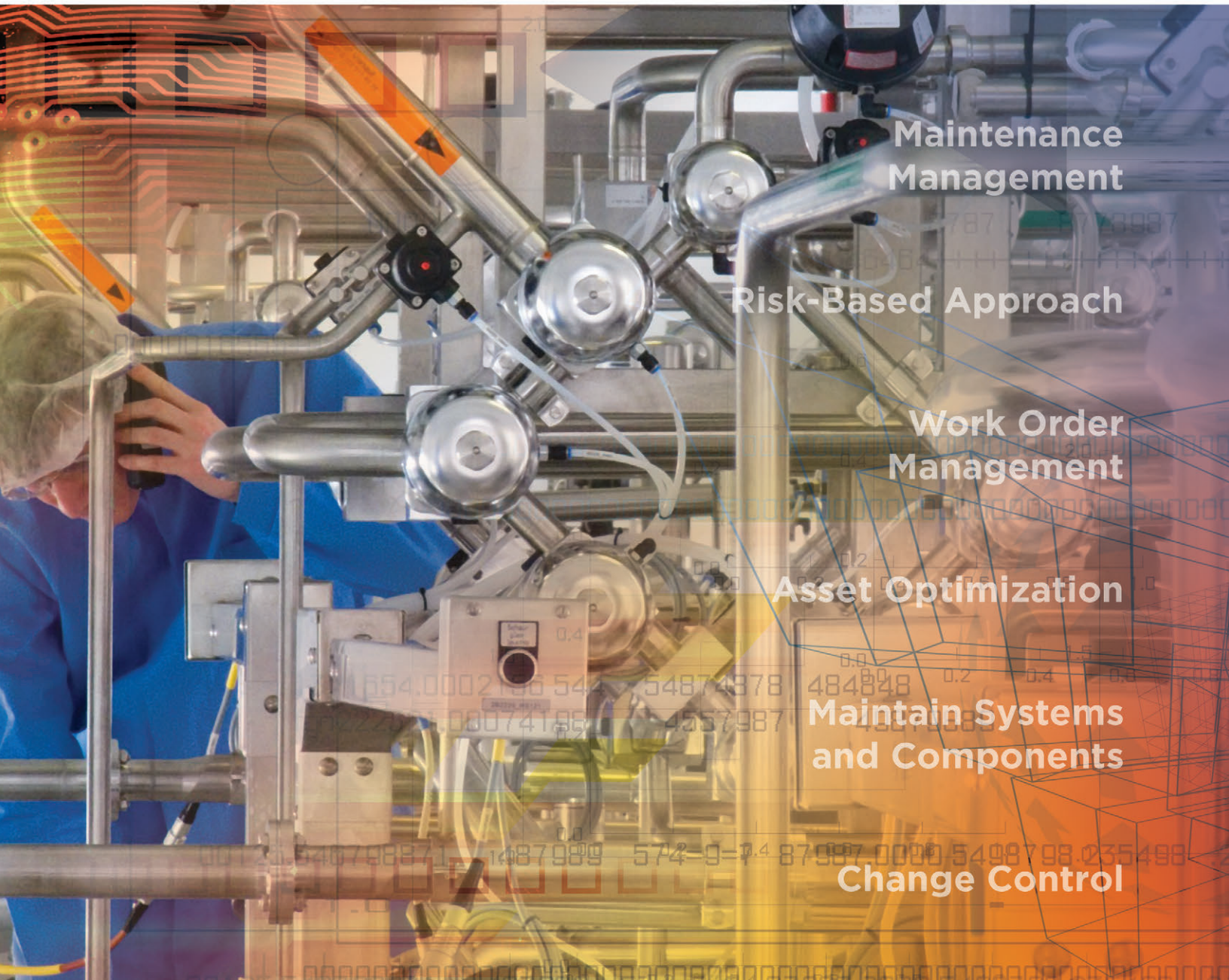




GOOD PRACTICE GUIDE: **Maintenance**

Second Edition



**Maintenance
Management**

Risk-Based Approach

**Work Order
Management**

Asset Optimization

**Maintain Systems
and Components**

Change Control



GOOD PRACTICE GUIDE: **Maintenance**

Second Edition

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ISBN 978-1-946964-38-0

Preface

Maintenance can impact both the quality of products and the compliance of pharmaceutical processes. Maintenance Programs have long been recognized as critical to the success of the operations they support.

This Guide focuses on achieving cost-effective compliance with existing regulations and associated guidance. It describes current established good practice and seeks to provide a practical and consistent interpretation of the required elements of a pharmaceutical Maintenance Program, while offering maximum flexibility to enable widespread adaptation and encourage innovation.

This Guide focuses on maintenance in GMP areas and is intended to be used as a tool for the development, implementation, and execution of a Maintenance Program in a pharmaceutical manufacturing environment.

Since the first edition of this Guide, the ICH Q9 risk-based approach has been widely adopted worldwide. This edition reflects alignment with the risk-based approach with respect to maintenance and the industry as a whole. Updates to this edition include consolidating basic and good practices categories, adding clarification on terminology for users, and updating examples.

Acknowledgements

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Special Thanks

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The Team would also like to thank ISPE for technical writing and editing support by Nina Wang (ISPE Guidance Documents Technical Writer/Editor) and production support by Lynda Goldbach (ISPE Guidance Documents Manager).

The Team Leads would like to express their grateful thanks to the many individuals and companies from around the world who reviewed and provided comments during the preparation of this Guide; although they are too numerous to list here, their input is greatly appreciated.

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Facility cover photo courtesy of F. Hoffmann-La Roche Ltd., <https://www.roche.com>.



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Table of Contents

1	Introduction	7
1.1	Background	7
1.2	Purpose	7
1.3	Scope	8
1.4	Benefits	8
1.5	Objectives	9
1.6	Key Concepts	9
1.7	Structure of the Guide	9
2	Key Principles and Relationships	11
2.1	Introduction	11
2.2	Philosophy	11
2.3	Maintenance Practices	11
2.4	Maintenance Program	12
2.5	Spare Parts and Materials	17
2.6	Training	17
2.7	Culture	18
2.8	Maintenance Key Relationships	18
3	Maintenance Good Practices and Maintenance Best Practices	21
3.1	Introduction	21
3.2	Overview	21
3.3	Maintenance Good Practices	22
3.4	Maintenance Best Practices	23
4	Maintenance Program	29
4.1	Overview	29
4.2	Examples of Maintenance Program (Outline), Maintenance Strategy, and Maintenance Plan	29
4.3	System Maintenance Strategy	32
4.4	Maintenance Plan	36
4.5	Types of Maintenance	39
5	Maintenance Management	43
5.1	Records for Facilities, Systems, and Equipment	43
5.2	Labor Resources	44
5.3	Planned Maintenance	45
5.4	Spare Parts	46
5.5	Paper-Based Maintenance Management Systems	49
5.6	Computerized Maintenance Management Systems	50
5.7	Maintenance Documentation	52
6	Work Execution	53
6.1	Work Order Management	53
6.2	Self-Inspection and Continual Improvement	64
6.3	Contract Management and Outsourcing	67
6.4	Change Management	69
7	Roles, Responsibilities, and Interfaces	73
7.1	Introduction	73
7.2	Roles and Responsibilities	73
7.3	Production and Maintenance	73
7.4	Project Engineering and Maintenance	74

7.5	Health, Safety, and Environment and Maintenance	75
7.6	Quality and Maintenance	75
7.7	Organizational Structure	76
8	Training	77
8.1	Purpose.....	77
8.2	Knowledge and Skills for Maintenance Personnel.....	77
8.3	Training Scope and Curricula Management	77
8.4	Training Methods and Trainers	79
8.5	Training for Vendors, Contractors, and Consultants	80
8.6	Training Effectiveness.....	81
8.7	Training Record Keeping and Regulatory Requirements	82
9	Appendix 1 – Regulatory Citations	83
10	Appendix 2 – Health, Safety, and Environment in the Maintenance Environment	87
10.1	Introduction	87
10.2	HSE Program Management for the Maintenance Unit.....	88
10.3	Hazards and Risk in the Maintenance Environment	91
10.4	Control of Hazards and Risks in Maintenance Work Areas	92
10.5	Permit to Work System	96
10.6	Control of Hazardous Energies, Lockout/Tagout	98
10.7	Confined Spaces and Restricted Spaces	99
10.8	Hot Work	101
10.9	Flammable and Explosive Atmospheres.....	102
10.10	Working at Heights.....	102
10.11	Working with Compressed Gases.....	103
10.12	Mandatory Maintenance Practices.....	103
10.13	Facility Design for Maintenance Safety.....	104
10.14	Environmental	106
11	Appendix 3 – Science-Based Quality Risk Management.....	111
11.1	Purpose.....	111
11.2	Risk Management.....	111
11.3	ICH Q9 Quality Risk Management Approach.....	111
11.4	Overview of the Quality Risk Management Process	112
11.5	Initiating Quality Risk Management	113
11.6	Risk Assessment.....	114
11.7	Risk Control	115
11.8	Risk Communication	116
11.9	Risk Review	116
11.10	Quality Risk Management Tools	116
12	Appendix 4 – Templates and Examples.....	117
12.1	Example Scenarios	117
12.2	Maintenance Strategy Template	118
12.3	Example Maintenance Plan	119
12.4	Example Maintenance Plan Checklist.....	121
12.5	Example Change Control Request/Approval Form.....	122
13	Appendix 5 – References	123
14	Appendix 6 – Glossary.....	125
14.1	Acronyms and Abbreviations	125
14.2	Definitions	126

1 Introduction

1.1 Background

Maintenance Programs have long been recognized as critical to the success of the operations they support. Maintenance has the potential to affect both the quality of products and the compliance of pharmaceutical processes.

Many pharmaceutical organizations have realized the importance of maintenance, and this has resulted in an increased focus on maintenance processes. This had led to the escalation of requirements being imposed on maintenance operations. In many cases, these increased requirements resulted in added cost and slower execution. In more recent years, the risk-based approach described in ICH Q9 [1] has been applied to Maintenance Programs.

Key themes and practices have become prevalent with respect to Maintenance Programs, e.g.:

- The pharmaceutical industry is using more condition-driven Maintenance Programs based upon operating data derived from Predictive Maintenance (PdM) technologies, rather than performing maintenance on a calendar basis. PdM practices are mature and have been in use in other industries for many years.
- Lean manufacturing concepts and self-directed work teams, borrowed from other industries, affect how maintenance services are delivered.
- Reliability-based techniques, which focus on asset functionality, failure modes, and criticality in the design of Maintenance Plans. Wireless sensors and connected real-time monitoring are becoming more and more prevalent and provide critical information to the user. Smart building techniques are changing the way that facilities are maintained.
- The movement to outsourcing or out-tasking more of maintenance activities adds a level of complexity to Maintenance Programs. A number of organizations are utilizing an Integrated Facilities Management (IFM) model which requires a paradigm shift in the way these services are managed and utilized.

1.2 Purpose

Maintenance practices and trends, coupled with the adoption of the ICH Q9 risk-based approach and the deployment of new technologies, have brought pharmaceutical industry professionals together to update this Guide. This *ISPE Good Practice Guide: Maintenance (Second Edition)* seeks to:

- Help ensure the quality and compliance of maintenance operations and the products impacted by maintenance
- Provide guidance on the latest trends in the maintenance, repair, and improvement of facilities and systems to ensure that organizations are afforded flexibility without impacting the quality of the products
- Recommend a systematic approach aimed at the continual improvement of maintenance operations
- Recommend flexible, standard practices for maintenance professionals that can be applied globally
- Recognize the continuing impact of outsourcing services to third parties and the impact of technology in the production processes
- Control the escalation of non-value generating requirements and cost

This Guide seeks to provide a practical and consistent interpretation of the necessary elements of a pharmaceutical Maintenance Program, while offering maximum flexibility to enable widespread adaptation and encourage innovation.

The practices defined in this Guide aim to address the escalation of cost that results from increasing requirements on pharmaceutical maintenance operations.

This Guide has been developed with the philosophy that the quality and compliance of a Maintenance Program takes precedence over cost elements.

1.3 Scope

This Guide is intended to be used as a tool for the development, implementation, and execution of a Maintenance Program in the pharmaceutical manufacturing environment. This Guide focuses on maintenance in a GMP environment.

Individual systems or equipment and their components may have a potential impact on product quality.

In this Guide, the term GMP, when applied to systems, equipment, or components, indicates a range of practices and controls that can be used to satisfy the requirements and manage potential risk to product quality to an acceptable level. The need and extent of these practices and controls will be based on risk.

This Guide uses the term non-GMP when applied to components, systems, or equipment, as determined through the application of Quality Risk Management (QRM), that do not have an impact on product quality.

Note: The *ISPE Baseline® Guide: Volume 5 – Commissioning and Qualification (Second Edition)* [2] describes a QRM approach (based on ICH Q9 [1] and ICH Q8 [3]) for the classification of systems and equipment based on its potential impact to product quality. Direct impact systems have an impact on product quality (GMP), and systems that are not direct impact do not have an impact on product quality (non-GMP). In addition, the Baseline Guide applies the risk assessment process for identification of the Critical Design Elements, within the direct impact systems, that is used to identify and document the quality impacting components.

The term maintenance, as used in this Guide, is intended to include the various types of maintenance performed on systems, equipment, and facilities.

Good Engineering Practice (GEP) is the foundation upon which a successful Maintenance Program is built. When considering the application of the Maintenance Program to GMP versus non-GMP elements, a risk-based approach that takes into account product quality, novelty, and complexity should be considered to scale level of effort and cost. Refer to *ISPE Good Practice Guide: Good Engineering Practice* [4].

This Guide does not address calibration or cleaning programs. For further information, see *ISPE GAMP® Good Practice Guide: A Risk-Based Approach to Calibration Management* [5] and *ISPE Guide: Cleaning Validation Lifecycle – Applications, Methods, and Controls* [6].

To avoid replication of materials and issues already addressed in other Guides, reference is made to related ISPE Guidance Documents for a complete discussion of the support issues affecting Maintenance Programs and the operations which they support. This Guide is intended to be complementary to the *ISPE Good Practice Guide: Equipment Reliability* [7] and the *ISPE Good Practice Guide: Asset Management* [8].

1.4 Benefits

This Guide provides professionals in the pharmaceutical industry with guidance on the approach to the maintenance of pharmaceutical facilities, equipment, and systems. This Guide is intended to be flexible to permit organizations to develop solutions to maximize performance and minimize the total cost of asset ownership.

1.5 Objectives

This Guide has been prepared to help pharmaceutical maintenance professionals develop and implement Maintenance Programs in accordance with GMPs. It is intended primarily for industry professionals in the US and Europe; however, many of the concepts are considered to be applicable in any pharmaceutical environment, irrespective of the size or location of the organization.

This Guide is intended to facilitate pharmaceutical maintenance, and as such, it does not attempt to address applicable codes, standards, and policies beyond the GMPs, which need to be considered in the development and execution of a Maintenance Program.

1.6 Key Concepts

This Guide introduces the concept of a range of maintenance practices organized into two categories:

- Maintenance Good Practices
- Maintenance Best Practices

Maintenance Good Practices parallel the GEPs and GMPs described in other ISPE Guidance Documents [4, 9].

- Maintenance Good Practices should be performed on equipment, systems, and facilities to ensure a level of reliability and asset performance as determined by the organization. Maintenance Good Practices are recommended for systems, equipment, and components where risk assessment indicates that patient safety and product quality could be impacted.
- Maintenance Best Practices are those practices that go beyond Maintenance Good Practices and typically are applied only for business purposes. Maintenance Best Practices incorporate program refinements, optimization, and advanced maintenance approaches, capabilities, and methodologies.

This Guide supports a risk-based approach to the determination of which category of maintenance practices should be applied to a system or its components. Risk management should be part of the analysis performed prior to an asset being placed in service and in many cases will involve the maintenance unit. The maintenance unit should apply its Maintenance Program and develop Maintenance Plans according to the risk assessment. An overview of the ICH Q9 [1] risk-based approach is described in Chapter 11 (Appendix 3).

The concepts and definitions used in this Guide build upon those from other ISPE Guidance Documents [7, 8, 9].

1.7 Structure of the Guide

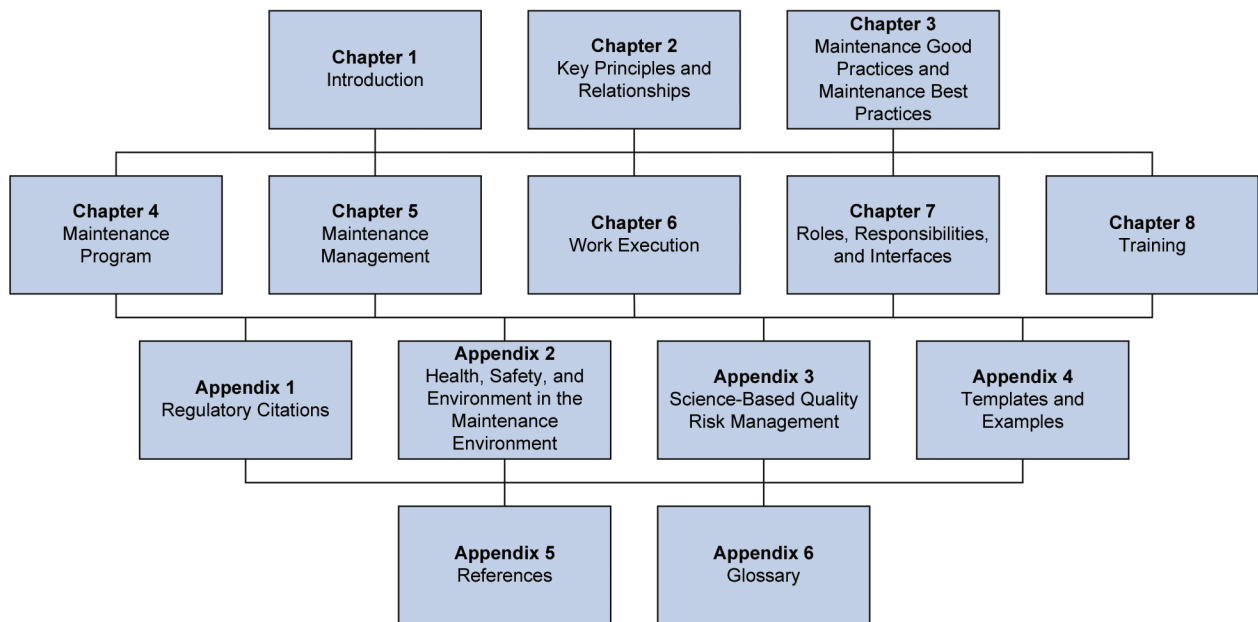
This Guide is divided into three main parts:

- Chapters 1 through 3 describe the philosophy and provide details of the key concepts of this Guide, introducing the two categories of maintenance practices described in this Guide: Maintenance Good Practices and Maintenance Best Practices
- Subsequent chapters elaborate on each of these categories of maintenance practices and consider:
 - Maintenance Program, its elements, and regulatory requirements
 - Work order management, including: Work Requests (WRs), Work Orders (WOs), planning and scheduling, WO completion including calibration work orders, and emergency work

- Roles and responsibilities involved in executing Maintenance Good Practices
- Training to ensure that personnel performing maintenance have the technical and procedural knowledge necessary to ensure patient safety and product quality
- Appendices provide information on regulatory citations, Health, Safety, and Environment (HSE), science-based QRM, and examples and templates which may be useful to the reader

The chapter structure is shown in Figure 1.1.

Figure 1.1: Chapter Structure



2 Key Principles and Relationships

2.1 Introduction

This chapter outlines philosophies and regulatory concepts for maintenance operations in a pharmaceutical manufacturing environment, regulated by the FDA [10], EMA [11], and other regulatory agencies for Active Pharmaceutical Ingredients (APIs) and finished pharmaceuticals. Regulatory concepts are outlined for both the development and execution of a Maintenance Program. In pharmaceutical manufacturing operations, there is a direct dependency upon systems to operate within tolerances in order to achieve drug product quality. Maintenance activities are directed at ensuring system performance, and thus, drug product quality. The Maintenance Program should help to ensure that the equipment is continually maintained in a qualified state and is suitable for intended use.¹

See also Chapter 9 (Appendix 1) for regulatory citations.

2.2 Philosophy

The process to establish regulatory concepts should start with the development of a list of all the elements of a Maintenance Program for a pharmaceutical manufacturing facility. These elements may range from strategic (Maintenance Strategy, organization, etc.), to tactical (work order execution, spare parts application, etc.). Each of these elements should be reviewed in the context of the GMP requirements.

This Guide focuses on those elements of maintenance where GMP requirements apply. In addition to the GMP requirements, a comprehensive Maintenance Program should address other drivers for performing maintenance, such as:

- Health and safety
- Environmental protection
- Business continuity

It is expected that many of the recommended practices described in this Guide will contribute toward meeting or exceeding other requirements of a Maintenance Program. It should be noted that requirements based upon drivers, other than GMP requirements, may result in additional controls or activities that extend beyond the Maintenance Good Practices recommended in this Guide.

2.3 Maintenance Practices

The GMP requirements permit flexibility and provide scope for innovation and improvement. The regulations are not intended to prescribe exactly what needs to be done for any particular activity, including maintenance. In general, the regulations require that maintenance is performed and documented to ensure affected operations consistently produce drug product that meets predefined specifications. However, how maintenance is performed is subject to change, depending upon an organization's philosophies, requirements, and capabilities.

Maintenance Good Practices are aimed at ensuring drug product quality and operational compliance, and are intended to meet the requirements of GMP. Maintenance Good Practices are also aimed at ensuring that operations do not experience unexpected downtime or system failures.

¹ FDA Guidance for Industry on Process Validation: General Principles and Practices [12] states that "activities undertaken to demonstrate that utilities and pieces of equipment are suitable for their intended use and perform properly" is referred to as qualification.

Maintenance Best Practices are practices that go beyond Maintenance Good Practices and involve tools and analysis typically aimed at optimization and increasing asset performance and lifecycle. Maintenance Best Practices go beyond GMP requirements.

The practices described in this chapter are part of Maintenance Good Practices, unless specifically noted otherwise, and subsequent chapters of this Guide elaborate on these two categories of maintenance practices.

2.4 Maintenance Program

2.4.1 *Establishing a Maintenance Program*

A Maintenance Program is a written document establishing the requirements for performing and controlling maintenance activities and should be approved by stakeholders. Maintenance Programs normally include sections on:

- System inventory and risk assessments
- Criticality analysis for key assets
- Reliability Centered Maintenance (RCM) plan
- Computerized Maintenance Management System (CMMS)
- Bar codes and Radio Frequency Identification (RFID) tags
- Change management
- Roles and responsibilities
- Documentation requirements
- Critical spare parts identification and storage requirements
- Turnover process for new facilities and equipment
- Training for client and partner/subcontractor staff
- Preventive Maintenance (PM) plan

Maintenance Programs should encompass management processes and controls, such as how new systems are brought into the Maintenance Program and who has the authority to approve and make changes.

The Maintenance Program's inventory of systems that require maintenance facilitates the determination (or confirmation) of system impact via a risk assessment. In most cases, the risk assessment is completed, and Maintenance Plans are established in conjunction with the maintenance unit during the Commissioning and Qualification (C&Q) phase and prior to putting the asset into service.

Maintenance Programs should document the rationale for determining when Maintenance Good Practices apply.

Maintenance Programs should have a process for handling unplanned maintenance activities. Typically, the program should detail how unplanned work should be evaluated for impact on drug products and how approvals and documentation should be managed. Unplanned activities, e.g., an equipment malfunction, by definition may require some degree of immediate judgement and action.

Organizations may apply common Maintenance Programs across their manufacturing sites. When a significant issue arises at one site, it should be addressed at all sites where there is potential for the same issue to occur. (Note: this is not a regulatory requirement.)

2.4.2 Maintenance Plans

Maintenance Plans contain tactical maintenance tasks performed to:

- Maintain systems (and their components) in proper working order
- Monitor performance in order to detect abnormalities or conditions that might lead to failure

Maintenance Plans are prepared in accordance with requirements established in the Maintenance Program. These tasks are usually time based or condition performance based, depending upon the asset, process requirements, and the organization's capabilities. Maintenance Plans are usually considered as PM WOs although they may be considered as other practices, e.g., corrective WOs.

Maintenance Plans can be established and performed on a system level or a component level. Instructions for maintenance can apply to several systems or be specific to a particular system or component (such as an individual equipment item).

Tasks outlined in the Maintenance Plan should be described in sufficient detail to ensure proper and consistent work implementation by persons qualified to execute the work. Maintenance Plans should include a predetermined frequency or trigger to execute the work to ensure asset performance.

Maintenance Plans and their frequency of execution are typically developed from various inputs including:

- Equipment manufacturer's original recommendations
- Experience with similar equipment
- Review of historical data (trending)
- Process requirements
- Risk assessments
- Complexity and novelty of equipment

For the execution of Maintenance Plans, a Maintenance Management System (MMS) can provide scheduling and documentation capabilities that assist maintenance management. Manual systems tend to be used in smaller sites and can be equally effective from a regulatory perspective. Most CMMSs (Computerized MMSs) are hybrids in that they produce a paper document (i.e., WO) that becomes the record of maintenance. When the record of maintenance and the schedule for maintenance are managed and recorded using a paper copy outside of the CMMS, the CMMS may not require software validation or hardware C&Q, as these are typically the only two maintenance system functions that have GMP regulatory impact. If the CMMS is used to maintain the record of maintenance or the schedule for maintenance, it should be in compliance with 21 CFR Part 11 [13]. For further information, see *ISPE GAMP® RDI Good Practice Guide: Data Integrity – Key Concepts* [14].

2.4.3 Change Management

The Maintenance Program should include procedures or reference to procedures for addressing change management. Throughout the lifecycle, there will be times when nonroutine repairs, modifications, and/or replacements will be necessary, creating the possibility of impact on process parameters (and ultimately drug product). The process for assessing, executing, and documenting these events or changes to systems should be established in the Maintenance Program. Organizations may refer to their quality organization's change management process.

When changes are implemented, some degree of testing and/or verification is required to ensure that the original equipment/component qualification status has not been impacted. The need to perform routine repairs, adjustments, and the like, within pre-established tolerances that have no impact on the process or drug product, should be considered when developing a change management program.

Refer to *ISPE PQLI® Guide: Part 3 – Change Management System as a Key Element of a Pharmaceutical Quality System* [15].

2.4.4 Roles and Responsibilities

The regulations are flexible regarding how the maintenance unit organization is structured and how specific roles and responsibilities are defined and performed; this is critical when third-party providers are utilized to perform this work. For GMP systems and equipment, the roles and responsibilities of maintenance staff should be documented. The regulations specifically state that assignment of responsibility for maintenance and maintenance scheduling shall be included in the written procedures for maintenance. It is also an expectation that roles and responsibilities be established for an overview of the maintenance activities, including processes such as:

- Writing maintenance procedures
- Authorizing changes
- Review and approval of work processes
- Response to deficiencies
- Training
- Documentation

Where maintenance personnel are engaged in these activities, their roles and responsibilities should be documented. In addition, where there is a review and approval of a process or procedure, it should be independent and unbiased.

Table 2.1 outlines the typical roles and responsibilities of stakeholders of maintenance activities with respect to the key elements of a Maintenance Program.

Table 2.1: Typical Roles and Responsibilities for Maintenance Activities

Maintenance Activity for GMP Systems and Equipment	Integrated Facilities Management (IFM) Provider or Subcontractor if Present	Maintenance Unit (Client Representative)	Subject Matter Expert (SME)	System Owner	Quality Unit
Maintenance Program	Prepare	Approve	Prepare and Approve		Approve
Risk Assessments	Prepare	Prepare and Approve	Prepare and Approve		Approve
Maintenance Plan	Prepare	Prepare and Approve	Prepare and Approve		
Change Control	Prepare	Prepare and Approve	Prepare and Approve	Approve	Approve
Deferred Maintenance		Prepare and Approve	Prepare and Approve		
Training Program		Prepare and Approve			Approve
Training Plans	Prepare	Prepare and Approve	Prepare and Approve		
Deficiencies		Prepare and Approve	Prepare and Approve		Approve (Process only)*
Spare Part Application (Like-for-like)	Prepare	Assess and Approve	Review		Approve
Spare Part Application (Not Like-for-like)	Prepare	Assess and Approve	Review	Approve	Approve
*The Quality unit should approve deficiencies that have the potential to affect Critical Process Parameters.					

2.4.5 Maintenance Documentation

2.4.5.1 Procedures

There are several approaches that organizations use in the application of procedures to maintenance processes. Organizations may develop governing procedures which provide a framework for maintenance practices, within which the maintenance unit is able to create plans, instructions, check-sheets, task lists, etc., to carry out the maintenance work. Alternatively, organizations may use specific procedures that are associated with an individual work process, e.g., the PM for a particular filling line might have a PM procedure specific to the line. There also might be hybrid approaches to maintenance procedures. The key difference between using governing procedures or specific procedures lies in where the approvals are conducted: within the maintenance unit or outside of the maintenance unit. Typically, the Quality unit approves governing procedures and the Maintenance Program; however, Maintenance Plans, instructions, or check-sheets, etc., would be approved and managed locally within the maintenance unit. The Maintenance Good Practice approach is to use governing procedures in the form of the Maintenance Program (which should be approved by the Quality unit) and to supplement these with Maintenance Plans that are developed, managed, and approved internal to the maintenance unit.

2.4.5.2 Deficiencies

When deficiencies are encountered on systems or equipment that may impact product quality and patient safety (GMP systems or equipment) during the performance of maintenance activities, they should be reported, investigated, and documented in a timely manner. If the deficiency is identified as an equipment or component failure that does not affect a Critical Process Parameter and has no potential impact to drug product quality (i.e., risk to meeting a Critical Quality Attribute (CQA)), then the deficiency can be reported, investigated, documented, and corrected within the authority of the maintenance unit. If the deficiency has affected a Critical Process Parameter, it should be reported to the Quality unit and the System Owner. Subsequently, the necessary course of action should be determined and typically would include an investigation, corrective measures, and reporting requirements.

Note: The *ISPE Baseline® Guide: Volume 5 – Commissioning and Qualification (Second Edition)* [2] designates Critical Design Elements as the engineering and automation design elements used to implement design controls (Critical Aspects) to ensure documented Critical Process Parameter operation. Examples of engineering design features include components, instruments, and materials of construction. Critical Design Elements are identified and documented based on technical understanding of the product CQAs, process Critical Process Parameters, and equipment design/automation.

2.4.5.3 Continual Improvement

Although not a specific regulatory requirement, continual improvement and innovation is encouraged by the FDA. [16] The regulatory requirement to investigate an abnormal event or occurrence with respect to maintenance activities is applicable where drug product may be impacted. Organizations may trend maintenance activities as a means of achieving a higher level of asset performance (Maintenance Best Practice). It should be noted that review and trending of maintenance activities is not a regulatory requirement. When a failure is experienced on a GMP system or equipment, however, the expectation is that any corrective action taken would be applied to similar systems where the same possibility of failure might exist, including other relevant locations within the organization. This should not be interpreted to mean that maintenance procedures on similar systems at all locations of an organization should be identical. Although there might be business reasons for harmonizing maintenance processes across an organization, this is not a regulatory requirement, nor is it always practical or appropriate.

2.4.6 Equipment

The US FDA 21 CFR Part 211.67 states “...records shall be kept of maintenance, cleaning, sanitizing, and inspection.” [17] The capability to track the maintenance activity on a specific piece of equipment in a manufacturing process for a drug product is important to demonstrate that proper controls exist. GMP systems or equipment should have a documented status at all times. When maintenance is being performed, a tag or identifier should be used to display clearly that the equipment or room that is undergoing maintenance is out of service.

Equipment that is used for producing a drug product should have a unique identification to distinguish it from other similar equipment. The use of a unique equipment identification scheme also provides a way to establish and track maintenance activities.

Maintenance activities may affect the cleanliness of GMP systems or equipment. Maintenance activities may also affect the performance of the equipment; a proper verification of operations is recommended.

Maintenance activities should be performed in a way that addresses drug product contamination and exposure concerns. Consideration also should be given to the tools, equipment, and materials that maintenance personnel use in the execution of their work.

It is recommended that if possible, all documentation should be performed electronically in the validated CMMS to ensure that the work is performed and recorded in the most efficient and effective manner.

2.5 Spare Parts and Materials

When parts and materials (lubricants, etc.) are applied, there should be some verification that the qualified state of the system has not been affected. Spare parts and materials management is not a specific requirement of the regulations. However, before a part is installed, its suitability for an application should be determined. Criteria should be established to determine whether a part is identical (i.e., functionally equivalent) or requires some additional evaluation or change control. The criteria should include defined roles to assess and implement part and material replacements.

When new equipment is installed, the Bill of Materials (BOM) should be established as part of the turnover package so that this information can be captured and stored in the CMMS system. A Best Practice is to have these items tethered to the CMMS system equipment ID for reference in the planning, scheduling, and ordering of parts for a work request or routine PM.

The Maintenance Good Practice approach to spare parts and materials application is to establish criteria for identifying spare parts and materials as like-for-like.

The maintenance unit should develop a procedure to determine if spare parts and materials are like-for-like. This procedure should be approved by the Quality unit. When parts or materials are deemed like-for-like, they can be installed as identical or functionally equivalent and do not require further documentation, beyond noting the installation on a WO.

If parts or materials are deemed not to be like-for-like, this constitutes a change that should be documented through the established change control process for GMP systems or equipment. Testing and requalification requirements should be established in advance of any part application. Appropriate testing should be conducted to ensure the equipment is working properly and is suitable for its intended use.

2.6 Training

A training program should be established as part of the Maintenance Program. The training program should determine the roles and responsibilities for:

- Training
- Training content
- Training delivery systems
- Evaluation of training
- Subcontractor training and qualification
- Role-based training based on job title and function
- Documentation practices

Training records should be housed in a validated Quality Management System (QMS) and include the training records of the organization's employees, contracted staff that performs work on validated equipment and systems, and all subcontractor employees who are working on GMP-related activities.

The Training Plan is the schedule of courses or learning activities that should be accomplished for a given period. Training is required for GMPs and job function. The basic skills that personnel bring to a job are normally confirmed during the hiring process. For instance, a trade qualified electrician is assumed to have the basic skill sets for their trade, and therefore documentation to that effect is not usually required by the regulatory authorities.

An important concept of GMP training is that personnel should understand how their duties may impact drug product quality.

All of the organization's employees, contracted staff, and subcontractors performing work on GMP-related equipment and systems should be included in the organization's role-based training system. A training curriculum needs to be established that clearly spells out the training program required for anyone assigned to a specific role or job description.

Refer to Chapter 8 for more information about training.

2.7 Culture

It is important to establish a culture for maintenance that is collaborative in nature, where clear lines of communication are established, SOPs are developed for the various processes, and all work performed follows the SOPs irrespective of whether it is executed by an employee or a subcontractor. The establishment of quality agreements for key services should serve as the model for which the roles, responsibilities, and approvals of work performed are addressed.

2.8 Maintenance Key Relationships

The Maintenance department must have a relationship with production operations, IT, quality, finance, purchasing, engineering, and all subcontractors including IFM providers, contractors, and vendors. These relationships can be the difference between having a successful operation or one that has issues with performance. Touch points and overlaps between functions need to be identified and a working relationship between departments established to avoid conflicts and confusion as to who is responsible for a given area or issue.

2.8.1 Safety

Safety should be built into the Maintenance Plans and not be performed as an afterthought. The safety SOPs should be integrated into the site's Maintenance Plans. As part of the PM and Corrective WO Management Plan, Job Hazard Analysis (JHA), Lockout/Tagout (LOTO) Plans, and Confined Space among others must be included in the work order planning and execution. The training on the HSE SOPs should be part of the employee's and subcontracted staff's training curricula and housed in the QMS.

Refer to Chapter 10 (Appendix 2) for more information about HSE in the maintenance environment.

2.8.2 Quality Management System

A Best Practice is for an organization to have a computerized QMS to track quality issues related to the performance of maintenance and calibration activities. These systems typically house training records and role-based training curricula, Quality and HSE SOPs, Corrective and Preventive Action plans, and related documentation. In addition, employee CVs, and subcontractor certifications and CVs are stored in the system as well.

2.8.3 Operations Management

The operations team adds requirements for product contact and GMP production equipment. These include the establishment of SOPs for a variety of areas including equipment access, removal of equipment from service, any unique cleaning or sanitization requirements, test runs to prove the equipment is calibrated and set up properly, and change control procedures related to a room, equipment, and/or system.

2.8.4 Equipment Reliability

The use of reliability maintenance tools and techniques is becoming more and more commonplace. Organizations can consider installing sensors that provide real-time monitoring of equipment and conditions including the addition of accelerometers, corrosion probes, current and voltage monitoring, and related types of sensors. The goal is to reduce unplanned failures and to ensure that equipment problems are promptly addressed.

See also *ISPE Good Practice Guide: Equipment Reliability* [7].

2.8.5 Physical Asset Management

The maintenance of the physical plant including support systems, walls, floors, and ceilings as well as the utility systems maintenance can lead to a more reliable and repeatable facility. One of the keys to this program is to have a PM program that is robust enough to keep the physical plant in a safe, clean, and reliable manner.

2.8.6 Risk Management

For critical production and utility related equipment, a strategy to consider is to utilize a technique such as a criticality analysis to identify the hierarchy of what the criticality of each piece of equipment is and how it fits into the overall plant operation. Once this is established, a PM program based on risk and criticality can be established for the facility.

3 Maintenance Good Practices and Maintenance Best Practices

3.1 Introduction

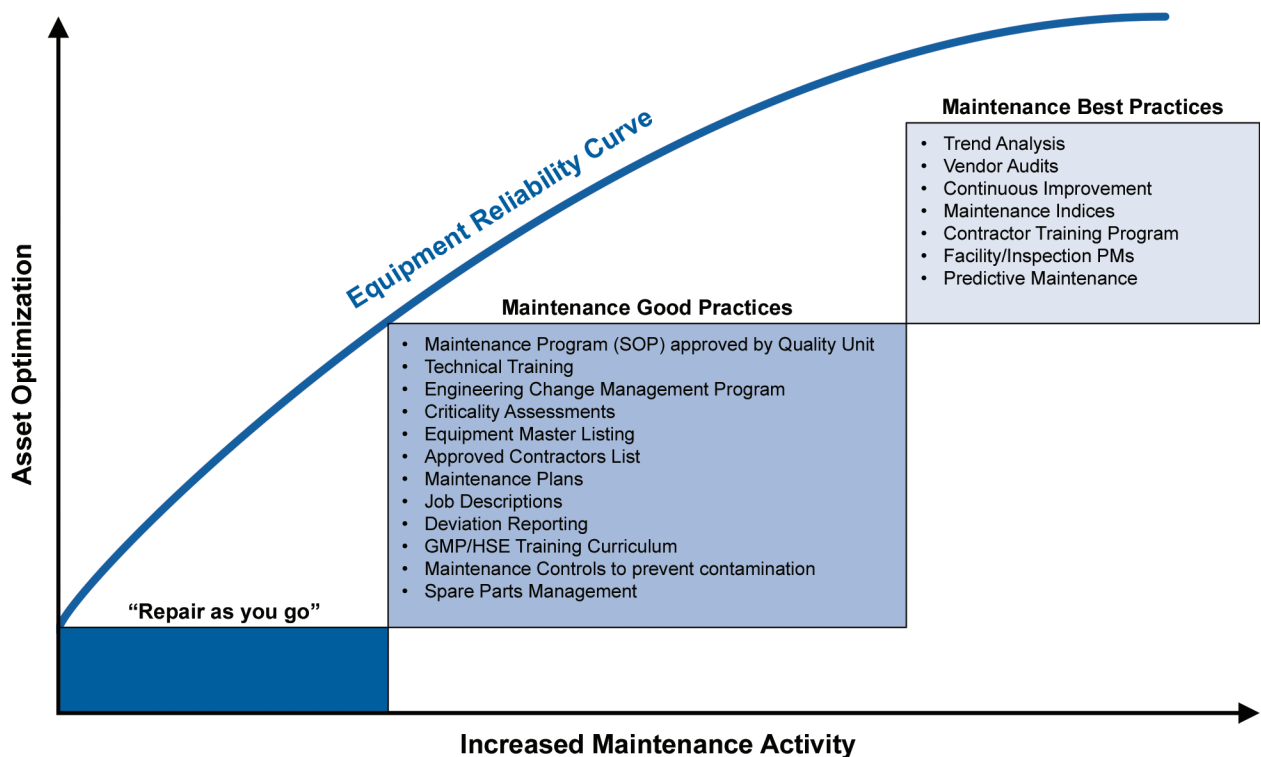
This chapter describes Maintenance Good Practices and Maintenance Best Practices for planning, execution, and management of Maintenance Program activities. Maintenance Good Practices are intended to meet or exceed the minimum requirements of GMP. Maintenance Best Practices extend beyond Maintenance Good Practices and incorporate program refinements, optimization, and advanced maintenance approaches, capabilities, and methodologies.

3.2 Overview

Design, Specification, and C&Q processes for systems and equipment supporting life sciences applications continue to mature and evolve with advances in technology and incorporation of science and risk-based approaches to asset delivery and lifecycle asset management. Maintenance activities must align with these evolving asset development and delivery approaches to support GxP compliant operations. Maintenance Best Practices described herein identify opportunities for improving maintenance performance, efficiency, and compliance beyond good practices for Maintenance Programs.

Figure 3.1 illustrates the relationship between Maintenance Good Practices and Maintenance Best Practices.

Figure 3.1: Relationship between Maintenance Good Practices and Maintenance Best Practices



3.3 Maintenance Good Practices

Maintenance Good Practices are performed to ensure and demonstrate regulatory compliance and/or because they make good business sense for asset reliability and preservation. This includes regular PM plans and schedules for each piece of equipment according to recognized industry practices and equipment vendor recommendations, technical training for personnel performing associated tasks, and maintenance documentation and records. Maintenance Good Practices are understood as those programs, actions, and processes necessary to meet the minimum needs for support of equipment performance and regulatory compliance. For Maintenance Good Practice programs, these documents and records may be paper-based or electronic. Required documentation and records include the following.

- Maintenance Policy and Philosophy
 - Maintenance actions planned and executed to meet minimum requirements of GMPs and other regulatory requirements
 - PM
 - Corrective Maintenance (CM)
- Maintenance Program
 - Basic Maintenance Plans
 - Basic equipment registry and asset management practices
 - Training for GMP and regulatory-related equipment actions
- Maintenance Management Program
 - Work execution with basic records
 - Roles and responsibilities
 - Training
 - > Training record keeping
 - > Training curricula management
 - > Training plan for vendors and contractors
 - Documentation and records
 - > User, Operation, and Maintenance manuals
 - > Engineering drawings, P&IDs, and vendor drawings
 - > Basic records for WO completion
 - > Inspection certificates, calibration certificates, and vendor support records

3.4 Maintenance Best Practices

Maintenance Best Practices build upon Maintenance Good Practices to optimize or refine Maintenance Program planning, execution, and management by the incorporation of approaches, analyses, tools, resources, and alignment with asset lifecycle activities. Examples of these include the following:

- Use of a CMMS
- Use of Maintenance Subject Matter Experts (SMEs)
- Roles and Responsibilities
 - Clearly defined for personnel including craft technicians, supervisors, managers, and approvers such as Quality Assurance (QA)
- Training Program
 - Use of computerized Learning Management System (LMS)
 - Well-defined training curricula
 - Training plans specific to crafts, vendors, and contractors
- Use of a Risk Assessment Process
 - To identify assets or components that support quality critical aspects of manufacturing systems and those supporting other regulated functions (environmental, safety, etc.)
 - To identify non-critical assets or components that may require less frequent maintenance action
- Use of a Reliability Assessment or Failure Modes and Effects Analysis (FMEA) process
 - To refine maintenance task and frequency requirements based on intended/actual use of equipment
 - To provide input for provisioning of spare parts, repair parts, and materials
- Incorporation of PdM and condition monitoring methodologies
- Integration with asset lifecycle activities such as C&Q, change control, process optimization, and decommissioning programs
- Maintenance Data and Documentation Management Program
- Proactive Maintenance Program Development and Delivery

These Maintenance Best Practices are further described in the sections that follow.

3.4.1 *Computerized Maintenance Management System*

The use of a CMMS provides numerous benefits and capabilities beyond what can be provided by paper-based systems. These capabilities include:

- Comprehensive asset management capabilities including asset registry, action/change history, asset information, hierarchy, location, status, and search capabilities

- Automated schedule management for maintenance actions (current/future WOs, completion status, open items)
- Generation of work plans that incorporate multiple maintenance tasks for the system or area that can be implemented at the same time while the system/area is scheduled for downtime
- Platform for management of maintenance and calibration work instructions, checklists, and completion records
- Work order planning, execution, and management
- Workload planning for maintenance resources and capabilities
- Comprehensive performance reporting and forecasting capabilities
- Activity event log and audit trail capability – suitable for support of compliance requirements
- Linkage to resource, training, and inventory management databases (internal or external platforms)
- Web-based access and management (offered by many CMMS providers)
- Automated management review of WOs

CMMS system use is widespread in the life sciences and general industry. Many organizations continue to rely on paper-based systems for a variety of reasons. Use of a CMMS-based maintenance management program offers the capabilities identified above and more in many cases, depending on the specific commercial product evaluated.

3.4.2 Maintenance Subject Matter Experts

Use of SME resources in key technical roles in the life sciences industry is considered a Best Practice and is also a developing industry practice. For maintenance applications, SMEs should be involved in multiple aspects of Maintenance Program planning, execution, and management including the review of maintenance and calibration:

- Plans
- Work instructions for technology-specific applications
- Schedules
- Task completion documentation
- Plans associated with Change Management actions
- Discrepancies, failures, and action items

3.4.3 Roles and Responsibilities

Roles and responsibilities are defined for all maintenance and calibration personnel including craft technicians, supervisors, managers, and approvers such as QA.

3.4.4 Training Program

Best Practice for training programs is the use of an electronic-based system that handles training requirements, materials, and records. All personnel are proactively trained on Maintenance Program procedures and requirements, GMP requirements, and task-level execution requirements. External training on novel technologies and best practices is provided for program development and technical advancement purposes.

3.4.5 Risk Assessment Process

During the Design, Specification and C&Q processes, quality risk assessments are conducted to identify critical components and critical design aspects (those components or aspects that have potential to impact product quality). Additional risk assessments may be conducted to identify components or design features that support other regulatory requirements (e.g., safety or environmental). The results of these assessments should be utilized as inputs to Maintenance Program development such that:

- Components or design aspects identified as critical from a GxP or other regulatory perspective are identified and assigned appropriate maintenance/calibration tasks and frequencies. QA functions should focus on this subset of components or design aspects to ensure maintenance actions are executed as planned and scheduled.
- Non-critical components or design aspects are identified and assigned appropriate maintenance/calibration tasks that may have longer intervals after initial maintenance actions and/or relaxed tolerances based on functionality and good business practice.

Refer to *ISPE Baseline® Guide: Volume 5 – Commissioning and Qualification (Second Edition)* [2] for more information.

3.4.6 Reliability Assessment Process

Another Best Practice for maintenance operations is the use of a reliability assessment process to refine scheduled maintenance requirements based on the inherent reliability of the equipment and its context of usage, potential failure modes, and expected operating life between failures. The results of reliability assessments provide maintenance task and frequency refinements beyond baseline recommendations provided by equipment manufacturers/vendors. Scheduled maintenance requirements, in turn, drive provisioning requirements for maintenance parts and materials necessary to support maintenance activities as well as workload commitments for skilled resources. Additionally, reliability assessment results can identify recommended spare parts to provision based on potential for failures or unscheduled CM actions.

Refer to *ISPE Good Practice Guide: Equipment Reliability* [7] for more information.

3.4.7 Predictive Maintenance and Condition Monitoring

PdM is a maintenance approach applied to specific types of systems and equipment based on known failure modes, likelihood of failure occurrence, and projected failure timing. The goal of PdM is to identify the optimal timing of maintenance actions; that is, perform maintenance actions just prior to projected equipment failure to avoid both unnecessary periodic maintenance and the result of equipment failures.

Condition monitoring is a type of PdM that utilizes real-time monitoring of equipment operating parameters to trend against known failure modes with the intent to intervene with prescribed maintenance actions prior to equipment failure. Condition monitoring is often used in rotating equipment applications to monitor the status of bearings or bushings based on monitoring of vibration or acoustic measurement data.

3.4.8 Maintenance throughout the System Lifecycle

Maintenance SMEs should participate in the Requirements Definition, Design, and Specification of new systems and equipment to ensure that requirements for equipment reliability, maintainability, and accessibility are addressed. C&Q activities for systems and equipment should include confirmation that appropriate maintenance and calibration programs have been established and are effective. During the Operations phase, incremental system changes or improvements should be assessed for changing Maintenance Program needs. At system retirement or decommissioning, certain activities may need to be performed (e.g., final validation and calibration close out) to confirm that the system was operating as it should at the time of decommissioning.

3.4.9 Maintenance Data and Documentation

System data and documentation are utilized as inputs for Maintenance Program development and maintenance task execution. Examples of documentation include:

- System drawings (e.g., Piping and Instrumentation Diagram (P&ID), General Arrangement (GA), piping isometric drawings, etc.)
- Installation, operation, and maintenance manuals
- Recommended spare parts lists
- BOM
- Recommended lubricants
- Recommended maintenance tasks and frequencies
- Instrument and equipment lists
- Controls information
- Sequence of operations
- Vendor equipment submittals

Documentation utilized to support Maintenance Program development should be retained throughout the life of the system.

System data is utilized by maintenance for the development of equipment registry information and maintenance task development. System data is also utilized by multiple other disciplines for testing and support programs. Typical system data includes:

- Manufacturer
- Model Number
- System Description
- System Number
- Drawing Number
- Specification Number
- Serial Number
- Equipment Range and Unit of Measure
- Process Range and Unit of Measure
- Location
- Component Tag Name(s)

- Component Service Description(s)
- Set point(s)
- Vendor Name
- Vendor Catalog Number
- Purchase Price

A Maintenance Best Practice is gathering, managing, and reviewing system documentation and data proactively as equipment is specified, procured, and received (prior to the creation of an equipment registry and Maintenance Program development). This facilitates accuracy, completeness, and timeliness of data and documentation to support program development needs. Availability and delivery of data and documentation can be scheduled to align with specific project milestones (e.g., drawings issued for construction, purchase order issued, equipment delivery, etc.) and in this manner, data and documentation can be anticipated, scheduled, accounted for, and managed in a proactive manner.

3.4.10 Proactive Maintenance Program Delivery

Maintenance Program development can be initiated as soon as system designs are confirmed and equipment design information is available. A Maintenance Best Practice is to develop the equipment registry, Maintenance Program, and spare/repair parts provisioning concurrent with system C&Q so that the systems are fully ready for operation upon turnover to operations. This helps avoid delays in initial system operation and ensures continuity of maintenance and calibration support throughout the C&Q and system turnover/delivery processes.

4 Maintenance Program

4.1 Overview

This chapter describes the Maintenance Program, its elements, and the regulatory requirements.

The hierarchy and associated terminology for an organization's Maintenance Program are as follows:

- Maintenance Program outlines the policies that describe the approach that an organization intends to use with respect to aspects of performing maintenance
- System Maintenance Strategy is the rationale (the “why”) for a particular approach being used at a system or process level
- Maintenance Plans are the specific details (the “what” and “how”) at a component or individual piece of equipment level

Note: Maintenance classifications apply to equipment, systems, and facilities. For the purpose of this Guide, the term asset is used interchangeably with equipment, systems, and facilities.

4.2 Examples of Maintenance Program (Outline), Maintenance Strategy, and Maintenance Plan

The FDA 21 CFR Part 211.68 [17] states:

“[Equipment] shall be routinely calibrated, inspected, or checked according to a written program designed to assure proper performance.”

Additionally, the EU EC Directive 2003/94 [18] states in Article 8(1):

“Premises and manufacturing equipment shall be . . . adapted and maintained to suit the intended operations.”

A Maintenance Program should document an organization's approach to performing maintenance regarding aspects and requirements. The Maintenance Program should outline the policies for:

- Maintenance Plans and WOs
- Maintenance classifications (preventive, predictive, condition monitoring, corrective)
- Maintenance systems and execution (e.g., equipment identification, documentation, work order management, resource planning, scheduling, maintenance materials management)
- Risk assessment
- Spare parts management
- Deviations
- Roles and responsibilities
- Training programs, plans, and records

- Performance management (e.g., continual improvement, maintenance metrics)
- Deferred maintenance
- Maintenance interfaces
- Change control
- Contract management and outsourcing
- Self-audits or assessments

The Maintenance Program should also include management processes and controls, e.g., for incorporating new systems and the associated equipment, supervision and overview of the processes and activities, and authority to approve and make changes.

Figure 4.1 depicts key aspects of a Maintenance Program.

Figure 4.1: Key Aspects of a Maintenance Program



The Maintenance Program should define how Maintenance Good Practices and Maintenance Best Practices are to be implemented.

Examples of Maintenance Good Practices of a Maintenance Program include:

- Describing long-term vision, drivers, and goals
- Establishing maintenance technical training
- Establishing the minimal requirements for performing maintenance in the organization
- Developing an asset management plan for assets from commissioning through decommissioning
- Identification of Maintenance Plans for GMP systems or equipment
- Identification of Maintenance Plans for GMP components associated with GMP systems or equipment
- Documented rationale (System Maintenance Strategy) for maintenance performed on GMP systems or equipment
- Maintenance Program (approved by Quality unit)
- Defined approval authority and change management program for GMP systems or equipment
- Equipment master listing
- Active, up-to-date Maintenance Plans
- Job descriptions with a skills matrix to define and track required skill sets
- Active, up-to-date GMP training curriculum (employees and contractors)
- Controls to prevent GMP impacts from maintenance activities
- Vendor audits
- Contractor training program
- Approved contractor list
- 5S/6S

Examples of Maintenance Best Practices of a Maintenance Program include:

- Asset criticality assessment (based on GMP, safety, and operational risks)
- Developing and monitoring Key Performance Indicators (KPIs)
- Maintenance analytics
- Emphasis on proactive maintenance
- Spare parts management

- Facility surveillances and inspections
- Establishing a continual improvement program
- Developing and implementing Maintenance Strategies for all critical assets (including non-GMP assets)
- Risk-based maintenance strategies

The Maintenance Program provides the framework for the risk assessment. It may be beneficial to involve maintenance/reliability engineering personnel in the stages of the risk assessments (i.e., during design).

The process for handling unplanned maintenance activities should be described in the Maintenance Program, including a procedure on how unplanned work is evaluated for patient safety and product quality in addition to how approval and documentation will be managed. The Maintenance Program should also include a procedure for returning equipment and/or classified areas back to service after maintenance activities are completed, which will verify a system is returned to the qualified state.

The Maintenance Program should be developed by a cross-functional team, led by the maintenance unit, including SMEs from:

- Engineering
- Quality
- HSE

4.3 System Maintenance Strategy

A System Maintenance Strategy is a rationale or set of criteria used to develop Maintenance Plans. Inputs to a System Maintenance Strategy may include:

- System or component classification
- Quality and maintenance risk assessment
- Original Equipment Manufacturer (OEM) recommendations
- Data analysis of key process and maintenance data
- Experience with similar equipment
- Process requirements
- Intervals and tolerances
- Spare parts strategies and requirements

An example of a Maintenance Good Practice is a documented rationale for maintenance performed on GMP systems or equipment, which includes a process for handling corrective or on-demand maintenance.

The inputs to the Maintenance Strategy may have been identified during the design, construction, installation, testing, and C&Q phases of system construction. If readily available and done so using GEP, this information should be first utilized. Otherwise the following sections describe the key aspects to developing a Maintenance Strategy.

4.3.1 System Description

The system description is a brief overview of the system or components to define operating context, functions, and system boundaries. Manufacturer and model numbers of major components should be identified. Items that may be contained in the system description include:

- Process Flow Diagram (PFD)
- Block Diagram
- P&ID
- Valve and Line Schedule
- Equipment Schedule
- Operating context from RCM analysis
- C&Q documentation
- Materials of Construction (MOC)

4.3.2 System and Component Classification

The system and component classification defines:

- Location priority/criticality ranking
- GMP impact
- Process safety management (e.g., mechanical integrity)
- Environmental classification of system and components (with rationale)

4.3.3 Science-Based Quality Risk Management

Risk management is a systematic application of management policies, procedures, and practices to the task of identifying, assessing, controlling, and monitoring risks. It normally is an iterative process.

Risk management should be based on good science and product and process understanding, e.g., an understanding of CQAs, which is based upon and ultimately traceable back to the relevant regulatory submission.

Qualitative or quantitative techniques may be used. The focus should be on the risk posed to patient safety and product quality.

Risk management should reduce risks to an acceptable level. Complete elimination of risk is neither practical nor necessary.

For a given organization, a framework for making risk management decisions should be defined to ensure consistency of application across functions. Such a framework is implemented most effectively when it is incorporated into the overall QMS.

4.3.3.1 *Quality Risk Management for Maintenance*

This Guide supports a risk-based approach to the determination of which category of maintenance practices (see Chapter 3) should be applied to a system or its components. Risk management should be part of the analysis performed prior to an asset being placed in service and in many cases will involve the maintenance unit. The maintenance unit has the responsibility to apply its Maintenance Program and develop Maintenance Plans according to the risk assessment.

A QRM approach should be used to identify and manage to an acceptable level the risks associated with maintenance activities and to identify those elements of maintenance that may impact product quality and patient safety.

Risks to patient safety and product quality are not the only risks to consider. In addition to the GMP requirements, a comprehensive Maintenance Program should address other drivers for performing maintenance. The organization also may apply the same approach to other applicable risk areas such as:

- Healthy and safety
- Environmental protection
- Business continuity

However, it is expected that many of the recommended practices of this Guide will contribute toward meeting or exceeding other requirements of a Maintenance Program. It should be noted that requirements based upon other drivers may result in additional controls or activities that extend beyond the Maintenance Good Practices recommended in this Guide.

Risk management provides an opportunity to scale activities appropriately. The benefit is achieved only if organizations are prepared to use risk assessments to justify a reduction or increase in the scale of activities or an omission or inclusion of an activity.

Risk assessments may help with determining which level of maintenance practices to apply by identifying:

- Systems and components which may affect patient safety and product quality
- Systems and components for which extra maintenance practices could be applied to minimize risk to HSE or business continuity

Risk assessments also describe functional failures, failure modes, consequences, and the mitigation approach, including:

- RCM Analysis
- FMEA
- Root Cause Failure Analysis (RCFA)
- OEM recommendations
- Data analytics of key process and maintenance data
- Input from SMEs
- Operational experience

The risk-based approach should be focused and resourced for maximum effectiveness. Organizations should not invest more effort and time into the risk management process than is commensurate with the potential impact on the supported business processes. Risk assessments should be periodically reviewed and continually reviewed as additional information, data and expertise, and new methods become available.

For more information on risk management from a reliability perspective, refer to *ISPE Good Practice Guide: Equipment Reliability* [7], Chapter 4.

4.3.4 Maintenance Tasks

Maintenance Tasks may describe CM, PM, and PdM tasks with supporting rationale, if not already included in the risk assessment and required by the site. This may include:

- CMMS records
- GMP library
- Equipment manuals
- Corrective Action and Preventive Action (CAPA) or discrepancy information
- Periodic asset reviews or evaluations
- Change controls

4.3.5 Intervals and Tolerances

Intervals and tolerances may describe the rationale for the selection of intervals, on-condition maintenance or calibrations, and the selection of failure and adjustment limits. This may include:

- Critical operational data and measurement uncertainty analyses
- CMMS records
- Periodic equipment reviews or evaluations
- Change controls
- CAPA or discrepancy information
- Data analytics of key process and maintenance data

4.3.6 Spare Parts

The spare parts section of the Maintenance Strategy may describe spare parts requirements, including sourcing information. This may include:

- FMECA (to identify critical spare parts)
- CMMS records
- GMP library
- Equipment manuals

- Periodic asset reviews or evaluations
- Change controls
- CAPA or discrepancy information
- BOM
- Vendor parts information (part number, description, lead time)
- Obsolescence strategy

An example of a Maintenance Strategy template is provided in Chapter 12 (Appendix 4).

4.4 Maintenance Plan

Maintenance Plans are the specific maintenance instructions or tasks, resulting from the System Maintenance Strategy, that are performed on components, equipment, or systems. Maintenance Plans should be prepared in accordance with requirements established in the Maintenance Program and System Maintenance Strategy. The plans should be executed to maintain systems (and their components) in proper working order and to monitor performance in order to detect discrepancies or conditions that might lead to failure.

Maintenance Plans may include:

- CM and On-condition/on-performance based maintenance
- PM
- PdM
- Job plans
- Spare parts management
- Operational inspections, surveillances, and checks

Maintenance Plans resulting from the System Maintenance Strategy are usually time based or use/condition performance based, depending upon the asset and process requirements. Maintenance Plans may be commonly known as PM WOs although they can take other forms as well (e.g., corrective WOs, predictive WOs). For further information, see Section 4.5 of this Guide.

Maintenance Plans can be established and performed on a system level and/or component level. Instructions for maintenance can be common and applicable to several systems or specific to a given system or component. Tasks outlined in the Maintenance Plan should be described in sufficient detail to ensure proper and consistent work execution by the range of persons qualified to execute the work. Maintenance Plans should provide clear and concise instructions to the technician performing the tasks and should take account of the technician's knowledge, experience, and skill sets. Maintenance Plans also could include acceptance criteria for any tests and inspections to be performed to ensure proper performance.

Maintenance Plans are documents that are used when developing the tasks needed to properly maintain systems (or their components, i.e., facility, site, or manufacturing equipment). Maintenance Plans provide a consistent approach to preparing and developing the list of maintenance tasks that should be followed to ensure the continued operation and maintenance of an equipment component, process, or system in a systematic way.

An example of a Maintenance Good Practice is traceability (e.g., documentation) of maintenance performed on components in a GMP system or equipment. This could include specific details on PM, PdM, CM, spare parts, etc.

Two examples of Maintenance Plans are provided in Chapter 12 (Appendix 4).

An estimated time to complete each step should be identified as well as any parts, tools, or special equipment that is required. Additionally, any required special permits to safely complete the work should be included (e.g., confined space, hot work, working at heights, etc.).

An example of a Maintenance Best Practice is to have visual aides to go along with the maintenance task list items in the Maintenance Plan. The aides could be overlays on a P&ID showing component locations and specific tolerance or a series of pictures showing what “good” and “bad” would look like on the specific component being maintained.

If the maintenance is performed on a large system (e.g., Water for Injection (WFI) distribution system) or piece of equipment with complex PM (e.g., bioreactor), a checklist can be created to help maintenance staff in performing the tasks. An example of a Maintenance Plan Checklist is given in Chapter 12 (Appendix 4).

Typically, the first section of a Maintenance Plan should contain the PM title and the equipment or system information, such as:

- Title
 - Must include information to help searching for and locating a job plan for future use (rebuild pump, replace seal, change oil, calibrate, etc.)
- Equipment/System Identification Number or Asset Number
 - Usually as identified in the CMMS system or Equipment Master List
- Equipment/System Brief Description
 - Identifies the specific equipment that is covered, e.g., Compressor 1, Tablet Press 40 stations
- Lockout/Tagout (LOTO), Job Hazard Analysis (JHA), Personal Protective Equipment (PPE) required to perform the task and permits required (e.g., fire or confined space permits)
- Customer contact information
- Equipment/System Location
 - Identifies the physical location of the equipment within the site or facility, i.e., building number or room number, etc.
 - > Equipment/System manufacturer
 - > Equipment/System model number
 - > Equipment/System serial number
 - > Equipment/System classification (i.e., GMP or non-GMP)

- Maintenance Plan Task Type
 - Identifies the overall type of work and usually related with the craft or workgroup that executes the task, i.e., mechanical, electrical, etc.
- Maintenance Plan Task Frequency
 - Establishes the periodicity or frequency at which the specific tasks listed in the plan will be performed, i.e., weekly, monthly, quarterly, meter based on running hours, differential pressure, etc.
 - In some instances, this overall Maintenance Plan frequency is not mentioned in the header; instead the specific tasks are organized in terms of the specific frequency of execution
- Maintenance Plan Version Control
 - Allows traceability of changes over specific tasks or equipment information.

The second section of the Maintenance Plan should contain the specific maintenance task instructions that have the following attributes:

- Task or Item Number
 - Identifies Maintenance Tasks listed in the plan and lists line item numbers.
- Maintenance Task Description
 - Includes the very brief description of the work to be performed, e.g., change the oil in the gearbox, inspect and lubricate pump. Include references to applicable SOPs here if stored in a different system of record.
- Frequency
 - Identifies the frequency at which the maintenance task is to be performed, e.g., 7 days, 30 days, 90 days, 180 days, or 365 days – usually days are used rather than weekly, monthly, quarterly, etc.
 - Meter based frequencies also can be used, i.e., 100 hours, 500 hours, etc.
 - Situational frequencies based on inspection results also can be included.
- Craft
 - Identifies the type of craft or workgroup skill required to perform the maintenance task, e.g., machinist, mechanic, or electrician
- Crafts Persons Required
 - Indicates the number of crafts persons required to perform the maintenance task
- Equipment Condition
 - If the equipment should be running or shutdown when certain maintenance tasks are performed, this condition should be indicated here.
 - In some cases where a specific task is not called out for pre or post-cleaning activities, the safety condition of the equipment may be indicated here, e.g., in biological or explosive operations, a chemical clean and flush may be required before executing work to protect the maintenance technician

- Type
 - Identifies the type of Maintenance Best Practice task, e.g., PM, PdM, CM
- Procedure/Task Number
 - Where specific procedures have been written for specific tasks, the unique procedure number should be entered, and typically, this will be the unique identifier used in the Plant Documentation System
- Estimated Time (hours)
 - Where the estimated time to complete the task should be entered, this is an educated estimate based on previous experience or established estimating best practice
- Special Tools/Materials
 - Identifies any special tools not usually carried in a crafts person's toolbox, e.g., torque wrenches, man-lifts, ladders, a hazardous waste container, or PPE.
 - Additional remarks that apply specifically to the performance of the task should be included
- Affected Equipment
 - If the maintenance task will require shutting down connected assets, the affected area owners should be listed and notified
- Requalification requirements
 - Examples include rotation verification, alignment, calibration, leak test, pressure check, sampling, temperature checks, vibration, IR scan, etc.
 - Additionally, any downstream equipment that may need follow-up action after maintenance is performed (e.g., changing High Efficiency Particulate Air (HEPA) filters, clean room certifications, etc.)

For GMP systems or equipment, the maintenance department should decide whether to develop an individual Maintenance Plan for each system or each piece of equipment installed. Alternatively, a Maintenance Plan for each type or class of system or equipment installed may be developed and applied to all systems or equipment of the same type or class. Where a system or equipment of the same type or class operates in different environments or conditions, it may be preferable to prepare individual specific Maintenance Plans.

4.5 Types of Maintenance

4.5.1 Purpose

Two modes of maintenance should be considered in building a Maintenance Program:

- **Proactive:** preventive, predictive, detective, condition monitoring (online through dynamic instrumentation methods, or offline utilizing particulate sampling) and planned CM
- **Reactive:** run to failure, emergency (breakdown) work, and unplanned CM

Either mode of maintenance may be appropriate. An effective Maintenance Program has a balance of proactive and reactive activities.

4.5.2 Proactive Maintenance Modes

4.5.2.1 Preventive Maintenance

PM is based either on calendar time or on run time. The intention is to perform the maintenance activity on a regular basis to ensure that the equipment is operating within tolerances, by minimizing wear and/or preventing failures. If a piece of equipment is operated a consistent number of hours each week, the maintenance can be scheduled based on calendar time. If use of a piece of equipment is sporadic, equipment run time is usually considered a better method.

The maintenance performed and the frequency at which it is performed should consider a variety of data sources, such as the manufacturer's recommendations and historical data. The maintenance unit should have documentation and a clear rationale to justify the PM frequency and task selection. This should be included in the System Maintenance Strategy.

Another important element of a PM program is in the execution of the work. For example, clean room environments have a high cost of recovery and requalification when disrupted. Therefore, it is usually cost-effective to perform all PM during the same scheduled shutdown. Logically grouping PM activities also can reduce errors. If, for example, some amount of disassembly is required to perform PM, minimizing the number of times the machine is taken apart also minimizes possible assembly and adjustment errors. Further, consider that each time maintenance is performed, it may not be performed by the same person which may introduce another variable in the process.

Organizations may schedule entire site shutdowns (annually or even biannually). This may mean that PM may be done sooner or more often than necessary. This extra cost is typically much less than the cost of an additional shutdown and is usually acceptable. Care should be given to ensure compliance with PM frequency guidelines defined in the organization's Maintenance Strategy.

Where only a part or a section of operations or site is shut down for maintenance, separation of activities and proper controls should be implemented to ensure that ongoing operations are not affected. For example, HVAC systems may be interdependent within a manufacturing zone. Shutting down one system may impact pressurizations and will require special consideration.

In the design of equipment, systems, and facilities, consideration should be given to provide access to equipment with more frequent maintenance needs. Where possible, this access should allow PM to be accomplished without a shut down. Installing redundant equipment or extending grease fittings may provide appropriate alternatives to enable continuing operation during PM. Space and access are important considerations when designing for effective and efficient PM.

Due to the practicality of the PM scheduling, an acceptable time frame should be established for completing scheduled PM before the PM is considered past due and subject to a deviation process or change control. Acceptable time frames should be predefined in the Maintenance Strategy and should be applied consistently. Typical examples of time frames include:

- Weekly PM: Plus or minus 2 days
- Monthly PM: Plus or minus 7 days
- Three month PM: Plus or minus 14 days
- Six month or longer PM: Plus or minus 30 days

The next scheduled date for the PM can either be scheduled on the same day of each week/month or be configured from the actual completion date of the previous PM.

A Maintenance Best Practice is to include a PM Optimization (PMO) strategy into the maintenance function. The PMO would include a look back at all maintenance activities completed within an acceptable time frame to verify that the correct level of PM is taking place. If, upon inspection during the PM activity, there were no faults found for at least three consecutive instances, then it may be acceptable to lengthen the PM interval. If, however, there were too many random failures between PM activities, then it may be advisable to shorten the PM interval. Consequently, an investigation should be initiated to determine the root cause, and a solution should be implemented. A standardized strategy for this interval modification should be established within the maintenance function.

4.5.2.2 Predictive Maintenance, Detective, and Condition Monitoring

PdM is based on identifying and monitoring key equipment operating parameters to determine the optimal time for performing maintenance. This method is considered Best Practice and has the advantage of performing maintenance when it is most needed rather than simply based on time. However, the monitoring of any parameter should be based on calendar time or equipment run time, and should be defined in the Maintenance Program strategy. Maintenance should be performed only if the operating parameters indicate that it is required.

While PdM can be used to inform the shutdown program, the limitation of PdM is that it may not be suitable for scheduled shutdowns. Parameters should be monitored to detect potential problems, allowing the maintenance unit to perform scheduled CM without shutting down production. Alternatively, work should be completed between production runs, without disrupting operations or conditions in classified areas. There may be opportunities when production is not running when specific maintenance tasks can be completed, as long as the integrity of operations is not put at increased risk.

Examples of predictive and detective maintenance indicators include:

- Vibration
- Pressure
- Ultrasound
- Chemical analysis of lubricants
- Thermographic analysis
- Infrared temperature readings
- Motor current analysis
- High speed videography
- Filter differential pressure

These readings usually can be accomplished while the equipment is in operation, minimizing disruption. If taken at the appropriate time, any required PM can be scheduled for the next shutdown. In most cases, if readings are being taken on a regular basis and a baseline has been established, a trend will be seen well in advance of a failure.

Monitoring and detective activities also can be performed without the use of instruments. This type of monitoring typically leads to corrective action as opposed to PM. Operations personnel should be trained to hear, see, feel, and smell changes in the equipment and environment. Changes to these attributes can predict a potential failure and allow a timely response to correct these observations to prevent deviations or failures. For example, an operator might observe a loose connection or hear a new sound. These abnormalities normally can be corrected with very little disruption to production. The extent of adjustments permitted without formal documentation should be defined.

4.5.3 *Reactive/Emergency Maintenance*

Reactive maintenance involves operating a piece of equipment until it fails and then repairing it. Failure may not involve a complete breakdown; the equipment may simply be operating outside specified parameters. Failures that result in product loss or pose a threat to the safety of personnel or the environment may incur greatest cost and should be defined and evaluated in the development of the Maintenance Program. When a failure results in system or equipment downtime, the downtime will normally be longer and more expensive than it could have been if the same repair were performed in a planned mode. Further delay may be caused by lack of availability of the required personnel or parts. A process for reactive maintenance should be established that includes measures to ensure that the qualified state of the equipment has not been put at increased risk. This may be accomplished through one or a combination of:

- Requalification
- Specified return-to-service requirements
- Start-up testing
- Use of functionally equivalent or identical spare parts

A written policy should be established to provide guidance on when each of these practices can be used.

Where proactive maintenance cannot be performed, reactive maintenance should be performed. This may be required for electronic components as well as hermetically sealed refrigeration systems, such as those used on coolers and freezers. Some proactive maintenance can be done on such items, but the sealed parts (such as the compressor, thermostatic expansion valve, and specific electronic parts) cannot be maintained or tested. Testing of the redundant systems and the switchover process should be part of the Maintenance Program for the asset.

5 Maintenance Management

Maintenance Management and work execution consist of the processes and controls used in the delivery of maintenance services. This chapter seeks to highlight the compliance aspects associated with the use of maintenance systems used to execute maintenance work. It is through the effective use of these systems that evidence is provided of the proper delivery and control of the maintenance service. Information in these systems should be collated, recorded, and managed accurately.

Information that is entered into an MMS (Maintenance Management System) is determined by the overall Maintenance Strategy and Maintenance Program strategy for the facility. An MMS is the collection of processes and work practices used by the maintenance unit to execute the work. The MMS can be computer-based, paper-based, or a mixture of both. In larger organizations with multiple sites and more complex MMS, it is often referred to as Enterprise Asset Management Systems (EAMS). In building the MMS, it is important to consider whether it will be deployed at a single site or across several sites. The latter requires significant effort to build a core framework for the MMS that can be applied across sites and customized to an extent that it can be deployed locally, but not to the extent that it becomes a different system which counters the benefit of harmonization. It is recommended that maintenance processes are harmonized across sites.

Maintenance processes and controls normally involve the following systems:

- Records for facilities, systems, and equipment
- Labor resources
- Planned maintenance
- Spare parts
- CMMS/EAMS
- Maintenance documentation
- Work order management
- Documentation assessment

5.1 Records for Facilities, Systems, and Equipment

The MMS serves as the repository of information for maintenance activities on quality critical systems. This has GMP relevance and therefore needs to be comprehensive and accurate. Various types of information should be gathered and recorded for equipment, systems, and facilities that will be tracked by the MMS depending upon a predetermined Maintenance Strategy.

Maintenance activities and the records of these activities are typically processed at the equipment level. It is important to establish a discrete and unique identity for each asset being maintained. In the case of systems such as fluid bed dryers, there may be several unique equipment components that comprise the system. Assets should be cataloged in a way that facilitates the maintenance processes. A parent-child hierarchy is often utilized to structure the facilities, systems, equipment, and components relationship for ease of organization. When an asset is put into operation, the MMS may include:

- Unique equipment identification number

- Equipment description
- Manufacturer
- Model number
- Serial number
- Equipment type, e.g., granulator, fermenter, blister machine
- GMP assessment (e.g., criticality risk assessment)
- Service agreement, warranty data
- Spare parts
- BOM/instrumentation
- Calibration requirements
- Technical data (i.e., hazardous area)
- Location (building, room, etc.)
- Owner information (e.g., cost center, production unit)
- Qualification status and documentation
- Historical data (in the case of a pre-owned asset)
- Changes/modifications
- Specifications

5.2 Labor Resources

The MMS system should include a list of roles and responsibilities. For example, a Maintenance team may consist of operators and technicians that are responsible for manufacturing steps or processes also in addition to light maintenance. Individuals should be identified and held accountable for activities completed. The MMS should contain:

- List of technicians and operators
- Qualifications and experience of technicians and operators
- Skills and training records
- Working shifts (to enable resource planning)
- Signature log

A Maintenance Good Practice for those working on GMP systems is to have GMP training with training and qualifications adequately documented.

In addition to the internal Maintenance team, external vendors may be included to perform specialized maintenance activities. The vendor should be qualified to perform work on GMP systems and be held at the same level of expectation with GMP activities.

5.3 Planned Maintenance

Planned Maintenance is defined as all documented and defined maintenance activities, where specific resources (labor, materials, tools, equipment) have been predetermined in order to carry out the predetermined tasks and to ensure their availability before initiating any job.

One characteristic of Planned Maintenance is the use of data and information gathered through the regular execution and documentation of maintenance activities following a routine or continuous monitoring process and Maintenance Strategy program.

5.3.1 Preventive Maintenance

PM is defined as all necessary measures to maintain and ensure satisfactory operating conditions of assets, by providing a fixed interval or trigger point, for systematic inspection, detection, and correction of incipient failures either before they occur or before they develop into major defects.

It is important to establish PM tasks and frequencies in an MMS and these should be established before the equipment or asset is placed in service. Typically, the PM is drafted and implemented during the commissioning phase of a certain equipment/system, and the established PM is a required component in the qualification testing of equipment/system. The specific tasks and respective frequencies are developed in accordance with the Maintenance Program strategy and consider the various inputs available, including aspects such as recommendations from the OEM. The PM program and procedure should be documented and controlled as GMP documentation.

The level of detail contained within the tasks and the specific tasks that are documented as part of the PM are important considerations when developing the PM program. Some organizations have general tasks (e.g., lubricate motor) while others use more specific tasks (e.g., remove shield, lubricate three fittings on top of motor, lubricate three fittings on bottom of motor, etc.). The correct level of specificity depends upon the equipment, risk assessment, skill of the persons performing the work, and numerous other factors. Regardless, there should be an appropriate level of detail in task instructions such that the organization can substantiate proper execution of the work.

Tasks and frequencies can be modified, expanded, or deleted based on actual experience with the equipment or system. The MMS should provide a mechanism to analyze the PM program and provide confirmation and guidance for task execution and in some cases, modification. Typically, a “notes” or “comments” section is included in a PM task sheet (or electronic record) for recording information about the maintenance task or equipment condition that can facilitate continual improvement of the program. This is considered Maintenance Good Practice.

The MMS should be capable of keeping track of when PM tasks are due, when they were completed, and the as-found condition for the respective machine or system when the PM work is initiated. When a discrepancy is discovered as the result of performing PM, this should be reported, documented, and acted upon. The nature of the condition and its potential impact generally will determine the level to which a discrepancy will be escalated. An out of specification finding on a critical component that may affect patient safety and product quality should be documented and investigated with the Quality unit at the time of observation. Minor items that do not impact drug quality could be handled within the maintenance department. This is Maintenance Good Practice for GMP systems. After the PM tasks have been completed, a return-to-service check should be performed and notification of completion should be produced. The PM tasks should be documented on the WO form or electronic record.

Time-based PM tasks should have provisions to be completed when the task due date falls on a non-working day. Most programs provide flexibility by establishing a window within which the PM can be completed. Time-based PM tasks should have a means to verify that all of the tasks that are due are in fact generated and completed per the established program. The organization should have a system that ensures all required PM tasks are being executed. Many organizations issue PM tasks 30 to 45 days in advance of the anticipated start date and cross-check the list of PM tasks issued against a master schedule that is kept for the site. A CMMS has the advantage of being able to report on upcoming, due, and past due work.

PM tasks also can be based on hours of operation (run time) or other measurable parameters or conditions (as in PdM). The organization should substantiate the rationale for this approach and also ensure that when a machine hits a milestone that it receives the appropriate maintenance.

5.3.2 Corrective Maintenance

CM comprises measures for restoring the original state of the asset and includes appropriate documentation and analysis of data. Part of a CM activity is proper planning with alternative solutions if necessary, creating maintenance task lists, including costs, scheduling, labor, and materials.

After the tasks have been completed, a functional test and acceptance inspection (e.g., return to service) should be performed and notification of completion should be produced. The repair tasks should be documented on the WO form or electronic record.

As with PM activities, the MMS should be capable of tracking when CM activities are requested, when they are completed, and the as-found condition for the respective machine or system when the repair work is initiated. The as-found condition of the reported defect and its potential impact to patient safety and product quality should be assessed with the Quality unit, and a discrepancy may be escalated if necessary. The MMS should also monitor the timeliness of maintenance request completion, and proper notation and justification should be provided for maintenance requests not completed within the pre-established time frame to assess the impact of equipment defect or malfunction on product quality or patient safety.

During emergency equipment or asset failure, CM may need to be performed on the spot without following the sequential activities in the Planned Maintenance framework. Procedural controls should be in place to describe the approved response process with adjusted sequence to accommodate the urgent nature of the situation, and it should also provide a mechanism for retrospective documentation on the WO form or electronic record to comply with maintenance record requirements.

5.4 Spare Parts

Spare parts are used to replace existing parts that show signs of wear during routine maintenance and parts that break during routine operation. This section considers like-for-like parts and covers the identification, management, and storage systems for spare parts to ensure compliance with GMPs.

The spare parts for each system should be divided into product impact or non-product impact parts during the initial C&Q risk assessment. This will help maintenance staff in the future to know if they have to replace a component with a like-for-like part or may purchase a part from a source other than the initial manufacturer/vendor.

Recommended spare parts also should be captured in the CMMS. The initial setup of these items should be based on the OEM recommended parts. This list can be expanded or reduced based on actual experience with the equipment and its intended duty, SME inputs, and experience from FAT/SAT, etc. The parts that have been identified as having the potential to impact product quality typically are identified during the qualification process.

A “where used” tag for spare parts may be useful to optimize the utilization of the parts. Spare parts may be dedicated or labeled for a specific machine or product; in this case, it is usually considered essential to have a system that controls the application of parts.

The point of control should be identified for spare parts. Organizations may control spare parts at the point of installation, i.e., the part and installation are documented on the WO. Alternatively, organizations may document or control the part as it is issued from the spare parts inventory.

Appropriate controls should be established for the application of spare parts to GMP systems and equipment, e.g., when an organization contracts to have the resin replaced in its water system, the new resin being installed should be verified as identical to the existing resin. An appropriate method would be to perform the resin change under a change control or work order with necessary documentation and signatures verifying the replacement. Critical spare parts should have a specification, certification, and/or manufacturer part number to facilitate the verification.

A purchase order is not considered sufficient control, as the item that is delivered and installed by the contractor could inadvertently deviate from the original.

When determining how and where to control the application of spare parts or materials that have been identified as having the potential to impact product quality, consideration should be given to the possibility that the application could be performed by personnel outside of the maintenance unit. Spare parts management could also be outsourced, with the external provider supplying people and expertise while located on site and utilizing the site MMS systems and processes.

5.4.1 *Like-for-Like or Functionally Equivalent Replacement Parts*

The preferred spare part is an identical replacement with the same:

- Manufacturer
- Part number
- Material of construction
- Version

Obtaining an identical part may not be possible and a decision will be required regarding the equivalence of a spare part with the part which it replaces. Criteria should be established for determining whether a spare part is acceptable or requires additional evaluation or change control.

The more extensive the documentation to show that the replacement part is functionally equivalent to the part used during qualification, the less the expectation to demonstrate that the system or equipment will function in its original qualification is needed. Requalification or adequate testing may be required to ensure that the system or equipment will work identically to when it was originally qualified.

Acceptability is determined at the point of control for the application of spare parts. The Maintenance Program should define a process for making the determination, and appropriate training should be provided for personnel involved, such as the maintenance SME.

Considerations in determining functional equivalence typically involve fit, form, finish, and function. More specific characteristics include:

- Performance
- Specifications
- Physical characteristics (e.g., dimensions and materials of construction)
- Usability

- Maintainability
- Cleanability
- Safety

If the supplier of the spare part is not the OEM or an approved alternate of the spare part is provided by a supplier other than the OEM, an assessment should be performed.

Requalification of the equipment or system is generally not required for like-for-like or functionally equivalent changes. Maintenance Good Practice is to define like-for-like and functional equivalence in a controlled document with all involved stakeholders and to establish a predetermined process to document like-for-like replacement.

5.4.2 Controlling and Managing Spare Parts

5.4.2.1 Bill of Materials

A BOM for a particular item of equipment is a list of the spare parts that are required to support the maintenance and continued operation of the equipment. These spares should be accurately specified with part numbers, etc. They may not be stored on site, but should be available from the supplier, as required. For non-urgent or quick delivery items, a business decision may be made not to stock an item.

A system should be established at the point of control to ensure that the correct critical spares are used. This may be achieved electronically, in a validated system, or controlled as part of the WO process.

If a piece of equipment (e.g., a pump) is replaced by another and then repaired or returned to stock, traceability through its life should be visible (i.e., products on which it has been used, decontamination, cleanliness, etc.). A system to document decontamination/cleaning, repair, bagging, and fitness for use should be established. The equipment history of the part should be both maintained and retrievable; this also can apply to tools and materials.

A spare parts policy should include consideration of the use of repaired items (e.g., pumps). For example, in a potent compound area, all parts may be dedicated to that area or product (e.g., penicillin). In this case, the parts should be appropriately labeled.

5.4.2.2 Identification and Traceability

Information should be maintained on the origin of maintenance materials and spares, manufacturer, storage conditions, etc. Where the criticality of the equipment is high, spares should be inspected and have appropriate certificates (e.g., piping that will be used in high purity water systems).

5.4.2.3 Identifying and Categorizing Spare Parts

When determining how to deal with spare parts, aspects such as economics, manufacturer's recommendations, prior experience, and structured reviews (FMECA, RCM, etc.) should be considered. Options include:

- Spare parts to be specified and held locally, either in a central organized and controlled store or on site
- Spare parts to be specified and not stocked
- Spare parts not to be specified and not stocked
- Spare parts to be specified and held by supplier

Critical spare parts should be identified within the spare parts list. Critical spare parts are those that must be readily available to minimize equipment and system downtime when repair is required, and they are determined through risk assessment considering the organization's tolerance level to production delay from equipment and system downtime.

5.4.2.4 Storage of Spares

Controls may be established on the procurement and storage processes for spare parts as part of good business practice. Depending on the size of the site, a central store may be required. If a central store exists, it should be cataloged, secured, and carefully managed. Uncontrolled stores may increase the risk of error and lack of auditable documentation.

Typically, locally controlled stores are used where spare parts are applied frequently or when they are required immediately (i.e., faster than a central store could provide).

5.4.2.5 Stores Management

Spare parts should be stored in appropriate conditions and in line with manufacturer's recommendations. Spare parts can rust or become damaged or dirty if not stored in a suitable environment. In addition, where parts, unused materials, or equipment are returned to the store room, proper handling procedures should be in place to protect against cross-contamination. For example, only those parts and materials that are needed for a repair should be issued (e.g., an entire box of filters should not be taken into a granulation suite to make an emergency filter change, as there is a risk to unused filters of exposure to product).

It is considered an important business practice to maintain an inventory of spare parts at the correct level. Monitoring the usage of spare parts will help to establish the correct stock levels. Monitoring the cost will help to decide the right spare parts policy, where the cost of spare parts is a significant parameter in determining the Maintenance Strategy and contributing to the organization's financial performance.

Considerations for the storage of spares include:

- Manufacturer's recommendations, e.g., temperature and humidity ranges
- Security of stores
- Potential for cross-contamination
- Cleanliness requirements
- Accessibility
- Shelf life

5.5 Paper-Based Maintenance Management Systems

Manual or paper-based systems may be used where the initial investment and ongoing operating expenses of a computerized system are difficult to justify. However, when deciding whether or not to have a computerized system, the organization should consider factors in addition to the financial analysis. For example, scheduling and reporting are facilitated more easily by a computerized system, data integrity is more rigorous with system audit trails to detect unauthorized changes in a computerized system, manual processing errors can be reduced, and more opportunities are available to harmonize processes within and across several sites with a computerized system.

From a GMP compliance perspective, either system is acceptable, as long as it is designed and implemented appropriately.

In a manual system, it is considered Maintenance Good Practice for each piece of equipment or asset to have the following attributes in order to be effectively managed and to meet GMP requirements:

- Dedicated equipment file for each unique asset
- Detailed plan of required PM tasks and frequencies
- Method of tracking upcoming and completed PM tasks
- Method of tracking scheduled WOs
- PM and WO history file by asset
- BOM and spare parts lists

Controlled access to all equipment files and documentation is required to maintain the integrity of the files. The program strategy should detail how much legacy data to retain in each file before archiving. Typically, organizations retain data from two or three years in the local files before archiving. For archived records, a system should be established to ensure that documents can be retained according to a predetermined long-term storage procedure and that the documents can be retrieved when required. Linkage to other asset information management systems (i.e., engineering data systems, GMP libraries, etc.) should be in place to ensure that all asset information is synchronized.

5.6 Computerized Maintenance Management Systems

With the increasing digitalization of operations and work processes, CMMS utilization has become very common and is considered a general good practice. Market competition also makes many CMMS products readily accessible and affordable to organizations. Types of CMMSs include:

- Mainframe-based
- PC network-based
- Web-based
- Standalone

In selecting a system, organizations should first develop detailed user requirements and evaluate options against these requirements.

Off-the-shelf systems can be configured to accommodate the requirements of an organization and have the advantages of support availability and less development work. CMMS may also have linkage to other organizational data system such as accounting or training systems.

Where the CMMS will control the maintenance and history of GMP systems, then Maintenance Good Practices apply and the CMMS should have the following capabilities:

- Audit Trail
 - To track changes to the CMMS data files.
- Security
 - Password protection to prevent unauthorized access and changing of data.

- Role-Based Access
 - Varying access levels based on specific roles and responsibilities.
- PM Scheduling Module
 - Should automatically schedule PM WOs based on a predetermined frequency.
- Work Order Module
 - Should allow the maintenance unit to approve WRs and create WOs for execution
 - A method of closing out the WO usually is required
 - Parameters (e.g., work type) and classification information (e.g., breakdown codes) on the WO can help both in the routing of the WO and with analyzing and improving asset performance
- Equipment Information Module
 - To capture all relevant equipment information.
- Equipment Work History Module
 - Should capture all work performed on a particular piece of equipment and should allow engineering and maintenance personnel to evaluate any recurring issues
 - This module may provide the required justification for equipment replacement and problem/root cause analysis
 - Materials, service contracts, and labor costs should be attached or linked to the equipment on which work is performed
- BOM and Spare Parts Module
- Report Generation

5.6.1 Paperless Systems

Where a paperless system is used to manage the maintenance, calibration, and history of GMP systems, it should be validated and all users trained on how to extract and enter data.

Computer system validation is covered in *ISPE GAMP® 5: A Risk-Based Approach to Compliant GxP Computerized Systems* [19].

5.6.2 Hybrid Systems

CMMSs usually are hybrids, using the CMMS for most processes and reporting. A paper WO (generated by the system) is normally produced, upon which the task data and signatures are recorded. Organizations need to determine how GMP records are managed between computerized and paper systems in order to determine if the CMMS needs to be validated. If all required regulatory information is provided by the paper WOs, the CMMS does not need to be validated.

5.7 Maintenance Documentation

Maintenance activities should follow a defined documentation process, as outlined in the Maintenance Program. The program should refer to the documents required, approval and review processes, document lifecycle management, and electronic records procedures. More specific examples include:

- Equipment File
 - Manuals and all other turnover documentation
 - Spare parts list
 - Instrument list with calibration parameters
 - Relevant Standard Operating Procedures (SOPs)
 - Maintenance Plan
 - Specifications
- History File
 - WRs
 - WOs
 - Procurement documentation
 - Change close out documentation
- Change Management Documentation
 - Change control documents
- Human Resources Documentation
 - List of technicians
 - Position descriptions
 - Calendar, working time, shifts
 - Training needs assessment
- Contractors
 - Qualifications

6 Work Execution

6.1 Work Order Management

This chapter outlines work order management and includes WRs (Work Requests), WOs (Work Orders), planning and scheduling, WO completion, and emergency work.

Effective work order management is an integral part of a maintenance operation. It is the process by which work is:

- Requested
- Prioritized
- Structured
- Planned
- Scheduled
- Executed
- Completed

The information collated during execution is recorded against the WO, forms the basis of the equipment history record, and is the means by which traceability is achieved and trends are established.

A significant amount of work initiated through the WR process is typically for repairs and modifications and may include project work. This type of work should follow the process steps outlined in a WO Flowchart (example provided in Section 6.1.2).

Work originating from the Planned PM Program is normally generated by the MMS, according to the predetermined schedule.

WRs should be reviewed by the appropriate maintenance supervisor or planner, to evaluate if the work is required before they become WOs. The requests should be reviewed for completeness and clarity, as well as for appropriate assignment.

The WO Flowchart should show planned preventive work introduced after the planning stage. Planned preventive work may be prioritized and screened, depending on local requirements.

Work should be subject to work scheduling with the exception of emergency work.

Where work order management is well established, work typically is not started without a WO, but this depends on site specific arrangements.

Work on GMP systems and equipment should follow a prescribed WO process, such as that described in this Guide, to ensure that site history can be maintained and traceability achieved.

Where emergency work is required, as an exception, a WO may not be created prior to work commencement. When emergency work is performed, an appropriate assessment with documentation should be completed in a timely manner to confirm the rationale for completing the work on an emergency basis.

6.1.1 Work Request

The WR process formally initiates a request for work to be performed and may be used as a means of clarifying and screening the need for the work. An initial review of the work requested should be used to confirm that the information provided is relevant and accurate, to establish or confirm the priority or urgency of the work with the Work Requester, and to assign a unique identifier for traceability purposes. The WR also should be assessed to determine the potential of the work to impact product quality. This assessment should be used to trigger change control. For requests that do not result in work being performed, it is not necessary to retain these requests; however, it is advisable for completeness. This is considered Maintenance Best Practice.

Many different methods can be used to initiate a WR, including:

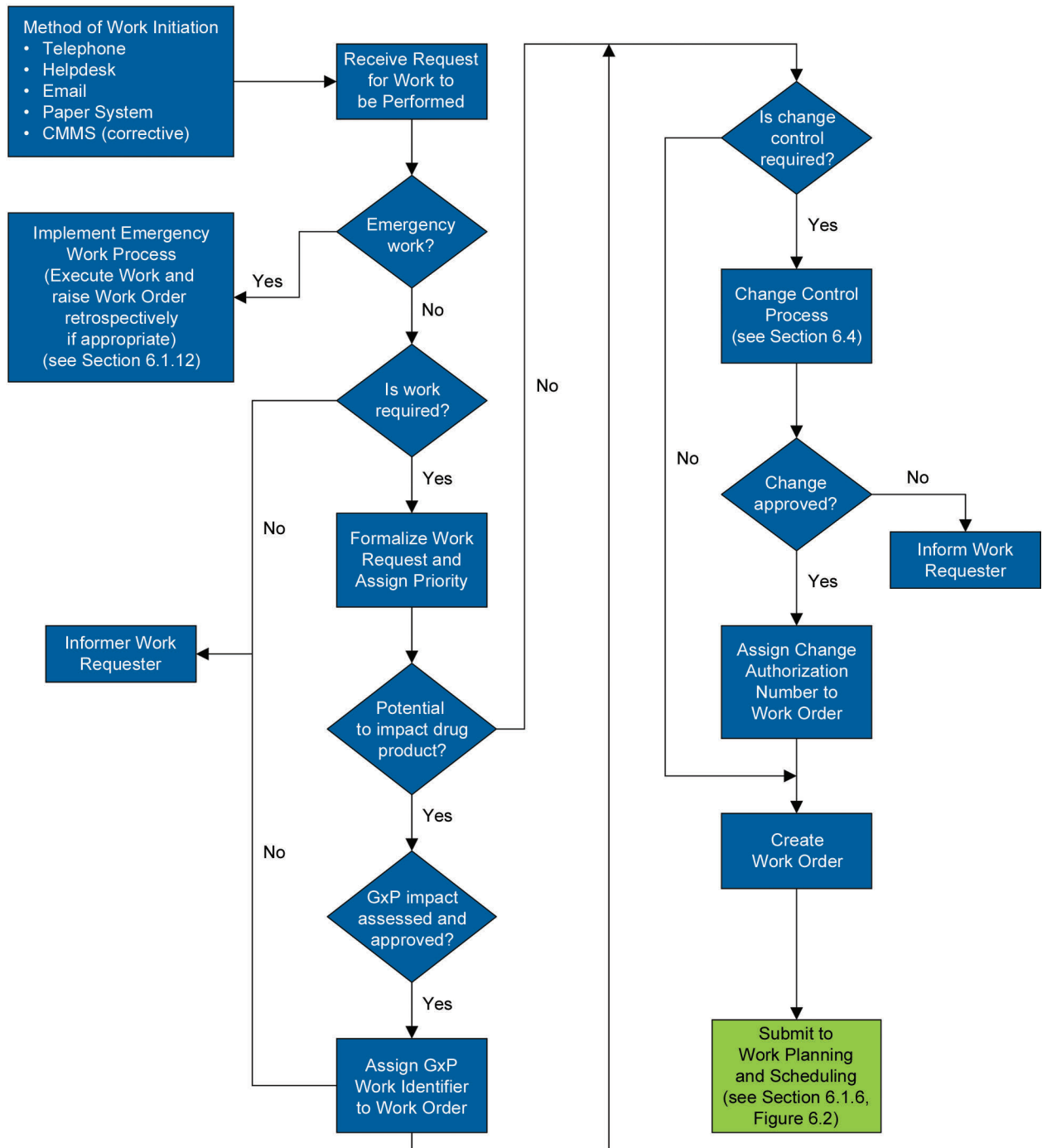
- Paper systems
- Email
- Telephone help desks
- Electronic systems that are part of a CMMS
- Small project request

6.1.2 Typical Work Request to Work Order Flowchart

It is recommended that the maintenance unit develops a work request/work order flowchart to assist in standardizing, optimizing, and training. See Figure 6.1 for a typical WO Flowchart.

The process should consider change control and how it applies to various types of work performed, e.g., emergency work. Although change control carries a particular meaning in a GMP environment, the process of making and recording changes is equally significant for areas such as HSE. Non-GMP critical changes may be differentiated under a separate process, such as engineering change control. The process of implementing changes should be well-defined and documented. This should be GEP compliant. Refer to *ISPE Good Practice Guide: Good Engineering Practice* [4] for more information. Maintenance Good Practice for GMP systems requires the involvement of the Quality unit.

Figure 6.1: Typical Work Order Flowchart



6.1.3 Information Requirements for Work Requests

WRs should contain sufficient information to facilitate later activity, such as planning and scheduling or performance analysis. This is considered Maintenance Good Practice and typically requires:

- Description of work required: Brief outline of the problem being experienced by the originator or site user

- Equipment or system identification number(s): A unique equipment identifier to enable accurate and prompt identification of the equipment
- Whether the work involves or suggests a change or modification
- Location
- Date of request (the time of request also may be included)
- Priority or urgency rating: Means by which work with conflicting demands for resource can be assessed, as agreed by originator and maintenance management
- Classification of work: Means by which the impact of the work on product quality, safety, environment, or the business can be highlighted
- WR number: Unique reference number for traceability and progress monitoring
- Name of originator and contact information: Required for advice on progress, priority adjustment, etc.

The maintenance unit has the responsibility to ensure both the entirety and accuracy of information during the work screening process.

Organizations may request costs as they are incurred.

6.1.4 Work Order

A WR normally progresses to a WO after initial work screening. The WO should contain sufficient information to allow qualified technicians or engineers to perform the work safely, effectively, and efficiently and to minimize the potential for the product quality to be impacted.

The unique WO number assigned to the work provides a necessary means of reference for the collation, recording, and traceability of information relevant to the support of regulatory or statutory compliance.

6.1.5 Information Requirements for Work Orders

A WO may include:

- Unique identifying WO number
- Short description of the work or problem
- Issue date
- Work classification for GMP, e.g., asset identifier
- Reference to change control document if applicable
- Reference to method statement or procedure to be used, if applicable
- Date and time of work performance
- Comments area for any conditions found or recommendations
- Date and time that work is scheduled

- Location details
- Permits required
- PPE required
- List of spare parts and materials used
- QA/HSE involvement

6.1.6 Planning and Scheduling

Planning and scheduling allow work to be executed effectively and efficiently and ensures that work is completed within the predetermined tolerances set out in procedures. It also facilitates decisions regarding:

- Work method
- Allocation of resources
- Use of contractors
- Use or sourcing of spares and materials

The planning and scheduling process does not have direct GMP impact, but may link to some GMP processes (e.g., training, change control). It is considered Maintenance Good Practice.

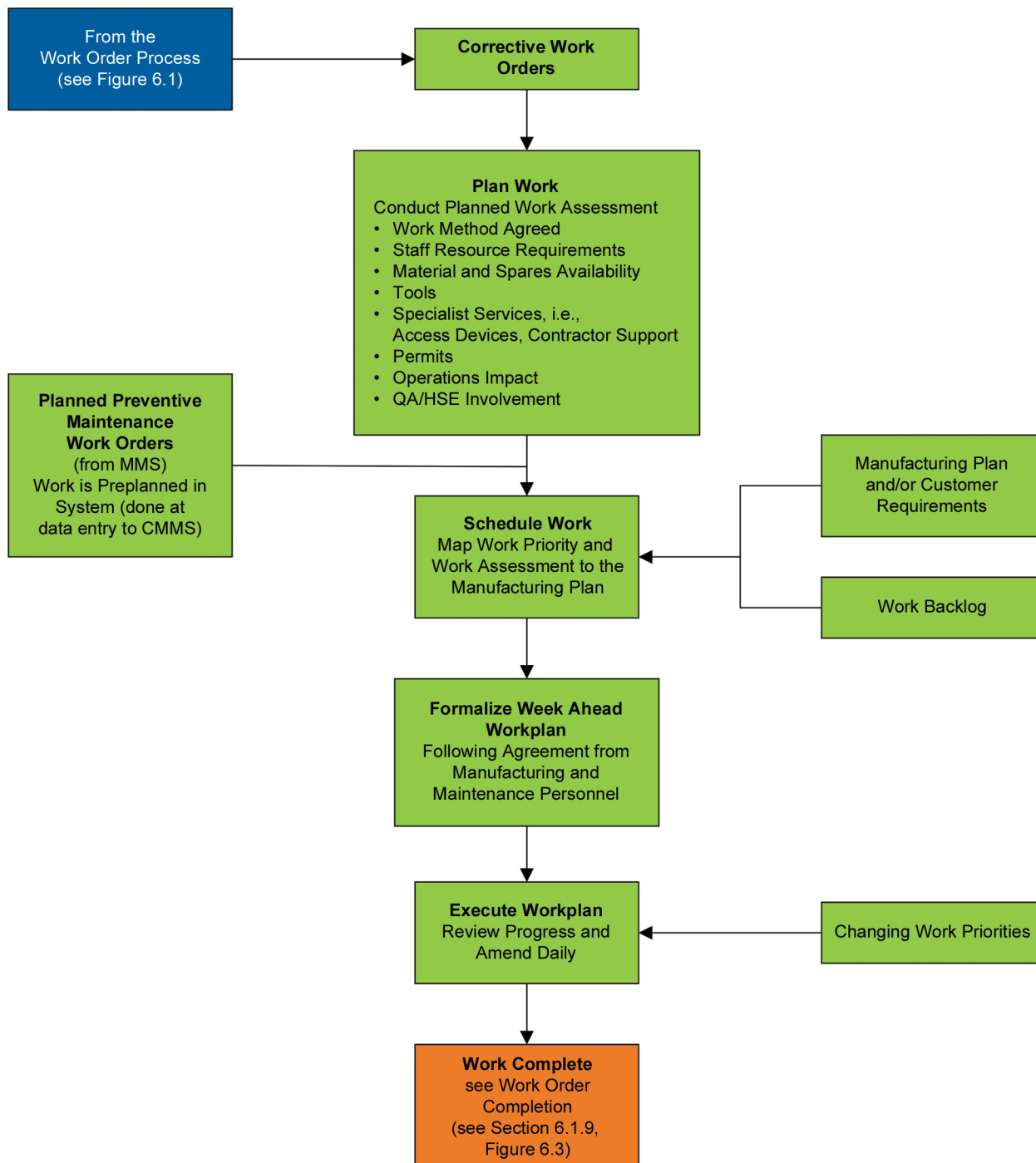
Planning is defined as the activity that seeks to determine:

- How the work will be performed
- How long the work should take to perform
- Material resources required to perform the work
- Skills required to perform the work

Scheduling is defined as the activity that aligns the planned work requirements with the available resources and determines when the work is to be performed.

See Figure 6.2 for a typical planning and scheduling flowchart.

Figure 6.2: Typical Planning and Scheduling Flowchart



6.1.7 Requirements for Planning and Scheduling

Maintenance work should not impact ongoing operations. However, this is not always possible due to complex maintenance work; in such cases, the maintenance management should work closely with operations to schedule a mutual optimal time to perform the work. Where PM work is required, it should be scheduled during windows in the production schedule. These windows may be short and fall in between batch campaigns; therefore, the need for good preparation and coordination with all relevant asset owners is a crucial factor. Maintenance work may need

to be performed in rooms where product is staged for the next run. Typically, these areas are cleaned prior to entry of maintenance personnel and all products are sealed and secured. These measures are intended to mitigate the potential for contamination and protect personnel from product exposure.

6.1.8 Information Requirements for Planning and Scheduling

As part of the planning and scheduling processes, information should be collected that can be used for performance analysis, such as schedule adherence or percentage of work planned. This can be used to optimize the work as well as to confirm the time required to perform the work. The use of such data is considered Maintenance Good Practice. Information normally generated for planning and scheduling purposes includes:

- Description or outline of the proposed work methods
- Estimate of the expected duration of the work
- Personnel and skill resource requirements
- Materials and spare part requirements
- Specialized tool or equipment requirements
- Specialized contract services
- Work permit requirements (isolation requirements)
- Necessary approvals for the work (pre and post)
- Operations/customer impact, e.g., shutdown requirements and coordination
- Agreed date for the work to be performed and systems returned to service

6.1.9 Work Order Completion

WO completion is a discrete process step where:

- Key data is:
 - Collected
 - Reviewed
 - Recorded
- Formal closure of the maintenance WO is documented

It is also the process that records key information that will demonstrate that the work has been performed in accordance with stated procedures and guidelines.

Consistency, accuracy, and completeness of the information recorded during WO completion are considered crucial to ensure compliance. Data must be recorded contemporaneously to comply with data integrity requirements. Certificates specific to a replacement part should be updated for the asset (e.g., materials of construction certificates, surface finish certificate, pump curve) and old documents may be removed or archived.

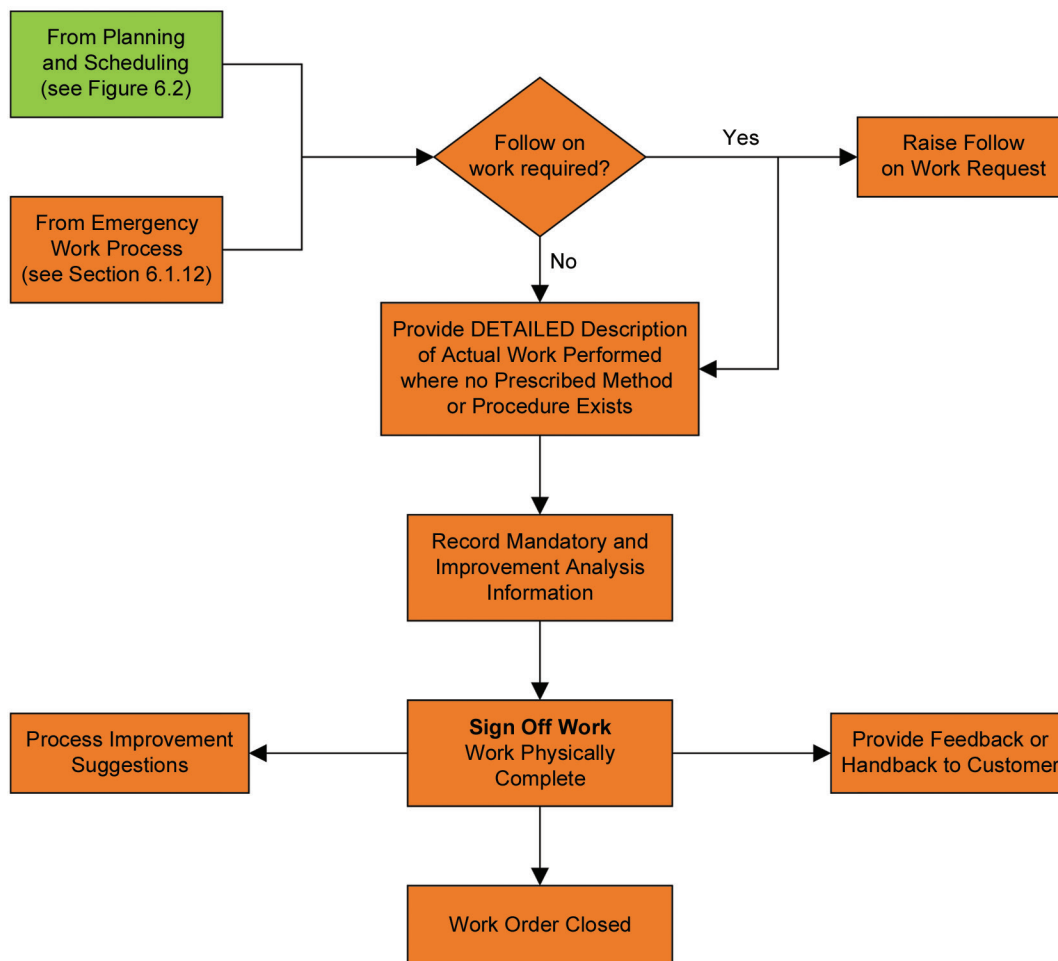
Personnel authorized and trained in the WO completion process should sign off the WO (for both electronic and paper-based systems). A guideline also should be established to ensure timeliness of WO completion.

The information captured may be used for maintenance history analysis, problem solving, or problem identification. It may be the basis from which decisions are made on changes to the planned PM plan or to implement site improvements, equipment redesign, or equipment replacement.

To aid consistency, failure (or closure) codes may be used to improve the ease with which information can be analyzed.

See Figure 6.3 for a typical work completion flowchart.

Figure 6.3: Typical Work Completion Flowchart



6.1.10 Information Requirements for Work Order Closure

For GMP systems, the following information should be recorded to satisfy regulatory requirements and as such is Maintenance Good Practice:

- As-found condition
 - Brief description of the problem, cause or probable cause, and any observations noting abnormalities
 - Discrepancies should be handled according to a procedure

- Work description
 - Detailed description of the actual work performed
 - Reference should be made to any recognized work procedure or method statement that was followed; if there are no procedures or method statements covering the work, a more detailed description should be included on the WO
 - > Organizations may use detailed task instructions (on WOs), whereas others prefer to have work procedures which are attached to the WOs
 - > Regardless of the preferred method, an appropriate level of detail that enables a competent technician or mechanic to complete the work is warranted
 - > Organizations should focus on critical steps that form the basis of the work.
- Completion date
 - The completion date when the work is 100% complete
 - WOs may have many steps that are completed over an extended period of time (i.e., spanning days).
- Work performer(s)
 - Work performers should be named, including the names of employees or any contractor and its employees where they have been used
- Approvals
 - Work performers should sign off that the work is completed and the equipment or system is ready to go back into service
 - If change control is required, appropriate signatures should be completed on the change control documentation
 - Where necessary, individual work steps may include a sign off to indicate when and who executed the step
 - It is considered good practice to have sign offs and date/time recorded for respectively completed tasks whenever the work goes beyond one shift
- List of spare parts and materials used during the course of the work (e.g., lubricants, barrier fluids)
 - Parts or materials that deviate from the system qualification process should be identified.
 - Reference to stores issue numbers and procurement order numbers may be recorded for traceability although this is not a GMP requirement
- Equipment movements
 - Detailed records of equipment movements and replacements should be recorded, e.g., if a machine is repaired in the maintenance shop versus in the production suite
- **Note:** Attachments to work order should follow Good Documentation Practice requirements (e.g., file names, WO number, attachment number, page number, initials, and date).

Any follow-up WRs generated as the result of observations or findings during the execution of the work should be confirmed and linked to the original WO.

The handover of the asset to and from the operating department should be a clearly defined process where each party has ownership. Refer to Section 10.4.1 for more information on handover of systems and equipment.

Maintenance units expect specific items to be complete:

- **Before** they execute work, e.g., that operations has provided all relevant information to the maintenance unit to enable them to perform the work, and that the equipment has been suitably cleaned and the area is prepared for their maintenance work
- **While** they work
- **After** the work is complete

Operations may expect that when they get the asset back, they can prepare to use it normally, unless the maintenance unit has stipulated otherwise.

Each department should communicate with the other to ensure that errors are avoided. It is not considered appropriate for operating departments to leave a machine outside the maintenance shop with a sign stating “broken.” It also is not considered appropriate for the maintenance unit to complete a repair and not inform the operating department that they can resume use of the asset.

6.1.11 Work Order Information for KPI and Continual Improvement

WOs should provide sufficient information to facilitate the continual improvement process and to provide an accurate asset history. Activities such as failure mode analysis, PMO (PM Optimization), and performance reporting and monitoring are examples where feedback from the work execution process can be valuable. The following information in addition to that listed above is suggested:

- Schedule confirmation (e.g., whether the identified window is large enough to properly perform the work)
- Work priority
- Failure (or closure) code
- Root cause of failure
- Work duration: planned versus actual
- Downtime incurred
- Improvement suggestions and ideas

6.1.12 Emergency Work Management

Work Order Management Systems should recognize and address the need to handle emergency work in such a way to ensure compliance of the maintenance operations. Emergency work by definition requires immediate attention and will, in all probability, follow a modified process that differs from the normal procedures for the management of maintenance work. While immediate action might be necessary when addressing an emergency WR, it is still important to ensure that a proper appraisal of the work being undertaken is performed and that appropriate procedures are followed. This is particularly true with respect to HSE concerns.

Any direct impact of the work on product quality should be assessed and approved before the site is returned to operation. Documentation requirements for emergency work generally should follow the same guidelines as outlined for planned work.

With emergency work, the WO may be created during or after completion of the work. In either case, a WO should be created to properly document the work. It is normally acceptable for the WO to be created retrospectively, but it should be raised as soon as practical following the initial work appraisal (typically during the same shift).

6.1.13 Typical Features of Emergency Work Processes

It is acceptable for WOs to be created after the work has started.

HSE procedures should be followed and not be overlooked.

Where there is potential to impact product quality, the Production and Quality units should be consulted immediately. Change control and product quality assessments, if applicable, should be approved before sign off of the work and return to normal operation.

Documentation and record keeping requirements apply and should be completed before the WO is closed.

Personnel involved in managing emergency work should have clearly defined roles and should be trained and proficient in the procedures used to control and manage work.

6.1.14 Performance Measurement – Key Performance Indicators

Common metrics of maintenance units include:

- GMP versus non-GMP work
- GMP work past due
- Changes implemented
- HSE incidents
- Response times
- Number of complaints and non-conformances
- Improvement plan progress
- Cost: savings and productivity
- Equipment availability/downtime
- Mean Time Between Failure (MTBF)
- Split between normal/emergency requests
- Waiting time for getting a Permit to Work (PTW) after arriving on site
- On time payment of invoices
- Labor utilization % (Best Practice would imply >98% completion rate)

- Planned work completion % on time
- Planned work schedule adherence (Best Practice would imply >90% completion rate)

6.2 Self-Inspection and Continual Improvement

6.2.1 Self-Inspection

Self-inspection (self-audit or assessment) is considered to be Maintenance Good Practice. The purpose of a self-inspection program is to review performance against standards and procedures for the purpose of ensuring compliance and identifying actions to deliver compliance. There should be a mechanism to enable significant issues to be raised to the attention of senior management. A Maintenance Best Practice related to self-inspection is to use metrics data to demonstrate that the maintenance system is in a state of control and to feed this data into the overall compliance of a site's quality and manufacturing systems (based on the FDA's [10] system-based inspection approach). For EU GMP, inspection could be done against all items relevant to maintenance activities under each GMP chapter [20].

6.2.1.1 Planning for the Self-Inspection

Consider risk-based number and duration of the self-inspection (self-audit) on maintenance activities. Deviations, changes, failure rate, key personnel changeover rate, newly installed equipment, and criticality and complexity of equipment to be maintained are among the criteria to define inspection numbers and duration.

Considerations for planning include:

- Sending to the auditee the audit plan, agreed upon date/time, purpose, scope, and inspection criteria (GMP audit only or combined audit including HSE).
- Making sure the assigned auditor or audit team have the necessary auditing skills and have received required training to audit the relevant engineering activities. Auditors with specialized backgrounds (e.g., engineering) may be necessary to accompany the team in addition to a lead auditor that is capable of leading the QMS auditing team.
- Preparing a checklist for the audit and reviewing critical and major deviations and changes to help guide the focus on high risk areas. Reviewing main maintenance procedures and samples of specific equipment SOPs before the audit will help to focus and shorten the duration of the on-site audit and improve audit efficiency.

6.2.1.2 During the Self-Inspection

After the opening meeting, the inspector(s) can go on a tour of the production and utilities areas to check the actual status of repair and performance of equipment. The inspection would then cover, for example, the following sections of the GMPs relevant to maintenance [20]:

- **Pharmaceutical Quality System**
 - Check how QRM is used in maintenance activities.
 - How are changes handled? Is there a defined procedure to identify like-for-like changes and how to handle them?
- **Personnel**
 - Check qualifications and training required for the Maintenance team.

- Is there a list of persons in the Maintenance team and what activities each person is qualified to perform?
- Does the Maintenance team receive training from a certified trainer (e.g., from the equipment manufacturer)?
- Are training records available and complete covering all the maintenance activities performed?
- Check if training covers how to prevent contamination and cross-contamination during maintenance activities.
- Check for an SOP that covers hygiene and gowning. Check for an SOP that covers precautions to prevent contamination and cross-contamination from maintenance persons covering more than one department.
- Are there dedicated maintenance tools for each area and procedures to decontaminate them before use of equipment?
- **Premises and Equipment**
 - Check for main maintenance procedure, risk-based maintenance schedule, individual equipment maintenance instructions, PM and CM records, and statistical analysis of CM.
 - Check for an SOP that identifies communication channels with production personnel before performing maintenance activities.
 - How are maintenance schedules tracked?
 - Are there maintenance SOPs for each piece of equipment? Do the SOPs consider all items specified in the manufacturer's maintenance manual? Does the maintenance frequency consider manufacturer's maintenance manual, risk assessment, and historical performance of the equipment?
 - Is there a list of lubricants used? Do the lubricants comply with the recommendations of the equipment manufacturer? For the lubricants that may come in contact with equipment product contact parts, are they food grade?
 - Is there a mechanism to detect abnormally repeated CM? Are root causes identified and are actions taken to prevent recurrence?
 - How are deviations from the maintenance schedule handled?
 - Are the instruments used for maintenance calibrated at suitable frequencies?
- **Documentation**
 - Are maintenance SOPs available to the Maintenance team?
 - Are there records for maintenance activities? Are these records signed by the persons who actually performed the maintenance activities and countersigned by the supervisor?
 - Are SOPs, schedules, and records retained for the period specified in the SOPs?
 - Are reference documents (e.g., manufacturer's manual) retained? How are they distributed and controlled? Are they accessible to the maintenance staff? How are changes to the equipment reflected in these reference documents?

- **Production**
 - Is there a risk-based stock of spare parts?
 - How are spare parts and lubricants quarantined before being released for use?
- **CMMS**
 - Is there a process to request access?
 - Have there been unauthorized logins?
 - Have there been unauthorized changes?
- **Quality Control**
 - What inspection steps are done before the release of spare parts or lubricants for use?
 - Are the certificates for food grade lubricants checked and retained?
 - Are the qualification/inspection records for spare parts retained?
 - What procedure is followed to release equipment for operation after maintenance activities?
 - Check role of Quality Control (QC) unit in maintenance activities.
- **Outsourced Activities**
 - Is there an SOP that covers handling of outsourced activities?
 - Are there quality agreements with contractors for outsourced maintenance activities? Are there proper initial and frequent assessments of these outsourced activities?

6.2.1.3 After the Self-Inspection

The self-inspection findings should be reported and the closure of any non-conformities should be followed up as per any other inspection.

6.2.2 Continual Improvement

Continual improvement should be part of all maintenance activities, and the philosophy of continual improvement should be well established and promoted regularly.

From a maintenance perspective, continual improvement is the application of reliability engineering principles to Maintenance Programs. The efficacy of maintenance activities is enhanced when maintenance is scheduled based on an evaluation of reliability metrics and the analysis of equipment failure. Continual improvement promotes the increased reliability of pharmaceutical manufacturing equipment, facilities, and systems using feedback processes developed to monitor and enhance performance. It is not a regulatory requirement to have a continual improvement program; however, some regulatory authorities encourage it. It is considered Maintenance Best Practice to have a continual improvement program.

For more information, refer to *ISPE Good Practice Guide: Equipment Reliability* [7].

6.3 Contract Management and Outsourcing

6.3.1 Outsourcing Strategy

The use of outside contractors for maintenance activities is considered a business decision. Organizations can choose whether to develop and provide maintenance resources in-house or to selectively use contractors to provide services. Organizations should build a service model that clearly identifies the service provider for each maintenance work activity. The model should be challenged and evaluated for effectiveness periodically, as it is subject to changes in internal and external environment. For example, if an organization outsources maintenance for Building Automation Systems (BAS) and the contractor experiences high turnover of personnel, it may be necessary for the organization to look at alternatives including bringing the expertise in-house.

A key principle with any contracted work is that the same procedures and guidelines apply as if the work were performed in-house.

Product quality is the responsibility of the manufacturing organization. It is the responsibility of the maintenance unit to ensure the compliance of contractors.

For organizations that outsource the maintenance function completely, the interface or point of control may reside in a non-operating unit or a different part of the organization. Compliance requirements apply and the contractor should, in this case, have an acceptable level of understanding of the regulatory requirements and the organization's internal SOPs and guidelines, etc.

6.3.1.1 What can be Outsourced?

Any maintenance activity can be outsourced to contracting organizations, providing the manufacturing organization ensures compliance with the appropriate procedures and standards.

6.3.2 Procedure for the Selection of Contractors/Outsource Organizations

6.3.2.1 Assessing the Contractor's Capabilities

Contractors performing maintenance activities on GMP regulated equipment should have relevant qualifications prior to being employed. This will help to demonstrate that the contractor has been assessed and is considered competent to perform maintenance work in a GMP regulated environment. Contractors also should satisfy other applicable regulatory requirements, e.g., HSE regulations, and policies. Assessments should be performed for those persons who will actually perform the maintenance work.

The assessment may be in the form of an audit involving a visit to a supplier and may include the following considerations:

- Discussion of the scope of services, requirements, service levels, etc.
- Experience of those designated to be directly involved in the services with a focus on GMP-related experience
- Supplier quality systems, including documentation systems
- Training programs
- Existing systems and programs to support operations at the manufacturing organization
- Verification of employees against the FDA Debarment List [10]
- Management team credentials

- Safety and environmental records
- Financial stability
- Performance management systems
- Rewards and recognition programs
- Degree of automation of processes
- Reporting and metrics utilized
- Continual improvement programs
- Memberships, licenses, and accreditations

6.3.2.2 Contract Duration and Long-Term Planning

The selection of a supplier to perform maintenance activities can be complex, particularly if the scope of the services is broad. A long-term, partnering approach should be developed that focuses on quality and execution of the services rather than immediate cost savings.

Organizations may enter into agreements that last for several years, showing a commitment by both parties. From a GMP perspective, it is not desirable to have a high turnover of contractors, due to increased training requirements, a higher probability of errors, and the need to harmonize with the new contractor's systems.

6.3.2.3 Bundling of Contractor Services

If properly managed, bundling (grouping) of contractor services under an umbrella contract with a consolidated management and reporting team can be effective. It is an option to consider for smaller organizations or organizations lacking competencies in GMP maintenance, but is effective only where the added value exceeds the added costs for the increased layer of management.

6.3.3 Engagement of Contract Maintenance Suppliers

6.3.3.1 Specification of Requirements

The specifications of requirements for contract maintenance suppliers should include:

- Schedules of equipment, systems, and facilities to be maintained
- Relevant SOPs
- Change control procedures
- Historical data
- Site specific training requirements
- Maintenance schedules
- Schedules of materials
- Reporting and documentation standards

- Performance measures
- Service levels
- Maintenance strategies

6.3.3.2 Contracts

A written contract is usually considered essential and creates the foundation for the partnership. The contract should reference GMP and other requirements and cover commercial and legal arrangements. Additional processes also may be included, such as:

- Complaint handling procedure
- Audit programs
- Improvement programs
- Help in conveying mutual expectations

6.3.4 Performance Management

Performance management or contract management is considered key to success and is a way to drive improvement into processes. Performance management may be used to determine what should be measured and to develop mechanisms to capture and report data collected. Data and metrics should be both meaningful and usable.

6.3.4.1 Performance Review and Feedback

Performance should be reviewed on a regular basis (e.g., annually). For larger or more critical contracts or where performance levels are not being met, reviews should be more frequent (e.g., monthly or quarterly).

The review should have a structured agenda so that all parties involved know what is expected during the review. The contract manager or account manager for both parties should attend. Feedback should be obtained periodically from customer groups and the Quality unit. Feedback should be provided to the customer groups on the outcome of the reviews and the actions resulting from the raised issues.

6.4 Change Management

6.4.1 Equipment/Facility Change Control/Notification

Operating parameter changes, failures, and breakdowns may result in equipment and system modifications, upgrades, or nonroutine repairs. External factors, such as changes in specifications or process changes, also may trigger such changes.

Procedures should be established to evaluate and implement changes so that effects on product quality are minimized.

Mechanics, technicians, and contractors should be properly trained, and formal guidelines should be established to define what constitutes a change in the context of change control. Change control procedures should be followed whenever GMP systems and equipment undergo a change as defined by the site's procedure. This process also should be followed for computer related changes that fall under the guidelines of 21 CFR Part 11 [13]. Non-GMP critical changes may be differentiated under a separate process, such as engineering change control, project change control, etc. Particular types of changes may not follow the formal change control process, e.g., routine adjustments within predefined tolerances.

The engineering and maintenance departments should follow the organization's normal change control procedure. Documenting and logging of changes should be harmonized across the site.

Maintenance departments should establish a process for emergency changes; these are changes that are sometimes necessary as a result of breakdowns or incidents. This process may work with parallel approvals of changes being implemented; however, the production outputs are typically "quarantined" or placed on "product hold" pending approval of the final change control paperwork. A generally accepted industry practice is to obtain verbal approval prior to implementing the emergency change, and then follow-up with the proper documentation.

6.4.2 Equipment Change Control Request

A typical method for determining which equipment/component changes require change control is shown in Figure 6.4. The approval process may include a multi-disciplinary team (e.g., engineering, manufacturing, and Quality unit) to review and approve the change request and subsequently the implemented change control document. A change should be reviewed and approved before the change is processed. The process should include verification that the changes implemented will not impact drug product quality.

The documentation should be tracked and controlled. This can be accomplished through a logbook, the site documentation practices, or using a serially coded change control numbering system. One method of capturing this information is to utilize an existing WO system and attach a change control form to the WO. The change form could include sections that:

- Explain the reason(s) for change
- Document approval of the change
- Indicate the testing that needs to be completed after the change is completed
- Release the equipment back to production for use

An example Equipment Change Control Request is provided in Chapter 12 (Appendix 4).

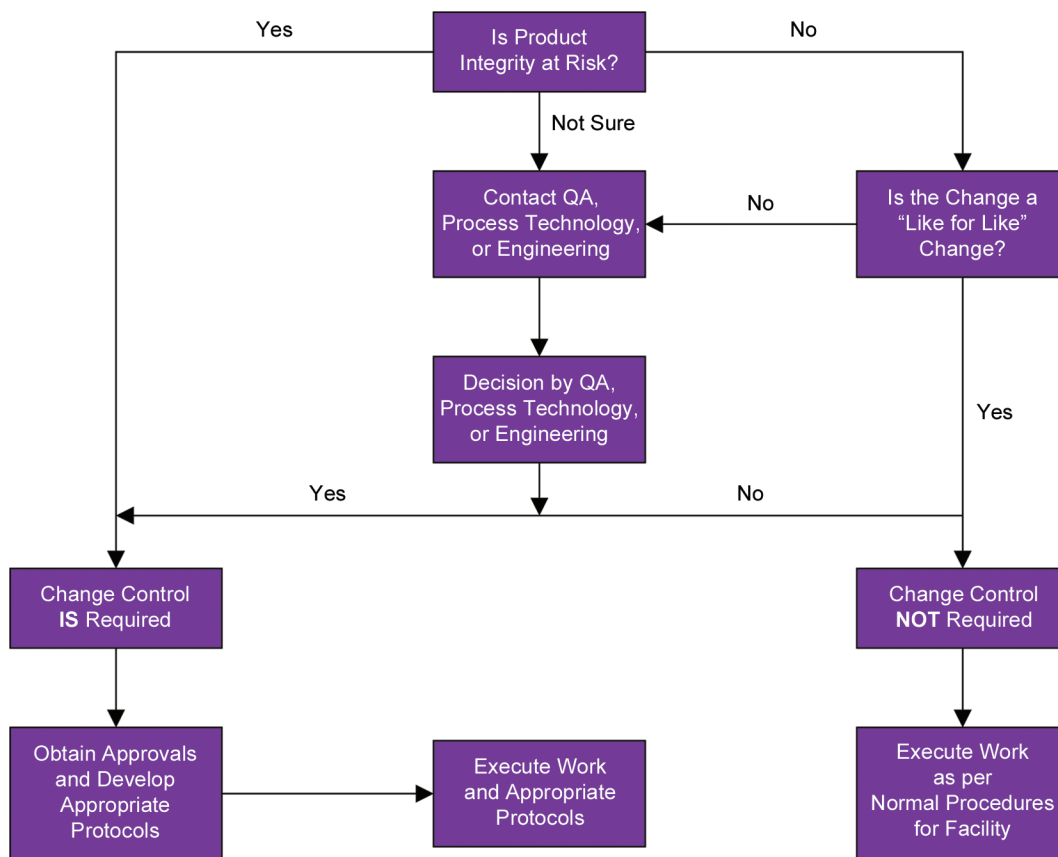
The change control documentation should include:

- Document tracking number (e.g., WO number)
- Equipment identity and location
- Rationale for the change (why the change is needed)
- Brief description of work
- Expected end results of the change
- Tests necessary to prove the change provides the desired results
- Criteria used to prove test results are acceptable

Upon completion of the authorized change, the person/assignee responsible for implementing the change should obtain the appropriate approval for releasing the equipment back to the production department (i.e., return to service), as well as notification of other affected departments. The Quality unit should have final approval for any implemented change.

The completed documentation, including all test protocols/results should be filed and easily retrievable for audit purposes as part of the equipment qualification/validation documentation for the site or in the equipment history file.

Figure 6.4: Example Decision Tree to Assist in the Application of Change Control



Question to Ask:

Will the change I make today allow the equipment to produce the same product tomorrow as it did yesterday?

7 Roles, Responsibilities, and Interfaces

7.1 Introduction

This chapter considers the roles and responsibilities involved in executing Maintenance Good Practices. It also examines the relationships between the various roles, as the responsibility with respect to equipment/asset performance and compliance with GMP and other regulations is a shared one.

Interfaces between the maintenance unit and other key areas in a pharmaceutical organization should be managed to ensure that maintenance activities do not have an adverse effect on GMP systems or components. The relationship between the maintenance unit and operations should be a partnership with mutual accountability for asset care.

To reduce the risk of undesirable events, such as production delays or impacts on product quality, Maintenance Best Practice processes should be established, documented, and audited. Examples of these processes are materials management (Maintenance, Repair, and Operations (MRO)/spares), maintenance planning, maintenance scheduling, and reliability engineering functions. These processes should also establish links to production, quality, and any other impacted organizational function.

7.2 Roles and Responsibilities

The GMPs state that assignment of responsibility for maintenance and maintenance scheduling are included in written procedures for maintenance [17, 20]. Maintenance Good Practice is to define these responsibilities in the governing procedures for the Maintenance Program implementation and management. It is also an expectation that where there is a review of the maintenance activities with respect to any maintenance processes related to quality systems (such as change control, deviation, or training), that these responsibilities be documented. Maintaining data integrity is thereby a responsibility of all. Typically, maintenance manager(s) are given these responsibilities, but depending upon the size of the organization, these responsibilities also could reside with maintenance supervisors. SMEs for maintenance activities and craft skills should also be identified as a Maintenance Best Practice.

7.3 Production and Maintenance

Production operators should act as “continual equipment monitors.” When problems occur, operators can provide valuable troubleshooting insight as well as diagnosis when initiating WOs. Which maintenance activities should be performed by the operating department and which should be performed by the maintenance unit should be clearly defined. Operators typically perform functions such as:

- Cleaning
- Lubricating
- Inspecting
- Minor adjusting
- Changeovers

These tasks should generally be defined in a procedure.

The methods used and record keeping procedures should be harmonized between operations and maintenance. Maintenance Best Practice would be to have all maintenance and related work performed under a single Maintenance Program at a site. To ensure that equipment history is preserved, only one system should be used to document performed maintenance and repair activity on equipment. Operations and maintenance should record their activities in a shared logbook. The recommended approach is to have a single system that the operations and maintenance departments share.

7.4 Project Engineering and Maintenance

Engineering project managers, who are responsible for all phases of asset realization from design throughout C&Q, can have a major impact on asset maintainability and cost.

If incorporated at the start of a project, maintenance can be significantly eased over the life of the asset.

Maintenance teams do not normally dedicate members to project teams and therefore rely on project engineering to implement project activities. This is usually true from design through the commissioning phases. For example, during commissioning of a large facility, the project team normally retains full responsibility for maintenance of the assets put into service until they are turned over. Although there are contractual obligations until handover of a project, it is still an opportune time to involve maintenance technicians who will ultimately be responsible for the assets. Where GMP systems are involved, maintenance should participate in the development and implementation of the Maintenance Strategy and Maintenance Plan during the C&Q phase or earlier.

Maintenance units should be involved early in projects. The level of involvement will vary greatly depending upon the size and nature of the project, but at the end the maintenance unit needs to be part of each project with equipment that will require maintenance. The maintenance unit needs to know how the equipment will be used and which maintenance efforts will be implemented into the existing Maintenance Plan. If everything is properly organized, much of the training of maintenance mechanics and technicians can be completed during the execution phases of a project. The advantages are less time spent on rework later, which can result in cost savings after handover of the project. Additionally, the Maintenance team should have input on equipment selection at the User Requirement stage of a project to ensure maintenance requirements can be achieved. Key aspects and questions to answer include:

- Which Maintenance Strategy is to be employed?
- Is there a Maintenance Plan for the asset?
- What are the training requirements?
- What are the tools and equipment required?
- How will initial calibration settings be established?
- Are critical spare parts required?
- Can the equipment be maintained properly (accessibility)?

Maintenance Best Practices suggest that project engineering and maintenance units have clear agreement on documentation, start-up, and operational procedures. The equipment verification program may form the basis of documents that will be turned over to the maintenance unit upon completion of a project.

Documents may be issued as drafts during a project to facilitate processes, and revisions or versions of these documents should be tracked.

7.5 Health, Safety, and Environment and Maintenance

Maintenance units should clearly understand and comply with HSE requirements affecting their areas of responsibility—HSE is integral to the performance of maintenance activities. It is very important to have HSE engaged throughout the project, same as project engineering. Early alignment with both parties ensures less rework regarding maintenance planning later on. All required HSE items should be fitted within the maintenance work.

Chapter 10 (Appendix 2) provides an overview of maintenance and regulatory requirements generally covered by HSE programs.

7.6 Quality and Maintenance

The Quality unit should ensure that all products manufactured meet predetermined requirements. The Quality unit is the custodian of compliance and owns and maintains the quality systems within which the maintenance unit operates.

One of the key activities of the Quality unit is compliance monitoring of GMP facilities and processes. This would typically include reviews, audits, self-inspections, and approvals associated with the day-to-day activities of the maintenance unit. Examples may include the following:

- Reviews
 - Periodic reviews of GMP systems, including maintenance performed
- Audits/Self-inspections
 - Maintenance systems and controls
 - Documentation
 - Training records and plans
 - Equipment change control
 - Maintenance outsourcing
- Approvals
 - Overall Maintenance Program
 - Change control
 - Notice of events or out of tolerance reports
 - Management of maintenance non-conformances

7.7 Organizational Structure

Organizational structures to support Maintenance Good Practice can vary greatly and regulations allow flexibility. Size, structure, and division of responsibilities are dependent on elements such as the nature of the site, resource capability, and operational characteristics. An appropriate level of staffing to deliver the Maintenance Program is expected. These resources can be internal to the organization or externally sourced, or as is most typical, a combination of both. Regardless of the organizational structure, the requirements, as defined in the Maintenance Program, apply equally.

8 Training

8.1 Purpose

Maintaining pharmaceutical GMP equipment to meet GMP requirements and ensure drug quality requires a highly skilled workforce. Whether the work is done by production personnel, maintenance staff, or contractors, all should have the technical and procedural knowledge necessary to perform and document the job correctly to ensure patient safety and product quality.

8.2 Knowledge and Skills for Maintenance Personnel

Maintenance work ranges from simple skills, such as setup changes on a machine or cleaning and adjustment, to complex tasks, such as complete troubleshooting and repair of aseptic operation equipment for product processing. These skills usually are acquired through training and experience.

Maintenance personnel are often hired with the basic or general skills required for their trade. Simple documentation to that effect, such as a copy of a trade qualification certificate or a resume in a training file, is usually sufficient to show technical competence. If employees are hired without these basic skills, they should be trained and that training should be documented. Such employees also may need special technical training for specific equipment, difficult, unusual, or highly tedious tasks; this training also should be documented.

8.3 Training Scope and Curricula Management

8.3.1 Training Scope

Maintenance personnel training typically includes general and HSE training, general GMP training, and job specific GMP training as well as training for technical knowledge, skills, and procedures. The main concept behind training for Maintenance Good Practice is that personnel should understand how the performance of their job has the possibility to impact drug quality.

Considerations for maintenance personnel training include, for example:

- General training and HSE training
 - Site and building layout
 - Security and access policies
 - HSE policies
 - Bio-safety policies and procedures
 - Procedures for high risk hazards (chemicals, steam sterilizers/autoclaves, high voltage, working at height, etc.)
 - Safe work procedures (LOTO, confined space, hot work)
 - Emergency response procedures
 - Environmental policies and green sustainability best practices

- General GMP training
 - Basic GMP
 - Personal hygiene
 - Good Documentation Practice
 - Change control and change management procedures
 - Deviation reporting and management
 - CAPA management
 - Data integrity
 - Material and personal flow
 - Control of tools in and out of GMP areas
 - Management of contractors
 - General facility maintenance and pest controls
- Job specific training
 - PM and Calibration program
 - Gowning requirements
 - Control and use of maintenance materials such as lubricants
 - Aseptic procedures
 - Work order management and procedures
 - HVAC and clean utility operation and maintenance
 - Building Automation System (BAS) operation
 - HEPA filter certification procedures
 - System P&IDs
 - Specific system operation and maintenance procedures
 - Specific instrument calibration procedures
 - Equipment changeover procedures
 - Problem diagnosis and troubleshooting

- Replacement parts assessment, identification of changes that can alter the validated state of the machine
- Equipment documentation and record keeping

Work performed by the maintenance unit should not alter the qualified state of the equipment and the validated state of the process and/or room. Specific procedures for gowning, moving tools in and out, cleaning procedures, etc. should be written and the maintenance unit personnel should be trained in the procedures. These procedures may be established and controlled by the operating department and maintenance personnel should follow the same training protocol as the operating personnel.

Maintenance personnel should have sufficient knowledge to understand the processes on which they work to know when drug quality may be affected. For example, a technician greasing a fan bearing in an Air Handling Unit (AHU) is unlikely to have adverse impact on product, as normally the fan is on the “dirty” side of the fine and HEPA filters. Conversely, a technician replacing a light fitting in a sterile product isolator is at high risk of adversely impacting on product. It is important that technicians who perform the tasks and other maintenance personnel who are involved in the process (planners, supervisors, and managers) are able to assess the tasks and impacts and make the correct judgement. A sound training program ensures the technicians are capable of doing so.

8.3.2 Training Curriculum Management

The training curriculum for employees is determined by their specific job descriptions and responsibilities. A training curriculum typically includes general mandatory requirements for all employees or certain groups of employees as well as role specific training for a particular job.

As many procedure documents are frequently updated, it is important to ensure the employee training curriculum is clearly defined and training completion status is closely monitored, so that employees are always up-to-date on the knowledge required to perform the maintenance tasks for the GMP systems. As a Maintenance Best Practice, using a computerized Learning Management System (LMS) can improve efficiency to manage the training curriculum for the staff.

Job specific training curricula are usually reviewed periodically to ensure they are commensurate to the job requirement.

8.4 Training Methods and Trainers

8.4.1 Training Methods

Planning how to test knowledge and skill retention is useful and encourages personnel to take an active role in learning. Testing, as an integral part of training, helps to address several questions:

- Does the program deliver the required knowledge?
- Does the trainee understand and retain important knowledge?
- Is it possible to document how well the training works?
- What is required to improve the training?

Table 8.1 provides a comparison of various training methodologies.

Table 8.1: Comparison of Training Methodologies

Methodology	Advantages
Reading Documents	• Lowest cost • Individual can train at any time or place
Read Documents and Test	• Individual can train at any time or place • Knowledge checks can be built into materials to ensure memory is sustainable
Electronic Media Training	• Individual can train at any time or place • Knowledge checks can easily be built into the materials • Easy to keep up-to-date – picture and video can be easily added to improve learning experience • Built-in training progress and completion is possible
Instructor-Led Training (ILT)	• Students can be guided with hands-on training exercises • Student questions can be answered immediately • Instructor can gauge the knowledge of the students • Students comfortable with this common approach
On the Job Training (OJT)	• Students physically active with hands-on training • Expert available for immediate questions • Instructor can gauge the knowledge of the student • Phase approach can be used to progress from “Observe” to “Assist” and “Perform”
Specialist (e.g., Vendor/School) Training Provided	• Equipment specific technical content in as compressed a time possible • Learn from the equipment SMEs • Instructor can gauge the knowledge of the student • Students comfortable with this common approach

8.4.2 Trainers and Instructors

For both ILT and OJT sessions, trainers may be required. A trainer is an internal or external SME who has in-depth knowledge of the specific field in the review. This person shall possess the documented evidence for his/her education, training, and/or experiences in the particular field. The trainer should also have the skills and ability to deliver materials to the students.

When a trainer qualification procedure is in place in the quality system, the trainer as an SME should go through this procedure to become a Qualified Trainer. This will ensure the SME also has the skills and capability to effectively deliver the knowledge to the students.

For training provided by either internal or external instructors, the training session should be properly documented with the trainer qualification information included. This document shall follow the company Good Documentation Practice (GDP) format and procedures.

8.5 Training for Vendors, Contractors, and Consultants

Maintenance work is often completed by external vendors, contractors, and consultants. These external personnel provide special or proprietary technical knowledge and skills to maintain and repair the equipment in GMP facilities. It is important to ensure that these external personnel possess the same general and job specific GMP training related and that their technical training records are kept up-to-date. Due to the skill level and criticality of the maintenance work and the frequency of the external personnel performing the work, it is usually easier to categorize the external vendors, contractors, and consultants in these three groups and manage their training requirement accordingly:

- For external personnel who come to perform maintenance work in low frequency (e.g., one to two times a year), their training qualification should be reviewed at each visit. Typically, the training requirement should be communicated before the visit to provide external personnel enough time to review the training material. For site-specific GMP knowledge, it may be more effective to arrange a full escort for the contractor personnel rather than to train them in all required GMP courses.
- For external personnel who work on site on a regular basis (similar to full-time employee), their training should be managed the same as the full-time employees.
- For external personnel that fall in between the above categories, proper justification should be applied to determine how the training is to be managed considering all factors and risks.

For maintenance work requiring specific technical skills in detailed steps (such as the calibration of a conductivity meter), the vendor/contractor personnel should follow either the internal SOPs or SOPs from the vendor/contractor organizations. In the latter case, vendor/contractor training and documentation should be reviewed in the initial vendor approval process and maintained by the Quality Agreement with the vendor/contractor.

8.6 Training Effectiveness

Verification of training effectiveness is an integral part of the training program required by GMPs.

8.6.1 Possible Ways to Evaluate Training

Prepared test questions: These may take time and several iterations to prepare but when well thought out can provide a reliable depiction of employee understanding. Test questions should provide a record of learning that can be used for both individual feedback and training program improvement.

Sample problems which are designed to simulate an actual situation: These provide a test of knowledge without risking failure in a real-world situation. This type of evaluation can take more time to set up than prepared test questions but may be performed over a period of time and can reinforce key learning points several times. Examples of problems should provide a record of learning that can be used for both individual feedback and training program improvement.

Demonstration and witnessing of skills on the job: An objective checklist of behaviors and skills expected during the witnessed demonstration should be prepared in advance.

Training programs should be monitored periodically to ensure that they provide appropriate levels of training and address the maintenance skills necessary to meet business needs. A formal annual monitoring program should be considered. Monitoring techniques for training programs may include:

- **Incident analysis:** Maintenance or GMP incident analyses could indicate whether training of personnel was a factor in an incident. (Note: training should not be cited as the root cause of an incident and retraining should not be cited as the solution.)
- **Formal certification:** Formal qualification or certification processes for some specialty skills should be considered. Government regulations may require certification.

8.7 Training Record Keeping and Regulatory Requirements

Training curricula should be maintained for all maintenance personnel working on GMP systems. Records can be maintained electronically or in paper files. If they are stored electronically, the system should be in compliance with 21 CFR Part 11 [13]. Retraining or annual training may be required for certain GMP topics, and these should be built into the annual training schedule. Proof of attendance should be maintained for all required training. Records should be auditable for on time completion of training and retraining.

The need for good training is highlighted in GMP requirements and is routinely audited during agency inspector visits to sites. For Maintenance Good Practice, there should be an auditable record of training activities for all maintenance personnel. Such records should also include the initial document for their basic and general skills from the hiring process. If government regulations do not mandate a file retention limit, individual organizations should set their own retention limits to dispose of the outdated records.

Examples of training records include:

- Maintenance role or job description
- Job related professional or trade union certification
- Ongoing Instructor-Led Training (ILT) and On the Job Training (OJT) documents
- Training objectives and training materials used
- Training schedules and attendees
- Training certificates and diplomas

9 Appendix 1 – Regulatory Citations

Table 9.1 lists specific US and international references relating to maintenance in facilities supporting the manufacture, processing, or holding of pharmaceuticals, APIs, and medical devices. The citations selected are intended to be representative but are not necessarily comprehensive.

Table 9.1: GxP Regulatory Citations

Maintenance Related Regulatory Reference and Topic		Maintenance Good Practice
US FDA 21 CFR Part 211 (Current Good Manufacturing Practice for Finished Pharmaceuticals) [17]		
Subpart B – Organization and Personnel	Section 211.25 Personnel qualifications. Paragraph (a)	General GMP training and job specific GMP training must be performed. GMP Training should ensure that maintenance persons understand how their work impacts or might impact drug product quality. A GMP training curriculum should be in place for all maintenance staff. Training should be documented with sufficient frequency. A process to ensure qualifications of individuals performing maintenance activities should be in place. Contractors performing maintenance activities are subject to the same requirements as internal resources.
	Section 211.34 Consultants.	“Consultants” refers to those who advise the maintenance unit and is not intended to include contractors who perform maintenance.
Subpart C – Buildings and Facilities	Section 211.42 Design and construction features. Paragraph (a) Paragraph (c) Subparagraph (10)	GMP facilities design and equipment layout must consider maintenance activities, and therefore, it would be expected that the maintenance unit is involved in the design review of facilities. Maintenance activities should be controlled to prevent contamination.
	Section 211.58 Maintenance.	Inspections of facilities, buildings, and building systems should be performed and documented. When inspections identify deficiencies, they should be corrected expeditiously.
Subpart D – Equipment	Section 211.63 Equipment design, size, and location.	The maintenance unit should be involved at appropriate points in the equipment specification, procurement, and deployment processes.
	Section 211.65 Equipment construction. Paragraph (b)	Materials used to perform maintenance activities should be evaluated for their potential impact on product prior to use.
	Section 211.67 Equipment cleaning and maintenance.	Maintenance should be performed on equipment and systems to ensure its required performance. In addition, maintenance should be performed in a way so as to ensure there is no impact to the product, such as contamination. PM plans should be in writing. Plans should be sufficiently detailed to ensure the range of skilled and trained persons called upon can properly execute the work. The work should follow a predetermined schedule and should be documented.

Table 9.1: GxP Regulatory Citations (continued)

Maintenance Related Regulatory Reference and Topic		Maintenance Good Practice
US FDA 21 CFR Part 211 (Current Good Manufacturing Practice for Finished Pharmaceuticals) [17] (continued)		
Subpart D – Equipment (continued)	Section 211.68 Automatic, mechanical, and electronic equipment. Paragraph (a)	CMMSs should be evaluated for their impact on product quality. Systems that are used for scheduling or recording the work should be evaluated to determine whether and to what extent commissioning, software validation, or hardware qualification are applicable. Maintenance programs solely relying on electronic data need to be 21 CFR Part 11 compliant.
Subpart F – Production and Process Controls	Section 211.100 Written procedures; deviations. Paragraphs (a), (b)	Change management procedures should be in place to assess and approve equipment/component changes performed during maintenance that may have an impact on product quality. Changes made to maintenance processes or procedures need to be properly reviewed and documented. Any observations noted on WOs should be reviewed and acted upon accordingly.
	Section 211.105 Equipment identification. Paragraph (b)	GMP components or systems need to be identified and have a unique identification number.
Subpart J – Records and Reports	Section 211.182 Equipment cleaning and use log.	When maintenance is being performed and equipment, systems, or an area is out of service, this should be clearly indicated. Major GMP equipment should be identified, and the maintenance performed should be recorded. An appropriate verification of the maintenance work should also be performed. Recording routine and non-routine maintenance in the same manner is recommended, as this facilitates documentation, reporting, and investigation.
US FDA 21 CFR Part 820 (Medical Device – Quality System Regulation) [21]		
Subpart G – Production and Process Controls	Section 820.70 Production and process controls. Paragraph (c) Environmental control Paragraph (d) Personnel Paragraph (g) Equipment Subparagraphs (1) Maintenance Schedule, (2) Inspection, (3) Adjustment	Maintenance must be performed on environmental control systems having the potential to affect product quality. Such environmental control systems should be monitored and routinely inspected to ensure proper function. Procedures and records should be documented. Maintenance personnel must be trained not only in their craft specialties but also in cleanliness and contamination control practices while working in the manufacturing area and controlled environments. Maintenance personnel supporting these activities should have periodic training and training records should be documented. Maintenance SMEs should be involved in the design, fabrication, installation, and placement of systems and equipment to ensure that accessibility for maintenance, cleaning, and inspection is considered. PM Plans should be in writing. Plans should be sufficiently detailed to ensure the range of skilled and trained persons called upon can properly execute the work. The work should follow a predetermined schedule and should be documented. Complete maintenance records should be kept to include the action(s) taken, person performing the action, and date. Adjustment limits and acceptable tolerances must be posted and available to personnel making adjustments.

Table 9.1: GxP Regulatory Citations (continued)

Maintenance Related Regulatory Reference and Topic		Maintenance Good Practice
US FDA 21 CFR Part 820 (Medical Device – Quality System Regulation) [21] (continued)		
Subpart G – Production and Process Controls (continued)	Section 820.72 Inspection, measuring, and test equipment Paragraph (a) Control of inspection, measuring, and test equipment Paragraph (b) Calibration Subparagraphs (1) Calibration Standards, (2) Calibration Records	Inspection, measuring and test equipment used to support manufacturing activities should be verified to ensure fitness for use (e.g., Design Qualification) and to ensure capability of producing valid results (e.g., Verification). Preventive Maintenance plans and procedures should be in place to ensure that routine inspections and calibration actions are performed as scheduled and documented. Calibration procedures must include limits/ranges for accuracy and precision. Calibration procedures should include a process for conducting adjustments when specified limits/ranges are not met and evaluating whether such out of tolerance conditions could affect device quality. These processes and results must be documented. Calibration standards used to calibrate inspection, measuring and test equipment must be traceable to a national or international standard. In the absence of an applicable standard, an in-house standard may be developed and maintained. Appropriate periodic maintenance and verification of in-house standards should be conducted. Calibration records for Inspection, Measuring and Test Equipment must be documented and additionally posted on or near each equipment item or instrument. Operations and Maintenance personnel should reference these records routinely while performing their work.
Subpart G – Corrective and Preventive Action	Section 820.100 Corrective and Preventive Action Paragraph (a) Subparagraph (1) Paragraph (b)	Corrective and preventive Action processes include documented investigations, corrective actions, verification of corrective actions, and appropriate procedure revisions applicable to maintenance and calibration activities.
EU Eudralex Volume 4 (GMP guidelines) [20]		
Chapter 2 – Personnel	Section (2.7) Head of production Section (2.8) Head of Quality Control Section (2.9) Heads of Production, Quality Control, Quality Assurance/Quality Unit	Requirements to be supported by each of these key personnel include ensuring that department, premises, and equipment are maintained and kept in a state of cleanliness in a manner suitable to support production and processing activities. These responsibilities also include ensuring that personnel supporting these activities, including consultants, are properly trained.

Table 9.1: GxP Regulatory Citations (continued)

Maintenance Related Regulatory Reference and Topic		Maintenance Good Practice
EU Eudralex Volume 4 (GMP guidelines) [20] (continued)		
Chapter 3 – Premises and Equipment	Section (3.2) General Section (3.10) Production area Section (3.32) Ancillary areas	Maintenance should be performed on equipment and systems to ensure its required performance. In addition, maintenance should be performed in a way so as to ensure there is no impact to the product, such as contamination. Maintenance should be performed on all aspects of the facility to ensure intended design conditions are maintained. Maintenance SMEs should be involved in the design, fabrication, installation, and placement of systems and equipment to ensure that accessibility for maintenance from outside the manufacturing area is considered. Maintenance areas, tools, and parts should be stored in areas separate from production. Dedicated tools for production may be considered to prevent contamination. Tools and parts may need to be wiped down with a cleaning or sanitizing agent as a good practice prior to bringing them into production areas.
	Section (3.34) Equipment Sections (3.35) and (3.37) Manufacturing and cleaning Section (3.41) Measuring, weighing, recording and control equipment	Maintenance should be performed on equipment and systems to ensure its required performance. Maintenance and cleaning actions should be performed in a way so as to ensure there is no impact such as contamination to the product or the environment, Measuring, weighing, recording, and control equipment should be calibrated at scheduled intervals. Calibration intervals should be determined by an appropriate means such as manufacturer recommendations, quality risk assessment, or other. Calibration schedules, procedures, and results must be documented.
Chapter 4 – Documentation	Sections (4.3) and (4.4) Generation and control of documentation	Documents containing instruction (including PM, calibration, inspection, and cleaning work instruction) should be approved, signed and dated by appropriate authorized persons and an effective date defined. These procedures and work instructions should be written in an unambiguous, declarative manner and should be reviewed by an SME prior to approval.
	Sections (4.7) to (4.9) Good Documentation Practice	Handwritten entries made to maintenance records and documents should follow applicable company quality procedures for Good Documentation Practice, including alteration of document entries.
	Sections (4.10), (4.12), and (4.29) Retention of documents	Maintenance and calibration records for systems supporting production must be retained in a designated, controlled area. Maintenance and calibration records should be retained for a period at least as long as the records for all batches whose release has been supported on the basis of that maintenance or calibration activity.
Chapter 9 – Self Inspection	Sections (9.1) to (9.3) Self inspection	Periodic self-assessments should be conducted to ensure that procedures and practices related to scheduling, performance, record keeping, and training are being followed as directed by company quality system and procedural requirements. All self-assessments should be documented along with any needs for improvements and for implementation of those improvements.

10 Appendix 2 – Health, Safety, and Environment in the Maintenance Environment

10.1 Introduction

Health, Safety, and Environment (HSE) is fundamentally important and critical to Maintenance Good and Best Practice. Pharmaceutical facilities, systems, and equipment must be maintained in a validated/qualified state and be compliant with HSE requirements. Maintenance activities can be potentially hazardous and carry varying degrees of risk to personnel safety. Specific facility systems and equipment may be designated as critical to HSE and should be maintained accordingly, perhaps requiring compliance with vendor recommendations and local, national, or federal regulations. The maintenance unit should clearly understand and comply with HSE requirements for their areas of responsibility. Additionally, the maintenance and manufacturing units should collaborate proactively to ensure that all work on manufacturing facilities, systems, and equipment is carried out in a compliant and controlled manner.

This chapter intends to provide general guidance concerning specific aspects of HSE in a maintenance environment. The content presented here is not a comprehensive treatment of the subject area, and it is strongly recommended to consult with HSE SMEs in the development of suitable HSE programs to identify, quantify, and mitigate hazards and risk and to promote safe and environmentally friendly work practices.

This appendix covers the following:

- HSE program management
- Hazards and risks
- Control of hazards and risks
- Permit to Work (PTW) system
- Control of Hazardous Energies (COHE) and Lockout/Tagout (LOTO)
- Confined spaces
- Hot work
- Flammable and explosive atmospheres
- Working at heights
- Working with compressed gases
- Mandatory maintenance practices
- Facility design for maintenance safety
- Environmental

Training of personnel and management of outsourced service providers (i.e., contractors) are also key components of Maintenance/HSE management. These topics are discussed in Chapters 6 and 8, respectively.

10.2 HSE Program Management for the Maintenance Unit

Given the significant hazards and risks associated with maintenance work, it is considered Good and Best Practice to develop and implement a Maintenance HSE Management Program. Such a program should be developed in cooperation with all stakeholders, including cross-functional management and staff (maintenance, manufacturing, and quality), and with SME input provided by the HSE unit. The program should encompass the areas discussed in this section.

The Maintenance HSE Program may be expected to operate an effective documentation system. At its discretion, the maintenance unit may choose to leverage the QMS document control system to manage and control the relevant program documentation, such as SOPs and Work Instruction, and records such as permits, handovers, training records, risk assessments and other records. The application of GDP may also be useful. However, it is recommended that these approaches are applied with discretion, as the HSE system may not require the higher levels of control associated with GMPs. For example, while it would be useful to apply document revision and record keeping controls, it may not be considered necessary to maintain full Quality oversight and approval.

Conversely, maintenance, repair, and service documentation and records will usually be held within the MMS and subject to GDP, GMP, and full Quality oversight.

10.2.1 Management Support for the Program

A successful program will require inputs from all site stakeholders:

- **Senior management** support is critical to the effective implementation of any site HSE program including that for the maintenance unit. Such support includes active support through leading by example, continual emphasis on the importance of HSE, visible presence in HSE activities, and provision of personnel and financial resources.
- Support from the **HSE unit** is normally a prerequisite for success. The HSE unit should provide SMEs for the critical elements, typically through an HSE generalist for most matters and supported by specialist expertise as required, e.g., fire safety, confined spaces rescue, etc.
- **Maintenance unit management and supervision** needs to actively support the program through good example, coaching, mentoring, and, if necessary, enforcement. They are primarily accountable and responsible for ensuring that maintenance practices and task execution are compliant with HSE. Maintenance systems, practices, SOPs, and work instructions must be robust in regard to HSE. Breaches of discipline in this regard should be actively followed up, investigated, and sanctioned if appropriate.

In addition, a culture of collective responsibility should be developed. The success of HSE programs depends on compliance by all personnel with its policies and procedures. Unsafe behaviors, such as adoption of unauthorized alternative practices, shortcuts, etc. will likely result in accident and injury.

10.2.2 Supporting Processes

It is assumed and expected that the HSE unit operates a number of critical site processes. The key processes are described below:

- **Crisis Management**

A program for the effective management of crises, such as serious site incidents (e.g., fire or explosion, multiple injuries, serious breaches of security), should be implemented. The process should be governed by an SOP, documented, and regular drills held to simulate an incident.

- **Pandemic Preparedness**

It is recommended that the company operate a pandemic preparedness program to allow effective management of the impact on the business and its people of pandemics or epidemics of contagious diseases, such as influenza and coronavirus. The program should be integrated with the Crisis Management Program described above. The program should include control measures relating to facility occupancy, interpersonal contact, disinfection, distribution of PPE, and management of suspect and actual medical cases, amongst other measures. Expert medical advice should be sought in the development of such a program.

- **Health Surveillance**

The company should operate a health surveillance program for staff, typically under the auspices of the Human Resources and/or HSE units. It is recommended that all staff receive a comprehensive pre-employment medical examination, tailored to the unique characteristics of the site, e.g., the nature of the products, specific hazards etc. This should be used to record a baseline for the health of each staff member, including general health, hearing, eyesight, etc.

It is suggested that the company adopt a program of ongoing health assessment including medical checks, such as general medical condition, eyesight checks, and hearing checks. There should be a comprehensive program covering hearing and eyesight conservation, including staff awareness training and mandatory PPE (such as ear and eye protection) as applicable.

- **Incident and Accident Reporting**

This process governs how accidents, incidents, and near misses are identified, investigated, and resolved by means of CAPA. As general guidance, all incidents, accidents and near misses must be reported, investigated, and CAPAs proposed, agreed, and implemented. Generally, a minor incident can be a precursor to a more serious incident if action is not taken. For this reason, all injuries, fires, and unlicensed emissions, no matter how apparently minor and innocuous, should be reported.

10.2.3 Specific Considerations for Maintenance Risk Assessments

Maintenance work and tasks are varied. Many tasks are generic, routine, and carry a reasonably predictable level of hazard and risk. Equally, many tasks are nonroutine and may be “first-off” and/or “once-off” for which the level of hazard and risk is not as predictable.

The maintenance risk assessment program should focus on maintenance work and tasks. It must accommodate the variety of tasks while adopting a reasonable and practical approach to the development of risk assessments. The risk assessments should encompass the tasks and associated risks and hazards that are reasonably likely to be encountered and be accessible and comprehensible to users. The following is guidance for the development of maintenance risk assessments:

- Risk assessments should be developed by a cross-functional team comprising maintenance supervisors and practitioners, operations, and HSE. The Quality unit may be consulted where maintenance work has GMP implications.
- Tasks which are generically similar may be grouped under a single risk assessment, e.g., maintenance of AHUs, electrical distribution, packaging machinery, etc.
- Maintenance practitioners should be trained on risk assessments and have ready access to them.
- Risk assessments should be reviewed and updated periodically, at an interval no more than two years, to ensure they reflect current practices.

- Specific risk assessments should be developed in advance for all high risk tasks, including and especially working in confined spaces, working at height, and working in flammable atmospheres.
- Routine, simple, or low risk tasks may be risk assessed through a short risk assessment process, sometimes referred to as a “one minute” risk assessment. The practitioner is guided through a risk assessment of the task using a form or template, which may be incorporated into the general PTW form.

10.2.4 5S and 6S

5S is based on an industrial Lean philosophy which is about the organization of operating spaces. With origins in Japan, 5S represents a Japanese acronym which may be loosely translated in English as Sort, Set in Order, Shine, Standardize and Sustain. The term 6S is used to incorporate Safety.

In terms of practical application, the implementation of 5/6S is usually managed by the Operational Excellence unit and essentially includes the following as part of the approach:

- All materials and items in an area are Sorted. Redundant, extraneous, and unnecessary items are disposed of.
- All required items are Set in Order. All items are stored, displayed, organized, and labeled so that all required items are easily located and retrieved. For example, in a workshop, tools may be put on a labeled shadow-board.
- Equipment, components, and consumables will be Standardized, e.g., all site areas will use the same implements, pens, knives, tools, brushes, etc.
- All areas and equipment are Shined, i.e., cleaned and maintained. This makes it easier to spot problems such as leaks, etc.
- The above is Sustained through ongoing effort.
- The ideal state for any area is established and captured, e.g., by photo and displayed locally.
- Areas should be periodically audited and scored for 5/6S compliance.

A full treatment of 5/6S is beyond the scope of this Guide. However, the application of a 5/6S program is strongly recommended due to the benefits that good space organization and housekeeping brings to maintenance in terms of efficiency and safety.

10.2.5 Integration of HSE Into Maintenance Systems

HSE should be regarded as an intrinsic part of maintenance and be built into all aspects of the maintenance unit systems, policies, SOPs, and instructions. The following are typical examples of integration of HSE into maintenance ways of working:

- SOPs and Work Instructions should include relevant HSE information, usually at the start of the document
- Maintenance WOs should cite and cross-reference risk assessments, contain a short synopsis of relevant risks and specify applicable PTWs
- The Work Permitting, Work Order, and Handover/Hand back processes should be integrated, mutually supportive, and cross-referenced
- Statutory inspections and contractor visits should be managed through the Work Order system

- HSE CAPAs requiring physical work by engineering/maintenance should be managed through the MMS or the project control system
- Contractor risk assessments and method statements should be integrated with the MMS

10.3 Hazards and Risk in the Maintenance Environment

10.3.1 Hazard and Risk Agents

Maintenance workers perform a wide variety of tasks and are exposed to a correspondingly wide variety of hazards and risks. The following is a list of hazard and risk agents (the list is not exhaustive):

- Physical Agents
 - Noise
 - Vibration
 - Electricity
 - Compressed air and other gases
 - Ionizing radiation (e.g., radioactive)
 - Non-ionizing radiation (e.g., lasers)
 - Thermal stress (hot/cold surroundings)
 - Thermal shock (hot/cryogenic materials)
 - Ergonomic injury (repetitive motion injuries)
 - Moving parts
 - Sharp objects
 - Fabrication processes and tools
 - Heavy and awkward loads
- Chemical Agents
 - Oils, greases, and lubricants
 - Solvents, degreasers, alcohol
 - Corrosive substances (acids, caustics)
 - APIs (fine chemicals, biopharmaceutical products)
 - Pharmaceutical excipients
 - Asphyxiant gases (e.g., nitrogen)

- Asbestos
- Polychlorinated Biphenyls (PCBs)
- Disinfectants and sanitizers
- Biological agents
- Flammable dusts, liquids, and gases
- Sensitizing agents
- Reactive or oxidizing chemicals

10.3.2 Control and Mitigation of Hazard and Risk

While hazard and risk are inherent to maintenance work, these can be mitigated and perhaps eliminated by using suitable controls. The following are the controls in the generally accepted hierarchy:

1. Elimination of the hazard at source through engineering, redesign, and continual improvement of the process. This is the most desirable approach.
2. Substitution of the hazardous agent with a less hazardous one. For example, use of citric acid instead of nitric acid for purified water loop passivation.
3. Use of engineering controls, which involves utilizing protective physical systems and equipment to reduce hazard, e.g., air extraction, guarding, light curtains, automatic fire curtains, etc.
4. Use of administrative controls by managing how people work safely, e.g., effective supervision, SOPs, training, work permitting, contractor management, project controls, change control, accident management, etc.
5. PPE to protect the personnel from the hazard. This is the least satisfactory approach as the hazard continues to exist and the worker is dependent on the correct functioning of the PPE as a barrier between the worker and the hazard.

10.4 Control of Hazards and Risks in Maintenance Work Areas

Maintenance work must be performed in a safe and environmentally friendly manner. Equally, the execution of maintenance work may potentially be invasive to the facility, system, and equipment and thus presents a risk to pharmaceutical product integrity and the patient. For both reasons, it is important and recommended that suitable controls be implemented at and around the site of maintenance work. The nature and extent of the controls required will vary according to the task, the location, and the degree of disruption caused by the work. For example, working on a filling machine during a live production batch should be considered as requiring a high degree of GMP and HSE control, while a task in an external area or technical area may require a strong element of HSE control with lesser GMP oversight.

Maintenance work should therefore be planned and implemented in consultation with the area owner (e.g., the manufacturing unit), Quality unit, HSE unit, and other stakeholders, with a commensurate degree of control applied. This section offers general guidance on such controls.

10.4.1 Handover and Hand Back of Facilities, Systems, and Equipment

Each element of a system should have a defined System Owner who is accountable for its operational status. For example, the manufacturing unit may own all manufacturing process equipment. The System Owner should control and authorize the release of the system to the maintenance unit for work to be carried out (handover) and acceptance of the system back from the maintenance unit upon work completion (hand back or acceptance).

Handover and hand back should be formalized through an SOP, and each transaction should be documented. The transaction should be documented, unambiguous, and authorized through any suitable means, such as a System Logbook, Handover Form, Manufacturing Execution System (MES), PTW, etc.

The handover/hand back process may be appropriately simplified for simple tasks such as running adjustments. Nevertheless, such events should be suitably recorded and/or documented in the MMS.

Facilities, systems, and equipment may be subject to concurrent work such as PM and cleaning to take full advantage of downtime windows. These tasks may have differing and sometime conflicting requirements, e.g., maintenance workers may need the system to be operable while cleaners may need it de-energized and locked out. These situations must be carefully managed. Responsibility for system ownership and the system status must always be well defined and clear. Involved parties need to closely communicate and collaborate.

10.4.2 Conflict Between Safety and Product Quality

Some manufacturing processes are inherently hazardous, e.g., processing of toxic, carcinogenic, and corrosive materials. These processes may be performed in controlled and contained environments, such as an isolator. Situations may arise where a maintenance intervention may require containment to be breached, introducing both a hazard to the workplace and potentially compromising product integrity.

These situations must be carefully preplanned and managed, with generation of risk assessment and task-specific SOPs, with input by the maintenance, manufacturing and quality units. Ideally, the situation should not compromise safety or product integrity. However, where conflict arises and cannot be reconciled, then safety must take precedence.

10.4.3 Segregation of Work Areas

It is often necessary to segregate the workplace from normal operations so as to isolate and protect one from the other. The nature and degree of segregation is dependent on the type of work, the criticality of normal operations, and the associated risk assessment. Segregation may take many forms, and the following is general guidance:

- Segregation may comprise physical barriers, such as hoardings, fences, traffic cones, tape, etc. The degree of penetrability will vary according to need and the risk assessment. Segregation can vary from being non-penetrable (e.g., a semi-permanent partition) to being merely indicative and easily penetrated (e.g., cones with tape).
- Segregation may be reinforced with suitable signage, which may be advisory, mandatory, prohibition, or directional.
- Working at height presents risks due to falling objects, such as maintenance materials and tools. Additional precautions such as overhead safety nets or hoardings should be considered.
- Dust screens should be considered if the work is dusty, particle-generating or otherwise impacts GMP area air quality. Such work includes plastering, painting, grinding, cutting, etc. Local extracts and filtration should also be considered to supplement the barrier.
- Specialist advice should be sought if dealing with exceptionally hazardous materials such as asbestos. In such cases, additional precautions will be required.

- Welding screens must be erected if carrying out electro-arc welding, to protect third parties from ultraviolet radiation.
- Invasive maintenance and construction work in a GMP area may necessitate dust-tight hoarding and complete isolation of the work area from the GMP area.
- Where segregation is in place that restricts access for normal operations, alternative means of access may have to be planned and provided.

10.4.4 Personal Protective Equipment

PPE is used to protect workers from hazards when performing maintenance tasks. As stated above, PPE is the least desirable method of hazard mitigation. Other controls, i.e., elimination, substitution, engineering, and administrative, should be applied in preference. The use of PPE should be based on risk assessment of the task, the hazards present, degree of risk, etc. Expert advice, e.g., from an HSE SME, should be sought on its selection and use. Additional general considerations include:

- Personnel must be thoroughly trained in the use of PPE. Lack of training and incorrect use of PPE can negate the protective effect of the PPE or even exacerbate the risk. For example, a poorly fitting respirator could lead to ingestion of noxious gases.
- Persons using respirators and breathing apparatus should receive fit-test training to ensure they are wearing the equipment correctly.
- PPE may be mandated to be periodically tested and certified, e.g., body harnesses, breathing apparatus, respirators. This is a critical requirement.
- PPE may have expiry dates which should be checked, e.g., activated-carbon filter elements. Out-of-date PPE should be disposed of and must not be used. This is also a critical requirement.

10.4.5 Lone Working

Lone work refers to working alone in remote or isolated areas. Maintenance personnel are sometimes required to perform lone work in plant rooms, technical spaces, and void spaces. The following considerations apply to lone working:

- Risk assessment should be performed for all lone working activities.
- Execution of lone working activities should be covered by an SOP.
- The execution of planned high risk tasks by a lone worker should generally be avoided. Examples include working in confined spaces, working at height, and working in restricted spaces.
- Emergency responses should generally not be carried out by a lone worker, although situations will arise where this may be necessary. These lone responders should be trained in emergency response procedures and exhibit due caution.
- The tasks most suited to a lone worker are those that are low risk such as patrol and surveillance, visual maintenance checks, response to some alarms, and emergency responses subject to risk assessment and safety.
- Lone working procedures should make provisions for man-down situations. A lone worker may be injured without a direct means of raising the alarm. Lone workers should ensure as a minimum that their whereabouts are known to a nominated trained and responsible third party, e.g., site security, and should check in with their nominated contact periodically. In the event of a failure to check in, there should be a preplanned search and rescue response.

- Lone working communication systems are becoming increasingly affordable and cost-effective. The following are suggested features:
 - Communication using mobile/cellular phones is readily available and achievable and should be regarded as a minimum requirement.
 - Two-way radio communication with a central manned base, such as security, is recommended.
 - Radios should have a “man-down” feature, to indicate when a person has fallen and is lying prone, indicating that (s)he has been incapacitated.
 - Radios should have a “dead-man” feature, which regularly obliges the holder and transmit an acknowledgement, indicating that (s)he is healthy and safe.
 - It is suggested that radio systems have a graphics-based location-finding facility, to allow the quick location of a casualty.
 - The system must be satisfactorily maintained.

10.4.6 Transport of Materials

It is frequently necessary to transport hazardous and other materials for use on maintenance tasks. Transport may be inter-site or intra-site. General considerations for transport of materials are as follows:

- Inter-site
 - Carriage of hazard substances in vehicles is potentially hazardous, e.g., there may be possibility for the emission of noxious fumes and vapors.
 - In some jurisdictions, the vehicle is considered as part of the workplace and workplace regulations apply in full.
 - Materials should be carried in suitable and approved containers.
 - The storage space should be well ventilated and segregated from the driver's cab.
 - The carriage of dry ice is hazardous due to the generation of CO₂ gas.
- Intra-site
 - Transport of hazardous substances on site should be controlled through SOPs.
 - Hazardous substances must be transported in suitable approved containers.
 - Transport of large volumes of hazardous substances, e.g., bulk containers of acid, should be carefully controlled and managed. There should be a risk assessment and method statement, and the operation may necessitate local evacuations.
 - Special care should be taken when moving materials and tools in and out of a classified area, such as a clean room. All items should be decontaminated, cleaned, and disinfected. There should be an SOP covering such practices.

- Lifting and transport of heavy loads
 - Persons using forklifts must be suitably trained and licensed.
 - The load and reach rating of a forklift must not be exceeded.
 - Forklifts and other load-lifting equipment must be periodically tested and certified.
 - Load configuration should be known in advance of a loading/unloading operation, i.e., dimensions, weight, weight distribution and center of gravity.
 - A single defined person should be in charge of a lift.
 - Personnel should be trained on and observe good manual handling practices at all times.

10.5 Permit to Work System

Permit to Work (PTW) systems provide the means for defining, authorizing, and controlling specific tasks which have an inherent environmental and safety risk. PTW systems provide a means for effecting control over maintenance work that can be potentially hazardous and a documented means for requesting authorization to complete a task. While a PTW system is normal in industry and not unique to the pharmaceutical environment, the rigors of a good PTW system is complementary to those of GMPs.

10.5.1 Key Features of a Permit to Work System

The PTW system may be paper-based or electronic. It should be governed by an SOP which defines and prescribes the applicability, procedures, methods, and forms associated with the PTW system. Where a PTW is required, the PTW form(s) are completed by the person responsible for completing the work (PTW requestor). The following information describing the work should be provided on the form(s):

- Date and time of work commencement and expected completion
- Name of person(s) doing the work (and name of company if applicable)
- Location: building, room, area
- Description of work
- Hazards identified
- Flammable and noxious gas readings if applicable (e.g., for hot work and confined spaces)
- Reference to applicable risk assessments and/or a short risk assessment
- Mitigating controls to be applied, e.g., isolations of services, pre-cleaning, PPE etc.

PTW forms are signed by the requestor and reviewed and approved by an authorized person (PTW issuer) and may require further approval by the operational owner of the work area/system/equipment and by the HSE unit. The signing and approval of the PTW form constitutes an acceptance by the requestor of the terms of the permit and the controls specified and handover to the persons completing the work and for work to commence.

Following completion of work, the PTW is again reviewed and approved by the original PTW issuer. Approval of the PTW constitutes an acknowledgement that work has been completed satisfactorily and a hand back of the area/system/equipment.

The PTW has a defined and limited validity period, typically one day. A hot work permit may have a shorter validity, e.g., one shift. If the work duration exceeds the validity, then the permit should be reissued or extended. The limited validity period obliges the PTW requestor and issuer to periodically evaluate the work and facilitates the necessary supervision and control.

It is necessary and strongly recommended that the PTW issuers be nominated and receive formal and thorough training on the PTW system and associated topics, e.g., hot work and confined spaces.

10.5.2 *Types of Permit to Work*

Examples of the PTWs for various types of work are as follows:

- **General:** Covers relatively low risk tasks with lesser inherent hazard. May reference out to other required permits as listed below.
- **Hot Work:** Strongly recommended for all work which may generate a source of ignition and cause a fire or explosion risk. Specifies additional controls not necessarily specified in the general permit.
- **Confined Spaces:** Strongly recommended for work in confined spaces, due to the demonstrated significant risk of serious injury including asphyxiation.
- **Working at Height:** Used when working at significant height, e.g., roof working and working from a mobile elevated work platform.
- **Electrical:** Used to carry out electrical work on high voltage systems and equipment, typically exceeding 24 VDC.
- **Excavation:** Used where the work requires excavations, due to risk of collapse and possible interference with underground services.

10.5.3 *Applicability of the Permit to Work*

The work for which a PTW is required is variable and a matter for definition by the maintenance and HSE units based on maintenance risk assessments. The following is general guidance:

- The PTW is intended to be adopted for work that is nonroutine in nature and/or where there is the reasonable likelihood of foreseeable and unforeseeable hazards and risks.
 - The PTW may not apply to many routine, innocuous, and low risk tasks, e.g., routine corrective interventions on manufacturing equipment, plant surveillance, and workshop activities. This decision should be based on a risk assessment.
 - A PTW may be required for certain high risk corrective interventions, e.g., invasive work on an isolator containing hazardous product. A PTW should always be issued for hot work, confined spaces working, pressurized systems, systems containing flammable materials (e.g., solvent or gas lines), systems containing toxic materials, working at height, and work invasive to a controlled/classified area, amongst others.
- While the PTW introduces a desirable level of control of certain work where such control is deemed to be required, it also introduces administrative delays and additional costs. Organizations should strive to strike a practicable and reasonable balance between the often-conflicting requirements of working effectively and efficiently versus applying required HSE controls.

- Contractors should generally be obliged to work under PTW, as they are usually less familiar with site procedures and norms and can thus be considered as a higher risk. Exceptions may be made for those contractors who work extensively or full-time on the site and can therefore be regarded as permanent and thus lower risk.

10.6 Control of Hazardous Energies, Lockout/Tagout

Systems and equipment can contain sources of energy that can represent a hazard when performing maintenance. Examples include:

- Electricity, e.g., live conductors and capacitors
- Excessively high temperatures, e.g., ovens, boilers, hot thermal fluid generators
- Excessively low temperature, e.g., freezers, cryogenic units, cold thermal fluid generators
- Compressed gases in pressure vessels, actuators, and pipe lines
- Flywheels
- Counterweights, e.g., passenger and goods elevators (lifts)
- Compressed springs and elastomers
- Parts that may fall under their own weight

Prior to conducting maintenance activities, precautions should be taken to ensure such energies are neutralized so as not to represent a hazard to maintenance personnel. It is recommended that a system of controlling hazardous energies be implemented. There are two aspects to consider: COHE and LOTO.

10.6.1 Control of Hazardous Energies

COHE involves making equipment safe prior to work commencement by isolating the equipment from energy sources, such as electricity and compressed gases, and by neutralizing internal sources of stored energy, such as springs or counterweights. If this cannot be completely achieved, residual energies should be identified and controlled through risk assessments and SOPs.

In some jurisdictions, there are statutory requirements governing the design of equipment so that energies are neutralized automatically when guards are opened for routine operational access. Refer to, for example, the EU Machinery Directive (2006/42/EC) [22] and US OSHA [23] codes.

In many cases, making equipment safe and de-energized must be performed manually, e.g., making a compressed air receiver safe by isolating the supply and exhausting the vessel. It is recommended that all such de-energization processes be governed by task-specific SOPs.

10.6.2 Lockout/Tagout

When equipment is being made safe for maintenance, it is highly recommended that energies and hazardous services be isolated by the person(s) performing the work. The means of isolation should be controlled by the persons performing the work and should not be interfered with by third parties.

LOTO is a complementary process giving effect to COHE and provides an effective system of isolating energies and services in a controlled manner.

Services such as electricity, compressed gas, water, etc. should be isolated and a lock placed on the valve or isolator (lockout). For valves, a protective lockable cover may also be used. A warning label ("Do Not Use", "Do Not Switch On", etc.) is placed on the lock (tagout) with the lock owner's name and contact details. Where a lock cannot be used, e.g., on non-lockable components such as Miniature Circuit Breakers (MCBs), a flexible tie such as a cable tie may be used instead.

The COHE/LOTO system should be regarded as a critical safety process and be appropriately managed. Advice should be sought from an SME. General guidance is provided as follows:

- The system should be governed by an SOP, and records and logs should be maintained.
- The system should govern all LOTO events on the site, including for example replacement of legacy locks left in place from site construction activities.
- Task-specific SOPs, WOs and PTWs should cite any relevant LOTO requirements.
- Maintenance practitioners should use individual personal locks, and the system should make provision for the use of group locks in addition to (and not instead of) individual locks. Usage of locks should be logged, including details of the user and lock location.
- There must be close control and documentation of the removal of abandoned locks. Removal should be sanctioned by designated authorized persons after verification that the lock is redundant and no longer necessary.
- A comprehensive range of LOTO equipment should be provided to cover all requirements, including valves, electrical isolators, MCBs, and pipe lines (e.g., blanking spades).
- It is permissible for locks to be left in place permanently, e.g., lockout of spare pipe line spurs and spare electrical feeds. These must be recorded/logged.
- The system should also govern the practice of bypassing or disabling protective safety devices, such as safety guard switches and the use of "jogging/inching" devices. These practices are often required during maintenance interventions and should be governed by risk assessment and SOPs.

10.7 Confined Spaces and Restricted Spaces

Maintenance work frequently needs to be performed in confined spaces. The Ireland Health & Safety Authority [24] provides the following definitions:

"Confined Space refers to any place, including any vessel, tank, container, pit, bund, chamber, cellar or any other similar space which, by virtue of its enclosed nature, creates conditions that give rise to a likelihood of an accident, harm or injury of such a nature as to require emergency action due to

- *the presence or reasonable foreseeable presence of:*
 - *flammable or explosive atmospheres*
 - *harmful gas, fume or vapour*
 - *free flowing solid or an increasing level of liquid*
 - *excess of oxygen*
 - *excessively high temperature*

- *the lack or reasonably foreseeable lack of oxygen*

The key characteristics of a confined space are:

- *the space must be substantially enclosed*
- *there must be a risk of at least one of the hazards listed above occurring within the space*
- *the risk of serious injury from the hazard must be created by virtue of the enclosed nature of the space*
- *the potential injury must be serious and be such as to require emergency action to rescue the person involved.”*

While confined spaces are not common in the manufacturing areas of pharmaceutical facilities (exceptions include bioreactors and API reactors), they are commonly found in the utilities and service areas. Examples include:

- Storage vessels for purified water, WFI, and compressed air
- Wastewater treatment vessel
- Foul and surface water drainage manhole

It is strongly recommended that SMEs be engaged in advising on work in confined spaces. General information and suggested areas on which to focus are as follows:

- Working in confined spaces should be governed by an SOP that covers the methods, procedures, and controls. The SOP should integrate with other HSE controls, such as the PTW, WOs and COHE/LOTO systems, to ensure that critical control measures are highlighted and applied.
- The Confined Space PTW is a critical document. In addition to the usual details associated with a PTW (as discussed in Section 10.5), it should also detail and/or confirm the following:
 - Task-specific risk assessment, risks/hazards identified and associated mitigating controls
 - Identification and isolation of services, application of COHE/LOTO)
 - Verification of satisfactory oxygen levels and absence of noxious gases
 - Verification that there is no flammable atmosphere present
 - Verification of availability and fitness for use of breathing apparatus and rescue breathing apparatus
 - Verification that a work area is cleared and safe for work
 - Verification that a watchperson has been nominated and is continuously available
 - Communications system, e.g., two-way radio, is available and used by workers and watchpersons
 - Verification that rescue equipment is available, e.g., body-harness, rescue line and hoist
 - PPE to be used
 - Persons performing the task and the watchperson are trained on the work being performed and all associated HSE controls, including rescue and use of breathing apparatus.

- First aid response is on standby
- Persons working in confined spaces must be satisfactorily trained in all aspects of the work, including specific training on working in confined spaces, use of breathing apparatus, use of gas detector, use of PPE, and rescue.
- The atmosphere in the work area must be checked for noxious and flammable gases, and readings noted and approved. The person working in the confined space must either wear a personal meter or have one in close proximity.

A restricted space is not a confined space; however, it shares some of the characteristics of a confined space in terms of restricted access/egress, difficulty in rescuing an injured person, and potential for injury. Examples of restricted spaces include above-ceiling and below-floor voids, AHUs, and technical spaces. Work in restricted spaces should be risk assessed and subject to a general PTW and perhaps other permits as appropriate. Hazards should be identified, and appropriate controls specified. Controls may include rescue arrangements, PPE, buddy/watchperson, etc.

10.8 Hot Work

Hot work represents a potential fire and explosion risk, especially in the presence of a flammable or explosive atmosphere or combustible materials. Hot work can be defined as any work that may give rise to generation of sources of ignition (e.g., flame, heat, and sparks) such as welding, cutting/grinding, electrical work, brazing/soldering, and use of hot tools. Hot work activities pose safety hazards and fire risk. Enhanced controls are required within the wider MMS.

General considerations for hot work are as follows:

- Risk assessments should be performed for hot work activities and appropriate mitigating controls applied.
- Hot work should be governed by an SOP that covers the methods, procedures, and controls. The SOP should integrate with other HSE controls, such as the PTW, WOs and COHE/LOTO systems, to ensure that critical control measures are highlighted and applied.
- Hot work should be governed by a hot work PTW that details the following:
 - Task-specific risk assessment.
 - Hazards identified and associated mitigating controls.
 - Verification that the work area has been cleared of flammable, explosive, combustible, and hazardous materials, and has been cleaned and made safe for work.
 - Verification that there is no flammable or explosive atmosphere present.
 - Verification that fire sensors have been disabled through a formal disablement process. This is necessary as smoke or fumes may trigger the sensors.
 - Verification that suitable fire extinguishing equipment is available adjacent to the work.
 - Verification that a fire watch, by a designated trained person, will be maintained of the work area for at least one hour after the completion of work to ensure that there is no danger of a fire starting.
 - PPE to be used by the person performing the work.

10.9 Flammable and Explosive Atmospheres

Flammable and explosive atmospheres may occur in certain areas of pharmaceutical manufacturing plants, e.g., areas used for the processing of fine chemicals, APIs, fine powders, and volatile flammable solvents such as alcohols, as well as solvents used for cleaning purposes. The hazard arises due to the generation of a flammable mixture of either volatile vapors or powders with air.

Areas that may contain such hazardous atmospheres should be designed and constructed so that there are normally no sources of ignition present which may ignite or explode the atmosphere. Such design features include the specification and installation of intrinsically safe equipment, enclosed electrical equipment, or positively pressurized electrical equipment.

Facilities that may possibly contain such hazardous areas are subjected to Hazardous Area Classification. This is a site survey that studies each area for its propensity to generate a hazardous atmosphere. Each area is zoned accordingly. Refer to local and national regulations for the specific details regarding Hazardous Area Classification.

Note: The classification and maintenance of hazardous zoned areas is a highly specialized subject. It is strongly recommended that expert advice be obtained.

10.10 Working at Heights

Working at heights is a common maintenance activity especially in the area of building maintenance. Working at height can be broadly defined as any work that takes place above ground level, such as cleaning and maintenance of high-level lighting, roofs, high-level pipelines, raw material silos, and building fabric. The relevant hazard involves fall of either personnel and/or equipment/tools, both of which pose potential for injury. The degree of risk and potential injury increases with increasing height, although serious injury can result from a fall from even a modest height.

General considerations for working at height are as follows:

- Working at height should be governed by an SOP that covers the methods, procedures and controls. The SOP should integrate with other HSE controls, such as the PTW, WOs and COHE/LOTO systems, to ensure that critical control measures are highlighted and applied.
- Risk assessments should be performed for working at height activities and can provide input into the determination of whether a PTW is required. If a PTW is required, a general PTW may suffice or an additional work at height PTW may be required.
- Persons working at height should receive specific training relating to working at height, correct operation of equipment (such as work platforms), and PPE.
- Access equipment should be maintained, tested, and certified periodically by a suitable professional. In some jurisdictions, this is mandatory. Equipment should be clearly labeled as having been tested and is fit-for-use. A color-coding label system is recommended. Scaffolding should be erected, checked, and certified by a qualified scaffolder. In some jurisdictions, this is mandatory.
- The working at height PTW is typically used for higher risk tasks, e.g., working on a roof close to an unguarded ledge. It is a critical document and should contain the usual details associated with a work permit as well as the following:
 - Task-specific risk assessment
 - Hazards identified and associated mitigating controls

- PPE to be used by the person performing the work, including fall arrest harness and lanyard
- Verification that the person carrying out work is appropriately trained, e.g., work at height training, operation of mobile elevated work platform, etc.
- Verification of condition of access equipment to be used, e.g., mobile elevated work platform, ladder, scaffold, etc.

10.11 Working with Compressed Gases

Compressed gases (e.g., air, argon, oxygen, etc.) represent a considerable hazard and risk to maintenance workers due the presence of significant stored energy. Additional hazards and risks arise in relation to flammable gases (such as butane, propane, and acetylene), flame-promoting gases (such as oxygen), and very hot gases (such as steam).

General considerations for working with compressed gases are as follows:

- Risk assessments should be performed for work involving compressed gases.
- Specialist advice should be obtained in relation to working with steam systems and flammable gases. The maintenance and operation of steam systems is a specialist subject requiring a relevant SME.
- COHE/LOTO should be correctly applied.
- Compressed gas systems should be regularly monitored and maintained.
- Compressed gas cylinders should be stored correctly at point of storage and point of use, and care should be taken to transport them in a suitable conveyance. The storage area must be protected, not subject to risk from damage, collision, extreme temperatures, and direct heat and sunlight.
- Compressed gases must be clearly labeled to include identification, pressure, and special precautions required.
- Compressed gas pipelines must be clearly identified to include identification and flow direction.
- Correct lubricants should be used when maintaining compressed gas systems and equipment such as manifolds, valves, fittings, etc.
- Smoking must be prohibited in the vicinity of compressed gas storage.

10.12 Mandatory Maintenance Practices

Maintenance practices and work may be mandated by local, national, or federal regulation or statute. Such requirements will vary according to the jurisdiction. Additionally, further requirements may be mandated by property loss insurers. Periodic inspection and maintenance may be mandated for systems such as life safety protective systems, pressurized systems, refrigeration systems, environmental protection systems, etc.

The following is a non-exhaustive list of example systems and equipment for which maintenance may be mandated for one or more of the reasons cited above:

- **Pressurized systems:** Pressure vessels (air, steam), Pressure Safety Valves (PSV), refrigeration coils, steam boilers

- **Waste systems:** Wastewater treatment plant, HVAC exhaust filtration, fire water retention, air exhaust scrubber, chemical spill kits
- **Fire safety systems:** Fire alarm systems, sprinkler systems, fire extinguishers, automatic fire suppression, automatic fire curtains
- **Electrical systems:** Main switch, medium voltage systems, lightning protection, low voltage socket circuits, residual current protective devices, earth-leakage protective devices, earthing and grounding circuits, emergency lighting, portable appliances
- **Life safety systems:** Breathing apparatus, oxygen meters, noxious gas meters
- **Lifting gear:** Passenger and goods elevators, chains/ropes/shackles, forklifts, powered pallet trucks, hoists and lifters, A-frames
- **Working at height equipment:** Mobile elevated work platforms, fixed work platforms, scaffolding, ladders, body harnesses, fall arrest systems, lanyards, roof tie-on lines

Considerations for maintenance practices include:

- All maintenance events should be managed through the MMS, leveraging the reporting systems.
- Within the reporting and archiving system, there should be readily available access to the subset of maintenance records and documents relating to mandatory maintenance. It is likely that such records will be sought by regulatory, insurance, or company compliance inspectors.
- Maintenance work requiring system shutdown should be coordinated with the general site shutdown, subject to remaining in schedule compliance.
- Statutory inspections should be scheduled to ensure that they are completed on or before the mandated date. It would be prudent to adopt a maintenance interval less than that prescribed. e.g., use a 12 month interval where 14 months is prescribed.
- Loss insurers may wish to inspect and survey equipment.
- Maintenance records should be readily available for inspection for auditors including regulatory inspectors and insurance inspectors.
- Systems and equipment should, if practical, be clearly labeled to indicate the inspection status and fitness for use. Calibration labels should be clearly visible.

10.13 Facility Design for Maintenance Safety

Early input to a developing project may identify opportunities to ensure that facilities, systems, and equipment are safe and maintainable and to reduce or eliminate hazards and risks. It is recommended that maintenance personnel be embedded into development project teams at an early stage. Hazard and risk may be reduced in the following ways:

- Influence the selection of equipment from the operation and maintenance safety perspective, e.g., standardization of equipment specification, provision of protective features, etc.
- Participate in C&Q activities to ensure that equipment is correctly installed and operating safely and effectively, and that safety features and alarms are functioning correctly

- Monitor and influence the installation to ensure maintainability, e.g., access for maintenance, facilities for ready removal and replacement of heavy components and provision of isolation valves
- Build knowledge of the facility, system, and equipment to allow advance preparation of risk assessments

10.13.1 Maintenance Safety Considerations in Project Design Phase

This section provides general guidance regarding critical issues to be considered at the design and build stage. It is not intended to be a comprehensive overview of the topic.

- **General**
 - Regulatory documentation should be obtained from the vendor in advance of operation, e.g., type and test certification, safety documentation (e.g., in EU, CE Certificate of Incorporation, Declaration of Conformity, etc.).
 - The risk assessment process should commence at the installation and C&Q stage.
- **Systems and Equipment**
 - Adequate space should be allowed around equipment to allow maintenance access.
 - Services to equipment, e.g., electricity and compressed air, should be routed so that they do not represent a trip hazard or head injury hazard.
 - Equipment installed in restricted spaces should have adequate maintenance access through suitably sized access openings. Where heavy equipment is installed in such spaces, e.g., an AHU installed in a ceiling void, a safe method of removing and replacing the entire equipment and/or major components must be defined and provided at the installation stage.
 - Adequate isolation valves should be installed on services to facilitate safe maintenance. Double isolation valves are strongly recommended for steam systems.
 - Equipment interior spaces, e.g., electrical cabinets, should have adequate lighting.
 - Electrical cabinets should be fitted with standard electrical mains sockets.
 - Filters which may become contaminated with hazardous substances should be fitted with a safe-change facility, e.g., bag-in/bag-out or similar.
- **Buildings**
 - The building design should allow for ready and safe access for substantial equipment to all areas and levels. This may comprise provision of roller doors, demountable panels etc.
 - "Walk-on" ceilings should be load-rated for a maintenance person and tools and be clearly signed to that effect. Non-compliant ceilings should have restricted access.
 - Void spaces should be as tidy and organized as possible as regards pipe and cable runs. Delineated crawlways, adequate ventilation, and work lighting should be provided.

- Design must enable and facilitate maintenance work at height. For example:
 - > Ground level layout should allow for access by wheeled work platforms or at least have free space to allow placement of a fixed platform or scaffold.
 - > Luminaires should be accessible from an elevated work platform or similar without need to overreach.
 - > Elevated areas (such as ceilings, walls and catwalks) requiring cleaning should be accessible from a work platform using long-handled mops but without overreaching.

10.13.2 Changes to Systems

The maintenance unit should be an active participant in the site Engineering and Quality Change Control processes. The maintenance unit is responsible for maintenance of almost all systems and equipment on site and should be an active stakeholder in all proposed changes, being best placed to offer input on technical and safety aspects.

10.14 Environmental

The impact of maintenance activities upon the environment can be significant. The maintenance unit should understand the operations being performed and the environmental risks associated with those operations. The HSE unit, and other SMEs as required, should be consulted and involved in the planning of maintenance activities that are potentially environmentally sensitive.

Sites may be regulated by an environmental regulatory agency such as the US Environmental Protection Agency (EPA) [25] and be issued with an environmental license accordingly. The licensed emission limits generally have legal force with substantial penalties for breaches of the license. The penalties can include fines and, in more extreme cases, imprisonment and site closure. These requirements will differ according to jurisdiction.

The following are general classifications of emissions, which may be subjected to mandated limits:

- Emissions to atmosphere, e.g., HVAC, combustion engines, gas-fired equipment, refrigeration systems, process venting
- Emissions to public wastewater, e.g., wastewater treatment plant, fire water retention, chemical spills
- Emissions to ground and surface water, e.g., rainwater, leaks from underground tanks, oil interceptors, chemical spills
- Noise emissions, e.g., external utilities, vents

Considerations for maintenance impacts and controls are as follows:

- The regulator may mandate the measurement and recording of licensed emissions at defined intervals. Records must be archived and readily available for inspection. The regulator may carry out periodic verification measurements or mandate the use of an independent third party to do so.
- Equipment giving rise to licensed emissions should be properly maintained in accordance with vendor recommendations and demonstrated operating experience.
- Pipe lines and valves are subject to leakage and failure which may result in unplanned or fugitive emissions. Such equipment should be included in the Maintenance Program.
- Waste materials, e.g., contaminated filters, should be correctly disposed of.

- Equipment fitted with emergency relief systems, e.g., bursting discs, may give rise to sudden emissions in excess of licensed limits. Such equipment should be audited and emergency response plans developed in the event of an emission.
- Bioactive wastewater treatment plants must be monitored for bioactivity, which must be maintained at the required level.
- Spills of prohibited substances should be contained and cleaned up immediately. Spill control kits should be readily available, and staff trained in their correct use.
- Drains in areas which may be subject to oil or grease spills, e.g., parking lots and kitchens, must be fitted with oil/grease interceptors which should be cleaned and maintained periodically.
- External liquid storage tanks must be contained in liquid-tight bunds which should be periodically checked for integrity.
- All maintenance, manufacturing, and laboratory staff should be fully trained in the correct disposal of waste and the necessity not to allow prohibited substances from entering stormwater and surface drains.

10.14.1 Waste Management

Waste management is of critical importance in pharmaceutical manufacturing sites. The wider subject of waste management and environmental impact is beyond the scope of this Guide and the following sections focus on waste management implications for maintenance.

The responsibility for waste management varies by site; however, it is typically a responsibility of the wider engineering/maintenance function or the HSE function.

Collection and disposal of hazardous waste is strictly regulated with site operating permits required in many jurisdictions. Even non-hazardous solid wastes may be controlled by weight or volume due to limited off-site disposal facility capacity. The recommended practice is to continually seek opportunities to minimize waste disposal volumes or recycling opportunities either on site or as secondary use materials. Management should implement programs to eliminate, reduce, reuse, and recycle waste in a manner that increases the overall efficiency of the business.

However, it is important to note that such waste reduction programs must not compromise the effective and safe disposal of hazardous waste containing highly toxic and potent substances. Such materials are generally not to be recycled unless the method has been validated as safe.

10.14.1.1 Sources of Waste in Maintenance

Many maintenance activities result in the generation of waste. The following are examples (the list is not exhaustive):

- Used lubrication oil from gearboxes and drives
- Used oils and oil filters from hydraulic and hydrostatic systems
- Spent grease cartridges and other oil containers
- Used HVAC and process filters containing contaminants
- Contaminated PPE (e.g., coveralls, respirator cartridges, dust masks)
- Defective product contact parts (e.g., filling parts, hoppers, needles, tubing, seals, filters, etc.) – such parts are likely to be contaminated

- Defective non-product contact parts (e.g., drives, valves, etc.) – these are less likely to be contaminated
- Degreasing and other solvents

10.14.1.2 Maintenance Impact and Controls

- The maintenance unit should collaborate and cooperate closely with the site waste management authority and HSE unit, and rigidly follow the waste management policies, procedures and methods.
- Maintenance safety procedures should be strictly adhered to, e.g., bag-in/bag-out method for filter changes, use of correct PPE, etc.
- Waste disposal procedures and methods should be included in relevant maintenance SOPs and on relevant maintenance documentation, e.g., work instructions, WOs, etc.
- Waste should be correctly streamed.
- Maintenance staff should be aware of and watchful for complacency in the disposal of apparently innocuous items, which may have critical implications if incorrectly disposed of, e.g., a defective mechanical seal which may be contaminated with highly potent or toxic material.
- Maintenance staff should be aware not to “cut corners” on waste disposal costs. Specialist waste disposal methods can be expensive, e.g., incineration; however, such budget and cost decisions have been decided by management and SMEs, formalized by approved policies and procedures, and should not be countermanded.

10.14.2 Energy Management

Energy management is of increasing importance worldwide with increasing emphasis on the environmental impact of energy generation and waste, as well as the focus on energy cost reduction as an important site efficiency tool. As for waste management, the wider subject of energy management and environmental impact is beyond the scope of this Guide and the following two sections focus on energy management implications for maintenance.

The responsibility for energy management varies by site; however, it is typically a responsibility of the wider engineering/maintenance function or the HSE function.

Maintenance can play a significant part in optimizing the energy usage of the site.

10.14.2.1 Major Energy Users

Within a pharmaceutical manufacturing plant, there are many significant energy users. The following are examples (the list is not exhaustive):

- HVAC
- Refrigeration including chilled water generation, office air conditioners, cold rooms, and freezers
- Compressed air generation
- Space heating and cooling, including associated hot and cold water systems
- Process heating, e.g., large bioreactors and mixers
- Lighting

10.14.2.2 Maintenance Impacts and Controls

Within the wider energy management program, there are many energy waste reduction initiatives that fall within the maintenance unit responsibility through effective and focused routine maintenance activity. Example activities are as follows:

- All equipment should be maintained as per manufacturer's recommendations and operating experience.
- Review and optimize HVAC systems, including replacement of filters on a timely basis.
- Review and optimize compressed air usage. Consider implementation of a compressed air leakage reduction program.
- Optimize lighting systems: LED lighting, smart lighting features (occupancy sensing, reaction of lighting level to available daylight level, dimmable light levels, etc.), and public lighting passive infrared sensors and timers (in working order and correctly set).
- Check steam systems: repair leaks and check pressure relief safety valves (replace/repair as needed). Leaking valves represent a potentially huge loss of energy and are frequently not detected and/or are ignored.
- Adopt waste heat recovery where possible and subject to reasonable payback.
- Check for proper insulation of hot and cold fluid systems, e.g., hot, cold, and chilled water and thermal fluid systems. Insulation should be periodically inspected; damaged and missing insulation should be repaired. This has implications for both energy usage and health and safety, i.e., prevention of hot/cold burns.
- Consider a program of electrical load shedding at peak times.

10.14.3 Retirement and Decommissioning

Due consideration must be given to environmental issues when retiring, decommissioning, and disposing of equipment. This important topic is covered comprehensively in the *ISPE Good Practice Guide: Decommissioning of Pharmaceutical Equipment and Facilities* [26].

11 Appendix 3 – Science-Based Quality Risk Management

11.1 Purpose

The Maintenance Program for a GMP facility and equipment should be built on its risks. When the equipment and systems are initially registered in the MMS, as well as when PM tasks are generated for specific equipment or component, it is important that such documents for scoping the maintenance effort are created from a science-based quality risk process. Identical pieces of equipment could have very different Maintenance Programs due to their different levels of science-based quality risk.

11.2 Risk Management

Risk management is a systematic application of management policies, procedures, and practices to the task of identifying, assessing, controlling, and monitoring risks. It is typically an iterative process.

Risk management should be based on good science and product and process understanding, e.g., an understanding of CQAs, which is based upon and ultimately traceable back to the relevant regulatory submission.

Qualitative or quantitative techniques may be used. The focus should be on the risk posed to patient safety and product quality.

Risk management should reduce risks to an acceptable level. Complete elimination of risk is neither practical nor necessary.

For a given organization, a framework for making risk management decisions should be defined to ensure consistency of application across functions. Such a framework is most effectively implemented when it is incorporated into the overall QMS.

11.3 ICH Q9 Quality Risk Management Approach

ICH Q9 [1] describes a systematic approach to QRM. ICH Q9 is used as the basis of the QRM approach described in this Guide.

ICH Q9 defines two primary principles of QRM:

- The evaluation of the risk to quality should be based on scientific knowledge and ultimately link to the protection of the patient
- The level of effort, formality, and documentation of the QRM process should be commensurate with the level of risk

ICH Q9 is intended for general application within the pharmaceutical industry.

This Guide uses the following key terms from ICH Q9 [1]:

Harm: Damage to health, including the damage that can occur from loss of product quality or availability.

Hazard: The potential source of harm.

Risk: The combination of the probability of occurrence of harm and the severity of that harm.

Severity: A measure of the possible consequences of a hazard.

This Guide applies the general principles of ICH Q9 to describe a general process for QRM consisting of the following elements:

- Risk Assessment
- Risk Identification
- Risk Analysis
- Risk Evaluation
- Risk Control
- Risk Reduction
- Risk Acceptance
- Risk Communication
- Risk Review

The process is described in more detail in the following sections.

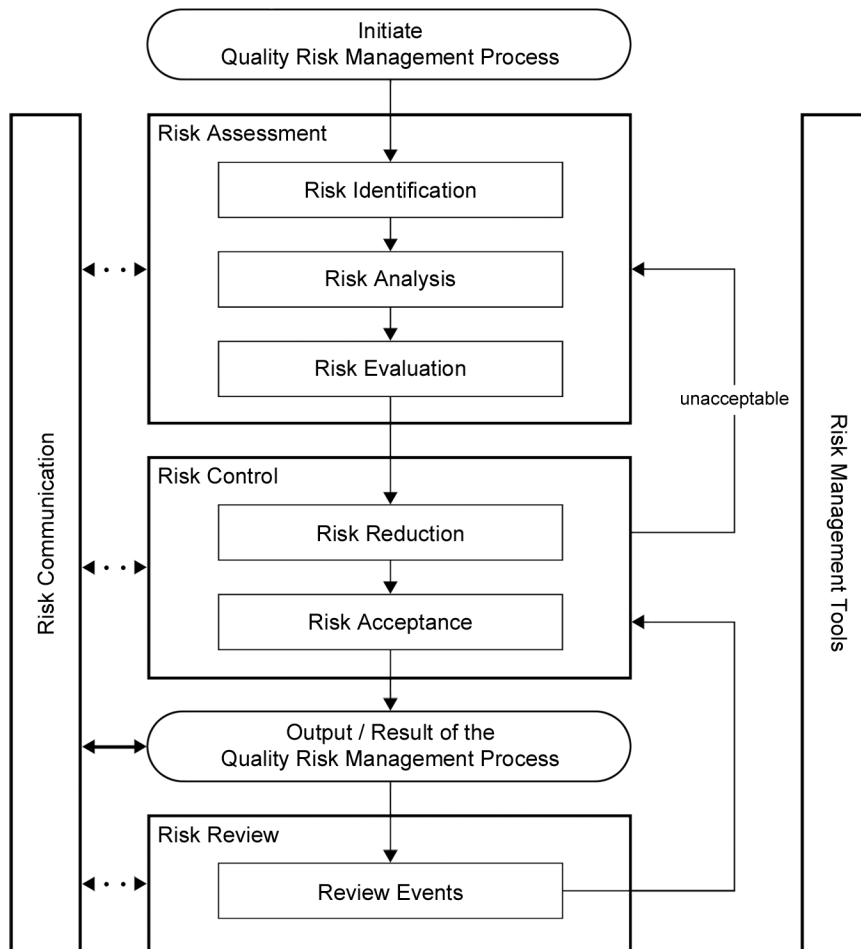
11.4 Overview of the Quality Risk Management Process

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

A model for QRM from ICH Q9 is provided in Figure 11.1.

The emphasis on each component of the framework might differ from case to case, but a robust process will incorporate consideration of all the elements at a level of detail that is commensurate with the specific risk.

Figure 11.1: Overview of a Typical Quality Risk Management Process – from ICH Q9 [1]



11.5 Initiating Quality Risk Management

QRM should include systematic processes designed to coordinate, facilitate, and improve science-based decision making with respect to risk.

The following steps should be considered when initiating and planning a QRM process:

- Define the problem and/or risk question, including pertinent assumptions
- Identify the potential for risk
- Assemble background information and/or data on the potential hazard, harm, or human health impact relevant to the risk assessment
- Identify a leader and necessary resources
- Specify a timeline, deliverables, and appropriate level of decision making for the risk management process

Determining the risks associated with maintenance requires a common and shared understanding of factors such as:

- Impact of operational tolerances on patient safety and product quality
- Impact of design of facilities and equipment on maintenance activities
- Impact of methods and materials used during maintenance activities
- Maintenance Programs and Maintenance Plans
- Training

11.6 Risk Assessment

Risk assessment consists of the identification of hazards and the analysis and evaluation of risks associated with exposure to those hazards, and consists of identification, analysis, and evaluation activities.

Risk assessment addresses the following questions:

- What might go wrong?
- What is the likelihood (probability) it will go wrong?
- What are the consequences (severity)?

Risk identification is a systematic use of information to identify hazards referring to the risk question or problem description. Information can include historical data, theoretical analysis, informed opinions, and the concerns of stakeholders. Risk identification addresses "What might go wrong?" including identifying the possible consequences. This provides the basis for further steps in the QRM process.

Examples of GMP risks include:

- Contamination of product caused by maintenance practices, e.g., use of inappropriate spare parts that contaminate product
- Facilities or equipment design that does not facilitate appropriate levels of maintenance
- Lack of GMP training for maintenance technicians
- Maintenance activities cause (critical) equipment to be (unknown to production) out of service

Systems or equipment that may impact product quality or patient safety (GMP systems or equipment) should be identified as part of the commissioning process.

Risk analysis is the estimation of the risk associated with the identified hazards. It is the qualitative or quantitative process of linking the likelihood of occurrence and severity of harm. The ability to detect the harm also should be considered in the estimation of risk.

Risk evaluation compares the identified and analyzed risk against given risk criteria. Risk evaluations consider the strength of evidence for all three of the fundamental questions.

Typically, the outcome of the risk assessment will be expressed using qualitative descriptors, such as "high," "medium," or "low." These terms and how they are used should be defined in as much detail as possible.

11.7 Risk Control

Risk control includes decision making either to reduce risks or accept them, or both. The purpose of risk control is to reduce the risk to an acceptable level. The amount of effort applied to risk control should be proportional to the significance of the risk.

Risk control addresses the following questions:

- Is the risk above an acceptable level?
- What can be done to reduce or eliminate risks?
- What is the appropriate balance among benefits, risks, and resources?
- Are new risks introduced as a result of the identified risks being controlled?

Risk reduction focuses on processes for the mitigation or avoidance of quality risk when it exceeds a specified (acceptable) level. Risk reduction might include actions taken to mitigate the severity and probability of harm. Processes that improve the detectability of hazards and quality risks also might be used as part of a risk control strategy. The use of PdM technologies can increase the detectability of an equipment failure and might be implemented where the associated risk warrants such an approach.

The implementation of risk reduction measures can introduce new risks into the system or increase the significance of other existing risks. For example, frequent maintenance on equipment increases the probability of error in disassembly or reassembly. Hence the results of risk assessment should be revisited to identify and evaluate any possible change in risk after implementing a risk reduction process.

Risk acceptance is a decision to accept risk. Risk acceptance can be a formal decision to accept the residual risk or it can be a passive decision in which residual risks are not specified.

For some types of harm, even the best QRM practices might not entirely eliminate risk. In these circumstances, it might be agreed that an appropriate QRM strategy has been applied and that quality risk is reduced to a specified acceptable level. This specified acceptable level will depend on many parameters and should be decided on a case-by-case basis.

Procedural and technical controls available to reduce risks to an acceptable level include establishing a Maintenance Program that includes, for example:

- System inventory and risk assessments
- Maintenance Plans
- Change management
- Clearly defined roles and responsibilities
- Documentation requirements
- Spare parts
- Training

11.8 Risk Communication

Risk communication is the sharing of information about risk and risk management between the decision makers and others. Parties can communicate at any stage of the risk management process.

The output and result of the QRM process should be appropriately documented and communicated, e.g., to regulators, to the patient, within a company.

The relationship between the maintenance unit and operations should be a partnership with mutual accountability for asset care. Each department should communicate with the other to ensure errors are avoided. For example, operating departments need to provide detailed information about equipment when in need of repair rather than indicating "it is not working." Similarly, the maintenance unit should inform the operating department that they can resume use of the asset following completion of a repair to avoid partially repaired equipment from being placed into service.

11.9 Risk Review

Risk management should be an ongoing part of the quality management process. A mechanism to review or monitor events should be implemented.

The output and results of the risk management process should be reviewed to take into account new knowledge and experience. Once a QRM process has been initiated, that process should continue to be utilized for events that might impact the original QRM decision, whether these events are planned (e.g., results of product review, inspections, audits, change control) or unplanned (e.g., root cause from failure investigations, recall).

Use the data gathered by the Quality system to find opportunities to further minimize the GMP risks.

11.10 Quality Risk Management Tools

No one tool or set of tools is applicable to every situation in which a QRM process as described is applied. ICH Q9 [1] provides a general overview of and references for some of the primary tools used in QRM by industry and regulators:

- PM
- PdM
- RCM Analysis
- FMEA
- RCFA

Typically, the maintenance unit is involved in these types of processes and analysis.

12 Appendix 4 – Templates and Examples

12.1 Example Scenarios

The following examples describe possible scenarios and their effects on the Maintenance department.

Example 1: Walk-in Cold Room

A company installs a walk-in cold room designed to maintain product at 2°C to 8°C. Per the URS (User Requirement Specification), the temperature is determined to be critical to product quality.

The company does not perform a risk assessment and assumes that all of the system components including mechanical refrigeration equipment, controls, and instruments have potential to impact product quality. The cold room undergoes temperature mapping during C&Q and all maintenance activities on the cold room equipment are considered critical because of the potential to impact product quality. This approach has increased their operating cost and regulatory risk because they have categorized all maintenance activities on the entire system as critical; this approach requires enhanced documentation that is auditable for all routine maintenance, change control, training, parts, etc. Because they have considered all of the components with potential impact to product quality, any changes to spare parts (in terms of parts, part numbers, or suppliers) in the lifetime of the cold room will require extensive and unnecessary documentation review and approval process. This scenario frequently happens with refrigeration compressors as new technologies emerge and old compressors become obsolete.

Alternately, the company could have performed a risk assessment and determined that the only potential impact to product quality is the temperature of the cold room. This will allow the maintenance technicians to work on the equipment, even change out compressors, as long as the temperature stays within its validated range. This system could be verified as fit for the intended use by performing temperature mapping and calibrating the temperature sensor with a chart recorder or digital data recorder.

As a general note, even for non-critical parts, it is recommended to review/compare the functionality of the replacement parts from a reliability perspective. In some cases, the value of product in the cold room may justify redundant refrigeration systems. This would allow time to order and replace parts on one system, while the other system maintains temperature. It might even allow for a strategy of “run to failure” on many of the components.

Example 2: Chilled Water Control Valve

A chilled water control valve controls water to a tank jacket used in a temperature sensitive process. The control loop includes the valve and a sensor/transmitter to record and alarm the tank temperature. A Risk Assessment determined that the sensor/transmitter and the recording device are critical components with potential impact to product quality. On the other hand, the control valve is considered non-product contact with no direct risk to product quality. The sensor/transmitter would detect any malfunction of the chilled water control valve. If the process control system will not allow separation of these two loops, the entire control system would have to be 21 CFR Part 211 [17] compliant. Another concern with this arrangement is that if the sensor/transmitter should go out of calibration, it could drive the tank temperature out of range and likely not be discovered until the next calibration. This will initiate a deviation and all production since the last calibration would be in question in this scenario.

The second option is the installation of a separate sensor/transmitter for the chilled water valve that will separate the two control loops and would allow the maintenance of the chilled water valve and its control loop to be managed under non-GMP procedures. In addition, if the sensor/transmitter controlling the chilled water valve should go out of calibration, then the sensor on the recorder will alarm. Similarly, if the sensor/transmitter on the recorder should go out of calibration, then it will also alarm because the chilled water valve control loop would still be maintaining the correct temperature. The additional cost of the second control system needs to be evaluated against the ease of maintenance and process reliability.

12.2 Maintenance Strategy Template

1. System Description	Brief overview of the system or components to define operating context, functions, and system boundaries. Check all that apply: ☐ Process Flow Diagram (PFD) _____ ☐ Piping and Instrumentation Diagram (P&ID) _____ ☐ Operating Context from Reliability Centered Maintenance (RCM) Analysis _____ ☐ Equipment Schedule _____ ☐ Valve and Line Schedule _____ ☐ Commissioning and Qualification (C&Q) Documentation _____ ☐ Block Diagram _____ ☐ Change Controls _____ ☐ Other _____
2. Classification and Criticality	Define location priority/criticality ranking, GMP impact, and Process Safety Management/ Mechanical Integrity classification of system and components with rationale. Check all that apply: ☐ Criticality Ranking/Location Priority _____ ☐ System Impact via Classification Assessment (Per <i>ISPE Baseline® Guide: Commissioning and Qualification (Second Edition)</i> [2]) _____ ☐ Process Safety Management: Mechanical Integrity _____ ☐ Environmental _____
3. Risk Assessment	Describe potential functional failures, failure modes, consequences, mitigation approach, or other supporting rationale. Check all that apply: ☐ Reliability Centered Maintenance (RCM) Analysis _____ ☐ Failure Modes Effects Analysis (FMEA) _____ ☐ Original Equipment Manufacturer (OEM) Recommendations _____ ☐ Root Cause Failure Analysis (RCFA) _____ ☐ Corrective Action Preventive Action (CAPA) _____ ☐ Change Controls _____ ☐ Critical Measurement/Measurement Uncertainty Analyses _____ ☐ Other _____
4. Maintenance Tasks	Describe maintenance tasks, including preventive maintenance, predictive maintenance, inspections, intervals, tolerances, etc. Source is: ☐ CMMS Records _____ ☐ GMP Library _____ ☐ Equipment Manuals _____ ☐ Other _____
5. Spare Parts	Describe spare parts requirements, including sourcing information. Source is: ☐ CMMS Information _____ ☐ GMP Library _____ ☐ Equipment Manuals _____ ☐ Vendor Parts Information (part number, description, lead time) _____ ☐ Other _____
Developed by: _____ Date: _____	

12.3 Example Maintenance Plan

12.3.1 Example 1: Pump Rebuild PM

Maintenance Plan Operations				Completed		Associated Procedures	
8	Print the preventive maintenance plan from CMMS to document the completion of the maintenance activities. Conduct pre-job brief with maintenance supervisor.			☐ Yes / ☐ No			
9	Collect required PPE (safety glasses, gloves, safety shoes, and hearing protection).			☐ Yes / ☐ No			
10	Review Lockout/Tagout (LOTO) and Job Hazard Analysis (JHA). Verify with P&ID. Check the tools required to perform the task.			☐ Yes / ☐ No			
	Collect spare parts kit.			☐ Yes / ☐ No			
20	Electrician to unwire, mark, and protect leads.			☐ Yes / ☐ No			
30	Uncouple and remove motor to side using crane and use 2 × 4s to crib and cover with weatherproof tarp. (See child WO 1234567 for crane).			☐ Yes / ☐ No			
40	Disconnect pump casing from foundation.			☐ Yes / ☐ No			
50	Use crane to rig and pull pump and transport to be cleaned (sand or cob blast). See child WO 1234567 for crane and child WO 12345678 for cob blasting. Transport the pump to shop after cleaning.			☐ Yes / ☐ No			
60	Dismantle pump and save parts for reliability personnel inspection for root cause analysis.			☐ Yes / ☐ No			
70	Rebuild pump using parts supplied in work kit. Reference pump maintenance manual supplied with work kit. Record clearances and torque settings on hard copy for entry into closing failure remarks.			☐ Yes / ☐ No			
80	Transport the pump to location and install pump and leave uncoupled.			☐ Yes / ☐ No			
90	Install motor and leave uncoupled.			☐ Yes / ☐ No			
100	Electrician to wire up and bump for proper rotation.			☐ Yes / ☐ No			
110	Couple pump to motor and laser align.			☐ Yes / ☐ No			
115	Set the lift.			☐ Yes / ☐ No			
120	Post-maintenance requirements include amp check, discharge pressure, and record both for closing notes. Record vibration reading to verify alignment and pump operation. Vibration has child WO 9876543.			☐ Yes / ☐ No			
130	Clean up job site.			☐ Yes / ☐ No			
140	Return any unused parts to stores with WO number.			☐ Yes / ☐ No			
145	Return Equipment Manual to file.			☐ Yes / ☐ No			
150	Fill out all documentation and enter into CMMS.			☐ Yes / ☐ No			
Labor				Material			
OP#	Craft/ Lab Code	Qty	Est. Hours	OP#	Item	Qty	Used
	EL	1	2.00		103460	1	
	MM	2	12.00		107672	1	
					110185	1	
					110424	1	
					113416	1	
					114203	1	
					117231	1	
					117860	1	
					118707	1	
					121279	1	
					121844	1	

12.3.2 Example 2: Cold Room Quarterly PM

☐ Print the Preventive Maintenance plan from CMMS to document the completion of the maintenance activities.
☐ Conduct pre-job brief with maintenance supervisor.
☐ Collect required PPE (safety glasses, gloves, safety shoes, and hearing protection).
☐ Review Lockout/Tagout (LOTO) and Job Hazard Analysis (JHA). Verify with P&ID.
☐ Check the tools required to perform the task.
☐ Collect spare parts kit.
☐ As required, refer to the equipment maintenance manual for equipment diagrams and/or parts list.
☐ Check compressor oil level (compressor must be running for >30 minutes). If low, check system for leaks and repair as needed. If loss of oil is identified, then recharge the system as needed per manufacturer specifications.
☐ Check compressor crankcase heater by utilizing a clamp on amp-probe to determine if the heater is drawing current. The compressor and heating element should be warm to touch, if not replace heating element per manufacturer specifications.
☐ Check refrigeration system moisture indicator/sight glass for signs of moisture. If moisture is indicated, check for leaks and repair as needed per manufacturer specifications.
☐ Check refrigeration system for proper refrigerant charge. If charge is low, check for leaks and repair/recharge as needed per manufacturer specifications.
☐ Check entire system for refrigerant leaks on all flare connections, suction lines, discharge lines, and all other components with an electronic leak detector. If leaks are found, repair leaks.
☐ Check outdoor condensing units for proper operation. Ensure fan motors are operating and fan blades are balanced and adequately supplying enough air to coils. Inspect unit for abnormal vibration, noises, and any other obscure issues. Clean coil as needed with chemical coil solution and water.
☐ Check defrost heater and defrost cycle to ensure proper operation by inspecting evaporator coils to ensure that there is no frost or ice buildup on the coils. Initiate a defrost cycle if applicable.
☐ Clean evaporator drain pan lines and ensure there are no blockages.
☐ Check the drain line heat tape for rated current draw with amp-probe. Heat tape should be warm to touch; check for abrasions. Repair as needed.
☐ If applicable, dry air added to the cold room should be between 25–35 CFM (Cubic Feet per Minute) (708–991 Liter per Minute) from plant air supply.
☐ Check the integrity and condition of the door and door frame seals. If damage or degradation is noted, repair or replace seals.
☐ Check door hinges and latch for proper operation and for loose or missing fasteners. Repair or replace as required.
☐ If equipped with door frame heater, inspect and test the function of the door frame heaters by utilizing a clamp on amp- probe to determine if the heaters are drawing current. The door frame should be warm to the touch. If not working repair or replace heating element.
☐ Check to make sure door rolls freely without any drag or binding during manual operation. Refer to the manufacturer's manual for further information and drawings of the door mechanisms.
☐ If equipped with an automatic door opener, check to make sure door opens and closes properly in power operation mode. If adjustments are required for the door seal, floor guide wheel, door drive chain, door travel limit switch chain, or pedestrian opening adjustment, refer to the manufacturer's manual for further information and drawings of the door mechanisms.
☐ Check to make sure the door safety edge strip functions properly. Refer to the manufacturer's manual for further information and drawings of the door mechanisms.
☐ Fill out documentation and enter to CMMS.
☐ If recharge is needed, refrigerant loss form must be completed and submitted to safety department.

12.4 Example Maintenance Plan Checklist

The following is an example of a checklist used in conjunction with a Maintenance Plan to perform PM on a WFI distribution loop. The 5 year PM requires replacing all of the valve diaphragms (for automated, manual, and sample valves) in the loop.

[illegible]

12.5 Example Change Control Request/Approval Form

Change Control Number: _____	Work Order Number: _____																												
☐ Emergency Work – Verbal Approval received: _____ ☐ Computer System Change																													
Change Description (as is): _____ Change Description (to be): _____ Justification: _____ High-level Plan: _____ Contingency Plan: _____ Associated Change Control/Work Order: _____																													
SME Assessment: _____ Deliverables (detailed list of all items/actions to update/perform based on SME assessment): _____ _____ _____ _____ _____																													
Risk Assessment and Mitigation: _____ Effectiveness Check Assessment: _____																													
Status of Equipment	<table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="width: 33%; text-align: center;">YES</th> <th style="width: 33%; text-align: center;">NO</th> <th style="width: 33%; text-align: center;">Document Number</th> <th style="width: 33%; text-align: center;">Initials</th> </tr> </thead> <tbody> <tr> <td style="text-align: center;">☐</td> <td style="text-align: center;">☐</td> <td></td> <td></td> </tr> <tr> <td style="text-align: center;">☐</td> <td style="text-align: center;">☐</td> <td></td> <td></td> </tr> <tr> <td style="text-align: center;">☐</td> <td style="text-align: center;">☐</td> <td></td> <td></td> </tr> <tr> <td style="text-align: center;">☐</td> <td style="text-align: center;">☐</td> <td></td> <td></td> </tr> <tr> <td style="text-align: center;">☐</td> <td style="text-align: center;">☐</td> <td></td> <td></td> </tr> <tr> <td style="text-align: center;">☐</td> <td style="text-align: center;">☐</td> <td></td> <td></td> </tr> </tbody> </table>	YES	NO	Document Number	Initials	☐	☐			☐	☐			☐	☐			☐	☐			☐	☐			☐	☐		
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Change Implementation Date: _____ Supervisor/Engineer Signature: _____ Date: _____ QA Approved – Final Approval: _____ Date: _____																													

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14 Appendix 6 – Glossary

14.1 Acronyms and Abbreviations

AHU	Air Handling Unit
BAS	Building Automation System
BOM	Bill of Materials
C&Q	Commissioning and Qualification
CAPA	Corrective Action and Preventive Action
CGMP	Current Good Manufacturing Practice (FDA)
CM	Corrective Maintenance
CMMS	Computerized Maintenance Management System
COHE	Control of Hazardous Energies
CQA	Critical Quality Attribute
EAMS	Enterprise Asset Management System
EMA	European Medicines Agency
FDA	Food and Drug Administration (US)
FMEA	Failure Modes and Effect Analysis
GA	General Arrangement
GDP	Good Documentation Practice
GEP	Good Engineering Practice
GMP	Good Manufacturing Practice
GxP	Good “x” Practice
HEPA	High Efficiency Particulate Air
HSE	Health, Safety, and Environment
HVAC	Heating, Ventilation, and Air Conditioning
ICH	International Council for Harmonisation
IFM	Integrated Facilities Management
ILT	Instructor-Led Training
JHA	Job Hazard Analysis
KPI	Key Performance Indicator
LED	Light-emitting Diode
LMS	Learning Management System
LOTO	Lockout/Tagout
MMS	Maintenance Management System
OEM	Original Equipment Manufacturer
OJT	On the Job Training
P&ID	Piping and Instrumentation Diagram
PdM	Predictive Maintenance
PM	Preventive Maintenance
PMO	PM Optimization
PPE	Personal Protective Equipment
PSV	Pressure Safety Valve

PTW	Permit to Work
QA	Quality Assurance
QC	Quality Control
QMS	Quality Management System
QRM	Quality Risk Management
RCM	Reliability Centered Maintenance
RFID	Radio Frequency Identification
SME	Subject Matter Expert
SOP	Standard Operating Procedure
URS	User Requirement Specification
WFI	Water for Injection
WO	Work Order
WR	Work Request

14.2 Definitions

Component

An element within a system, such as a pump or a valve, or a piece of process equipment. Components can be critical or non-critical depending upon their potential impact on drug quality.

Critical Component

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

Non-Critical Component

A component within a system where the operation, contact, data control, alarm, or failure will have an indirect impact or no impact on drug quality.

Deficiencies

For the purpose of this Guide, an engineering or automation design element and/or operational or performance characteristic observed in a status not meeting documented commissioning or qualification conditions during the performance of maintenance activities.

Discrepancy

A discrepancy is a condition that is unexpected or involves some variation from the expected condition (i.e., an event or occurrence outside the acceptable limits for a system).

Like-for-like (as applied to spare parts)

Functionally equivalent. Replacement of a part with a part that meets the original specification in terms of functionality (e.g., input range, output range, accuracy specifications, operational specifications, dimensions, etc.) and materials of construction.

Maintenance Best Practice

Those practices that go beyond Maintenance Good Practice. Maintenance Best Practice may include: reliability engineering, enhanced controls, trending and analysis, benchmarking, etc.

Maintenance Good Practice

The recommended maintenance requirements for the pharmaceutical industry to comply with GMP in order to ensure and document that the quality, safety, identity, purity, and strength of drugs or drug ingredients will not be compromised due to maintenance activities or lack of maintenance.

Maintenance Plan

The specific maintenance instructions or tasks, resulting from the System Maintenance Strategy, that are performed on components, equipment, or systems.

Maintenance Program

A document prepared by the maintenance unit and approved by the Quality unit describing the approach that an organization will use with respect to all aspects of performing maintenance. The Maintenance Program outlines the policies for system maintenance strategy, maintenance plans, discrepancies, change management, roles and responsibilities, documentation, training, equipment identification, continual improvement, etc.

Maintenance Strategy

A documented policy that describes a company's approach to performing maintenance. The Maintenance Strategy should include descriptions of the management processes and philosophies to ensure that assets fulfill their necessary functions.

Maintenance Types

Corrective Maintenance (CM)

Maintenance performed to ensure equipment, systems, or facilities remain in their qualified state and fit for intended and continued use.

Detective Maintenance

Task performed by an operator or technician without the use of instruments (i.e., using senses like sound, sight, feel, and smell) to identify a potential failure.

Planned Maintenance

Maintenance that is scheduled before it is performed. This includes Preventive and Predictive Maintenance.

Predictive Maintenance or Condition-Based Maintenance

Based on identifying and monitoring key operating parameters to determine the most optimal time for performing maintenance. This includes such practices as: vibration analysis, infrared technology, oil analysis, etc.

Preventive Maintenance (PM)

Typically based on calendar time or run time. The intent is to perform the maintenance activity on a regular basis so as to ensure the equipment is operating within tolerances, minimizing wear, and/or preventing failures.

Reactive Maintenance

Operating a piece of equipment until it fails and then making a repair or replacement. Failure does not necessarily imply a complete breakdown – it might just mean that the equipment is operating outside of specified parameters.

Routine Maintenance

Lubrication, minor adjustments, inspection, monitoring, and other activities where skilled individuals perform the maintenance and step-by-step procedures are not required. The determination is made by the frequency of the activity and skill of the person relative to the complexity of the activity such that detailed instructions are not required.

Scheduled Maintenance

Maintenance that is performed at regular intervals (days, months, cycles, tons of production, etc.) at prescribed points in an item's life.

Unplanned Maintenance

Maintenance that is performed without prior planning based on an immediate need either because a piece of equipment has failed or failure is imminent.

Maintenance Unit

The organizational element responsible for developing and executing maintenance processes.

Quality Unit

The person or organizational element at the site having oversight responsibility for ensuring that the drug or drug products produced consistently meet their predefined attributes through a proven process. Responsibilities of the Quality unit are typically divided between QC and QA functions.

Subject Matter Expert (SME)

An individual possessing in-depth knowledge of the particular subject based upon their education, training, experience, and expertise.

System Owner

The person or organizational element having overall (primary) responsibility for a system.

System

An organization of engineering components that have a defined operational function and can include processing equipment, facilities, utilities, etc.

Systems Maintenance Strategy

A rationale or set of criteria that is used to develop a Maintenance Plan.



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