should be used to protect against vessel over-pressurization.

A method should be identified for replacing vent filter cartridges (e.g., Steam-In-Place (SIP) with pure (clean) steam or autoclaving the filter in its housing prior to installation so that it does not contaminate the system). The process should be documented.

Vent filters (e.g., 0.2 µm) are suitable for microbial retentive gas filtration. Areas of concern for gas filtration are blockage of the filter caused by condensed water vapors or leakage caused by improper filter installation or defective filters.

Control measures to avoid accumulation of condensate vapors in the vent filter housing include:

- Electrical or steam heat tracing
- A self-draining housing orientation
- Placement of the housing at a distance far enough from the tank such that vapors do not accumulate

Where heat tracing[6] (such as electric jacket or steam) is used, the temperature should be set above the normal operating temperature of the water in the storage vessel so that the temperature is above the dew point temperature and below the manufacturer's maximum temperature rating for the vent filters.

[6] Heating by flexible electric heating elements.

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Vent filters should be constructed of specified and verified materials. They should be integrity tested in the housing prior to initial use and periodically thereafter. Regular visual inspections and testing procedures should be performed, including post integrity testing in the housing after removal.

Post integrity testing can be used to verify that the filter is not plugged or has not been leaking at the time the filter is removed from service. Post integrity testing can provide assurance that preventative maintenance schedules and procedures are appropriate. Filter integrity testing methods include:

- Bubble point
- Diffusion
- Water intrusion

Filter integrity testing methods can vary, depending on the filter manufacturer, application, and type of filter.

Vent filter integrity testing equipment may not be available at some “non-sterile” product manufacturing sites. Acceptance of a supplier certification of vent filter integrity may be considered sufficient based on an audit of the supplier’s manufacturing site and QMSs.

Commissioning documentation should contain information that confirms that the method selected for avoiding condensation is appropriate, that the filter orientation allows for drainage and that the filter integrity testing has been performed and successful results have been obtained.

2.5.2.9 Support Utilities

It should be determined whether support utilities are critical or non-critical systems. These utilities (i.e., instrument air, drains, power, cooling water, plant heating steam, etc.) should be commissioned. These systems should be connected to critical components in accordance with specifications (i.e., the URs).

Other system utilities (i.e., compressed air blow, N_2 blanket, etc.) may be required for use in the compendial water or pure (clean) steam system.

2.5.2.10 Loss of Utility

This test can be specifically planned for systems based on the likelihood of occurrence and potential water or steam quality risk. A risk assessment on the loss of utilities should be performed at the beginning of the project and documented. This should include the proposed testing to be performed or why testing does not need to be performed. The risk assessment should be approved by the system owner. The commissioning plan should include a strategy on how the system will be restored to service after loss of utilities, such as whether the system will need to be drained, flushed, sanitized, steam sanitized, or passivated, how it will be released for use, and who will release it for use.

The system’s response to loss of support utilities to the generation equipment and distribution system should be investigated. Response to loss of electrical power should be considered. This includes retention of critical data, as well as safe equipment and system response.

Equipment and system responses to loss of other utilities (e.g., compressed air, hot/cold process water, glycol, and nitrogen) should be documented to ensure that adequate protection is provided in the equipment and system design.

For short down times (i.e., due to loss and resumption of a given utility), equipment and system behavior should be adequate to prevent contamination of the system. Except for system specific extended downtime periods, a procedure for loss of electrical power should be developed, including the steps to perform in the event of a power loss. Upon power being restored, the system should automatically return to the service mode/cycle.

AVA Documents
Document Sharing Hub
Full document details: ISPE Good Practice Guide - Approaches to Commissioning and Qualification of Pharmaceutical Water and Steam Systems 2014