



Good Practice Guide

Project Management for the Pharmaceutical Industry



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Good Practice Guide

Project Management for the Pharmaceutical Industry

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ISBN 978-1-936379-25-5

Preface

The practice of Project Management within the highly regulated world of the pharmaceutical industry provides unique challenges and opportunities. The ISPE Good Practice Guide: Project Management for the Pharmaceutical Industry promotes the integration of GxP with relevant project management activities to ensure that compliance risk is managed both effectively and proactively.

The Guide aims to provide a reference source of good practices for project management for a wide variety of project types within the pharmaceutical industry and benefit to Project Managers and other professionals working on such projects.

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Acknowledgements

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1 Introduction

1.1 Background

The practice of Project Management within the highly regulated world of the pharmaceutical industry provides unique challenges and opportunities. It is considered good project management practice to integrate GxP with relevant project management activities to ensure that compliance risk is managed effectively and proactively. This ISPE Good Practice Guide (GPG): Project Management for the pharmaceutical industry provides good practice approaches which promote the successful integration of these additional requirements.

Throughout the Guide, references to the “pharmaceutical industry” are intended to include all aspects of the industry, including biopharmaceuticals and medical devices.

1.2 Purpose

The purpose of this Guide is to provide a reference source of good practices for project management for a wide variety of project types within the pharmaceutical industry.

The Guide considers how appropriate tools and techniques can support and promote good project management practices and aims to help in sharing of these good practices to facilitate their use within the pharmaceutical industry.

This Guide aims to:

- provide specific guidance on project management in the pharmaceutical industry
- provide a resource for Project Managers and other professionals who are involved in projects in the pharmaceutical industry
- provide a link to project management bodies of knowledge for industries other than the pharmaceutical industry (References 1, 2, and 3, Appendix 3)

The Guide aims to support the:

- development of a common language across the pharmaceutical Project Management community
- access to good project management practice information to enable Project Managers to complete a gap analysis
- development a culture of good project management practice throughout an organization
- development of organizational project management capability, e.g.:
 - a reproducible project delivery system
 - an understanding of the project management requirements for successful project execution
 - enabling project stakeholders to understand the complexities of running a project
 - regular training and skill development for the personnel delivering a project
- development of organizational and individual pharmaceutical project management capabilities through expanding the project management body of knowledge (References 1, 2, and 3, Appendix 3) specific to the pharmaceutical industry

- integration of different aspects of a pharmaceutical project which cross both functional and organizational boundaries, which need to be managed proactively
- integration of risk management into specific aspects of a project

This document contains good practice guidance, and any stated recommendations or requirements should not be regarded as mandatory (except where regulatory or legal requirements are directly referred to).

*The use of terms such as **must** is intended to indicate that these aspects are essential for maximum project effectiveness or success, and not that such aspects are mandatory from a regulatory or legal perspective.*

*Similarly, the use of **critical** (except when used as part of a defined term such as Critical Quality Attribute) is intended to indicate that these aspects are essential for maximum project effectiveness or success, and not that such aspects are necessarily critical from a product quality perspective.*

1.3 Benefits

This Guide is intended to be of benefit to Project Managers and other professionals working within the pharmaceutical industry.

It aims to provide the pharmaceutical context to project delivery and address unique aspects of project management within the pharmaceutical industry. The key benefit is intended to be an increased potential for successful completion of a pharmaceutical project.

A key purpose is to provide a common language and a way to use generic and specific tools in the context of a pharmaceutical project.

Additional benefits include:

- the collation of a comprehensive list of current good practices to aid project delivery success
- the development of a broader knowledge of pharmaceutical projects and project management for a wider variety of stakeholders
- knowledge to help to mitigate or eliminate risks common to pharmaceutical projects

1.4 Industry Context

This Guide is specific to Project Management within the global pharmaceutical industry and to projects typical within that environment. The main focus of the Guide is facility and engineering projects, including facility, improvement, and IT projects.

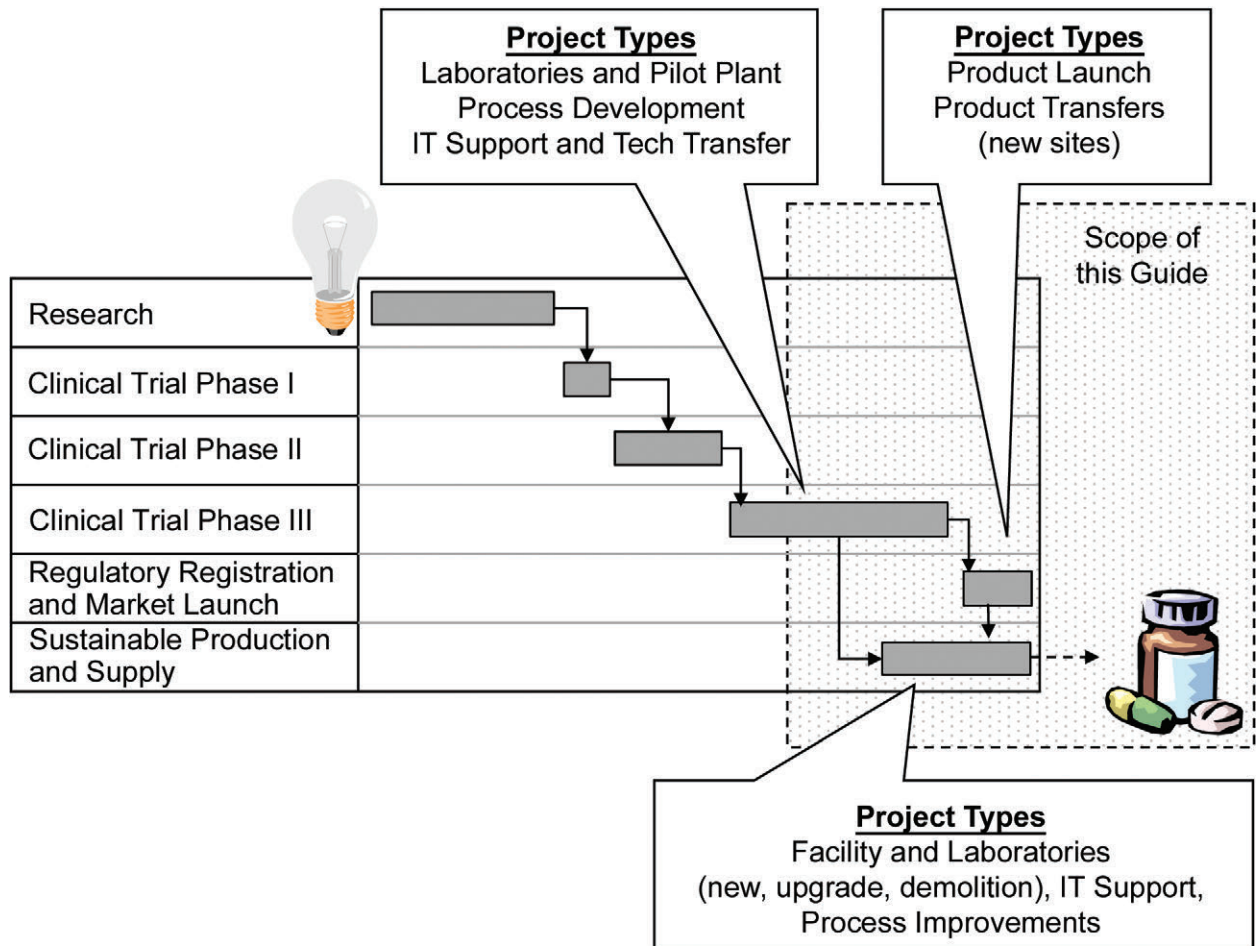
The concepts, principles, approaches, and tools are also relevant to other project types. The specific terminology of each type of project may differ, but the methods discussed in this Guide are applicable. For sources of further guidance on specific terminology, see Appendix 4.

The industry context and scope of the Guide was defined through considering the stages within the product life cycle (ICH Q10; Pharmaceutical Quality Systems (Reference 4, Appendix 3)) and Figure 1.1:

- Pharmaceutical Development
- Technology Transfer

- Commercial Manufacturing
- Product Discontinuation

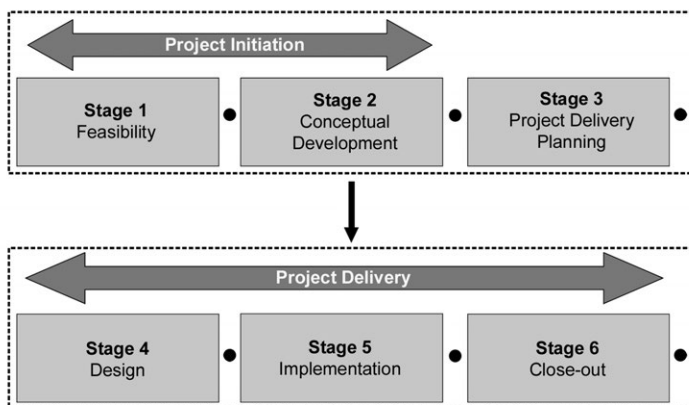
Figure 1.1: Typical Pharmaceutical Drug Product Life Cycle and the Scope of this Guide



1.5 Scope

The Guide will cover:

- the tools and techniques supporting project delivery
- the life cycle of a typical project (Figure 1.2) in the pharmaceutical industry
- how compliance to pharmaceutical industry regulations should be integrated with the project life cycle

Figure 1.2: Typical Project Life Cycle

This Guide considers new or novel aspects of project management which, although not unique to the pharmaceutical industry, are fundamental to pharmaceutical project success.

Generic areas of project management knowledge (e.g., project controls, safety, health and environmental, etc.) which, although not specifically covered in individual chapters, are discussed in chapters where they have a specific pharmaceutical relevance.

This Guide does **not** cover:

- Generic project management tools and methodologies that are not applied differently nor have a different context within a pharmaceutical environment.
- The technical challenges within any part of the project life cycle: Only the management of those challenges are covered, **not** the technical solutions. Technical Guides are referenced, where applicable.

This Guide is **not** intended to be a comprehensive or generic project management body of knowledge. For further information regarding general project management, see (References 1, 2, and 3, Appendix 3).

1.5.1 Project Types

In terms of the type of projects which occur in the pharmaceutical industry, this Guide is intended to be applicable to most types with the exception of pure discovery or research projects (see Appendix 1). These project types could include:

- Facility
 - New and Retrofit Facilities
 - New Equipment or Equipment Systems
 - Decommissioning and Demolition
 - Estate (whole site projects: purchase, development, sale)
- Improvement
 - Product, Facility, and Equipment
 - Audit (Safety or Quality) Preparation and subsequent improvement (typically linked to a facility)

- Product
 - New Product and Product Transfer
 - Technology Transfer
- IT
 - ERP Implementation
 - System Functionality Upgrade
- Automation
 - Process Control System

Case studies, for a variety of the above project types, are included in Appendix 2.

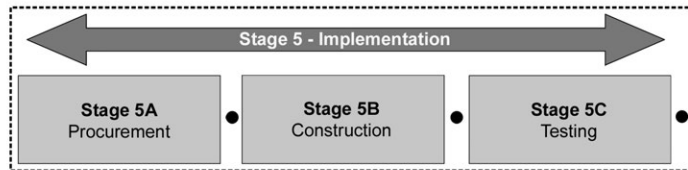
The lack of inclusion of any particular subject is not a reflection on its lack of importance within pharmaceutical projects, but a recognition that it is a generic subject and existing project management guidance is available (see References 1, 2, and 3, Appendix 3).

1.5.2 Terminology

The terminology in Figure 1.2 is generic and where specific terminology is used within a certain project type, then this will be introduced, explained, and defined in the glossary (Appendix 4) and also summarized in the Project Type Matrix (for further information, see Appendix 1). For example:

- Within Computerized System Projects, delivered following the GAMP approach, (Reference 5, Appendix 3) the life cycle stages are:
 - Concept
 - Planning
 - Specification, Configuration, and Coding
 - Verification
 - Reporting and Release
- In Facility Projects, the design can be broken up into distinct stages:
 - Concept Design or Conceptual Development (as used in this Guide)
 - Front End Design, Preliminary Design, Scheme Design, or Basis of Design (as used in this Guide)
 - Detailed Design and Engineering
- In Facility Projects, implementation involves three distinct phases following detailed engineering design (Figure 1.3):
 - Procurement

- Construction and Installation
- Testing (also called commissioning and qualification and also verification)

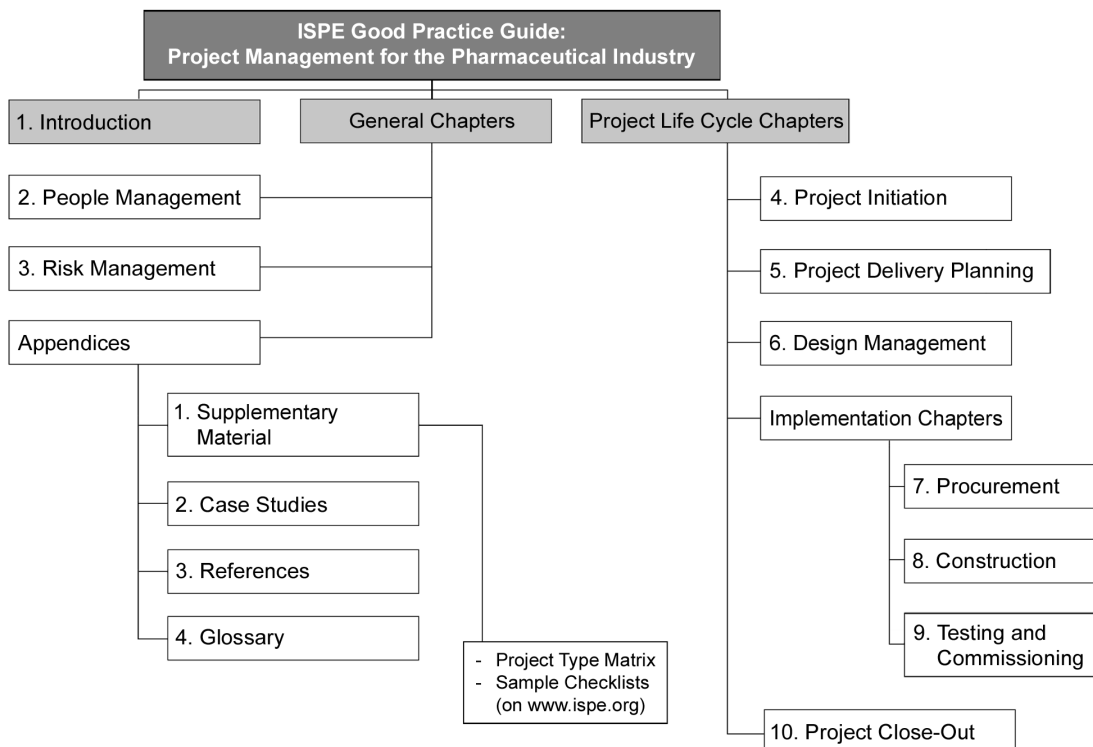
Figure 1.3: Typical Facility Project Implementation Stages

- In Improvement Projects, close-out involves not only demonstrating that the project deliverables are complete, but that the benefits from the project are also being realized sustainably, i.e., project closure and handover do not represent the end-point for the Project Manager although it will be for most of the Project Team.

1.6 Structure of the Guide

Figure 1.4 shows the structure of the Guide. Chapters 2 and 3 are applicable across an entire project life cycle. Other chapters cover a distinct phase of a project life cycle. Appendices are used to provide further information and background, e.g.:

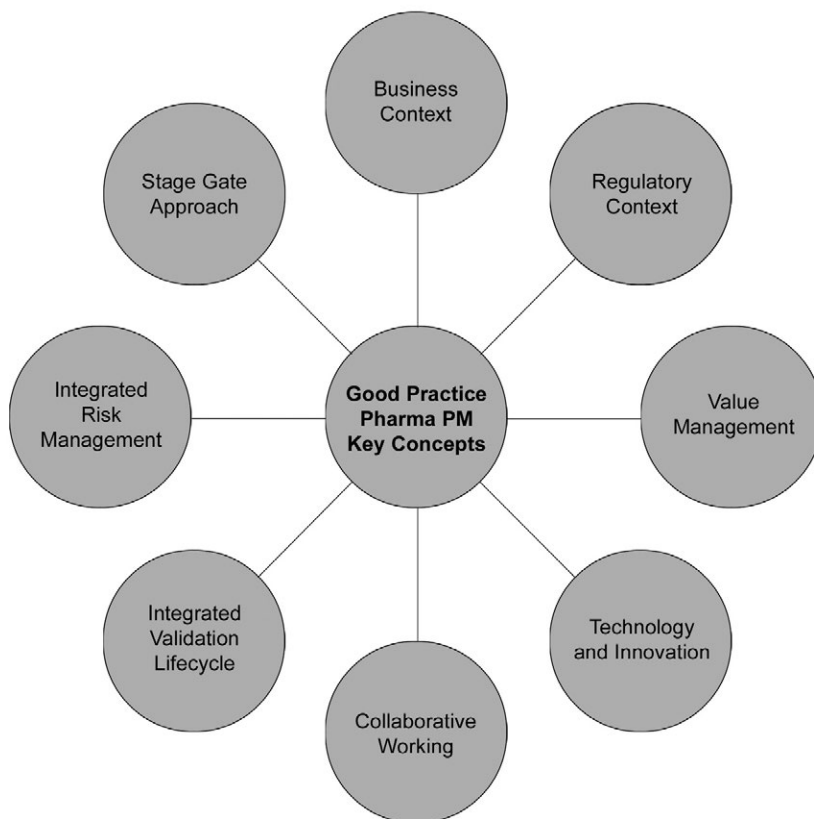
- Appendix 1 – either includes or provides reference to supplementary materials to give additional guidance in specific areas of project management.
- Appendix 2 – provides short case studies for a variety of projects to demonstrate how the guidance in this Guide can be applied.

Figure 1.4: Guide Structure

1.7 Key Concepts

The following key concepts (see Figure 1.5) are those which apply to all pharmaceutical project types and all parts of the project life cycle. They form the basis on which this Guide has been developed.

Figure 1.5: Key Concepts Summary



1.7.1 Business Context

A project is the result of an approved business case which demonstrates that its delivery will satisfy a business need within an acceptable cost-benefit analysis. Within a stable external environment, this cost-benefit analysis can be clearly linked to a defined scope and delivery approach which changes only in a minor way during the lifetime of the project.

Within the pharmaceutical industry, there are a large number of drivers which can affect the cost and benefit of a project. Project Managers have, therefore, a greater requirement (and responsibility) to have a formal benefits management process. This process can guide interaction with project sponsors and enable the management and delivery of the business case.

Benefits management in this context allows an organization to evaluate repeatedly all aspects of a traditional business case:

- **Cost** – the cost estimated at funding approval may be challenged as the external economic and political environment changes. Projects need to deliver cost effective solutions in an increasingly cost competitive environment. Organizations are cost conscious and operate in dynamic economic and political environments.
- **Scope** – as technology, regulatory, and competitive issues occur, the scope of a project has to be repeatedly challenged.

- **Time** – the importance for increased speed to market for new drugs has meant that most projects are under pressure to deliver faster while maintaining agreed cost and scope objectives.

The pharmaceutical industry is highly dynamic, with critical cost and time constraints within a shifting regulatory environment. Business expectations for a project often require consideration of risk and future needs on an ongoing basis, particularly where product pipeline flexibility is a key management goal.

The Project Manager's role involves managing the project business plan and linking that plan to regulatory requirements. A key part of that is to link several stakeholders through effective communications planning and delivery. If conflict or contradiction between business needs and regulatory requirements occur, Project Managers should educate stakeholders, including project sponsors, so that regulatory requirements are met.

1.7.2 *Regulatory Context*

Where applicable, GxP should be integrated into relevant activities to ensure that compliance risk is managed effectively and proactively. Regulatory policy can be dynamic. Project Managers should take note of changes in the regulatory climate that will be fundamental to a project's success.

Regulatory requirements are of high importance within the pharmaceutical industry. Compliance with specific industry regulations and local codes, legislation, and regulations is required. Failure to abide by these regulations can result in significant financial and operational penalties for a manufacturer. Managing a project's compliance to regulations is an essential undertaking to achieve success, but ensuring compliance can be complicated by fast track product and project development.

The pharmaceutical industry has adopted and embraced a systematic quality risk management process (as described by ICH (References 4, 6, 7, and 9, Appendix 3)). This process involves the assessment, control (risk acceptance or reduction through mitigating activities), communication, and review of risks to the quality of a product across its life cycle, and therefore, the risk to the patient. A quality risk management process provides an organization with effective and consistent risk-based decisions that will complement compliance activities and approaches.

Regulatory requirements should be managed throughout a project life cycle to ensure compliance. The key regulatory management functions include:

- **Regulatory Definition** – the identification of regulatory requirements early in the project life cycle and then the confirmation of the processes (see below) which will maintain these during the project. This includes compliance with GxP and other codes and regulations.
- **Management of Change** – the identification, analysis, and documentation of change occurs throughout the project and product life cycle. Within a project this process should proactively identify the extent to which a change may impact the ability for the project to successfully meet the regulatory requirements.
- **Management of Scope** – the identification and management of the scope required to successfully achieve the regulatory requirements. Within a project, this process should challenge the scope required to successfully meet the regulatory requirements while not necessarily essential to the success of the business case.
- **Quality Management** – to define the intended quality objectives and how to best deliver them (and the link to Quality Risk Management – ICHQ9 (Reference 7, Appendix 3)). This would typically involve processes to manage traceability and validation, for example.

Within a project management context, a Project Manager would not distinguish between the latter three functions; they are a part of the "business as usual" for a Project Manager:

- Change control is a process to manage cost, time, and scope.

- Scope management is a process to manage all aspects of the scope: quantity, functionality, **and quality**.

1.7.3 Value Management

Value management is a multi-disciplined process aimed at enhancing the value of a project from concept design through to final handover and use of the project outcome. The purpose of value management is to achieve the maximum benefit of an investment over the expected useful life of the project outcome based on resource availability and/or constraints. Value management is specifically targeted at the “business solution” rather than the “technical solution” (synonymous with Value Engineering). This methodology aligns with the principles of lean six sigma and requires the full participation from the customer, project team, and other key stakeholders.

The starting point for successful value management is a comprehensible scope, which allows the consideration of value from a specific project context. The value management process is a scope challenge process, i.e., the process aims to identify non-value adding activities, deliverables, or approaches, etc. Table 1.1 shows examples of what “is” and “is not” value management:

Table 1.1: Value Management Definition

IS Value Management	IS NOT Value Management
A cross-functional team based process that provides a ‘forum’ for the identification and evaluation of all design and project delivery options without constraint based on the definition of value for that project	A simple cost cutting process
The identification and elimination of unnecessary product cost (through elimination of non-value adding scope or approaches)	A design review
Encourages creativity, imagination, ingenuity and inventiveness with no restraints	Quality Control
A process that synergizes a better (a value added) solution	A consensus process
A Kaizen event	A regular project team meeting
A way of confirming and communicating project goals in support of an aligned project vision of success	A forum for individual agenda or preferential engineering

When performed successfully, value management can provide benefits such as:

- all assumptions are challenged
- documented proof that value has been added and integrated into the project at an early stage (typically pre final funding approval)
- a technique that recognizes both economic and intangible value
- the identification of missing cost or scope items
- the identification of risks and early discussions of how to manage them in a value-added manner
- a more competitive solution
- improved sustainability with respect to the environment

- emphasis on life cycle cost and equipment reliability

Life cycle cost is becoming an increasingly important aspect of value management and within this Guide, the term is used to describe the total cost of ownership over the life of an asset (e.g., building or equipment). Typical areas of expenditure which are included in calculating a complete life cycle cost include construction and acquisition, operations, maintenance, depreciation, and cost of finance.

1.7.4 Technology and Innovation

When managing projects, the introduction of technology and innovation should be considered in terms of its application to:

- The internal running of a project – when applied successfully, the performance of a project can be improved while reducing required investment.
- The project outcomes – in an environment where speed to market and cost are often conflicting primary drivers, technological and innovative solutions can become strategic enablers.

Key drivers for the introduction of technology and innovation include:

- a varied and expanding portfolio of products
- product and/or process improvement and remaining competitive (constantly reduce the cost of goods)
- the ability to accommodate new platforms and future generation technologies
- adaptability, flexibility, and interchangeability
- lower emissions and less environmental impact
- supply assurance with a less costly and simpler supply chain
- development of sustainable solutions
- innovative ways of working, including improved collaboration, communication, and information sharing for project teams
- streamlined approaches to technology transfer, process and equipment design, and testing of products, facilities, and processes

Optimum and innovative solutions may be achieved by avoiding traditional technologies; a solution which matches the context should be identified. For example, labor cost, product margins, and product volumes are considered when determining the appropriate level of process automation for a project.

Risk associated with using technology and innovation should be managed, e.g., confirmation that suppliers can provide appropriate support during ongoing use for the technology.

1.7.5 Collaborative Working

Collaborative working promotes the sharing of information and exchange of ideas to enhance overall understanding and enable stakeholders to achieve superior solutions.

A stakeholder is considered to be anyone who is influenced or affected by the project or who could influence or affect the project.

Senior stakeholders, the Project Manager, Project Team members, and Subject Matter Experts (SMEs), from stakeholder organizations, should be committed to collaborating constructively to help to bridge geographic, cultural, and technological boundaries. This working model should provide value-based solutions that are generated by the team, combining team success to solutions, and reducing time, effort, and cost over the project lifetime.

Characteristics of a collaborative working environment include:

- reciprocal respect of each stakeholder's viewpoints and expertise
- reduced risk of individual stakeholder failure and reward driving stakeholder ownership
- early and continuous involvement of all stakeholders with clearly defined roles and responsibilities
- communal decision making and innovation generation
- mutual perception of the project parameters and objectives
- avoidance of the duplication of effort and activities
- appropriate, timely, informative, and accurate communication
- an appropriate infrastructure

Processes which integrate these characteristics into a collaborative approach include:

- good communications planning and delivery
- robust development of team member roles and responsibilities
- development of pre-agreed business objectives for personnel involved in a collaboration

Project Managers and project sponsors should have the appropriate level of authority and capability to manage these processes (see Chapter 2 of this Guide).

1.7.6 Integrated Risk Management Approach

A risk-based approach should consider the variety of risks related to a project. This may include risks to the project, the process, or the product.

Chapter 3 provides details of the process of applying a risk-based approach across the project life cycle and how this links in with regulatory requirements. The project life cycle chapters demonstrate good practices within the context of the project stage being discussed.

1.7.7 Integrated Validation Life Cycle

The integrated validation process supports the management of the interaction between project management good practices and regulatory requirements. Validation requirements should be defined early and managed throughout the project life cycle. This approach is usually termed the “management of the integrated validation life cycle.”

The integrated validation life cycle should ensure that, where possible, validation activities are integrated into normal project activities. The project team, with SME support, should identify where GEP and GxP are applicable.

A Validation Master Plan (VMP) may be used to define and document a validation strategy at the start of a project. The VMP should:

- Define processes, testing, and documentation required.
- Define Critical Quality Attributes (CQAs).
- Define Critical Process Parameters (CPPs).
- Allow resource requirements to be determined (in terms of capability and capacity).
- Set the strategy to obtain documentary evidence and traceability from defined user requirements through design, testing, and acceptance.

Validation management can help Project Managers to:

- Integrate validation planning into the overall project delivery planning activities.
- Identify the SMEs required to support the validation process.
- Manage GxP risks through early development of mitigation strategies.
- Be assured that GxP has been integrated into the project outcome from an early stage.
- Streamline activities and avoid duplication during the project life cycle.
- Simplify project documentation, document approvals, and the flow of project information.
- Integrate reviews, checks, and decisions which assure that a project is moving forwards appropriately.

The integrated validation life cycle should continue after handover of the project outcome. Project Managers should ensure that requirements are defined to maintain the validated state of the project outcome following deployment.

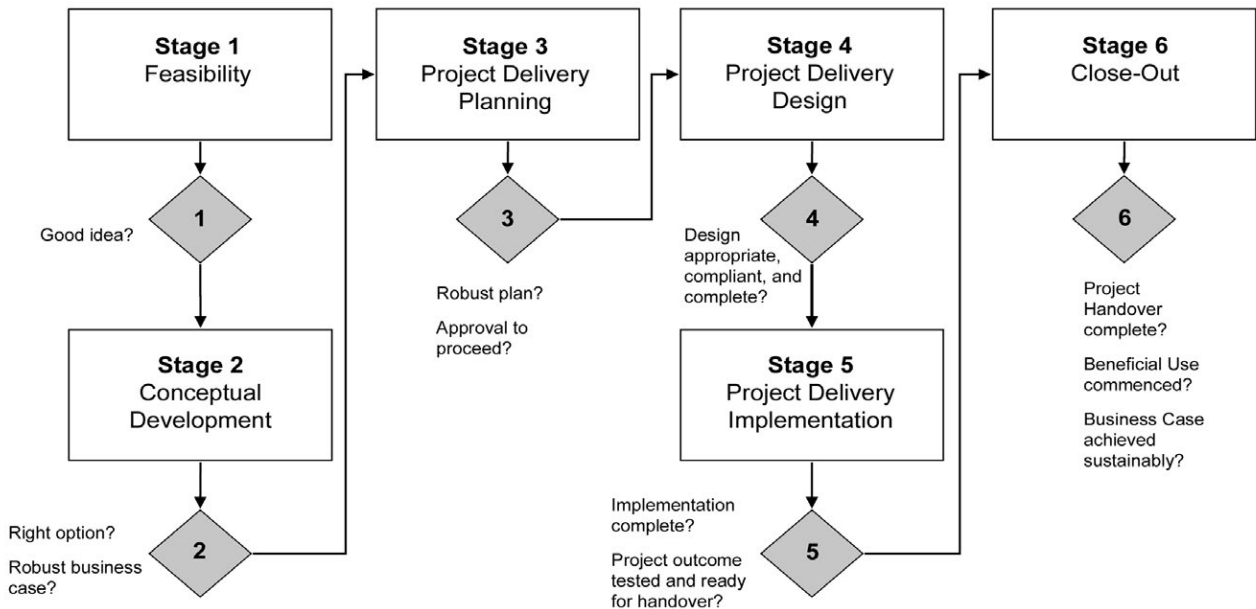
A key project management tool which supports the integrated validation life cycle is stage gate definition.

1.7.8 Stage Gate Approach

A stage gate approach is a project management good practice. Figure 1.6 shows an example of a project life cycle which has been divided into discrete stages.

Each stage is a bounded set of activities which deliver data to a stage gate decision. The stage gate decisions are go/no go points: A project has to pass through each stage gate to proceed to the next stage.

Figure 1.6: A Typical Project Stage Gate Approach



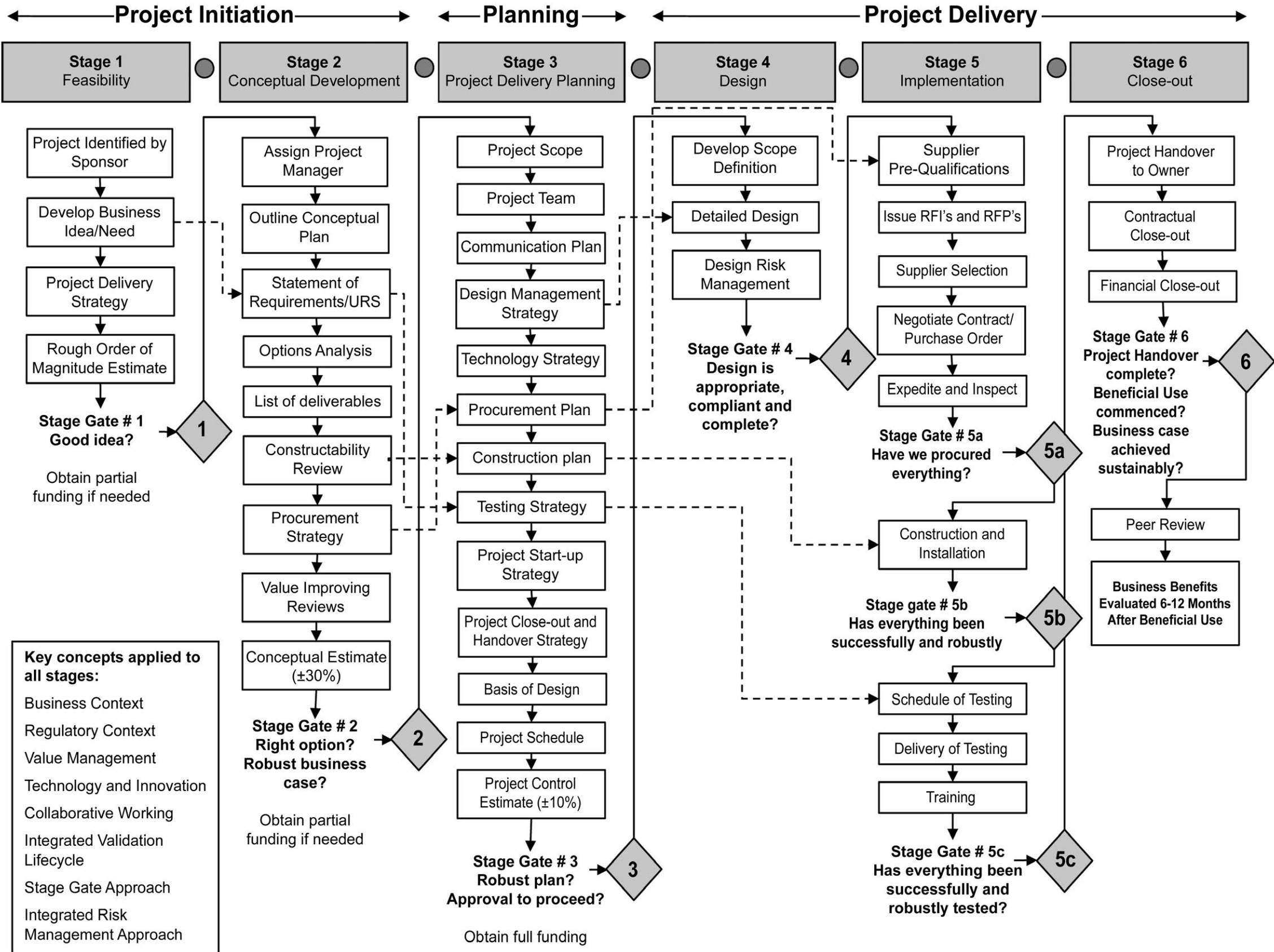
For this approach to be effective, each stage gate should have:

- **Inputs:** what needs to have been achieved before a decision can be made.
- **Acceptance Criteria:** the level at which the achievements are deemed to have been sufficient.
- **Value:** a reason why the hold point is required; why it adds value to an organization.

A project stage-gate approach can be used to develop clarity of scope and approach for a project team and key stakeholder groups. It can be used to develop an early view of the overall project time-line based on the key data needed at each stage gate and the decisions that the data can support.

This approach has been used throughout this Guide and Figure 1.7 expands upon Figure 1.6 making links to the contents of the Guide and the stage gate decisions within each part of the project life cycle.

Figure 1.7: Project Management Flowchart



2 People Management

2.1 Introduction

In a regulated environment, a wide variety of people and functions will typically be brought into a project, i.e., the project stakeholders as well as specialist subject matter experts. The interdependency of issues requires this wider variety of people and disciplines to interact, communicate, and collaborate effectively to deliver the intended project outcome.

The key areas of people management are:

- Roles and Responsibilities:
 - Defining the categories of project stakeholders, their roles and responsibilities, for effective management: The Project Manager, Senior Stakeholders, The Project Team, Consultants, and Contractors
- Knowledge Management
 - The extent of critical and/or confidential project information requires the definition of a project Knowledge Management Plan that addresses knowledge capture, knowledge sharing, and knowledge change management.
- Language, Communication, and Culture
 - Effective communication throughout a project requires the definition of a Communication Plan that addresses communication processes, defines the terminology and establishes the basis for a project culture.

2.2 Roles and Responsibilities: The Project Manager

Project Managers should manage communication, knowledge transfer, project goals, and maintain a conflict-free project delivery.

Within projects in the pharmaceutical environment, no matter the type, there is often a greater diversity of expertise required – both what and when. This is a challenge for the Project Manager who needs to be selected based on being able to cope with this diversity. A Project Manager has a continually moving team and is constantly making and realigning relationships; often managing through influence rather than power as matrix teams with part-time team members are used. Sometimes a Project Manager may not even be managing a face-to-face team – virtual teams are becoming more common when dealing with major organizational change projects where there is no one focal point in the organization for all the required resource. The establishment of a Project Management Office (PMO) is one way that organizations are handling this challenge; it allows implementation of a consistent project management process across an organization.

Some projects have part-time Project Managers or managers with minimal project management skill: they are selected for their technical expertise. While this is not an ideal situation, and may introduce risks to project success, it is often the reality. The Project Sponsor has a role to play in mitigating this risk and this is often through establishment of a Project Team with appropriate capabilities to manage any gaps.

Titles used for role of Project Manager can depend on project type and organization, e.g.:

- Project Leader (or Product Leader) may be used in R&D type projects.
- Project Director may be used in larger capital engineering projects.

- Program Manager may be used for large IT projects or programs.

Titles used may reflect the scale of the project or the hierarchy within an organization; roles or responsibilities can be comparable.

For other titles, see the Project Type Matrix (see Appendix 1). Within this Guide, the term Project Manager is considered to be the person responsible for delivering the successful project outcome.

2.2.1 ***Project Management Capability***

Project Managers may need to coordinate a wide range of knowledge in pharmaceutical industry projects and may not be a Subject Matter Experts (SME) for the project type. Project Managers usually require the ability to ask the correct questions and to respond to those questions appropriately, by having an understanding of:

- how to deliver successful projects in this highly regulated industry
- the challenge of science driven projects

The criteria for the selection of Project Managers, the organization around the role, and the responsibilities within the role may vary considerably.

The complexity and criticality of a project in relation to its size, duration, and project type should be understood when considering appointment of a Project Manager. Aspects to consider include the:

- required project management capability
- required leadership skills

Example

A complex project for a new drug launch which is critical to an organization's future sustainability requires a different level of project management capability to that for a small maintenance shutdown project on an API Manufacturing Facility.

Criteria for project management capability in the pharmaceutical industry include:

Knowledge:

- Has knowledge of the regulatory context in which a project is to be delivered.
- Has knowledge of the project type in terms of the typical life cycle, risks, and key success criteria.
- Has knowledge of the critical pharmaceutical processes or technologies that constitute a large part of the project (desirable, but not essential), e.g., the validation process and requirements.
- Understands how to engage with people.
- Understands business drivers.
- Understands when to apply value managements tools and concepts.

Skills:

- Able to manage at all levels throughout the organization with strong communication skills and good political and cultural awareness.

- Possesses appropriate project management skills:
 - Hard skills, e.g., project delivery strategy development, cost, and schedule planning, risk management techniques, negotiation, progress management, etc.
 - Soft skills, e.g., team building and management, facilitation, communication, motivation, influencing, decision making, stakeholder management, etc.
- Has good business acumen and the ability to manage the project throughout the project life cycle or has good business acumen and ensures that the project delivers the specified benefit to the stakeholders.
- Possesses appropriate leadership skills, e.g., thinking strategically, resolving conflict, and managing key business relationships.

Behavior:

- Encourages innovative thinking and the exploration of ideas and approaches.
- Able to drive engagement, via team based decisions and other approaches, encouraging input and involvement while keeping the team focused on the primary objective of the project.
 - Project Managers should drive team commitment and steer that team toward achieving a project's objectives.
 - Project Managers should create and manage a team that will meet, and where possible, exceed expectations.
- Able to focus on the business goal.
 - Project Managers should work closely with the Project Sponsor and stay connected with an organization's strategic plans.
 - This normally requires strong communication skills and the ability to effectively manage both up and down an organization.
- Can build a project team whether in the same location or virtually.
 - Project Teams should be encouraged to think innovatively and should be provided with an environment for the exploration of concepts such as sustainability and life cycle cost. This may be assisted by familiarity with value management tools and techniques.
- Is an effective leader; demonstrates leadership behavior such as honesty and integrity and has the ability to be strategic and inspirational and to engage the team in the longer term vision of success.

Performance:

- Is experienced in managing senior stakeholders from a diverse scientific and business background.
- Has proven ability to understand and manage the expectations of a diverse group of stakeholders.
- Has demonstrated success in managing projects within the pharmaceutical industry (or similar highly regulated industries).

- Where a Project Manager has experience of project management, but not of the pharmaceutical industry or specific project type (e.g., subject matter expertise), a project organization should be created with the required subject matter expertise and a robust process for the Project Manager to engage with that expertise.
 - For smaller projects, a Project Manager may be responsible for delivering technical work packages or content in addition to project management duties. In such cases, project activities may be delegated to other members of the project team to allow sufficient time for the Project Manager to manage the project,
 - Where an SME is appointed as a Project Manager, the Project Sponsor (with project steering team support, if applicable) should provide additional support to manage the project management capability gap.
- Has proven success in delivery of project outcomes which generate sustainable business benefits,
 - Meets responsibilities in an ethical manner,

Project management capability can be developed by, e.g.:

- Knowledge accumulated by learning and experience in other project roles.
- Skills acquired through training and practice.
- Behavior adapted by changing attitudes or values.
- Performance enhanced through new experiences.

The key responsibility of a Project Manager is delivering the required project outcomes (Table 2.1), i.e.:

- Achieving the project objectives by balancing, cost, scope, and schedule.
- Enabling the realization of business benefits.
- Developing and managing a project team and all stakeholder groups.
- Management of all regulatory and compliance aspects through appropriate management of risk.

A basic project management tool which supports clarity in role definition is the RACI Chart. A RACI Chart (see Table 2.1) defines:

R = Responsible – who does the work to complete an activity or task

A = Accountable – who is ultimately accountable for the correct completion of the activity or task

C = Consulted – whose opinion is sought during the completion of the task

I = Informed – who is kept up to date about the progress of a task and/or its completion

Only one person can be accountable for an activity and only one person can be responsible (this can be the same person, if appropriate). The level of consultation (2-way discussions with others) and informing (1-way communication at completion of an activity) should equate to that necessary for the success of an activity and the project. Table 2.1 is an extract from a typical RACI Chart used to clarify the role of a Project Manager.

Table 2.1: Example RACI Chart – The Role of the Project Manager

Role →	Project Sponsor	Process Owner	End User	Project Manager	Project Team
Activity ↓					
Development of the project delivery plan (see Chapter 5 of this Guide)	A	I	I	R	C
Delivery of the project outcomes	C	I	I	AR	C
Achievement of project objectives (cost, schedule, scope)	C	I	I	AR	C
Enable the benefits to be realized	C	I	I	AR	C
Develop and manage team performance	I	-	-	AR	C
Develop stakeholder management plans	C	-	-	AR	I
Manage project risk	I	-	-	AR	C
Deliver regular project reports	I	I	I	AR	C

The RACI Chart would typically be an Appendix within the Project Delivery Plan (PDP) (see Chapter 5 of this Guide). The PDP is a core tool for a Project Manager; it is considered a “contract” with the Project Sponsor and a key communications tool for the Project Team.

Project Managers are usually expected to have a diverse range of skills and experience. A suitably qualified Project Manager may need to be appointed from outside an organization if none are available internally. All candidates should be interviewed in a similar way to ensure the appropriate person is appointed to the role.

- **The “Internal” Project Manager** – if expertise is available within an organization, a Project Manager may be appointed to the role of Project Manager.
 - This is frequently the case for smaller projects, especially those in which the Project Manager might also be responsible for delivering some of the technical work packages in addition to managing and leading the work of others.
 - When an internal Project Manager is appointed based on their technical expertise their project management expertise can be supported/developed by the use of a part-time project management consultant.
- **The “External” Project Manager** – when an organization does not have the expertise to manage projects it typically appoints an experienced consultant to perform the project management role.
 - Selected based on their experience in managing the type of project to be delivered..
 - Consultant Project Managers should have a suitable personality, attitude, and leadership style to deliver a project within an organization’s corporate culture.
 - The Project Sponsor should provide the context and support necessary to:
 - > Ensure the consultant Project Manager undergoes induction training and understands organizational ways of working.

- > Clarify that the consultant Project Manager is leading the project within the organization.
- > Allow the consultant Project Manager to manage the organization's staff effectively.

2.2.2 Key Project Management Challenges

Key challenges for the Project Manager include:

- The management of a diverse, science-focused team.
- The operation of virtual, matrix, or co-located task teams that are potentially diverse in language, culture, and capability.
- The management of complexity across a lengthy product life cycle often managed as distinct projects in series to deliver a robust process, an operational facility and a sustainable manufacturing business.
- The clarity needed in assigning responsibilities for effective project delivery (using tools such as the RACI Chart).

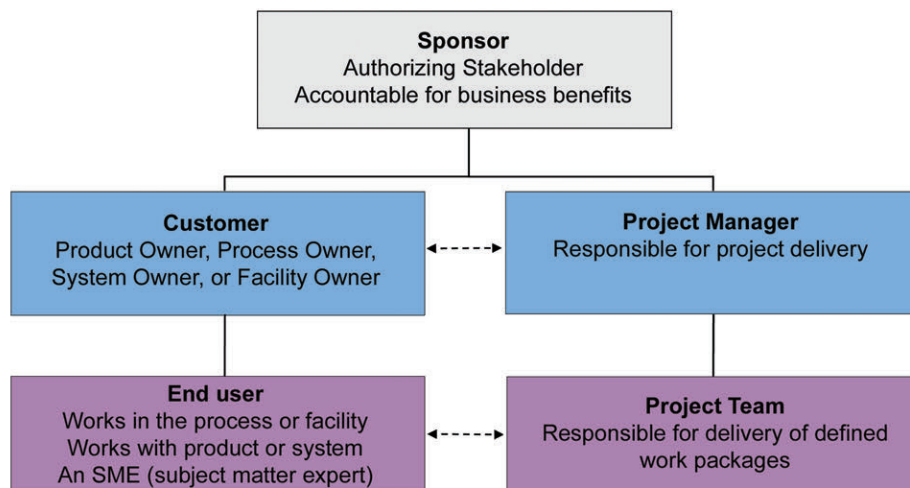
2.3 Roles and Responsibilities: Senior Stakeholders

Senior project stakeholders within the pharmaceutical industry normally have a technical background and focus on the patients for whom their products are intended. An effective partnership should be developed. The process of stakeholder management should involve the identification of those senior stakeholders who have both the authority and influence on the resources, pace, and direction of the Project and who have a technical or business driver for their involvement. The three key senior stakeholders can be categorized as:

- The Project Sponsor
- The Customer
- The End User

Figure 2.1 shows the relationship between these key senior stakeholder groups.

Figure 2.1: Stakeholder Relationship Map

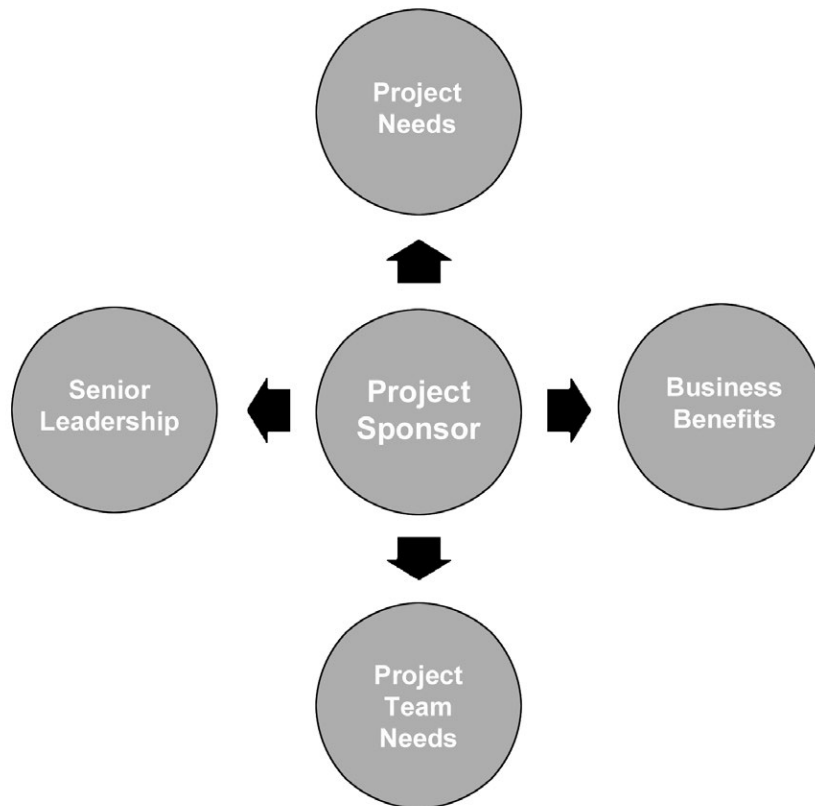


2.3.1 The Project Sponsor

The Project Sponsor should have the authority over the part of the organization being changed by the project. The Project Sponsor should:

- ensure the Project Team receives all the support and resources necessary for a successful delivery and is managed appropriately
- be an advocate for the Project Manager and Project Team
- provide guidance and support to the Project Manager
- manage Senior Stakeholders in line with the Stakeholder Management Plan
- act as a buffer between the Project Team and Senior Stakeholders to prevent the Team from being distracted or receiving information or guidance that could be misleading
- remove obstacles to project success: this may require close interaction with Senior Stakeholders
- mitigate all organizational issues which could undermine a successful outcome for a project
- approve the scope of the project and conducts regular reviews to ensure that the project meets both its technical and business objectives while being managed appropriately
- develop the External Communication Plan for the Project in liaison with the Project Manager and handle communication to and from the senior stakeholders within an organization
- create and ensure commitment to the project within the Customer's organization
- champion the project through the approval process and thereafter to completion/handover
- be a link between the project and the business at all times: remain actively engaged and identify current strategic information that could affect the project
- monitor the external environmental: assessing the "fit" of the project to the business on an ongoing basis
- obtain additional funds from the original approving authority (once the scope of the project is established and final funding received) before making substantial scope changes outside the approved/funded scope of a project

The role of a Project Sponsor can be summarized in four key areas, described in Figure 2.2.

Figure 2.2: Role of the Project Sponsor

The Project Sponsor is:

- accountable for the delivery of sustainable business benefits from the project
- responsible for confirming that the project meets business needs and is delivered within cost and time parameters within the customer's organization
- responsible for key decisions:
 - stage gates (project go/no go points)
 - resources (people, funds, assets)

Project sponsors may require training to help them prepare for the role. Project sponsors need to balance their project sponsorship role with their primary business role. This potential conflict of objectives can be detrimental to a project. Lack of support and guidance from a Project Sponsor may prevent a project from achieving its objectives.

2.3.2 The Customer

Within this Guide, the term "customer" refers to the actual group who will use the project's outcome to support achievement of business objectives. From a project perspective, the product, process, system, or facility owner is the customer. On smaller projects, the customer and Project Sponsor could be the same person. The Customer:

- requires the project outcome: the project deliverable
- should be able to express the benefits of the project and set the business acceptance criteria by which the project's completeness can be assessed at the end of the project

2.3.3 The End User

The End User is the customer's representative who has detailed knowledge about how the project's key deliverables should perform during operation. Key End Users (i.e., SMEs) have knowledge or experience which is valuable to the project team. In this regard, they are also key customers for the project team. The End User and the project team should collaborate to ensure that user required functionality is integrated into the project design and testing. The End User group should include representatives from other functions within the customer organization, as required by the project scope. For example, manufacturing projects end users would include Quality and Compliance. The End User:

- helps the Project Manager and Project Sponsor to define the project's objectives and develop the business case
- works with the Project Team to develop the User Requirements Specification (URS) (see Chapter 6 of this Guide)
- provides expert guidance and advice to the project team during design and delivery to reduce risk
- has access to SMEs in other areas of an organization and ensures their involvement, as required
- may have a role in the review and acceptance of activities during the project such as acceptance testing or formally accepting ownership of the project's deliverables once the project has been completed
- may have a role in confirming the business acceptance criteria have been met (this depends on the role of the Customer)

2.3.4 Senior Stakeholder Management

A Project Manager should develop a Stakeholder Management Plan to manage stakeholders, based on the analysis of:

- involvement of stakeholders in the project or in the use of the project outcome
- stakeholder influence on the project outcome
- stakeholder authority to give or withhold critical resources which the project requires
- stakeholder support or resistance to the project

Stakeholder management then goes through four basic phases:

1. Gaining Entry – making initial contact.
2. Contracting – clarifying and agreeing roles and responsibilities, decisions and information flows, etc.
3. Engagement – meeting the agreed “contract.”
4. Disengagement – agreeing that the “contract” is complete (at project end and/or when benefits have been realized).

Stakeholder management tools include:

- Role Identification Tool: Stakeholder Mapping
- Role Definition Tool: RACI Chart (see Table 2.2)
- Role Management Tools: Stakeholder Maps, Relationship Maps, RACI Charts, etc.

The RACI Chart is a good practice tool for the definition of responsibilities. The RACI Chart can also be used at project launch to help to plan how the group of senior stakeholders and the project team will work together, and to agree and communicate definitions on key activities. The RACI Chart may be considered a customer communications plan and a first step in customer relationship management.

Table 2.2: Example RACI Chart – Defining the Role of Senior Stakeholders

Role →	Project Sponsor	Customer	End User	Project Manager	Project Team
Activity ↓					
Defining the projects objective, business context, and rationale	A	R	C	C	I
Establishing and prioritizing the projects business objectives	A	R	C	C	I
Representing the projects interests and ensuring the project is allocated sufficient resources and priority within the customers organization	AR	C	C	C	I
Chair the Project Steering Committee	AR	C	I	C	I
Develop the Projects Business Case	AR	C	C	C	I
Define and establish the roles required to complete the project	C	C	C	AR	C
Manage project progress	C	I	I	AR	C
Remove organizational road blocks that might impede the progress of the project	AR	C	C	C	I
Endorse any Project scope changes	AR	C	C	C	I
Communicate impact of project on the business	AR	C	C	C	I
Ensure project benefits are realized throughout the life of the project outcome (immediate post project review)	A	R	C	C	I
Formally accept the completed project	A	R	C	C	I

Note for Table 2.2: The example RACI Chart represents a situation where all senior stakeholder and project team roles are within one organization. When defining roles and responsibilities, the potential effect of contractual boundaries should be considered.

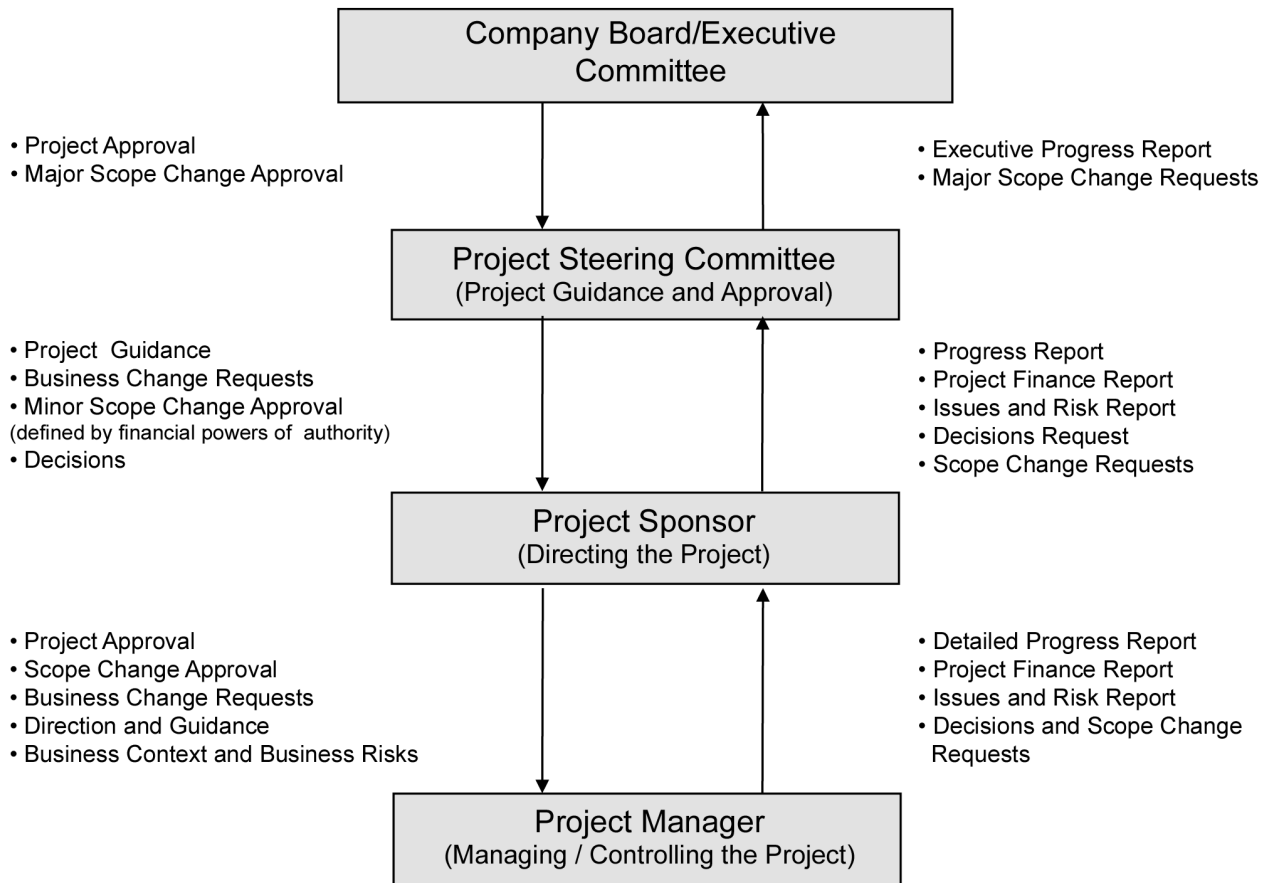
The defined roles form the Project Manager's basic stakeholder map. A stakeholder is anyone who is influenced or impacted by the project or who could influence or impact the project. The stakeholder map is considered a key customer relationship management tool and can be fundamental to managing business change issues.

2.3.5 Project Steering Groups

A project specific steering group or committee may be created to support management of key customer relationships. Figure 2.3 shows an example communication map and reporting structure for a typical project steering committee.

Steering committees should be formed at the beginning of a project and typically consist of senior stakeholders. The Project Manager should report to the Project Sponsor who chairs the steering committee.

Figure 2.3: Project Steering Group Structure



The roles and responsibilities of the steering committee typically include:

- acting as the ultimate decision taking body for critical project issues
- ensuring that adequate resources are available
- deciding on appropriate contracting models
- deciding on the utilization of the cost contingency
- providing recommendations to the organization's board/executive committee for investment approval
- steering the direction of the overall project
- nominating a Project Manager

- decisions regarding any changes to the project budget, timeline, and scope (quantity, quality, and functionality) following approval
- select the most suitable alternatives (usually presented by the Project Manager on behalf of the project team)
- providing guidance and feedback to the Project Manager and team, resolving disputes and ambiguity

In systems or process change projects that cover multiple areas of a business, it may be beneficial for the steering committee to remain together after delivery to allow on-going decisions related to system changes and updates.

Example

During the delivery of a new ERP system to controls production, sales, and financials, it was impossible to assign a single system owner; therefore, a steering committee was formed. This group of Senior Stakeholders was effective in steering the direction of the project and making timely decisions. Upon project completion, the group decided to remain “active” in order to steer any future system changes and ensure the sustainability of the project benefits.

2.3.6 Project Ownership

The handover of the project outcome should be discussed by the Project Manager, Customers, and End Users from the very start of a project. Early stakeholder discussions should include the transition of the project outcome into the business, e.g.:

- identify the business changes needed and responsibilities for their delivery, i.e., are they within the project scope or are they to be delivered by the business at handover
- identify potential compliance risks
- identify people and business process issues, e.g., the need for operational documentation to be developed, such as manufacturing procedures
- identify infrastructure issues, e.g., the need for more purified water

Example

A newly developed drug product is handed over for production within an existing manufacturing facility.

- Additional operators were recruited to operate the new process due to an increase in the number of manual operations.
- The new operating procedures were handed over.
- In process sampling and testing procedures were agreed.
- The facility team trained operators to manufacture to the new procedures.
- The support functions (quality, warehouse) were involved in handover discussions so that they could manage their own business changes.

2.3.7 Business Change Management

When a project is approved, it is typically because the business requires some form of business change. The project delivers outcomes which, when used by the business, supports delivery of this change thus realizing benefits of value to the organization.

Completed projects can lead to:

- new ways of working
- requirements for new capabilities and skills
- new organization structures and responsibilities
- new roles and will have an impact on resource levels

Managing the related business changes is a part of the project management scope. This includes the identification of the business change and also gaining support for successful delivery, often by resources outside of the Project Team.

Within the pharmaceutical industry, changes to the business also have to ensure compliance to regulatory requirements. This requires:

- Organizational change control documentation. This is documented proof that the project's outcomes meet regulatory requirements; that quality risk have been eliminated or reduced to an acceptable level, and that the new ways of working are reproducible and repeatable.
- Training – to enable people to operate according to the revised ways of working.
- Sustainability – checks that the new ways of working are being maintained.

Example

A laboratory business change project was implemented to decrease the time it took to test final drug products. The project changed the laboratory layout, the way samples were managed, and the way testing was completed. The success of the project was due to the early identification of key areas of business change requiring support from the laboratory team:

- an understanding of current ways ("as is") of performing tests
- an understanding of Good Laboratory Practices (GLP) or other applicable regulatory requirements
- assurance that the team would implement the new ("to be") ways of working

The Project Manager developed a project delivery strategy which engaged and involved the laboratory end users:

- The laboratory team, SMEs in this area, and representatives were asked to join the Project Team.
- The initial workshops involved all of the laboratory team as a way to collate issues or any differences in current ways of working.
- The laboratory team was involved in the design of the "future state."
- 2-way communication using the lab team representatives was a continuous process during the project delivery.

As a result of the business change strategy used, the project successfully delivered the required reduction in testing time and was able to sustain this improvement following project completion.

Inevitably, there can be resistance to change. Resistance is a natural human reaction to change; however, in a project, it needs to be managed so that the project's goals (both compliance and business objectives) are achieved and sustained. Key strategies to minimize and manage change resistance include:

- open communication with the affected business area through all phases of the project
- participation from all or some representatives of the business area; these may be SMEs and should be part of the project team

- development of handover strategies from the start of the project
- development and delivery of training programs
- robust stakeholder management planning and engagement (see Section 2.3.4 of this Guide)

The project team should develop the project scope with a clear understanding of the current (“as is”) business situation, so that the project is seen as solving current issues, and to highlight the benefits regularly throughout the project to maintain engagement of the End Users.

2.3.8 Key Project Management Challenges

Key senior stakeholder management challenges for a pharmaceutical project can be summarized as shown in Table 2.3.

Table 2.3: Key Customer Management Challenges

Challenge	Comments	Impact?	Mitigation Plans
Project alignment with business objectives	Business objectives change over time. Project sponsors are responsible for ensuring the project objectives remains aligned with the business objectives and to initiate any scope changes that may result from the changes in these objectives.	High	Regular Project Manager-Project Sponsor meetings should be held to ensure alignment between the internal project environment and the external business environment.
Poor communication between the Project Sponsor and project team	Project sponsors can also be an SME and involved on a day to day basis with the team.	Medium	The Project Sponsor should understand the dichotomy of these roles. This should be managed, as Team members may not see the distinction.
Changing key project members during the project delivery	Key SMEs can be moved from project to project due to changing priorities. This can cause risks to individual projects, if done without adequate knowledge transfer and without regard to impact on a project team.	Medium	The Project Manager should outline key SME roles and agree how SME redeployment (if necessary) should be managed.
Selecting the wrong Project Sponsor	Project sponsors need to have the appropriate authority in the area being changed by the project. This may not be the most senior person available or person who has the most interest, knowledge, or expertise in a project is selected.	High	Project sponsors should be selected from persons who have the appropriate authority in the business area being changed by the project. The Project Sponsor may need to be changed to someone with the appropriate authority.
Key stakeholder not adhering to the agreed terms of engagement	Inexperienced project stakeholders can be involved in projects.	Medium	A specific RACI Chart should be developed and a “contracting” session should be conducted.

Table 2.3: Key Customer Management Challenges (continued)

Challenge	Comments	Impact?	Mitigation Plans
No defined Project Sponsor	Small projects or large complex technical project may not have a single point of accountability.	High	A Project should have a Project Sponsor who is accountable for realization of the project deliverable and benefits, who is “active” and understands the role.
Poorly defined roles and responsibilities	The Project Manager should ensure that the project team understands their roles and responsibilities, to avoid duplication of effort, conflicting priorities, and aspects of the project being missed.	High	Formal roles and responsibilities should be developed, preferably using the RACI process described in Section 2.3.3 of this Guide.
Insufficient project team members with the correct expertise	Project team members should be appointed based on skills and/or authority to operate in the role, rather than status.	High	Project sponsors should understand and support the Project Manager in the selection of staff with the appropriate level of skill and authority.
Have resource available with strong knowledge of GxP and other regulations	A resource with knowledge of GxP and other regulations should be available to ensure the project is compliant with regulatory requirements and regulatory deliverables are optimized.	Medium	Appropriate regulatory expertise should be engaged when establishing the project team. Expertise may be obtained from within an organization or outside an organization.
Unrealistic expectations of project cost and schedule	Inexperienced Project sponsors may set unrealistic “stretch” goals with regard to a project’s schedule and budget.	High	The process of building project budgets and schedules should be transparent to both the Project Sponsor and Project Manager and methods of schedule acceleration should be openly discussed.
Diverging Process Owner priorities	Customers can be two different process owners, e.g., in developing and transferring a drug to a scale up facility there is usually a facility owner and a product owner.	High	Recognize that the project deliverables are going to two different owners. The Project manager should contract with both owners to understand, define, and align priorities.

2.4 Roles and Responsibilities: The Project Team

Team members need to understand their Subject Matter Expert (SME) role, and also the need to balance deliverables and expectations with cost and schedule, as the Project Manager does. They may need to be coached into joint ownership of project delivery within the sanctioned project constraints and this requires selection of a suitable coach and possibly provision of additional formal training. Being a member of a project team is different from the role of supporting production from a QA, Validation, or Operations position, yet team members might not understand this. Project success can depend upon this cross functional participation and team members may need additional training or support to contribute properly. These and several other people considerations will be discussed further in this chapter. However, above all, for project team members to be successful they need to be capable, available, and have the authority to undertake their defined roles and responsibilities. The Project Manager must ensure that this happens and recognize and manage the risks when it doesn’t.

This section looks at the team structure for a project, but it should be noted that the structure may change as a project matures. For the purposes of this Guide, a “team” is defined as:

- “Two or more individuals or functional units that join together to achieve a common goal, either under a permanent or temporary organizational structure.”

As the scope of a project increases the number of people supporting the project (either full or part time) and the number of relationships to be maintained also increase. Project Managers have a key role in the management of people and these relationships:

- The Project Manager defines a team structure which is communicated by project organizational chart. This is led by the project manager and any team member within the chart is managed by the Project manager. This is the vertical structure that defines the team depth.
- The Project Manager also determines additional support needs. These are not typically documented within the project organizational chart and may not be managed by the Project Manager. This is the horizontal structure that defines the team breadth.

The scope of work may be divided into specific areas or sub-projects with each being assigned a defined set of deliverables. A resource plan, such as supported by a RACI Chart or Role Profiles, should be developed for each area and sub-project; this should state the roles and responsibilities of team members.

In larger projects, the project life cycle may be divided into phases. As a project evolves, project participants may change or their roles may change within the project. This process needs to be defined and managed.

In a given project phase, the Project Manager can decide to divide the resource plan and/or organizational chart differently than in earlier or later phases. For example, during the engineering design phases of a Facility Project, it is usual to organize a project by function, whereas during the construction or implementation phase, a project may be divided into geographic areas or systems.

It is the intent of this section to reinforce existing concepts and introduce new ones that will address the following questions:

- How should a Project Manager structure the project team roles and responsibilities to deliver project scope?
- How should a Project Manager determine the size and type of team required to meet the project objectives?
- How should a Project Manager determine which roles are most critical to project success and how best to staff those roles?
- How should a Project Manager determine and manage the needs of the project team and balance those against project objectives?

These questions are critical activities which should be considered early and re-evaluated regularly throughout a project's life cycle. The term “team” should be predefined. The Project Manager should identify, formulate, and manage the team, including delegating activities appropriately to team members.

2.4.1 Critical Activity #1 – Structuring the Project Team's Roles and Responsibilities to Ensure Delivery of the Project Scope

Project Managers should:

- Understand the scope of a project and be able to assess resources needed, establish budgetary estimates, and determine schedule duration. The project scope should be documented.

- Ensure that a project team has a clear and complete understanding of the scope of a project.

Team member's roles and responsibilities should be established early in a project life cycle to help ensure a project's success. Using a RACI Chart can be beneficial, e.g., the definition of responsibilities supports the establishment of communication and reporting structures.

Typically, an outline project scope is developed by a small team of experienced senior staff. The Project Manager should use the outline scope to develop an executable plan which identifies the expertise and resources required to deliver the project. For further information on the development of scope, see Chapters 4 and 5 of this Guide.

Once the scope has been allocated by functional groups and resource types, the roles and responsibilities should be clearly documented and communicated to team members. This is the basis of establishing a team.

Where external resources are used extensively as Subject Matter Experts (SMEs), team members from within the organization may "shadow" the external SMEs. This practice can support project turnover (see Chapters 9 and 10 of this Guide), but should be evaluated against the project schedule and budget, as well as demands placed on other responsibilities of team members from within the organization.

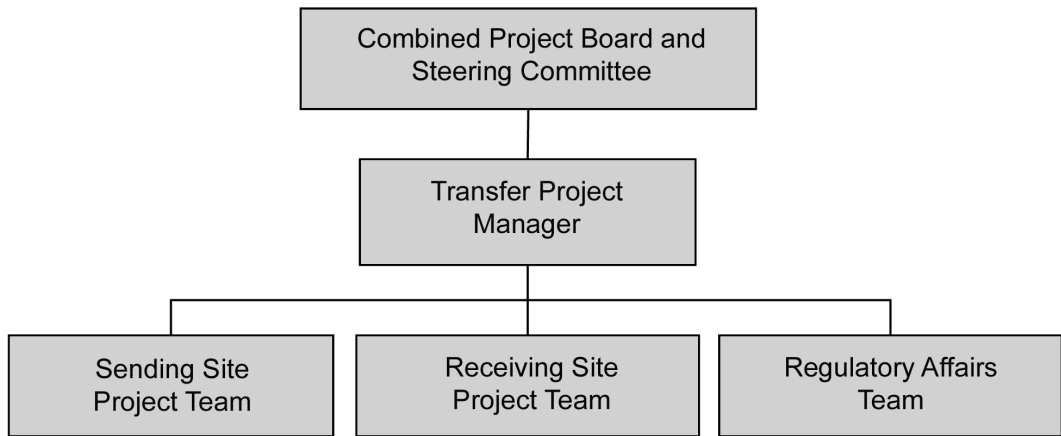
Assigning specific tasks to team members from within the organization, with SMEs providing mentoring and training, can be a more effective relationship.

2.4.2 Critical Activity #2 – Determining the Size and Type of Team Required to Meet the Project's Objectives

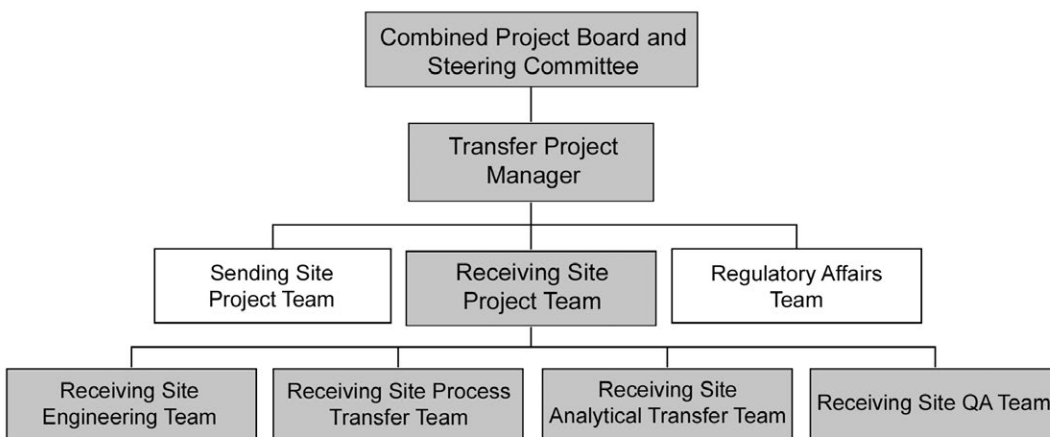
The project scope determines the type, size, budget, and duration of a project team. This is demonstrated using an example of a project for transferring production from one manufacturing site to another.

At a high level, the project may be organized into teams as shown in Figure 2.4.

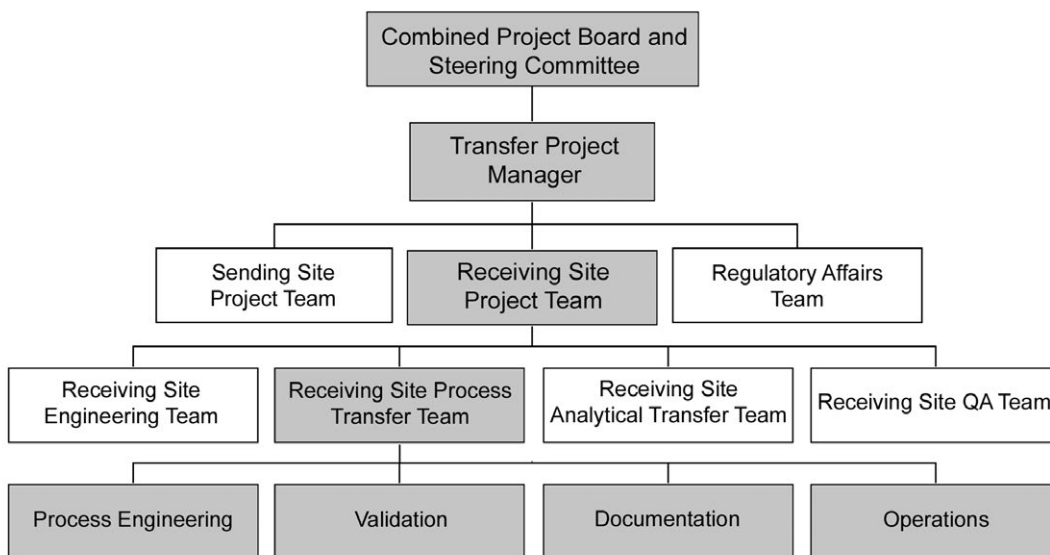
Figure 2.4: Typical Technology Transfer Project Team Structure



As shown in Figure 2.5, this team structure can be broken down into the sub-teams required to deliver various aspects of the project's scope.

Figure 2.5: Typical Technology Transfer – Receiving Site Project Team Structure

Each of these sub-teams may have a further sub-set of smaller teams, as shown in Figure 2.6.

Figure 2.6: Typical Receiving Site Process Transfer Team Structure

Project Managers should determine the best way to structure a project, regardless of the size of the project team.

The following steps provide an **example** for determining the size and type of team required to meet a project's objectives.

Step #1 – Determining Functional Needs

Functional areas needed to support the project should be listed. This list should help to define the skill sets and expertise required, but without determining hours of effort, budgets, or schedules. Roles and responsibilities for the project should have been identified previously to allow the required functional areas to be established.

The conceptual structure, defined during this step, may contain functions that can be achieved by the Project Manager or the project management team.

Step #2 – Defining the Project Management Role

Project Managers should develop the organizational structure considering the project requirements and the tools and methods appropriate to the stakeholder organization. Tasks such as scheduling, cost control, procurement, and document control may be included in the Project Manager's role, depending on the size and/or complexity of the project. Project Managers should balance such a workload with the requirements of managing the project. When staffing the project, Project Managers should ensure that other team members are able to provide support for these project management tasks.

Leadership is a core competency for Project Managers; management of activities is as critical as the execution of those activities.

Step #3 – Consolidating Remaining Functional Roles

For the remaining functional roles, the Project Manager should try to group like tasks into organized groups. These groups may be aligned with typical project responsible areas, e.g., in a Facility Project:

- Project Management (PM)
- Design (D)
- Construction (C)
- Testing (T)
- Operations (O)

Depending on the project type, other responsible areas may be required, e.g., Regulatory Affairs, R&D, or IT.

Step #4 – Re-Evaluation of Roles and Responsibilities

It may be beneficial for Project Managers to re-evaluate the roles and responsibilities to demonstrate the appropriate division of labor across the functional groups. The roles and responsibilities should be sufficiently detailed to identify any gaps or responsibilities not aligned with the project's scope.

Step #5 – Determining Contract Scope

This step allows the Project Manager to determine which functions can be managed internally by a Customer's personnel, and which functions need to be contracted out.

Identified functions can be organized into two groups within the project team:

- one for identified functions **“to be managed internally”**
- one for identified functions **“to be contracted out”**

This is a critical activity and will be the basis for determining a project's associated labor budget and the Project Manager should gain commitment for the “to be contracted out” scope of work.

Projects may be staffed entirely internally by an organization. Where projects require additional contract support, the internal versus contract scope of work needs to be defined and agreed in order to determine an accurate estimate of associated costs. For further information on the development of an appropriate contract strategy, see Chapter 7 of this Guide.

The internal groups and resource required to support a project should be determined early in a project. Draft roles and responsibilities should be shared with internal groups to enlist their support. Internal capabilities should be verified to ensure that assumptions made in developing roles and responsibilities of internal groups are addressed before outside support is contracted. Potential additional contract needs should also be identified.

The reporting structure and employee evaluation of internal staff assigned full-time to a project should be moved temporarily to the Project Manager. This should allow the Project Manager to manage full-time team members and assign team members' job function and goals. A matrix management approach to personnel management may be required in virtual, multi-site, and multi-national teams.

Example

During a facility improvement project, the overall project budget was established prior to the development of the detailed labor estimates. This delivered a staffing approach that met the available funding, but not necessarily the technical or compliance requirements.

The Project Team should be staffed with individuals having the necessary technical competencies to deliver the project scope. Less experienced individuals should be placed with those with more experience. Project Managers should identify skill sets required and conduct value management activities to correctly size the team, offer project specific training, mentor project team members, and maintain a project team focused on scope delivery.

Step #6 – Determining Duration of Functional Support

The duration of functional support required to support the project should be determined independent of how much time is needed at each stage. One approach is to mark on an outline project milestone schedule the functional groups required to support each project stage.

Typically, major milestones align with project life cycle stages, e.g., for a Facility Project:

- Conceptual Development
- Project Delivery Planning
- Detailed Design
- Procurement
- Construction – if a capital engineering project
- Testing
- Close-Out and Handover

This activity can help to develop an understanding of the hours of effort required to deliver each project life cycle stage and establish project staffing requirements. Functions may span multiple life cycle stages or may appear in non-sequential stages. This exercise should form the basis for identifying the structures of the project team throughout the life of the project.

The six steps above should allow Project Managers to organize team structures defined by Team Depth (Project Assigned Staff), Team Breadth (Project Support Staff), and Team Length (Duration of Assignment).

Step #7 – Determining Team Depth (Project Assigned Staff)

Steps #1 to #6 should help Project Managers determine the functional areas that will fall under their management structure. Typically, project structures are shown as top down reporting schemes; however, alternative methodologies can be employed. For the purposes of this Guide, a general structure of an organizational chart is assumed (see Figures 2.4, 2.5, and 2.6) with the intent to show both the reporting structure and the functional division of labor and responsibilities. Organizational charts should be included in the Project Delivery Plan (PDP) and communicated to all team members and the Project Sponsor. For further information on PDPs, see Chapter 5 of this Guide.

The depth of the team should be based on an evaluation of the level of staffing and level of skills required in completing the scope of work of a project. For example, a senior procurement manager may support the project throughout its entire life cycle, but it may be supported during peak workloads by a sub-team of procurement experts, etc.

The number of team members required to support a project is dependent on:

- the scope of work
- workload estimates
- available resource schedule analysis
- identification of roles and responsibilities
- skills and experience of key team members
- the division of available budget

Step #8 – Determining Team Breadth (Project Support Staff)

The functional areas not managed directly by the Project Manager, but supporting the delivery of the project, such as quality assurance, finance, or maintenance management, etc., form the breadth of a project and represent how the project scope can affect many areas of an organization. Communication should be managed, as these functional groups may not have close contact with the core project team. Individuals should be designated in the vertical (core) team structure with responsibility for maintaining linkage with the wider team so that information and communication can be managed and distributed as needed.

Correct sizing of communications becomes important where there is a mix between part-time and full-time team members. Full-time members are usually better informed. Part time members may lose connectivity and may become inefficient. A comprehensive communications plan should be developed to mitigate potential inefficiencies (see Section 2.7 of this Guide).

Project team members from a customer's functional organization may support more than one project in addition to normal working. The time required to be committed to a particular project, as a team member, should be planned, allocated, and documented in their annual objectives. Project team activities should be integral to an individual's annual objectives and be evaluated during performance reviews. This should help to ensure the team member's contribution is understood by both the project and customer leadership.

Other functional areas may not appear on the project structure or organizational chart. However, the activities that those areas need to perform to deliver a project should be identified and communicated to ensure that their roles and responsibilities are included in the PDP. For further information on PDPs, see Chapter 5 of this Guide.

Step #9 – Determining Team Length (Duration of Assignment or Support)

The duration of the different project life cycle stages may not be fixed during the early stages in project planning, but the level of effort required during the specific stages should be estimated.

There are several methods for communicating and representing the durations needed for functional groups during a project timeline. One of the simplest is to connect the start and end of involvement to specific project milestones and to highlight which milestones are on the schedule critical path.

These milestones should bookmark the major level of effort required by the functional groups. Groups may need to become involved prior to the start of their activities, especially during schedule development, or planning activities where time is required to significantly increase resource levels for a specific activity. Functional groups may also be involved after their primary responsibilities have been completed. The staffing plan should account for this.

These steps help the Project Manager develop a detailed view of the overall project team structure.

2.4.3 Critical Activity #3 – Determine Which Roles are Most Critical to Project Success and Determining How Best to Staff Those Roles

For functional groups with the longest time span across a project's life cycle, the Project Manager should consider performing a capability and capacity risk assessment to evaluate and mitigate any potential risk associated with lack of appropriate resources.

Functions identified as critical to project success are likely to have the highest resource budget and most scheduled items to manage. Typically, they will be on the schedule critical path, and represent potential risk to the project schedule and quality. The critical requirements of the key positions within project teams should be identified. The Project Manager should ensure that individuals chosen to fulfill these roles are suitably qualified, experienced, and sufficiently skilled to perform the designated function.

A project culture which aligns philosophies and management practices should be established early in the staffing life cycle. This should help to ensure ownership from key project team members and allow them to build sub-teams with team members who fit the project culture and can work together as necessary (see Section 2.7).

Key project team members form the core project team in the vertical project structure and should commit to the project scope and vision of success. The Project Manager should act as the interface between the core project team and the horizontal cross-functional team.

The core project team should communicate effectively with others and be available for the complete duration of their assigned roles and responsibilities. This may be achieved through the development and distribution of the project charter by the core team (See Appendix 1).

2.4.4 Critical Activity #4 – Determining and Managing the Needs of the Team and Balancing Those Against Project Objectives

Team members may be required to follow rigid processes in their daily job function, whereas in a project role, they may be required to adopt a more flexible way of completing their responsibilities. These differing role requirements can lead to conflict, as:

- Projects are less predictable and have a higher level of uncertainty.
- Projects can have changes of direction, as uncertainty is clarified.
- The project team has a definite start and end date and a focus on project outcomes.

- Project team members usually have differing skills and experience.
- Processes may be customized for a specific project (defined within the PDP).
- The Project Manager may not be an SME or an expert on the business area or the technology.
- Project participants may not have sufficient time allotted for project work.

Resource gaps can occur where insufficient time is allotted for project work.

Project environments are usually:

- high pressure, and therefore, more stressful
- less certain and require more flexibility, and problem solving and creative skills
- more transient in terms of developing relationships

Issues to be considered include:

- personnel being unclear about their role
- frustration from repetitive changes of direction
- loss of perspective
- lack of availability of key personnel
- splintering of a team into small groups who work independently and inadvertently deviate from project scope
- insufficient time to complete tasks
- exhaustion of personnel through increased workload as the project progresses

The impact of these issues can be mitigated by the use of good project management practice and general management tools and techniques, e.g.:

- RACI Charts and Role Profiles
- Project Charter
- Team Health-Check
- Time Management Tools (Importance/Urgency Matrix)
- Effective Meeting Checklist

Where personnel are in a new environment defined roles and responsibilities should be communicated, solving two problems:

- Two project members trying to do the same job because each believes they are responsible. This can lead to stress and a breakdown in working relationships.
- Omissions, where each project member believes someone else is responsible.

Roles and responsibilities should be discussed with the project team and adjusted, as required. As a project progresses, roles and responsibilities should be re-visited to ensure that they remain current.

Project leadership should be maintained. It can be beneficial for the Project Sponsor explain to the project team why the project is being undertaken and how it will change the organization.

Project Manager Role in Critical Activity #4

Project Managers should consider activities that will increase commitment and promote project ownership to the individual level, e.g., project team workshops to develop the detailed RACI and schedule based on the high-level predefined requirements.

Project Managers should manage their own workload as well as the workload associated with direct reports. There should be a balance in how the project maintains focus and absorbs increasing workload, e.g., flexibility in working hours or working from home (where company policy allows) may help to mitigate increased project workload.

Project Managers should use an appropriate change control process to evaluate change and determine the impact on project objectives such as schedule, quality, and cost as well as on the project team (capacity and capability).

Project Managers should develop methods that best fit their own project management style and keep each member of the project team engaged. Turnover of team members may be necessary for personal or disciplinary reasons, but can have a negative impact on a project.

Where issues arise that cannot be resolved within the team, but have not escalated to a point of conflict, a level of authority beyond that mandated to the team may be required. Plans should be established to address such issues and can have two clear benefits:

- provides a defined escalation process, ensuring problems can be addressed quickly
- defines authority levels and personnel understand who is making decisions

Conflict resolution planning should be part of a Project Delivery Plan. Conflict can prevent delivery of a successful project. The Project Manager should have the experience and skill to resolve conflict or the project should have a designate that has the experience and skill to resolve conflict. The Project Manager should be able to enforce the established project policies and agreed team ways of working. Example techniques to resolve conflict are given in Section 2.5.6.

Team Meetings

Interaction should occur within an individual team and between separate project teams. The full project team should meet on a regular basis, e.g., starting the week with a team meeting for all members of the project team. An overview of progress is usually presented and then each attendee (or team leads of the sub-teams) should discuss what they have planned for the week. If a team lead is the only person representing that sub-team's scope of work, that sub-team lead should mimic the weekly meeting process for their sub-team. This achieves:

- making team members focus on their goals for the week and encouraging good work practices
- giving team members a sense of commitment - they have stated their goals, and the following week they will have to explain if these have not been met
- alerting the Project Manager to problems
- enabling team members to see how the work of other people may be affected by what they are doing

- raising issues between different project team members
- providing a chance to set action items and follow-up the following week

The Project Manager should determine which methods work best for them, and allow for feedback and constructive criticism to focus their style to the project team's needs.

Example

A facility improvement project was approved and involved a large package of changes to an existing facility to be delivered over 18 months. The Project Manager identified a number of methods to maintain team communications and delivery focus over this time:

- A Project Team Meeting – to occur at a regular time each month and have an agenda and minutes. Where action items are created, they were documented in the minutes. The minutes were communicated by the afternoon of the same day.
- “Weekly Stand-up” only meetings – around project dashboards and used to convey project status in a visible way so that team members immediately got a “signal” to act or react in a specific way to maintain appropriate progress.

A Project Manager should recognize that management is the application of skills and experience. Project Managers should understand that people can be unpredictable and influenced by factors outside the project. An effective Project Manager should be patient and understand the personalities, skills, and capabilities within the project team members.

2.4.5 Key Project Management Challenges

Typical challenges faced by a Project Manager as a team is selected, formed, and managed include:

- Developing a “streamlined” team with the required capacity and capability, particularly with respect to an SME to address the GxP or specific technical considerations. For example, the design team needs to integrate compliance with and consideration of GxPs effectively into the detailed design and be able to support qualification/verification efforts to support validation.
- Working with technical experts – in terms of the technology challenges – who do not have the relevant compliance background; ensuring personnel who may be from other industries and not have the appropriate understanding of GxP and compliance receive the appropriate training.
- Using QA resources effectively (while maintaining their independence from commercial aspects of the project), e.g., QA personnel with an appropriate background in risk assessment working to develop a risk-based verification approach. Motivating team members and ensuring accountability for individual responsibilities.
- Decision making – recognizing that decisions with significant impact have to be made and ensuring appropriate team commitment to these.

2.5 Roles and Responsibilities: Consultants and Contractors

This section discusses the people aspects of the relationship between an organization and its key external resources: consultants and contractors. It focuses on communications from an internal Project Manager perspective to give an example of the type of challenges faced and how to mitigate risks. The exact nature of contracts is not discussed.

For further information on using external resources and strategies, see Chapter 7 of this Guide.

Communication is discussed from the point at which:

- A scope of work has been approved.
- A design consultant has been selected (if appropriate to project type).
- A contract has been signed.
- The Project Manager and design consultant are embarking on design.

Design is an iterative process and requires significant collaboration between the parties. A team of consultants with their own Project Manager may be contracted to provide project services to a Customer. In this case, the Customer's Project Manager may communicate contractual changes only with the consultants' Project Manager - as a single commercial point of contact. The consultant's Project Manager takes responsibility for managing the team of consultants and ensuring their adherence to quality, schedule, and budget. The consultants' Project Manager is responsible for reporting to Customer's Project Manager.

Contracts should contain clauses which make explicit what should happen where communications start to be challenged or breakdown; however, no contract can predict every situation or cover every contingency so the Project Managers' tasks are dependent upon their communications skills and processes.

2.5.1 Selection

Key criteria for selection of consultants and contractors include:

- previous experience in the specific type of project
- track record in the pharmaceutical industry
- adequate in house resources Client references for similar projects
- alignment of contractor and Customer's culture

In addition, each organization may have specific procurement policies for consultants and contractors, e.g., consultants and contractors may need to:

- be an approved supplier before being used on a project within an organization
- undergo specific training before commencing work on a project

For further information on selecting external resources, see Chapter 7 of this Guide.

2.5.2 The Contractual Relationship

The formal nature of contracts should ensure that they align to the way that a project needs consultants and contractors to behave (see Chapter 7 of this Guide).

Partnering and alliance approaches can be used to link the contractual relationship with an appropriate communication process by reducing or eliminating the adversarial nature of contracts. These typically involve the development of performance measurement applicable to both organizations, and appropriate to the contract type, e.g.:

- In a capital project the desire to achieve a key milestone for completion within a budget can be aligned in the contract through some form of sharing of the savings from good ideas. The incentive drives appropriate behaviors – looking for cost saving ideas – which support project success.

- In a product launch project, the need to launch on time can be aligned in contracts through use of bonuses linked to milestones achieved, e.g., completed acceptable scope delivered on time and in full.

Care should be taken that the contractual measures fully align with all project objectives, including quality related objectives, so that the contract supports the management of patient safety as well as other project specific goals.

In addition, contracts should outline how proprietary information is managed and how documentation should flow between each organization to enable project completion while managing knowledge appropriately (see Section 2.6 of this Guide). Restricting the flow of such information can cause risks to project success. Inappropriate alignment of confidentiality and information management contract clauses can cause a barrier to communication and relationship management.

Not all projects may be suitable for partnering styles of contract. The selection of this project delivery approach is specific to each organization and to each project.

2.5.3 *Negotiating*

In collaborative negotiations, parties should search for alternatives by conducting negotiations as a problem solving exercise.

Project Managers may be called upon to participate in competitive or distributive negotiations where the objective is to decide which party gets the larger scope of work. In other cases, a more collaborative approach may be used where what is mutually beneficial for all parties involved is identified.

A Project Manager should gain an appreciation of and experience in negotiating.

Example

During a competitive negotiation where cost was the highest priority driver for the project, a Project Manager was considering options:

- The project wanted to pay less than the selected supplier wanted to be paid.
- The supplier has issued a variation to contract as the scope change requested by the Project Team would deliver a change to the contract scope.

The Project Manager decides to only approve the change, and the associated contract variation to Supplier, if the Project Team and Supplier can identify how this change will deliver project delivery benefits in other areas such as reduced project schedule or less internal team effort. The change is not necessary for project success, but has the potential to deliver benefits of value. The negotiation concluded with a reduction in the cost of the variation as the Supplier would actually spend less effort elsewhere in their contract scope.

2.5.4 *Communications with Consultants and Contractors*

Consultants and contractors (including sub-contractors) should rely on the Project Manager for clear direction and communication. Project Managers should be able to deal with inter- organization and inter-departmental communications.

During the project delivery phase, the Project Manager should maintain visibility with the whole project team, including visits to sites where a project is being implemented, while still handling administrative aspects and team meetings. This includes maintaining an effective visible presence with consultants and contractors.

Communications requirements extend throughout all levels of an organizational hierarchy. Consultants and contractors can come from a variety of organizations with their own organizational cultures, interests, issues, and needs, which may conflict with those of a project. Project Managers should establish an environment through which the project team avoid, prevent, and resolve such conflicts. Economic conditions can also have a significant impact on projects (e.g., bankruptcy).

The Project Manager should seek alignment with consultants and contractors on common objectives. From a legal perspective objectives are established in contracts; however, the relationship should extend beyond what is stated in the contract. Project teams should establish a level of trust with consultants and contractors, who are judged mainly by competency and results and so having clear expectations in terms of deliverables and documentation is required, i.e., what documentation is to be provided, as well as where and in what form documents will be stored.

2.5.5 Collaboration

Communications should be collaborative, e.g.:

- working in an environment dedicated to finding common ground
- persisting with problem solving during disagreements (not participating in “blame” or using sanctions)
- working toward resolution through dialogue and discussion, and not abandoning communications
- using third party intercession, escalation, or arbitration when needed to resolve disputes

One process to establish collaboration is to instigate a partnering relationship wherein customer-consultant-contractor agree to a process in which all parties commit to a common project objective, e.g., “project success.” Partnering can:

- require that customer-consultant-contractor interact earlier in a project
- bring greater participation in owner policies and procedures, information sharing, and decision making
- have both benefits and risks and both should be managed in alignment with the agreed partnering goal
- be incentivized and can be written into a contract or operate without a contractual basis

It is usual to have an agreed arbitration process if this approach is used.

2.5.6 Avoiding, Preventing, or Resolving Conflict

Project Managers should communicate and manage relationships with the project team, consultants, and contractors to avoid, prevent, or resolve disagreements before they become conflicts, turn into disputes, and result in complaints. Project Managers should be able to recognize how to react to disagreements, conflicts, or disputes.

Project Managers may need to

- facilitate discussion between individuals in his project
- facilitate resolution
- mediate conflict
- utilize a project escalation/conflict process

Facilitating Resolution – Project Managers should help all parties involved by being in control of the process of information sharing, allowing the parties to better understand each other’s perspectives on the issues. Parties should use this information to resolve issues, preferably without needing the Project Manager to be involved in reaching agreement.

Mediating Conflict – Project Managers should work with the parties to find common ground, identify alternatives, and work with them parties through resolution or impasse. During mediation, information sharing may allow parties to work out a mutually agreeable solution.

Escalation/Conflict Process – Where facilitating resolution or mediating conflict is not possible, Project Managers should know and utilize a project escalation/conflict process.

Where a Project Manager is a source of conflict, has a conflict of interest in facilitating or mediating between parties, or the issues are such that parties need more experienced facilitators or mediators, the escalation process should designate an “objective” intercessor. Examples of approaches taken by third party intercessors include:

- Gathering parties involved and identifying the issue. Obtaining agreement on who is responsible for making the decision. Ensuring that the relevant party is present (it may be one of the protagonists) so that a decision can be made.
- Asking each party to define how they see the issue from the other’s perspective before they present their own case.
- Discussing with the parties involved individually. Asking whether it is an issue with the person or with their view on a particular topic. It may be both. If it is an issue with the person, asking them to list things they dislike and things they like about the person. Suggesting they focus on the things they like, rather than do not like.
- Talking to both parties and suggesting they can benefit from their differences by identifying how they can be applied to achieving the project’s goals.
- Talking to other project team members and asking how the problem can be resolved - a solution may be provided. Talking to the person and convincing them to be more compromising.

2.5.7 Key Project Management Challenges

In order to have successful working relationships with consultants or contractors, challenges to be addressed include:

- Recognition of the need for SMEs and that this expertise may need to come from outside an organization.
- Recognition that contractors and consultants may need training in an organization’s systems or processes.
- The need to be better at collaborative working rather than use prescriptive scope and contract document approaches.
- The need to develop long term relationships to manage post project issues, as well as those which may arise during project delivery.
- The management of knowledge to protect intellectual property rights and adherence to non-disclosure agreements.
- How new technologies (possibly from outside the industry) can be harnessed when an organization with the specialized skill does not have pharmaceutical experience.

2.6 Knowledge Management

Project Managers in all industries handle data and they support the conversion of that data into knowledge that can support project team success. The movement of knowledge within a project team and the transfer of knowledge as the team changes are all processes fundamental to project success.

There is a critical requirement for confidentiality and the handling of proprietary information and protection of intellectual property within pharmaceutical projects and this requires the Project Manager, team members, end users, and other key stakeholders to have clearly defined processes to manage sensitive data. The accuracy of data at the start of pharmaceutical projects can be quite low and as the knowledge increases the importance of change control and good communication increases.

Project management is also about the integration of cross functional activities from the start and continuously through a project to enable streamlined project success. A Project Manager has to manage a variety of project activities and work packages yet still maintain attention to fundamental project requirements, e.g., funding requests, design contracts, construction contracts, equipment orders, reporting progress in all areas, etc.

2.6.1 Knowledge Management Principles

There are two important terms in knowledge management:

- **Explicit Knowledge** – captured and recorded in documents, databases, or Web sites, etc. Explicit Knowledge is tangible and can be easily identified, accessed, and manipulated.
- **Tacit Knowledge** – the knowledge people have, their experience, and personal learning which translates into insights and ideas. People are often not aware of how useful the knowledge they possess can be to others.

The IT based tools and techniques available to help capture both types of knowledge are not discussed in this Guide.

Different strategies are required to gain benefit from each type of knowledge. Triggers for explicit knowledge include regular reporting and it is easy to distribute and make available. Explicit knowledge should be managed to allow searching for specific knowledge.

Tacit knowledge can be difficult to access (even from someone very willing to share it!). The appropriate role, environment, culture, and use of questioning techniques should be used to uncover valuable tacit knowledge that a person may, or may not, realize they have.

The sharing and use of knowledge is highly dependent on organization and individual culture. This can be influenced by the Project Manager who can also facilitate the creation of the right environment. Typical barriers to using collective and accessible knowledge for the benefit of the project include individuals view, i.e.:

- *“knowledge is power”*
- *“not invented here”*
- *“my colleagues will feel I am incompetent if I ask for help”*

For further information on project culture, see Section 2.7 of this Guide.

2.6.2 Knowledge Management and the Project Timeline

The integration of Knowledge Management (KM) elements into a project can be broadly classified into three phases:

- start

- during
- end

Start

During the start phase, the Project Manager should ensure that the project team draw learning from different sources and integrate it into the planning and set up of the project. Typical questions include:

- Has a project of this nature been done before, what issues were encountered, and what was learnt?
- Was it viewed as successful; what were the key factors which made it so?
- Who has expertise in this field and what can we learn from them?
- Can we get people who have relevant skills to review our plans, challenge our assumptions, and ask questions?

The overall quantity of information and knowledge will be relatively small at the start of a project. The projects objectives should have been defined, but the route map to their completion may have only loosely been determined. In addition, the information known at the start of a project is likely to be imprecise and may be inaccurate, e.g., budget estimates: accuracies of +/- 50%. As a project progresses the level of knowledge available increases, as does the accuracy of the cost estimate.

During

During a project, the level of knowledge to be managed starts to grow exponentially and the challenges, include:

- maintaining communication
- sharing relevant knowledge
- sharing the latest information
- working collaboratively to address issues and take opportunities
- maintaining alignment with other work which may affect the project

During a project, the accuracy of available information increases. Knowledge management and change control processes should be established and enforced to ensure that Project team members work with up to date information.

Knowledge established may be required to ensure GxP compliance of the project. The project team should assess which elements of project knowledge affect GxP compliance and manage this knowledge in a GxP compliant manner.

End

In the final stage of the project, the amount of knowledge about the project is at its highest, e.g., the project budget. The Project Manager should know the actual cost to complete the project in precise detail.

Before the project team disperses, a project review should be undertaken by the project team to capture project knowledge for subsequent projects and regulatory requirements. This knowledge capture should take the form of:

- Comparing what was supposed to happen with what actually happened and identifying why there were differences.

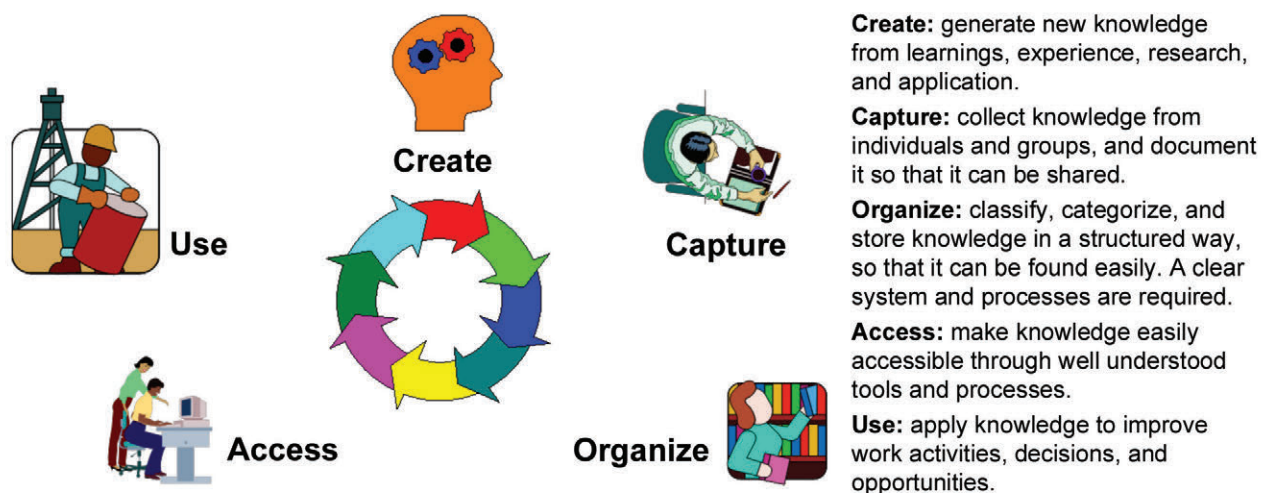
- Establishing what can be learned from these differences and how they were handled, and if there are any other “lessons learned,” both positive and negative, from the project.
- Identifying if there is anyone outside the project team who could benefit from this knowledge.

There may be an appropriate location for this knowledge to be stored for future reference by the organization.

2.6.3 The Knowledge Cycle

The model shown in Figure 2.7 illustrates the life cycle of explicit knowledge. These principles can be (loosely) applied to tacit knowledge.

Figure 2.7: The Life Cycle of Explicit Knowledge



At the hub of the cycle is the organization of a knowledge base which should be accessible to the right people in the right way. The principles of operation of the knowledge base, project team roles in populating and using it, and responsibilities for management should be established early in the project.

As the project progresses, redundant documents, drafts, and superseded versions should be removed to help to retain ease of access to useful information. IT tools and systems are available to manage knowledge bases. Project Managers should seek expert help in assessing the most suitable IT solution for their project.

The knowledge base can help to mitigate risks from changes to project personnel more likely within projects with lengthy timescales.

Cultural issues should be addressed to allow a successful application of the knowledge cycle, see Sections 2.6.1 and 2.7 of this Guide. Project Managers should set clear expectations, including the role specifications of project team members. For third parties, including contractors and consultants, these should be written into the contractual commitments. The Project Manager should also monitor and facilitate the knowledge cycle use and role model the desired behaviors.

2.6.4 Key Project Knowledge Management Challenges

Knowledge management can be a significant challenge, and therefore, a significant part of the overall management of a project. Project Managers remain responsible for the appropriate accuracy and precision of the knowledge available to project team members and other key stakeholders before, during, and after project completion. Key challenges include:

- handling confidential knowledge

- handling GxP knowledge
- motivating project team members to share specific knowledge which may be regarded as “intellectual property” and overcoming fears that in revealing this knowledge they are no longer required
- using benchmark data during a project and providing data to support continuous improvement of benchmarking knowledge after the project is complete

2.7 Language, Culture, and Communication

Communication is a critical aspect for all areas of a project and communications management is a core project management process. Challenges can be categorized as related to:

1. Language
2. Culture
3. Communications Process

The key message throughout this chapter is that effective communication is a critical success factor for all participants in all stages of the project.

2.7.1 Language

In the pharmaceutical industry, different languages are used across the product life cycle. For example

- a scientist developing a drug
- an engineer designing a new facility
- an operator running a manufacturing plant
- a QA Specialist releasing drug batches

The above groups each have their own “language.” Each may be required to convey critical information during a project. These challenges can be addressed using a project glossary which should be included in the PDP (see Chapter 5 of this Guide).

Having a common language and common terminology can assist in effective communication in an environment which is multi-disciplined, multi-organizational, multi-cultural, and multi-national. Issues to be considered include:

- Where project team members are not communicating in their native language, the Project Manager should test for understanding.
- The integration of industry best practices through the use of the “language” of improvement (lean six sigma).
- The “language” of quality aims to ensure that all participants in a project focus on product quality and patient safety.
- There should be an effective risk management process that ensures the potential impact of identified risks are communicated and understood by all personnel involved with a project.

- Cultural differences, particularly when working in cultural settings that have a distinct hierarchical structure, e.g., cultures may behave differently – there is no right or wrong, a successful team will allow for differences.

Project Managers, project team members, and senior stakeholders should speak the same “language” to ensure project success. Jargon, confusion over terms, and inconsistent terminology should be avoided. In addition, Project Managers should stay up to date with and adopt new terms to explain advances in current thinking and technology in the pharmaceutical industry, ensuring that the team understands them.

Companies may have their own vocabulary, or acronyms, a definition of these within a project document may help ensure a common understanding across the project team.

The Language of Project Management

Within the pharmaceutical industry, “life cycle” or “techniques/tools” terminology can have specific nuances, i.e.:

Life cycle – The life cycle of a project in the pharmaceutical industry follows a typical life cycle as described in Chapter 1 of this Guide. The terminology used by Project Managers is driven by the life cycle stage of the project. Each project life cycle chapter in this Guide develops the specific life cycle terminology for that stage of the project, for example

- A Project Manager is aware that the project initiation stage (see Chapter 4 of this Guide) typically culminates in a Business Case which states the cost/benefit criteria for that project; however, this has to be put in the appropriate context for the team and senior stakeholders to understand.

Techniques/Tools – Project Managers will always discuss scope, cost, time, and the tools and techniques required to develop these key project management themes. Within some parts of the pharmaceutical industry, however, the term conceptual scope may not mean the same as the development of an early User Requirements Specification (URS). A key role for the Project Manager is to understand the tools, techniques, and terminology used and to describe them to the project team.

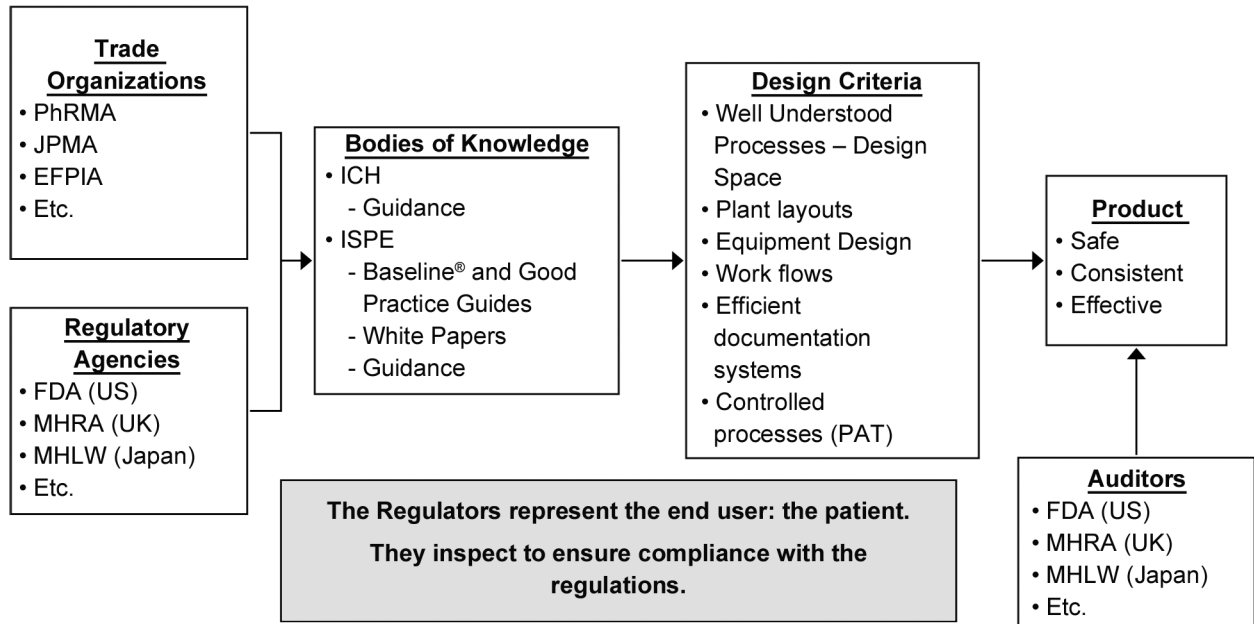
Project Managers should try to use concise everyday language to support communication to help to ensure that that they are understood. They should avoid making some common mistakes:

- Jargon can alienate team members and stakeholders.
- Terminology for the sake of terminology; using a specific term which may have no resonance within a part of an organization, e.g., the term “Project Delivery Plan,” may be referred to as a “Project Execution Plan.”
- Excessive use of acronyms can alienate stakeholders and limit good communication.

The Language of GxP

The pharmaceutical industry has its own language. The terminology can be categorized as that linked to regulatory agencies, other organizations or resources, and key industry terms (See Figure 2.8).

Figure 2.8: Example: The Language of GxP



The majority of the terms listed below can be found in the ISPE online glossary (Reference 8, Appendix 3) and are only further discussed here to show, by example, the necessity to develop a common language that supports good communication.

- **Regulatory Agencies** – include, e.g., US FDA, UK MHRA, and Japan MHLW. Project Managers should ensure their project team includes from an early stage in the project regulatory SMEs in the relevant agency expectations.
- **Organizations and Resources** – organizations within the pharmaceutical industry, e.g., ISPE, ICH, JPMA, may offer guidance in the form of documents or through training, conferences, seminars, and communities of practice (collections of SMEs). During project delivery, the team may require specific guidance and would usually refer to such bodies.
- **Key Industry Terms** – these are listed in the ISPE online glossary (Reference 8, Appendix 3). For example, the definition of terms such as GxP, Quality Critical Quality Attribute (CQA), etc.

Project Managers should use such terminology within the team to fully communicate the challenges being addressed and the need for specific responses to them. The project team should ensure:

- integration of regulatory requirements into every aspect of a project
- involvement of quality assurance and compliance functions as a core part of the project team
- streamlining the project process to integrate rather than have parallel processes

2.7.2 Culture

Project culture results from the personnel involved and the governance of a project. The project culture is shaped by each participant as described by three elements:

Culture = (1) how we behave + (2) values we hold + (3) things we do

The Project Manager can influence these three elements to promote a change in project.

Factors which can influence how team members behave and act include the way in which:

- The Project Manager chooses to communicate and react to team communications.
- Progress is measured and managed.

If specific behaviors are required, measures and communications need to drive to those behaviors; the way in which project controls and team management processes are set may prevent this, e.g.:

- Contractors may have a fixed number of hours to work each day, and by using techniques like earned value, need to complete specific deliverables within an allotted time. This can aid deliverable completion to target, but may not support quality goals.
- Where employees do not have their time monitored, their focus on quality can lead to a lack of focus on completion and schedule targets.

This can lead to a detrimental effect on the project team culture, where team differences cause misunderstandings and conflict.

Project Managers should work within the contractual and functional boundaries. There should be recognition of how team member performance is measured, as this can affect how team members behave. There should be an agreed shared goal which overrides other considerations. The development of critical success factors which lead to a shared vision of success is a key tool in this regard.

To drive the appropriate project culture, Project Managers should:

- Possess a high level of integrity; project team members should want to emulate the Project Manager.
- Be genuinely interested in the well-being of each member of the project team. Project team members should know that when a dispute is being settled all participants are respected.
- Show respect, e.g., by careful listening and giving prudent feedback to influence team culture and which project team members can emulate.
- Gain commitment with the appropriate use of SMEs.
- Consider the time zones that participants are in when scheduling meetings.

2.7.3 Communication Process

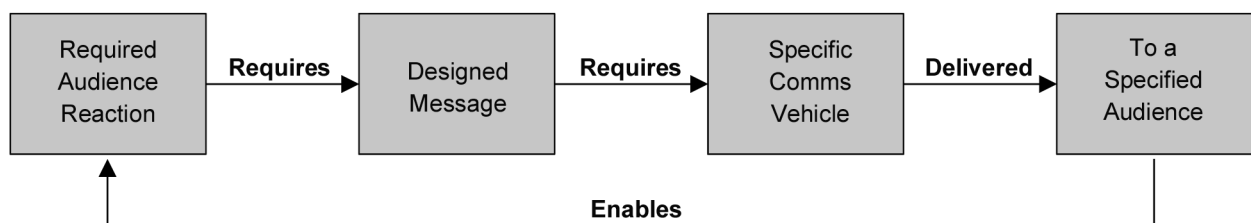
Projects should have a cross functional, formally agreed communication plan which describes how information will be disseminated and how decisions will be made. Typically, the communication plan should be a sub-set of the PDP (see Chapter 5 of this Guide). The communication plan should incorporate product quality and regulatory aspects of communications and decisions.

Approach for Developing a Communication Plan:

- Start with a communication plan template.
- Identify team members and functions.
- Identify stakeholder levels of management.
- Explain communications information scope, i.e., what will be communicated, how and when (frequency of communication).
- Link with the project timeline, deliverables, project metrics, and reporting.
- Agree the mechanism and frequency for each type of communication with the cross functional team.
- Identify decision analyses which will be employed and who will be involved.
- Obtain cross functional team approval.
- Maintain the communication plan as a covenant or contractual agreement – to be referred to regularly.
- Maintain a decision log – capture participants and rationale.

When designing specific communications, start with the desired readers' requirements (see Figure 2.9).

Figure 2.9: Focusing Communication Messages



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Example

A Project Manager wants to get more resources approved by the Project Sponsor and is developing an appropriate communication message. The communication plan is broken down as described in Figure 2.9.

Required Audience Reaction:

- Approval of Resources

Designed Message:

- What: we need more resource.
- Why: we have added project scope.
- Impact: we will miss a key deadline.

Specific Communication Vehicle:

- One to one meeting between Project Manager and Project Sponsor
- One page summary document, clearly stating the issue, the suggested resolution, alternative actions considered and why rejected, and the cost and schedule impact

Specified Audience:

- The Project Sponsor

The communications plan should be tracked to ensure that it is effective, meets the team's requirements, and current organization:

- Communication should include feedback from people being communicated to; that they understand the message and that they convey the appropriate, designed reaction.

Project Managers should be sensitive to a potential to lose the respect from team members by ignoring their input to the communications process; both in terms of developing and delivering the messages and also in tracking audience reaction.

Project Managers should maintain open communication paths with the project team; this can support building trust and project commitment.

3 Risk Management

3.1 Introduction

Project risk can occur at any stage in a project's life cycle. The uncertainty caused by the existence of project risks needs to be mitigated: whether this involves the cumulative impact of smaller risks or one major risk. Individually and collectively these risks can increase the cost and schedule and reduce the effectiveness of a project's ability to deliver on its business case. Effective risk management can mitigate uncertainty.

Project risk should be defined and managed. This is a key component of the project management process, and therefore, Project Manager should regularly ask:

"What is the overall likelihood of achieving project success?"

Identification and objective analysis of the risks and continuously controlling how the project has responded to them can provide an answer.

The scope of this chapter is the risk management challenges specific to the project types considered by this Guide, i.e., Facility, Improvement, Product, IT, and Automation.

As defined and described in ICH Q9 (Reference 7, Appendix 3) Quality Risk Management (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 life cycle.

The integrated risk management approach described in this Guide covers both project risk and risk to product quality and patient safety.

Many of the same tools and approaches are appropriate and useful for managing both project risk and risk to product quality and patient safety, but a clear distinction should be maintained between these types of risks in a pharmaceutical context.

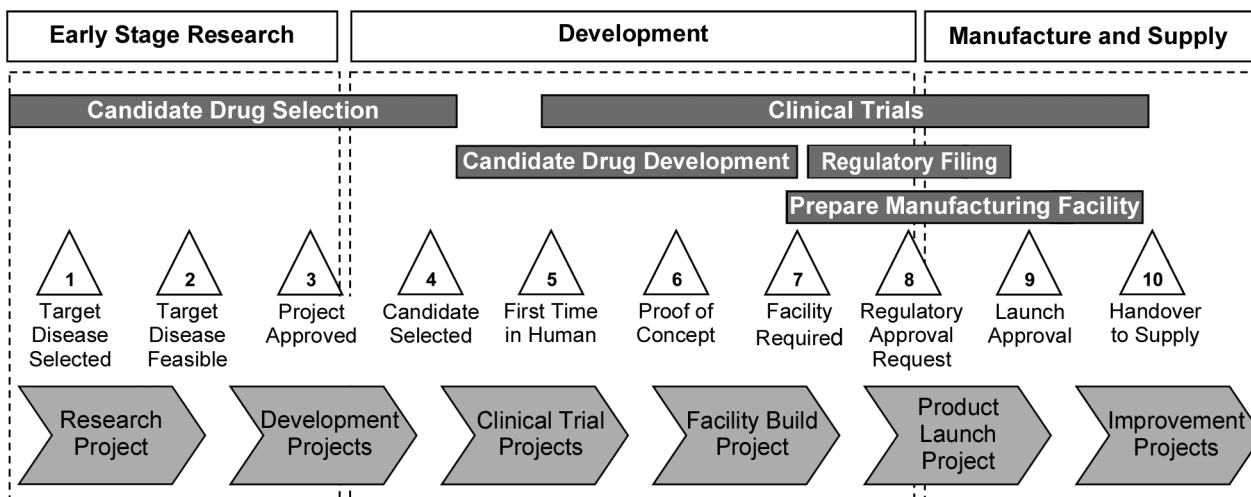
Management of risks to product quality and patient safety is covered specifically in Section 3.3. Pharmaceutical Risk Management.

Figure 3.1 describes the life cycle of a pharmaceutical product (see ICH Q10 (Reference 4, Appendix 3)):

- Pharmaceutical Development – early stage research and development
- Technology Transfer – linking development to manufacture and supply
- Commercial Manufacturing – supplying product to the market
- Product Discontinuation – when market supply and associated manufacture ceases

The life cycle can be viewed as a chain of projects of different types which together deliver a new product to the market. The points at which these projects interact and handover are considered major sources of risk.

Figure 3.1: Example – The Product Life Cycle Linked to Project Delivery



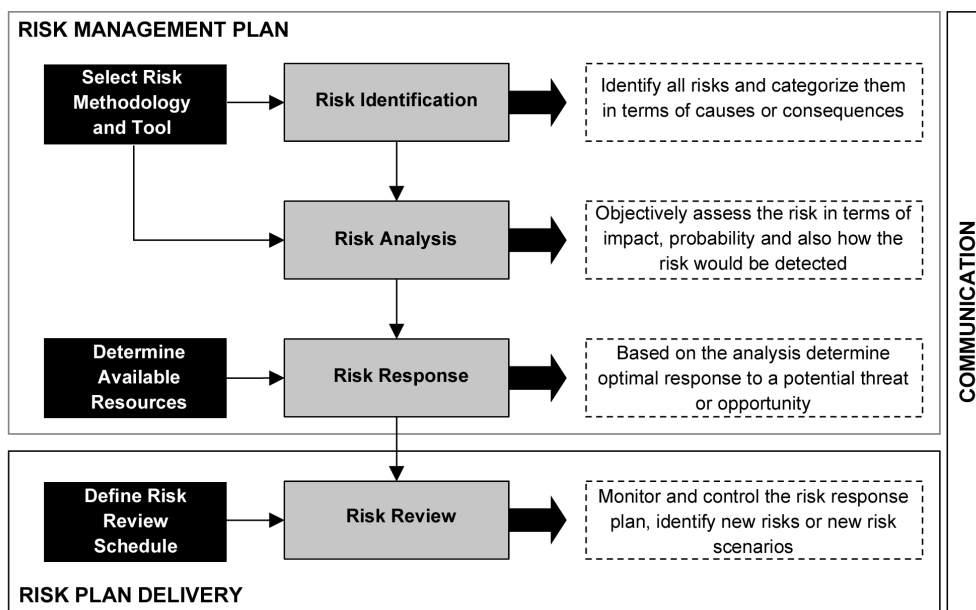
The complexity of the regulatory framework and the different functions required to complete the overall process introduce risks which can be mitigated by considering:

1. Generic non-industry specific good risk management processes which are applicable to the pharmaceutical industry and mentioned for completeness.
2. Specific risk management challenges typically seen within the pharmaceutical industry with guidance and how they are usually handled.

3.1.1 The Generic Risk Management Process

The management of uncertainty (whether giving positive or negative outcomes) is called risk management. Figure 3.2 describes a typical risk management process.

Figure 3.2: Typical Risk Management Process



Note: Within a project management context, a risk response is the act of prioritizing and selecting what to do as a result of identifying and analyzing a risk. The identified risk response has therefore to be reviewed regularly to ensure that it is appropriately managing the risk, i.e., Risk management = risk response + risk review. A risk management plan therefore comprises the risk response plan and the risk review plan.

This is a generic process, used across most industries and different project types to:

- identify an area of uncertainty (a risk)
- objectively assess that risk (typically impact and probability are assessed and, in some cases, detectability)
- collate data to allow a risk response plan to be developed

Within the pharmaceutical industry, this generic process is used for different project types (e.g., GAMP) and for specific risk types (e.g., Quality Risk Management). These processes should have the same basic stages of risk assessment, control, and review while maintaining communication.

The risk control phase starts with risk response planning, after a thorough and objective analysis has been completed using appropriate personnel and data, and once a Project Manager understands the project resources available, i.e.:

- people
- funds
- time
- assets

The risk plan should seek to provide:

- **Mitigation responses** – where actions are planned to either reduce or eliminate the probability that the risk will occur, or to minimize the impact should it occur. These actions should be integrated into the Project Delivery Plan (PDP) (see Chapter 5 of this Guide) and aligned to the protection of the project objectives. A key aspect of mitigation planning is establishing criteria to evaluate the effectiveness of the mitigation actions.
- **Contingency responses** – where actions are planned to minimize the impact if the risk occurs. Such “back-up plans” may be approved for implementation in advance of the risk occurring, but when its probability of occurrence is high, e.g., bad weather.

Risk techniques allow prioritization of the risk response; “traffic light” measures may be used to indicate risk levels, i.e., Red, Amber, and Green:

- Red and Amber risks require some form of risk response.
- Green risks are considered low priority and do not generally require a formal risk response.

The risk response strategy should review:

- The most appropriate location of risk management: who in the project is best placed to deliver the mitigating or contingent action.
- The resources available.
- The impact of the response strategy on the project objectives.

Tool selection should focus on the tool most appropriate to the situation under review. Table 3.1 provides an example of how risk tools have been used in a variety of project scenarios. This list of risk tools is not intended to be exhaustive.

Table 3.1: Example Risk Management Tools used in a Project Environment

Risk Technique	Description	Examples of Use within a Project Environment
Risk Matrix	Typically a 3 × 3 table which allows risk to be plotted and prioritized with reference to 2 parameters: typically probability of risk occurrence and severity of impact.	Overall project risk assessment – to identify which critical success factors are least likely to be achieved, and therefore, affect project success and support prioritization of the risk responses. GAMP 5 (Reference 5, Appendix 3) has adapted the risk matrix technique for use in functional risk assessments. Two matrices in series are used to assess severity, probability, and then detectability.
Fault Tree Analysis (FTA)	Identify the most probable failure route using logic trees.	Commissioning Planning – plan for risks with the potential to cause system test failures which shows the risk assessment related to a Factory Acceptance Testing (FAT) failure. Design Management – identify technical design risks with overall project impact.
Fishbone	Cause and Effect Technique. Identify potential factors causing an overall negative effect through considering 6 cause categories.	Overall project risk assessment – to identify most probably cause-effect relationships, and therefore, highest priority mitigating actions. Schedule and cost risk assessment – to identify high probability risks with specific project consequence.
(Hazard and Critical Control Point Analysis) HACCP	Identify potential hazards within critical risk areas.	Overall project risk assessment – to identify highest impact risks in critical areas of the project.
Hazard and Operability Study (HAZOP)	A standard hazard analysis technique using a guide word approach to assess impact of deviations.	The preliminary safety assessment of new systems or modifications to existing ones. The detailed design of an API facility would use HAZOP to ensure that the design is appropriate.
Failure Mode and Effects Analysis (FMEA)	A tool whose origin is from the requirement to eliminate defects within systems by identifying potential failure modes and analyzing them (effect, cause, and control).	Design risk assessment – to identify and mitigate risks around the design of briefly exposed process operations. The failure modes (leading to product exposure) can be identified and then analyzed and mitigated as appropriate.

Focus on the risk response plan should be maintained to avoid a lack of follow through in terms of tracking and maintaining the risk response plan.

3.1.2 Risk Management in the Pharmaceutical Industry

This chapter discusses three aspects of risk management in the pharmaceutical industry.

1. **Pharmaceutical Risk Types:** causes and consequences of risk may be unique to the pharmaceutical industry (see Chapter 3.2 of this Guide).
2. **Pharmaceutical Quality Risk Management (QRM):** risk to product quality and patient safety should be considered, managed, and mitigated (see Section 3.3 of this Guide).
3. **Integrated Project Risk Management:** the way in which the process and tools of risk management are integrated into a project team's way of working is distinct to the pharmaceutical industry (see Chapter 3.4 of this Guide).

Project Managers should focus on:

- Balancing the different types of risk and resources needed to manage them.
- Prioritizing risk responses so that the “red risks” (such as risks to patient safety, and product quality) are managed in preference to the “green” ones.
- Selecting and applying the most appropriate risk management tool or technique for the specific project situation.
- Involving the appropriate SMEs throughout a projects life cycle.
- The handover of project knowledge at the end of the project, which will allow risk management to continue where appropriate.

The life cycle sections of this Guide highlight the specifics of risk management during a particular phase of a project.

3.2 Pharmaceutical Risk Types

Risks can be categorized by consequence or by cause. This allows the development of mitigation or contingency strategies which address several distinct risks, usually in one cause or consequence category. Risk tools typically focus on cause or consequence and analyze risk impact within a particular scenario, e.g.:

- When launching a new product to market, the risk consequences of most concern are product acceptability and launch on time. This leads to a focus on using schedule and quality risk management tools and techniques. Fault Tree Analysis (FTA) may be used to consider the most probable failure routes to these two consequences (see Table 3.1). A Project Manager would typically manage risks linked to key go/no go decisions so that the project remains connected to the business.
- When improving an existing mature pharmaceutical process, it is usual to focus on what could potentially cause the process **not** to be improved and tools, such as FMEA may be used to look at a variety of potential failure modes (see Table 3.1).
- Within technology transfer projects, the focus on technical equivalence is linked to the regulatory and compliance consequences mitigated by effective documentation of the science and the Quality Risk Management (QRM) process. Risk checklists and flowcharts provide a way to assess specific aspects of the project looking primarily for GxP risk consequences.

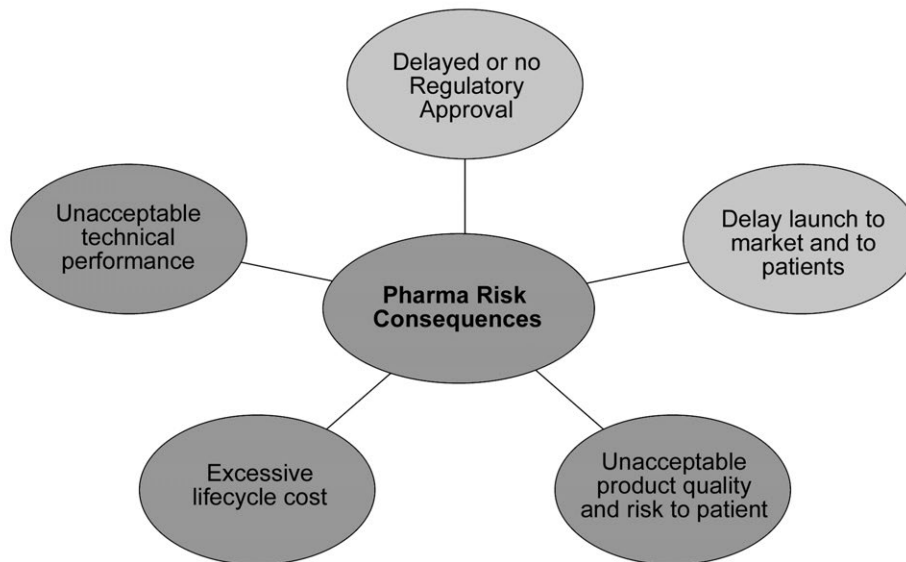
3.2.1 Risk Consequences

Specific consequences in pharmaceutical projects (see Figure 3.3) include:

- Not obtaining regulatory Approval

- Product being late to Market
- Unacceptable Product Quality
- Failure to meet Technical Performance targets
- Exceeding the Life Cycle Cost estimates

Figure 3.3: Example – Pharmaceutical Project Risk Consequences



Regulatory Approval

Pharmaceutical products are subject to continual scrutiny throughout the entire product life cycle, the function of which is to assure patient safety. A complex compliance framework exists to govern the ability of a manufacturing process and production facility to protect a drug substance from contamination and to safeguard personnel. There are multiple regulatory processes throughout a products life cycle (see Figure 3.1). Regulations vary around the world, requiring compliance with multiple regulations, sometimes simultaneously. The project management challenge is to manage the project process, while maintaining compliance with the relevant regulations. Reliance on SMEs is a key part of this process.

Product to Market

The business goal is usually to move a product from the initial idea, through the research, process development, clinical trials registration, and to launch it into sustainable supply as quickly as possible. Although other routes to market exist (e.g., third party R&D or contract manufacturing) the costs and risks remain in the product life cycle. In addition to the intricate compliance framework, the length of the product development process results in a large number of stage gates that a product needs to navigate. These create a unique set of challenges for a Project Manager. Each stage gate exists to mitigate the risk of continuing without specific data and this information and decision management becomes an important part of the project management framework, particularly as one project in the product life cycle hands over to the next.

Product Safety

Significant effort is required to document each step of the process to assure patient safety. As R&D progresses and product and process knowledge expands, this knowledge should be captured and documented. The documentation forms the basis of the manufacturing process design and all elements of the infrastructure needed to support

compliant product delivery. The development process should continue after the preliminary manufacturing data is captured in order to identify the limits of process safety – the extent to which the process operating conditions and raw materials can vary while continuing to assure the required product quality. Within the pharmaceutical industry, regulatory guidance on the development of both chemical and biotechnology Active Pharmaceutical Ingredients (APIs) can be found in ICH Q11 (Reference 9, Appendix 3), with analogous guidance for the drug product in ICH Q8 (R2) (Reference 6, Appendix 3) together with their associated Questions and Answers and Points to Consider (References 10 and 11, Appendix 3). While these guidelines are not regulatory requirements, they encourage the development of Design Space(s) which can illustrate enhanced product and process understanding (e.g., parameter and attribute interactions) and enable manufacturing flexibility.

The data captured is used as the basis of the validation cycle: documenting what is intended and the expected results; followed by testing to confirm that the expected results were achieved, and collating the results of the tests to prove to regulatory agencies that testing was successful. This should be managed as a part of the quality risk management process within a project (see Section 3.3 of this Guide).

Once into the sustainable supply sections of the life cycle, the cycle of demonstrating that the process stays within the defined operating limits should continue. At all stages, changes to the original plans, processes, and evidence should be documented and justified through a robust change control process. This should ensure that no change can be made to prejudice the process integrity, and therefore, prejudice patient safety. A project interacting with a product, therefore, should take these risks into account during project delivery.

Technical Performance

A Project can be stopped at any stage in the life cycle with the possible loss of investment and a robust risk management process should be used to ensure that the project can be terminated without excessive costs. Reasons for termination include:

- If clinical trials indicate a product is unsafe or lacks efficacy.
- If process development is unable to ensure the drug substance can be manufactured to consistent standards of identity, strength, quality and purity, it may not be possible to obtain permission to market the drug substance.
- If manufacturing operations are not operated within the parameters identified during development, regulatory clearance may be withdrawn and the right to manufacture (license) may be withdrawn.

Life Cycle Cost

At the start of a project, the life cycle cost considerations may determine which high level options are acceptable, e.g., whether to have a multi-purpose or dedicated facility; the variety of alternative design options: modular build for scalability, disposable technology for reduced operating costs, etc. These can have an impact of the total life cycle cost.

It is considered financially beneficial to start the revenue stream from a drug substance as early as possible to ensure maximum revenue before patent or marketing exclusivity expires. In this case, activities may be commenced before an approaching stage gates review is completed successfully. This could accelerate the delivery of subsequent stages, but may increase financial risk. If a project does not pass a subsequent stage gate, more cost has been expended than was necessary to stop a project. The Project Manager should:

- Understand the risks involved.
- Collect data to conduct an effective risk analysis.
- Balance the risk of additional cost against the earlier start-up of the revenue stream.
- Make decisions based on all the above.

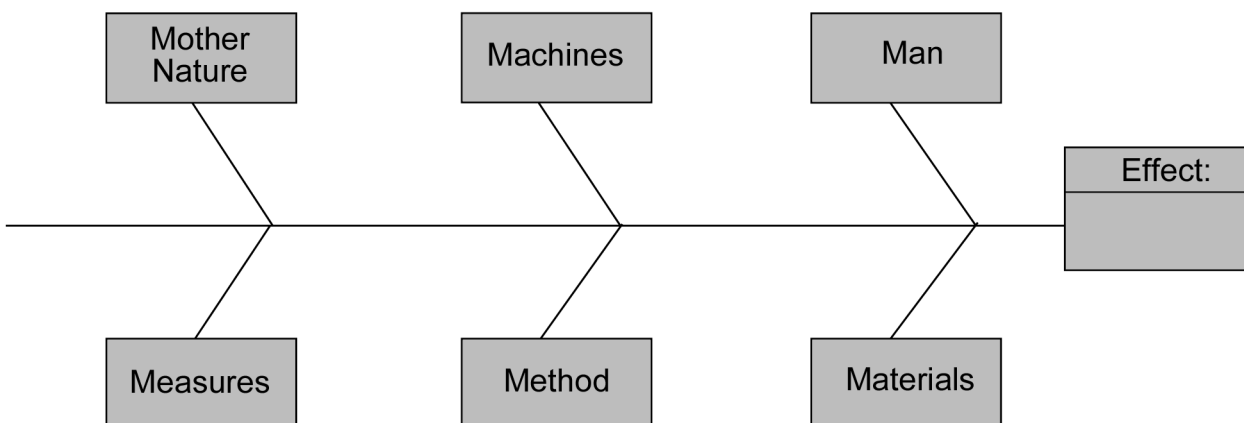
3.2.2 Risk Causes

This section considers the cause-effect relationships that are specific to the pharmaceutical industry.

A Cause-Effect diagram (see Figure 3.4) can be used to highlight different categories of cause. This is called a Fishbone or Ishikawa Diagram and is a way to develop an understanding of the root causes of an effect; whether positive or negative. The challenge for project management is to balance all risk causes and consequences to deliver a successful outcome. Typical causes of uncertainty in these categories include:

- Man
- Machines
- Mother Nature
- Materials
- Method
- Measures

Figure 3.4: Typical Causes of Uncertainty



Man

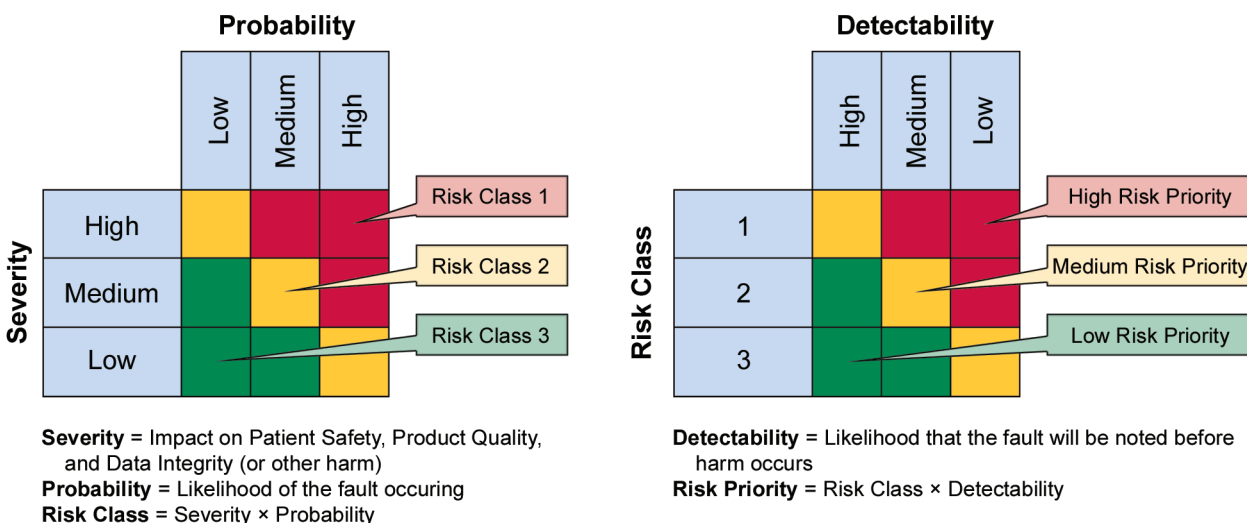
Human error and the variability in human response to issues can be mitigated through effective selection and management of project team members (see Chapter 2 of this Guide). The appropriate use of SMEs and quality and regulatory professionals, for example, can mitigate some typical human causes of failure seen in pharmaceutical projects. The Project Manager can mitigate project failure by role identification linked to an understanding of team member capacity and capability.

Machines

Decisions made regarding technical and technology outcomes, equipment or system selection, and the automation or IT strategies, require specific accurate data in order to manage the uncertainty. Typically, this type of risk assessment is managed within the design process (see Chapter 6 of this Guide).

For example: within computerized systems functional risk assessments are needed to identify and manage risks to patient safety, product quality, and data integrity that arise from the failure of the function under consideration. Automation may introduce specific risks (e.g., electronic record integrity, system availability, security infrastructure). The GAMP approach may be used to complete this assessment (see Figure 3.5).

Figure 3.5: Example – GAMP Approach



Mother Nature

The nature of the pharmaceutical industry does introduce specific risks. The Project Manager should maintain an overview of all project risks so that this interaction of risk cause or consequence is managed effectively.

Specific SME management, e.g., regulatory, GxP, or safety may be required. Challenges to cost and schedule can cause uncertainty as mitigation plans impact other areas of a project and cause regulatory, process robustness, or product quality risks.

Materials

How a project is specified in terms of the scope needed and the deliverables required to deliver that scope (e.g., documentation, systems, and equipment) can be a source of uncertainty especially where commenced at an early stage to test feasibility.

Method

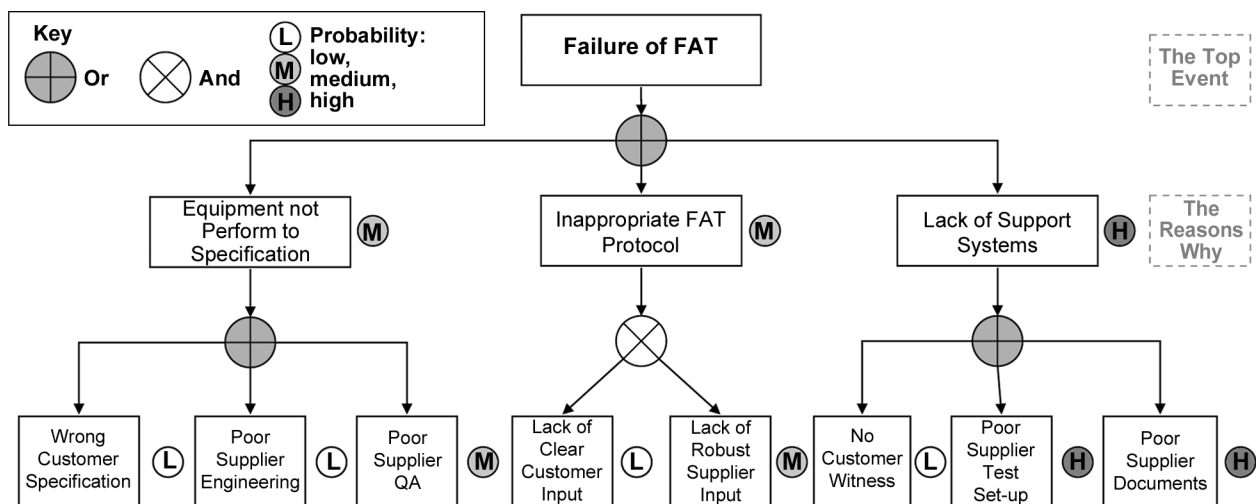
Projects usually concern product development or an element of design linked to a product or process within the overall product life cycle (see Figure 3.1). The stage gate process allows the uncertainty to be managed by successively reducing uncertainty as the stage gates are successfully passed, e.g., R&D should be challenged to provide a Design Space (see ICH Q8(R2) (Reference 6, Appendix 3)) before significant facility design is completed rather than just a list of Critical Quality Attributes (CQAs). Technology transfer: the interface between pharmaceutical development and commercial manufacturing is an example of a key process in the pharmaceutical industry (see case study in Appendix 2).

Measures

In a project, the team and Project Manager can only react to what they know and therefore what they measure – whether this is a formal or informal measure. The accuracy of that measurement and the technique used to deliver it can challenge the project risk strategy.

Example

In a Facility Project, a Supplier equipment package has been identified as “critical” because it is a part of a critical unit operation with associated quality critical parameters. The supplier has a reputation for poor QA leading to inadequate documentation and therefore that becomes the focus of risk management by the team. However, by only measuring single causes or considering one particular consequence, the overall view of uncertainty becomes compromised. Figure 3.6 shows how the analysis the team eventually conducted identified more than one cause which required measurement and management. The Fault Tree Analysis (FTA) led to a better understanding of the probable failure route and a clearer set of measures.

Figure 3.6: Example Fault Tree Analysis (FTA) – Equipment Project FAT Failure

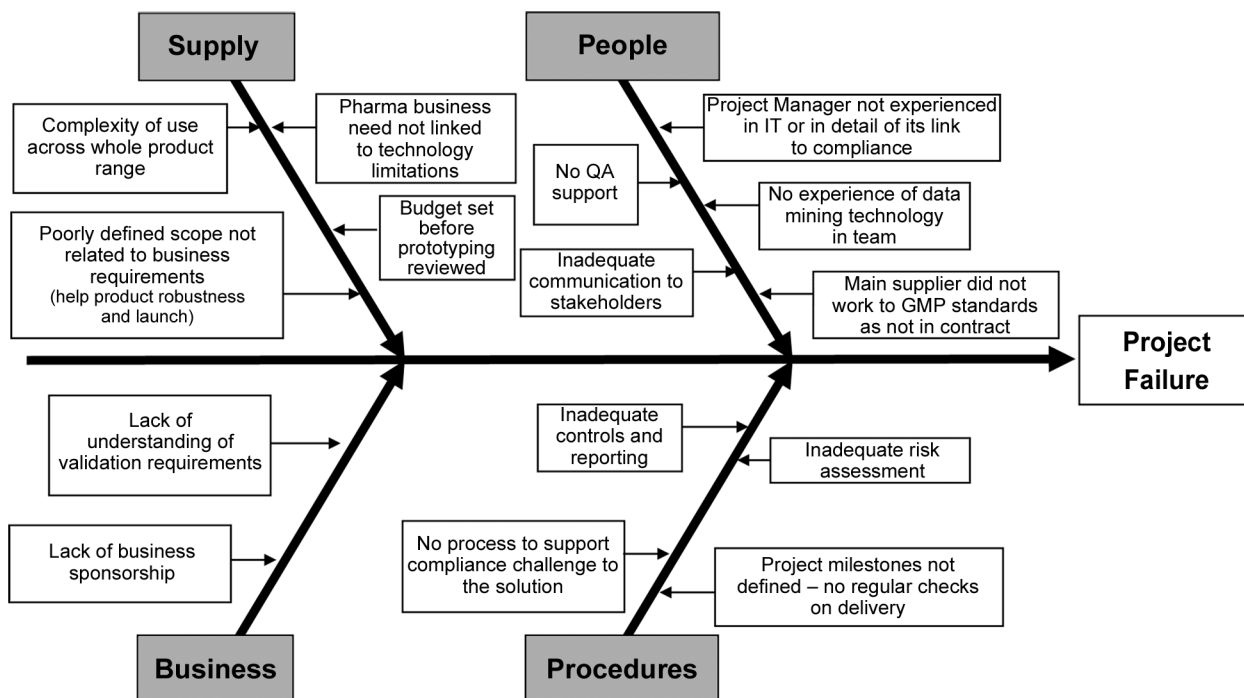
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The decisions on which measures are appropriate should be made in the context of the pharmaceutical challenges within the project.

Project Fishbone Diagnosis

The Fishbone tool can also be used to diagnose the root cause of project failure. Figure 3.7 illustrates an example of this use (the traditional categories used in Figure 3.4 have been converted here into 4 project oriented categories of Supply, Business, People, and Procedures).

Figure 3.7: Example Project Fishbone Diagnosis – IT Project



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In this example, an IT Project within a pharmaceutical manufacturing business failed to deliver on both project and business objectives. It was eventually terminated when it became clear that the technical solution could not deliver the required benefits (consolidation of business information from internal and external sources).

3.3 Pharmaceutical Quality Risk Management

3.3.1 Quality Risk Management (QRM)

Quality Risk Management is defined as a “systematic process for the assessment, control, communication, and review of risks to the quality of the drug (medicinal) product across the product life cycle” (ICH Q9 (Reference 7, Appendix 3)). Risk in this instance refers to risk to patient which arises from a risk to the product quality.

The impact of this for project management relates to those project requirements that relate to the product quality. These quality requirements are usually covered in the technology transfer process and are defined in ASTM E2500-07 (Reference 12, Appendix 3) as:

- Product Knowledge
- Process knowledge
- Regulatory Requirements
- Company Quality Requirements

These together form the section of the whole project requirements that relate directly to product quality and patient safety. These requirements are approved by the quality unit and will be used to develop aspects of the design that are critical to product quality.

The role of project management and engineering design team is to ensure that the design will provide the intended functionality, so that when the project is complete, these requirements are fulfilled. Changes necessary to the design or subsequent project phases that change these requirements will need quality unit approval. Change that does not impact these requirements can be approved by the project management or other approved SMEs. A collaborative relationship between the Quality Management and Project Management functions will increase the likelihood of a successful outcome.

For additional information, see Appendix 1.

3.3.2 QRM Life Cycle in a Project Context

When a project commences there are elements of QRM that may have already been performed which need to be formally integrated into the risk management aspects of the project. Similarly, as a project nears completion, the Project QRM information should be passed to those who will be managing the project deliverables going forward, whether they involve a new facility, a new product, etc.

The organization of QRM activities within an organization is a consideration for project management work, as opportunities to mitigate risks to product quality and patient safety exist not just during manufacturing activities. When quality risk management is applied across the product life cycle, from process and product design and development through to manufacture (incorporating change control) and product discontinuation, quality can be built in and maintained, from design and development onward, throughout the remainder of the product life cycle

Incorporating QRM activities into the product life cycle requires:

- formal organizational policies
- management buy-in and commitment
- QRM competency development
- robust intra and inter-site communication mechanisms
- resources and managerial oversight

This may represent a significant cultural change within a company. When done correctly, this can result not only in a high focus on mitigating risk to product quality and patient safety being present and promoted throughout all organizational operations within the company, but it should also result in more effective and scientific approaches to facility qualification and process validation, areas that currently are time-consuming and expensive, but not always value-adding. Table 3.2, although not exhaustive, shows example of QRM-related activities across functional areas and life cycle stages.

Table 3.2: Examples of QRM-related Activities During the Product Life Cycle

Area of Activity (function or life cycle stage)	Example QRM-related Activities
Development	Specification setting, test method selection and process development
Regulatory Approval	Regulatory scrutiny pre and post handover
Quality System Management	Auditing, deviations and discrepancies, complaints and recalls, change control management and Corrective and Preventative Action (CAPA)
Facility Systems Management	Design, hygiene, qualification (or verification), environmental control, preventative maintenance and computerized systems validation
Materials Management	Supply chain management including inventory and distribution controls, assessment and evaluation of suppliers and contract manufacturers, procurement and release of material
Production	Process Analytical Technology (PAT), validation and revalidation, in-process sampling, testing, reporting and trending, computerized systems management
Laboratory Controls	Validation, final product sampling, testing, reporting and trending, methods development, stability
Packaging and Labeling	Selection of container closure system and label controls
Regulatory Authority Activities	Audit and inspection
Product Discontinuation	Archiving and facility decommissioning, tracking of product in the market

The benefits of such an approach are the creation of an environment in which:

- Companies qualify and validate what is directly linked to patient risk mitigation.
- Good Engineering Practices (GEP), where appropriate, are sufficient to ensure compliance in certain areas.
- Documentation practices are value-adding and deliver streamlined output.
- Product and process understanding are derived from science- and risk-based pharmaceutical development leading to robust and streamlined commissioning, qualification, verification, and validation activities.
- Engineering/operational solutions are developed taking into account risk considerations supported by an appropriate level of documentation.

QRM is considered a key part of the integrated project process (see Section 3.4 of this Guide). A project is one part of the overall QRM life cycle, and therefore, a Project Manager should align established organizational processes to manage risks to product quality and patient safety. ICH Q9 (Reference 7, Appendix 3) describes an approach to risk management which aligns with typical risk management processes (see Section 3.1 of this Guide).

Resources available to support the Project Manager include:

- ICH Q9 (Reference 7, Appendix 3)
- ISO31000 (Reference 13, Appendix 3)

- ISPE API Baseline® Guide (Reference 14, Appendix 3) and associated white paper on API Facility Design and Qualification (Reference 14, Appendix 3)
- ISPE C&Q Baseline® Guide (Reference 14, Appendix 3)
- ISPE Guide: Science and Risk-Based Approach for the Delivery of Facilities, Systems, and Equipment (Reference 15, Appendix 3)
- ISPE Good Practice Guide: Applied Risk Management for C&Q (Reference 16, Appendix 3)
- GAMP® 5 (Reference 5, Appendix 3)
- ASTM E2500-07 (Reference 12, Appendix 3)

It is the decision of each organization to determine the most appropriate approach to QRM both within and beyond a project.

Key features of a project management approach to the management of the QRM life cycle are the effective use of risk management, design review, and Good Engineering Practices (GEPs), in particular:

- The responsibility for engineering quality control is placed on the technical experts (SMEs) with appropriate oversight by quality assurance.
- Non-critical discrepancies are addressed through GEP.
- Installation verifications and operational verifications conducted concurrent with project delivery.
- Documentation practices focused on technical content.
- Risk management is used as a tool to ensure that the effort is placed on delivery of the quality user requirements at each stage of the process.

The application of approaches to QRM can be managed only through balancing quality risks with other types of risk highlighted in this Chapter of the Guide.

3.3.3 *Human Heuristics in a Project Context*

When performing Quality Risk Management activities as part of project delivery in the pharmaceutical industry, it is useful to address the problems of subjectivity and uncertainty that may arise, particularly during the risk identification and assessment activities. This area of subjectivity and uncertainty in risk management is well documented in the more general literature (Reference 17, Appendix 3). It is likely that problems of subjectivity and uncertainty may also arise during QRM activities in pharmaceutical projects.

Within the GxP environment, many existing QRM tools do not formally deal with the problems of subjectivity and uncertainty that can arise during QRM exercises. Most of the currently available tools do not provide any formal strategies for addressing such problems during the application of QRM in GxP or other environments.

Example

During a Failure Mode and Effects Analysis (FMEA) exercise at the start of a project, the team was brainstorming to identify potential failure modes, their probabilities of occurrence and their causes. The Project Manager could find no documented means or clear guidance for ensuring the objectivity of the activity and therefore the results.

There is evidence that when people are performing QRM-related activities such as brainstorming (or when they are providing opinions on issues such as probability estimates) the judgments that are made are susceptible to what are called *heuristic-based behaviors*.

Heuristics are cognitive behaviors. They:

- come into play when people make judgments in the presence of uncertainty
- may be a source of significant bias and errors in judgment
- can be thought of as “cognitive rules of thumb”
- can be experience based, albeit on limited experience
- influence individual decision making, brainstorming, and forecasting
- influence group dynamics and meeting behaviors; impacting reliability of outputs

In the area of probability of occurrence estimates, three of the main heuristics are:

- **The Heuristic of Anchoring and Adjustment:** this heuristic affects how people make decisions, such as when estimating the probability of an event occurring. When this heuristic is in operation, people’s judgment can be heavily influenced by the first approximation of the value or quantity that they think of or hear.

Example

Early in a project, a Project Sponsor announces that this is a \$1million project and from that point on, the Project Team is “anchored” in this belief and work toward it. The belief is not challenged even though it is not based on objective data.

- **The Heuristic of Availability:** this heuristic relates to the fact that a person’s probability estimate is often determined by “the ease with which [people] can think of previous occurrences of the event,” or the ease with which they can imagine the event occurring.

Example

A Project Manager starting a similar project to a previous one dismisses a potential failure mode identified by a Project Team member because it did not happen in the previous project. The Project Manager is not “available” to the suggestion.

- **The Heuristic of Representativeness:** this heuristic also affects how people estimate the probability of an event occurring. A person’s probability judgment is often influenced by one “expecting in the small behavior that which one knows exists in the large.” Thus, when tossing a coin six times (H = Head and T = Tails), people tend to rate as more likely the sequence HTHHTH than either of the sequences HTHTHT or HHHTTT, even though all three sequences are equally likely.

Example

In estimating the probability of failure for a new IT system, a Project Team member uses his previous experience of similar packages and over estimates the failure probability due to this. The team member had seen previous IT projects fail due to poor scope management and forecasts that this project will fail in a similar manner even though the data available does not suggest this.

Within a pharmaceutical context, it may be beneficial to develop controls and design features for QRM methodologies that counteract the adverse effects that heuristics may exert. Doing so has the potential to reduce the extent of subjectivity and uncertainty that currently affect QRM activities. In this regard, several simple, practical strategies are available to improve the outcomes of QRM exercises with respect to problems of subjectivity and uncertainty (Reference 17, Appendix 3).

What this Means to Project Managers

Having a basic understanding of the potential adverse influences of human heuristics can be useful for Project Managers. This is because Project Managers can then work to ensure that the QRM activities that occur during projects are designed with a working knowledge of the problems that may arise as a result of those heuristics. For example:

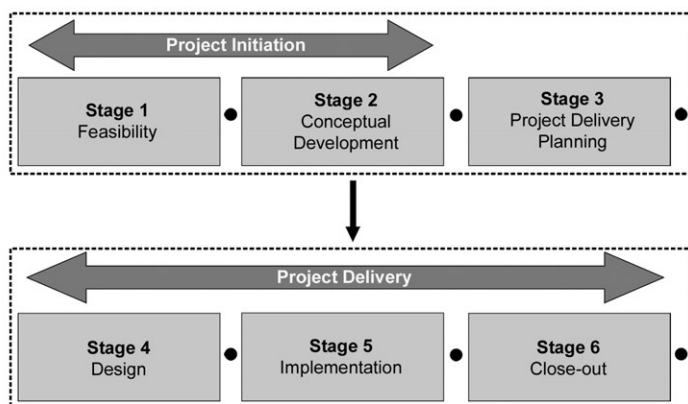
- During brainstorming sessions, when identifying failure modes or potential negative events and their probabilities of occurrence, Project Managers can, in conjunction with the Team Leaders or the facilitators of QRM exercises, ensure that controls and features are designed into brainstorming activities that serve to reduce the potential adverse effects of the above three heuristics. For example, the development of agreed scoring systems, which require data in support of the risk scenario.

Project Managers should ensure that the Team Leaders or those facilitating QRM exercises are appropriately trained in the area of human heuristics, so that they can recognize heuristic-related problems at an early point and address them in a timely manner.

3.4 Integrated Project Risk Management

Project Managers should consider the risk potential within projects and should develop a risk awareness culture where team members seek to identify, evaluate, and mitigate/eliminate risks at every stage of project delivery. The nature and impact of risk will change with time (see Figure 3.8).

Figure 3.8: Typical Project Life Cycle



A single risk management session held at some point during a project will capture some of the potential risks; however, Project Managers should develop an integrated project risk management approach where risk assessments and risk reviews are performed at regular intervals to maximize the probability that risks can be identified and mitigated. Generally, the earlier a potential risk can be identified, the easier it is to develop mitigation or contingency plans for that risk. “Lessons learned” may also exist from similar projects and may be obtained via consultation with peers and colleagues.

Stage gate reviews and integrated risk management can be particularly important for “Fast Track” projects where schedules are challenging and typically require parallel design, procurement, and other implementation activities with greater overlaps between stages.

For risk assessment and management related to Regulatory Compliance and on-going patient safety assurance, different perspectives, expertise, and approaches are required.

- A generic risk management process may be appropriate where the principle focus is on non-product quality elements like cost and time, equipment delivery, and performance. These risks are more likely to involve scientists, engineers, planners, and project management professionals than qualification, quality, compliance, or operational staff
- The generic process should be supplemented with, or replaced by, a non generic process of Quality Risk Management (as defined in ICH Q9 (Reference 7, Appendix 3)) where the focus is on product quality assurance and risk reviews usually involve qualification, quality, compliance, and operations staff in addition to the project team.

An integrated risk management approach should be developed which addresses the variety of risk types applicable to the project in a streamlined and integrated way across the life cycle of the project, e.g., a design review can incorporate review of operator and process safety and operability as well as GxP and constructability.

3.4.1 The Risk Management Life Cycle: Stage 1 and 2 – Project Initiation

The purpose of Project Initiation is to adequately define the project so that a robust business case can be developed to confirm whether the project should go ahead. Conceptual Development aims to narrow down the potential solutions to the business need and to develop the remaining solutions to a point where an informed decision can be taken on the selection of the preferred project for development and delivery (see Chapter 4 of this Guide). This is a risk mitigation activity:

- Data is collected to make risk-based decisions on whether the project can deliver an appropriate cost-benefit for an organization.
- Various potential solutions are reviewed and typically a single agreed solution, that will most effectively meet the business case, is selected.

By ensuring that a robust stage gate review, involving all key stakeholders, takes place before allowing the project to move into the delivery planning phase, the Project Manager can minimize the carrying forward of “open” questions which can introduce unnecessary risks into the project brought about by later changes to intent, strategy and scope.

During this phase, the project team should start their risk management activities by outlining a Risk Management Strategy or Plan based on the early identification and listing of those fundamental risk elements which could affect the delivery of the business case, e.g:

- Safety
- Time
- Location
- Cost
- Resource
- Schedule

- Scale
- Process Complexity
- Validation Complexity
- Operational Needs
- Regulatory Environment

Effort should be expended to mitigate fundamental risks; therefore, providing significant business benefit.

A project may be assigned an overall risk categorization in this stage. This is used to inform management of probability of success, and/or provide a basis for allocating estimating and schedule contingency factors. Although these early categorizations may be useful, Project Managers should maintain a focus on risk identification and elimination or remediation and update the summary risk profile as the project progresses.

The project team should begin categorizing risk into the generic or specific risk mitigation categories and ensure that the project identifies the appropriate expertise to understand the risks.

Example

The risk of schedule extension caused by a shortage of steel due to world demand would fall into the generic category which could be mitigated by advancing the steelwork design, whereas the risk of obtaining timely, accurate, and documentation which achieves the quality required by good documentation practice to support qualification preparation and execution from a key equipment vendor could be categorized as a pharmaceutical specific category and could involve discussions with formulation scientists to determine if the particular equipment is unique or if a piece of equipment from a more GxP aware supplier could be an acceptable substitute. The answer to the question begins to inform possible mitigation strategies and the internal expertise which may need to be involved in acceptance of the risk.

3.4.2 The Risk Management Life Cycle: Stage 3 – Project Delivery Planning

The purpose of Project Delivery Planning (see Chapter 5 of this Guide) is to adequately plan for the delivery of a project solution to meet the approved business case. This is the phase where the primary focus of the project team moves from defining and aligning on the scope of the business solution to consideration of the opportunities and obstacles that may exist to realize the project.

As Project Delivery Planning proceeds, the project team should refine the risk management strategies and add risk management activities to the project schedule. It is recommended that Risk Management reviews become a standing element of monthly (or other periodic) project progress reviews to guard against “risk complacency.”

A key part of the planning process is the development of the Validation Master Plan (VMP) which is a risk-based document: assessing validation need against quality risk.

Individual(s) within the team who are to be responsible for leading the risk assessment, mitigation planning, and reporting should be identified and the following related risks addressed:

- under-performance of the project team/team members
- poor management of the project team
- non-availability of part-time team members such as key SMEs
- non-availability of supplier SMEs due to other project work unrelated to the Customer organization

A Project Manager should be aware of the risks inherent in the dynamic nature of the project team and ensure that key project resources are identified, engaged, and aligned in their commitment to early and continuous risk identification and mitigation (see Chapter 2 of this Guide). Generating an appropriate understanding of the project life cycle within core, extended, and part-time team members is considered fundamental to this risk management.

3.4.3 The Risk Management Life Cycle: Stage 4 – Design

The purpose of Design Management (see Chapter 6 of this Guide) is to develop the project solution to a point where it can be implemented. For facility projects, this typically means the development of engineering documents to a point of completion which will allow the procurement of equipment and construction materials/contracts. For technology transfer or validation projects, this may be the development of planning, testing, and operating documents to allow experiments to be conducted and qualification activities to be executed.

Risk management reviews should be used to identify those areas which are likely to introduce risk into the specific project under analysis, for example:

- Operation
- Maintenance
- Compliance with GxP Regulations
- Compliance with EHS Regulations
- Generation of Verification/Validation Documents

Example risk mitigating activities conducted during this stage include:

- drafting and/or refining of commissioning/validation master plans
- defining test and inspection requirements
- ensuring clear definition of system boundaries
- conducting GxP reviews
- conducting safety, operational, and maintenance reviews

During design management, the project team should focus on detailed risk identification, analysis, and mitigation planning activities with regular sessions based on the design and eventual implementation schedules. An emphasis placed on risk identification and mitigation in this stage should significantly reduce the number and severity of unexpected or emerging risks to be managed during the implementation phase. Planning for implementation testing should take place, as this will begin to align the teams around system identification and documentation requirements.

The importance of identifying the risks on a particular project can be illustrated by looking at the following list of typical areas and activities which normally take place during this period which are directly or indirectly related to risk.

Stakeholder Involvement and Alignment:

- How is the project ensuring that stakeholders fully understand and accept what it is that the project is going to deliver?
- Are we relying on operational staff reading detailed engineering design drawings or are we providing spatial visualizations showing what a space may look like to operate within or maintain?

- How will new computer systems interface with the installed base?
- Have we discussed what alarms are necessary/important and how operational personnel need to deal with these alarms?
- What would be the impact to the project success criteria if misalignments were identified once the project was in implementation (or close to completion)?

Process Criticality and Critical Quality Attributes (CQA):

The science of a process will define which unit operations and associated process parameters are critical. While risk management cannot change the science, the potential risks to the process associated with incorrectly identifying and managing the CQAs should be recognized.

Design Quality Assurance:

The project team should ensure that they fully understand what quality systems are in place to ensure that design documents are developed, reviewed, and approved in a way that ensures that they are complete and accurate, and completely describe the intent before they are issued for costing and/or procurement and/or use. Typically, after completion of conceptual design a “design freeze” is used to clearly communicate the concepts that are to be built into the future detailed design activities. This also supports change control processes.

Design Review:

The project team should understand the value of design review (also known as design qualification). The potential drawbacks from “human heuristics” should be noted. Design reviews should be planned and structured with the correct participants in attendance. It is suggested that they be led by the team’s validation expert, this is especially important on more complex projects where a poorly executed review will generally **add** risk to a project. In small, simple projects the qualification of the design can be integrated into design review activities.

Quality Alignment:

- Does the project team fully understand the requirements and expectations of internal regulatory quality standards?
- Have the assumptions of this understanding been tested with subject matter experts or just assumed?
- Have we incorporated the alignments into design review activities?

These challenges should be addressed and risk appropriately mitigated.

Safety Assessments:

These include: Design Safety, Process Safety Assurance, Operational Safety, and Maintenance Safety, etc.

- Has the project team identified all of the safety related activities which must be completed during the design phase and the consequences of non completion in later stages?
- Does the team have plans in place to address these issues at the appropriate time in the project?

Typically, safety risk assessments are integrated into all aspects of the design process.

GxP Documentation:

GxP documentation should be accurate, timely, and compliant to support validation and qualification, or verification. Good documentation practices should be a core team process within the project.

Non-GxP documentation:

Non-GxP documents can pose a risk, e.g., contract terms where decisions taken can have unexpected consequences, e.g., is your contract language appropriate to the type of supply? Is it conducive to a collaborative open relationship (particularly with key suppliers) or is it adversarial where potential concerns (risks) could be hidden behind a closed contractual relationship?

Appropriate risk analysis of these key documents is a project management responsibility.

Documentation Management and Disaster Recovery:

- Does the project have a robust document management and recovery plan in place?
- Are documents stored in a secure and protected area?
- Is there appropriate revision control of documents?
- Could the project recover or reconstitute documents in the event of a loss?
- Does the project classify and segregate critical and non critical documents?

The risk is linked to business continuity through the management of important documentation.

Supplier Identification and Pre-qualification:

In parallel with the design activities, projects normally prepare for the implementation phase. For procurement, this usually means working with the Project Team members involved in design activities to identify potential suppliers for pre-qualification activities. Pre-qualification is a risk management activity that should encompass a review of commercial elements (pricing history, financial evaluations, etc. and non-commercial elements (a wider review of company capabilities and those of its key personnel, cultural alignment, etc.). The Project Manager should work with the procurement function to ensure that a balanced approach is taken in pre-qualification activities and that the Project Manager makes the correct internal resources available to the pre-qualification activities and interviews to address the commercial considerations, experience, expertise, and alignment questions.

Contractual Conditions:

An incorrect contract between an owner and a supplier can introduce significant risk into a project. Teams should avoid one sided owner driven contracts and strive for contracts that are fair and balanced with an appropriate sharing of responsibility and accountability and risk and reward (see Section 2.5 and Chapter 7 of this Guide).

Change Management:

Change is arguably the single most common cause of projects failing to meet their business objectives and there is little value in developing and executing a comprehensive risk management strategy, if this does not consider the risk introduced by change. Most people can remember a project where the consequences of accepting an ill considered change were severe; therefore, the project team should have an enhanced sense of the need to maintain a culture of vigilance and challenge where change is concerned to ensure that changes are broadly reviewed for all potential consequences (intended and unintended). Key project deliverables such as the Project Charter (Appendix 1) and the User Requirements Specification (see Chapter 6 of this Guide) form a good baseline from which to challenge change.

Qualification or Verification Management:

From the analysis of WHAT is to be qualified or verified through to the way these activities are integrated into other project activities there remains risks to be managed.

3.4.4 The Risk Management Life Cycle: Stage 5 – Implementation

Implementation encompasses the procurement, installation/construction, and testing activities within a typical facility project (see Chapter 1 of this Guide). For the Procurement and Installation/Construction activities, assuming that the team has done the mitigation planning in earlier phases, and that there is a continuing focus on change and change control; risk mitigation should involve delivered the established risk mitigation plan.

The Project Types Matrix Attachment (see Appendix 1) describes the typical implementation phases in other project types.

The focus of risk management should be shifting from delivery of the project to the delivery of an operational asset; the project outcome, while maintaining appropriate supervision of risk during implementation. The testing team (encompassing acceptance testing, commissioning, qualification or verification, validation, etc.) should identify and develop risk management plans and strategies targeted specifically on the testing phase. The planning should begin as early as possible to ensure that necessary prerequisites for testing (e.g., documentation, calibration, test points, spool pieces, and dummy servers) have been identified and are being supplied by other parts of the project team.

Areas of focus for the testing team would include:

- reviewing and addressing any residual risks in the risk management action log
- construction/installation records, walkdowns, and punchlisting
- safety – pre start-up and start-up safety, closure of HAZOP actions prior to the introduction of hazardous chemicals
- documentation – good documentation practices, quality, management, and availability
- operational SOPs
- master equipment and master instrument lists, calibration certificates
- prioritization of areas of the project to allow efficient testing

The testing team provides the critical bridge between project and operational teams and it is suggested that this team should be given a level of authority and control over the installation/construction teams to ensure that their requirements are properly addressed via documentation and a properly sequenced installation/construction schedule (i.e., prioritization of systems to allow the most effective sequence of testing). Roles and responsibilities should be established between the testing team and other project team areas. Risk strategies in this phase broadly fall into two categories:

1. Risks where mitigation strategies are within the boundaries of the project team and can be put in place by the project team. For example, the risk of a machine not reaching its design capacity where the risk can largely be mitigated (assuming the correct process was followed to select the supplier) by ensuring that robust acceptance testing is carried out at the suppliers before accepting the machine.

2. Risks which may not have an obvious mitigation or where the mitigation may take a longer time than the project schedule allows and/or which may impact outside the project team. An example of this could be the scale up and transfer of an established formulation process into larger equipment that fails to deliver the expected yield thereby putting a capacity risk into the supply chain.

The Project Team, and those within the team involved in testing activities, should ensure that risk identification activities look as broadly as possible at potential risks and their consequences and that risks which could have an impact outside the Project Team are communicated as early as possible to allow personnel, such as supply chain planning, to undertake their own risk assessments.

3.4.5 The Risk Management Life Cycle: Stage 6 – Close-Out

Close-out is an activity which formally transfers the project to the Customer and End Users, seeks their acceptance of the project outcome with any attendant residual risks, and then closes the project (see Chapter 10 of this Guide). A lack of control over close-out is likely to introduce risk both to the project team and to the Customer team who have accepted the project. These risks come in two main areas and it is in these areas that the Project Manager should maintain particular focus:

Documentation (Knowledge Transfer)

Typically, a large percentage of documents generated by a project are of limited or no value to the End User and are either interim deliverables (required to produce the eventual project outcome) or provide documented evidence and traceability of the project process followed. The project team should plan for the identification and classification of the documents early in a project such that they can be provided distributed to the correct location and owner as efficiently as possible. This transfer of project knowledge is a part of the transfer of the risk understanding and any residual project risk (see Section 2.6 of this Guide).

The Project Manager should make documentation classification and document management a high priority during the delivery planning phase and should have an established plan to align the various parties on which documents are being delivered where (operations, maintenance, finance, quality, archive etc). The document management function should be retained throughout close-out.

Commercial

Appropriate actions should be taken throughout the project to address and conclude contractual and commercial matters. Allowing these issues to remain open could introduce risk, via:.

- Claims, arbitration, and litigation which as a minimum may distract the project team.
- Adversarial relationships with suppliers, which may impact their commitment to delivery on current or subsequent projects.

4 Project Initiation

4.1 Introduction

A consistent, effective project management methodology applied throughout the full project life cycle is considered key to delivering changes within an organization. Individual projects are delivered within the context of an organization's overall project portfolio with the associated influences from factors such as organizational culture, business processes, project prioritization, resource allocation, and constraints.

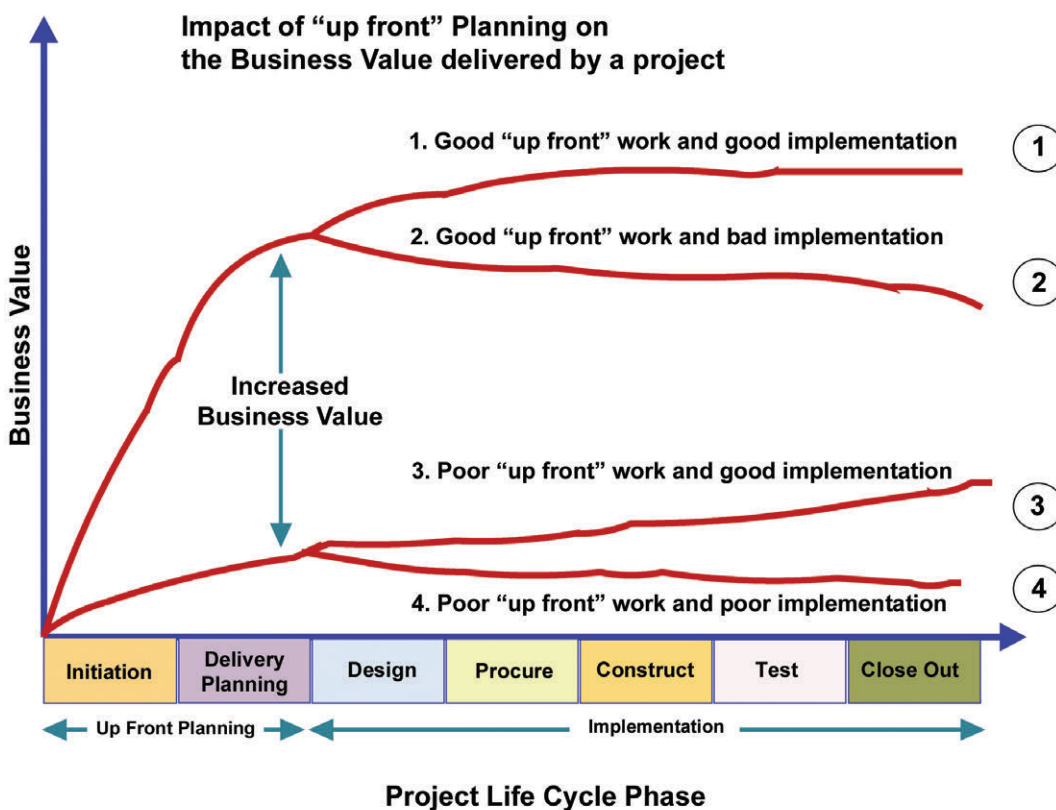
Although organizations may have individually tailored project management approaches, this section recommends a series of "good practices" for the project initiation stage.

Using the Guide terminology "project initiation" covers the period from "idea generation" through to being ready to start project delivery planning.

4.2 The Importance of Good Front End Definition

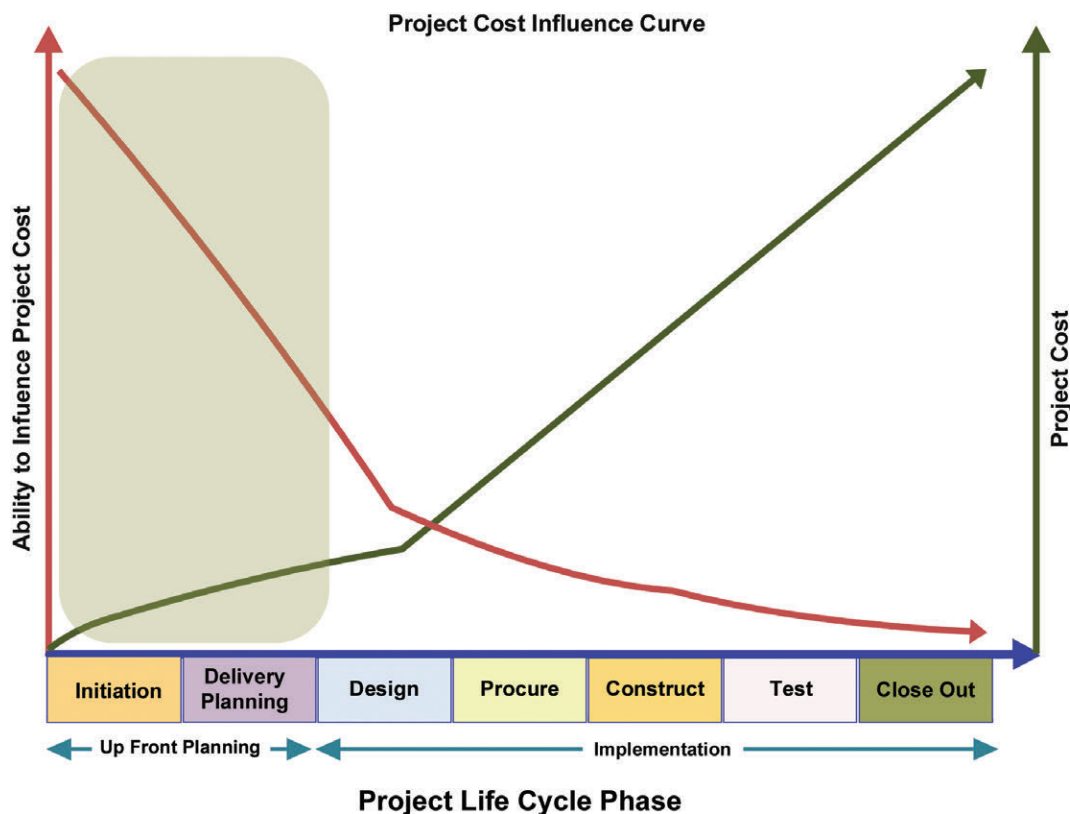
The greatest opportunity to influence the outcome of a project is at the start. The business value delivered by a project (measured in terms of the business benefits achieved) is heavily influenced by the quality of the "up front" work in the project initiation and project delivery planning phases (see Figure 4.1 for a non-quantitative illustration of this principle).

Figure 4.1: The Value of Front End Definition



During these early phases, the extent and quality of the work done and the resulting decisions made regarding project definition and project delivery strategy will drive the end result of the project. Beyond these initial phases, where more money is committed, the less the influence the project team has on the project outcome (see Figure 4.2).

Figure 4.2: Project Cost Influence Curve



These observations are particularly applicable to the pharmaceutical industry given the dynamic nature of the business environment, the technical complexity of projects, and the need for achieving regulatory compliance.

Benchmarking data from the pharmaceutical industry demonstrates that the successful projects are usually those that are developed through a rigorous and structured stage gate approach (see Chapter 1 of this Guide). This chapter outlines the key elements of a proven project initiation methodology for the pharmaceutical industry.

4.3 Stage Gate Project Approval Process

4.3.1 The Problem – Balancing Effort against Results

On a complex project an accurate cost estimate could require several months and considerable design effort to achieve.

At this early stage of the project, a broad range estimate may or may not be acceptable, and unless the estimate immediately casts doubt on the viability of a project, it could lead to more questions and demands for greater accuracy. To progress to greater accuracy requires resources, all of which have an associated cost. A methodology is, therefore, required to help management decide whether or not to spend money on progressing further with the project idea in order to improve the estimate accuracy.

4.3.2 The Solution – 3 Stages of Increasing Design and Estimate Accuracy

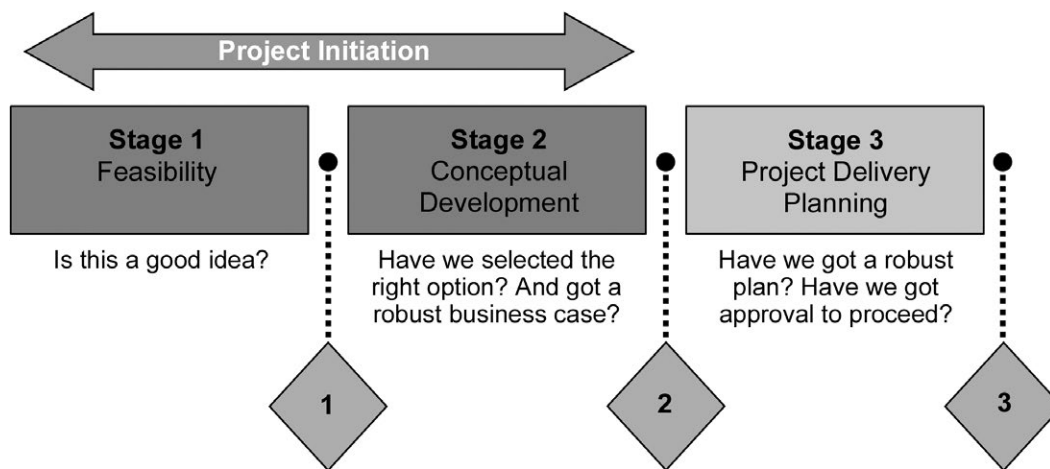
The stage gate system has been adopted across parts of the pharmaceutical industry as a “best practice.” This system takes a potential investment idea and develops it from a Rough Order of Magnitude (ROM) “50%” cost estimate, through a “30%” conceptual estimate to a “10%” control estimate. At the end of each stage, the idea goes through a “gate” where it can be challenged by the sponsoring business and a decision made on whether to proceed further.

The advantages of this system are that it provides the best compromise between expenditure and estimate accuracy (that has been found to date) and a controlling framework to ensure that project teams develop the project in the most cost and schedule efficient way.

The stage gate process requires a project team to develop the project cost estimate through each of those three estimate stages, but it also requires the team to pass through an approval gate after each estimate at which business management reviews the project and decides whether it is worth expending the next release of funds to develop the project further. The gates are intended to provide a set of information to allow decisions to be made in alignment with business needs. The objective of the process is to spend the minimum to provide the right level of information to allow a robust business decision to be made on whether to proceed.

4.3.3 Overview of the Three Stages

Figure 4.3: The Project Life Cycle – Front-End Stage Gates



Stage 1 – Project Feasibility – Is this a Good Idea?

The purpose of this stage is to establish if a project idea has a potentially viable business case and is worthy of further development. Resource expenditure at this point is minimal (typically < 0.5% of final project cost) and will probably only include input from a few key people led by the Project Sponsor. Sufficient information (principally business benefits and costs) has to be gathered at an appropriate ROM accuracy (+/-30% to 50%) such that an informed decision can be made as to whether or not to take the project to stage 2.

Stage 2 – Project Conceptual Development – Which Option is Best?

The purpose of this stage is to turn the idea into a project by refining the scope, developing options, and selecting the one that best delivers the business case. The project team will require input on a wider range of topics which may include regulatory, product development, sales, supply strategy, technical and engineering.

The business case is better defined and estimated, and along with a project cost accuracy of approximately +/- 25 to 30%, a decision can be made at the end of this stage, based on a conceptual design report and preliminary project delivery strategy, as to whether the business benefit justifies proceeding to stage 3. At this point, expenditure will be typically < 2% of final project cost, and any early funding requirements for items on the critical path will have been identified, along with any other critical resource issues such as availability of key personnel.

Stage 3 – Project Delivery Planning

The purpose of this stage is to take the option chosen in stage 2 and progress the project technical definition and delivery plan sufficiently to achieve a project cost estimate accuracy of +/- 10%. The project should be led by the Project Manager who should ensure that the project technical scope and delivery plan/schedule have been developed with the key deliverables in place for a stage gate decision as to whether to apply for funding to fully implement the project. Expenditure at this stage will be typically < 5% of final project cost.

For further information, see Chapter 5 of this Guide.

The Gatekeeping Process

The gatekeeping process is fundamental to the success of the stage gate approach. The process may be performed by a suitable senior individual or by a cross functional project review panel. The objective at each stage gate is to:

- Ensure senior management, independent of the project, review the project status.
- Ensure the project is closely linked to the business and not isolated.
- Allow the integration and sanity checking of the latest business need information.
- Check that sufficient quality information has been developed (using project readiness questionnaires and checklists for each stage).
- Ensure that the outcome of both business and project delivery risk analyses are considered.

The gatekeeping process provides the disciplined framework for making the decision as to whether to proceed to the next stage, conduct further work before proceeding, or cancel the project.

Front-End Loading

The term “front-end loading” refers to an increased extent of effort expended at the start of a project to initiate, define, and scope the project. Studies show that projects which have good front-end loading and use a disciplined stage gate process achieve significant quality, schedule, cost, and risk management advantages compared to those projects that do not.

Fast Track Projects and the Stage Gate Process

Fast track projects involve significant overlap of the project life cycle stages. A project is typically fast tracked because there is an immediate business opportunity/need with the time to market being an overriding business driver. Successful projects have good Front-end Loading and good decision making as a common theme; this applies particularly to fast track projects where it is essential to get things correct first time with little opportunity available to return and change decisions made early in the project. This is widespread in the pharmaceutical industry.

A stage gate process is applicable to a fast track project, but it may be implemented differently. Fast track projects need to proceed with minimal delays, but stage gate reviews should be made to ensure that decisions are made which are based on sound information, e.g., the Stage Gate reviews may include advance funding authorizations to allow the early award of long lead/critical path items. In these situations, Business Management should appreciate

that the project is proceeding at risk as these funds are being advanced ahead of the appropriate project definition being available. Fast track projects rely on robust risk management to be successful.

Those responsible for the gatekeeping process should keep close to the progress of the project and be prepared to conduct a stage gate review at short notice in order to minimize potential delays.

Project Size and Complexity Variables

A typical pharmaceutical company has a significant portfolio of projects to manage with, typically, 20% of the projects accounting for 80% of the investment cost. The business leadership team recognizes that not all projects will require the same level of stage gate supervision, those with the greatest impact on the business will require most analysis. Smaller or less risky projects should follow a formal gate process with an appropriate level of supervision at each gate, typically via the Project Sponsor role.

4.4 Stage 1 – Project Feasibility – Is this a Good Idea?

4.4.1 Focus and Objectives

The number of requests for capital and resource usually exceed that which is available. It makes business sense to select those ideas which have the greatest probability of realizing the greatest business benefits. Not all projects can be implemented; project portfolio prioritization decisions are required taking into account the:

- alignment of the project with the company's overall business strategy
- scale of benefits achievable
- investment required
- project risk profile
- probability of achieving the benefits
- financial resources available and the organizations current project delivery capacity

The objective of this feasibility stage is to conduct a preliminary filtering of needs in a structured way without spending too much time or money on making an assessment on a project's viability/feasibility. Once this has been completed resources can be concentrated on those projects that will be most beneficial to the organization.

4.4.2 Project Idea Origination

In the pharmaceutical arena, projects can be either:

- Top down, e.g., the project will involve a business owner wanting a capability installed to discover, develop, or manufacture a product. This project is rarely initiated by the site where the project eventually ends up; these sites may be involved in "bidding" for the project. The leadership of the project at this stage is usually the responsibility of the business owner.
- Bottom up, e.g., an existing site has identified a process improvement or a new technology which can improve quality, yield, reduce cycle time, improve safety, or replace old assets. In this case, the business benefit will be realized by the site concerned and for these types of projects the project leadership will typically come from within the site organization.

4.4.3 The Project Team Organization

Typically, the feasibility stage comprises from resources within an organization, with specific inputs from industry specialists, procured as required, to support the effort.

The Role of the Project Sponsor in this Stage

The Project Sponsor at this stage is usually the project initiator and champion, who has a particular interest in the success of the project and who should be held accountable for the realization of business benefits (see Chapter 2 of this Guide). This is a key role that should address business considerations such as:

- What is the likelihood of this product successfully completing clinical trials?
- How does this project fit with the organization's supply strategy? For example, after launch will this product be moved to a lower cost country/facility?
- What countries will it be marketed in?
- What are the licensing timelines?
- Which regulatory bodies will have to be approached?
- Are there any specific drug potency issues?
- What are the potential sales volumes?
- Is there new technology involved?

For bottom up type projects, the Project Sponsor should consider:

- Is there a likelihood of introducing business risk to an existing process?
- Does the extra cost of validation and the resource taken in submitting a regulatory license modification justify the outlay?
- Does this project reduce patient risk?

At this stage, the Project Sponsor (see Chapter 2 of this Guide) should:

- lead the project effort
- be directly involved with the project
- identify and quantify the business benefit via the business case
- obtain funding
- identify the main stakeholders
- set up project governance policy (especially steering group and gatekeepers)
- recruit project team members
- initiate a project communication plan

The Project Team

During feasibility, the team will be relatively small and consist of only those people who have direct knowledge of, or will have significant input to, the project. They should be capable of making decisions, be conversant with all the functions that need to come together to deliver the project, and have access to resources to help provide data and information to satisfy the stage gate requirements.

Typically, the team at this stage will have representatives or input from:

- Project Sponsor
- Primary Stakeholders
- Subject Matter Expert(s) (e.g., technical, quality, process, development, regulatory, validation, safety)
- Engineering (for preliminary costing)
- Finance (to help with viability and project location)
- Business Planning/Strategy Group (to align project with the organization's strategy)
- Project Manager (if already selected, may take over project leadership from Stage 2 onward)

4.4.4 Developing the Business Idea/Need

Developing the Business Case

This is a key task which can have a significant influence on the viability of a project. It is the responsibility of the Project Sponsor (see Section 4.3.3 of this Guide).

The development of the business case starts with the identification of benefits. Brainstorming may be beneficial to optimize the balance between scope, benefits, and cost. At a later stage in larger projects, a benefits delivery manager may be appointed, and their early involvement for this brainstorm can provide an understanding of the benefits that will form the basis of the business case. Benefits may not be financial, but should be identified. These can range from safety improvements and employee welfare improvements, to addressing regulatory requirements.

The assumptions on which the business case is built should be clearly stated, and interdependencies with other projects clearly identified.

Business Objectives versus Project Objectives – The Importance of Clarity

Requirements should be clearly defined and communicated. The scope of the project should be defined as accurately as possible at each stage of the project life cycle. The assumptions that decisions, benefits, and costs are based upon should be listed. (If the base assumptions change then a quick re-evaluation of the project should take place.) Items that are not included in the project scope should be listed for clarification purposes.

Example

During stage 1 of a project to add a new building to an existing site, an assumption is made: There is sufficient existing site utility capacity to run the new building and therefore costs for new utility raising equipment are not in scope.

As the project develops and the utility demands of the new building become known during the design stage, this assumption is revisited, and the original assumption was shown to be incorrect. By having documented the original assumption, it was easier to defend the scope change and associated cost and schedule impact, to the project steering group than if this assumption had not been made clear.

Aligning Business and Project Objectives

High level management consultations should be held early in the process to help guide project scope boundaries and give the project team guidance in project options to assess before a formal submission is made.

The project objectives can then be aligned with the business strategy which will aid the project through the ensuing stage gates.

Assessing the Need for being Schedule Driven

Specific parts of projects are pushed at greater speed (and hence greater cost) than may be necessary. This can be due to a misconception that the critical path of the project will be through a particular phase of the project, e.g., the construction of a facility. When the entire scope of a project is defined; however, the critical path may lie through the regulatory or licensing elements of the project.

The entire scope and activities of the project (which may include operational activities which are not financed from capital) may be defined and combined on a common schedule to show where the overall critical path lies.

At stage 1, the schedule detail should be sufficient to highlight where the project is time critical. Based on this, action plans can be formulated to accelerate a particular part of the project if necessary.

Documenting the Project Objectives – The Project Charter

The principal function of a project charter (see Appendix 1) is to encapsulate the headlines of a project, where possible on a single sheet of paper. Typically, this will outline the scope, financial authorization limit (if applicable), success criteria, main risks, constraints, business benefits, key project team members, and milestones, along with interdependencies to other projects. It should be authorized by the Project Sponsor, and will be a living document which should be updated as the project progresses. It should be modified only with agreement from the project steering group.

Defining the Cost Boundary (At what cost does this idea no longer make sense?)

At the early stage of a project, benefits and costs are expressed in wide ranges. As the project progresses, these ranges get smaller and it becomes increasingly easier to decide if the project is going to have a payback or benefit which fits with the business strategy. At stage 1, the question as to whether a project can be delivered for a particular figure based on the initial benefits calculation should be able to be answered.

This step should build confidence in the viability of a project. Alternatively, it can influence the design process if it is clear from the outset that the project has to be built below a certain capital cost threshold.

Communicating this business case threshold to the project team can make a more efficient and focused development of the project; not communicating it risks the project team expending significant wasted time and effort.

Cost Estimating

At feasibility stage, there will be insufficient project definition or design work completed to do a comprehensive “bottom up” cost estimate. A cost estimate prepared at this stage will take a “top down” approach and be based on benchmarks and historical data for similar projects, e.g., taking a simplified example:

“The last 5 facilities built had an average cost of \$X per 1,000 tablets/day of production capacity. Therefore, as our facility will produce 5,000 tablets/day, it will cost in the region of 5 times \$X.”

This type of estimate can be produced quickly and cost effectively as the feasibility stage of a project can typically cost less than 0.5% of the project total installed cost; the trade-off is that this estimate will have a wide accuracy of the order of -20% to +50%.

The development and communication of cost estimates is a critical, emotive, and high risk aspect of project initiation. Business management should clearly understand the reality of cost estimate development and the fact that early stage estimates carry this significant accuracy range. The Project Sponsor should insist that all cost estimate communications consistently flag the accuracy range and what it means.

Cost estimate contingency refers to the amount required in an estimate to cover uncertainties and unforeseeable elements of cost within the defined project scope; it covers inadequacies in project scope definition, estimating methods, and estimating data, but not project scope changes or major unforeseen events. It is money that will be spent to deliver the project scope. At this point in the project, the amount of contingency included will reflect the level of project scope definition. For example, if the project is to install a second identical production line in an existing building, the contingency will be low as the major part of the project cost will be equipment the cost of which will be known; a suitable contingency could be between 20% and 30%. However, if the project involves developing new technology, or where outcomes are uncertain, the contingency may be above 50%.

The difference between an estimate and a budget needs to be clearly understood by the funding organization. Establishing a budget for a project requires careful consideration of factors such as:

- the estimate accuracy range
- the organization’s philosophy on funding approvals
- what is included or excluded in the estimate
- revenue costs versus capital costs
- start-up costs
- utility costs
- investment grants
- taxation
- related projects in the program
- multi-currency implications
- cost inflation and escalation

Benchmarking and Independent Review

The stage gate process is designed to build confidence and accuracy in a project one step at a time. At the early feasibility stage, the estimates of cost and benefit will be broad. A good way of increasing confidence of where the true costs could lie in the range is to benchmark the project against similar completed projects, either within the organization or from industry published figures. These may be cost per unit area or cost per unit capacity. Factors can be used for different countries and for escalation since the benchmarked project was completed.

If insufficient projects are available against which to benchmark, the Project Sponsor may consider engaging an external company with the relevant experience to assess whether the costs and schedule are in the correct range of values. If the project is to be executed in a country where the organization does not have much experience, this could be especially appropriate.

Having an independent review can also prevent allowing favored projects which may not be fully and sufficiently developed or prepared for the next phase. It also removes any natural optimism bias of a project team when assessing project readiness.

Benchmarking and independent reviews should be performed using experienced project delivery personnel; if the skills are not available within the Customer organization, they may be sourced externally.

Benchmarking reviews can be appropriate for non-capital related business change projects where the level of internal resources needed to deliver the business change represents the biggest cost. Gaining an appropriate estimate of this resource cost is a requirement to achieve stage gate 1 for such projects.

4.4.5 Gatekeeping Decision at this Gate

The gatekeeping decision at the end of stage gate 1 is:

- “With the information available is this project viable? Does the organization agree to commit the resources identified to progress to stage gate 2?”

To be able to make this decision, the project Sponsor and gatekeeping team should answer fundamental questions regarding whether it is a good idea and warrants the organization expending more resources to pursue the project further, e.g.:

- Why is this project beneficial to the organization (Project Charter)? Is it value-added?
- Does it fit the organization's strategy?
- What is the business benefit, (and is there an impact on operating costs)?
- Is there an impending regulatory change that is driving the need for this project?
- Are there current compliance issues that are being addressed by this project?
- Is there a maximum capital spend above which the project does not become viable?
- Can the project be delivered for less than this cost? If so what is the capital cost range and accuracy?
- Have the key stakeholders been consulted?
- Is there a list of options to investigate during the next stage (not essential)?
- Is a simple project schedule in place, and are there any long lead items or lengthy activities which will dominate the schedule?

- Are there any immediate constraints on the project?
- What are the major risks and what is the strategy for their mitigation?
- What funding/resources will be required to complete the next stage?
- What impact will this project have on current operations?

For a checklist to support this stage gate decision, see Appendix 1.

4.5 Stage 2 – Project Conceptual Development – Identifying the Best Option

This section provides guidance on how a facility project should progress through the conceptual development stage. The principles used are applicable to other types of projects, e.g., those using significant capital like major IT Infrastructure projects, and those using internal resources such as business or operational improvement projects.

The conceptual development stage should provide sufficient information about potential options to allow a clear distinction to be drawn between them and an option selection made for further development in the Project Delivery Planning stage.

4.5.1 Focus and Objectives

This stage focuses on evaluating the possible alternative project solutions to meet the business objectives. At the start of the phase, the options to be examined should be clearly documented. Examples of alternative project solutions may be:

- Do I want process A, process B, or do I want to outsource manufacturing completely?
- Do I want to build in, e.g., the USA, Europe, India, or China?
- Do I want to expand plant X or build a new plant at site Y?

The object of this stage is to invest the minimum amount necessary to decide which **single** option gives the best fit with the business objectives and then whether the business opportunity is still a viable idea. That single option can then be detailed further in a subsequent Project Delivery Planning stage.

The key deliverables of this stage are a clear differentiation on return on investment between options in order that one option can be chosen and a $\pm 30\%$ estimate of that option.

4.5.2 Who Leads this Stage?

In this stage, the Project Manager typically takes over managing the project on a day to day basis as the work to develop the concept design becomes more technically focused.

4.5.3 Conceptual Development Stage Project Plan

An outline project plan should be developed to control the conceptual development stage; this should be a short document focused on communication and coordination.

- How the success of the project stage will be measured (i.e., for the conceptual phase, a clear indication on which option provides the best capital choice and is able to deliver the required benefits case).

- What the team is to deliver (i.e., for the conceptual development stage, the deliverable is the capital cost information to allow a decision to be made on options).
- How the team will go about delivering it.
- How the team will be organized and managed.
- How the team will communicate internally and with external bodies, including how it will report progress.

4.5.4 The Project Team Organization

The conceptual development stage requires a robust blend of technical/design and project management/delivery skills. The risk in the more technical projects is for the technical issues to dominate with project delivery strategy, procurement, cost, schedule, and risk, etc., being given inadequate attention.

Developing the concept design will typically require a mix of internal and external resources. (For further information on the selection/engagement process, see Chapters 2 and 7 of this Guide).

The key roles for the Customer include:

- Project Sponsor
- Project Manager
- Technical Team (particularly Process, Automation and IT)
- End User
- Regulatory and Quality
- Validation
- Procurement and Contracts
- Project Controls – Cost and Schedule

Given the project scale, complexity, risk, and business criticality the Project Manager, supported by the Project Sponsor, should ensure the correct mix of skills and availability to support an acceptable conceptual development effort.

The Project Sponsor

The Project Sponsor has a key role in mentoring/supporting the Project Manager through this conceptual development stage, particularly where major decisions such as country location are part of the option discussion. In these cases, the capital cost of the project will be only a small part of the business decision, with issues such as operating/production costs, tax regimes, and marketing regulations requiring the Project Sponsor to retain a high level of active involvement.

The Project Manager

The Project Manager is responsible for the management of the project to deliver the conceptual development package to support the Stage 2 gate review. The Project Manager reports to the Project Sponsor, who maintains business supervision of the project.

Technical Team

The conceptual development stage requires strategic technical inputs and decision making from the Customers technical team. In resourcing the concept design team, the following strategic technical inputs are typically required:

- Process Engineering – in the pharmaceutical industry, the process expertise is very often in-house with proprietary intellectual property rights to be protected.
- Automation – covering the process and facility automation systems.
- Equipment – global experts/specialists for critical process/utility equipment.
- Architect – developing building concepts together with the engineers.
- HVAC Engineer – developing different HVAC options.

End User

End Users should be involved during the early stages of project definition (see Chapter 2 of this Guide). End Users (with both operations and maintenance backgrounds) should be involved during the conceptual development and project delivery planning stages (when changes are relatively inexpensive). End Users should recognize that the conceptual development and project delivery planning stages are the place at which to provide input or comment on the project. This can help to avoid change requests during the detailed design and construction stages (when these changes become significantly more expensive). During this stage main tasks for the End User include:

- ensure the user requirements are complete and part of the agreed project scope
- input and sign off on the regulatory, quality, risk, and validation philosophy/strategy
- set acceptance criteria for a successful project
- approve the concept design and respect the “design freeze”
- be involved in integrated risk reviews and the overall value management process
- ensure that operational readiness issues such as personnel training are adequately catered for in the project scope

During the conceptual development stage, the team should address operational requirements, site standards, and operability. Maintenance concerns during this stage focus on the maintainability of the facility and setting the strategic requirements for the team regarding spare parts and required training handover documentation. The End User representative should have input into the procurement process, reviewing the lists of preferred equipment and material suppliers.

The End User representative should also act as the communication interface between the project team and the operations team. Where the project has to choose a “fit for purpose” option over a “nice to have” option, it is the role of End User representatives to support the project team in communicating the reasons why the option has been chosen.

Regulatory and Quality

The Project Manager should ensure that a senior representative from the regulatory/quality function forms part of the project team to ensure that the output from the conceptual development stage is aligned with the required corporate regulatory/quality policies. Regulatory and quality input should also feed into the Quality Management System (QMS) aspects of the proposed procurement strategy.

The conceptual development stage report should include a validation life cycle describing the agreed strategy/philosophy, the main life cycle activities to be performed, key documentation, testing, and proof of delivery. This is particularly important when considering qualified automation systems and their interfaces with process, utility, and building systems. QRM reviews may be facilitated by quality representatives; however, they involve and are the responsibility of all project team members.

Procurement and Contracts

During the conceptual development stage, the procurement and contracts strategy for the project should be prepared to support the project delivery strategy/master schedule. This strategy should cover both material/equipment procurement and contracted services.

At this stage, the emphasis should be on developing/matching an overall procurement/contracting approach with the required business and project needs. Key issues include:

- overall project delivery strategy, e.g., Design and Build, EPCMCQ, separate EP, CM and CQ teams, extent of Customer self-execution, etc. (see Appendix 1)
- approach to long lead equipment
- availability of agreed terms and conditions to support Project Delivery Planning procurement and contracting activities
- preparation for procuring the Service Provider for executing the Project Delivery Planning phase (see Chapter 7 of this Guide)

Project Controls

During the conceptual development stage, the Customer's project controls inputs will be focused on establishing the cost and schedule baselines for the project. Given the extent of option assessment that takes place in this stage multiple estimates and schedules will typically be prepared.

It is considered good practice on large projects for the project controls team to be in the project team with dual reporting to the Project Manager and functional head of project controls. On smaller projects the Project Manager may well take on the project controls responsibilities.

4.5.5 Conceptual Development Stage Kick Off – Statement of Requirements and URS

The business requirement for the project should be clearly defined and documented from the start of the conceptual development stage. The project charter will typically be a very short overview and should be supported by a statement of requirements that should address questions such as:

- How will the business measure success?
 - An ability to increase production in 2012 from X to Y tons per year?
 - Meeting the new government legislation, coming into force in 2011?
- At what capital cost will the business case no longer make sense (this knowledge may be restricted to Project Sponsor and Project Manager)?
- Is there a genuine business reason for spending more money to go faster or is capital cost the driving force (pharmaceutical projects can be schedule driven without a clear rationale why)?

- What options have to be assessed?

The first step in formation of the project design activities should be the development of a clear, detailed definition of the project requirements, i.e., scope and objectives. These should be clearly communicated to project participants and understood by members of the project team. During the kick-off of the conceptual development stage, the Project Sponsor should transmit information gained during Stage 1 (feasibility) to the project team. Acceptable documentation practices should be defined and used.

The Project Manager should consider business risks to ensure that the design meets all project objectives. Business elements that should be addressed include:

- life cycle costs
- capital costs
- operation and maintenance costs
- process and technology issues
- financing
- required quality standards

Project definition should have objectives that are measurable. Vague or misleading language should be avoided. The goals of the project should be clear and focused on the corporate business objectives, e.g., “product output of 5 million doses annually” or “provide product for commercial launch in the 3rd quarter.”

Benefits should be measureable so that they can be tracked and used to verify at project end that the project has delivered the business case.

The project definition should include clear scope in terms of technology and operational philosophy. For example: (1) Where the design focuses on ensuring product and environmental safety due to the handling of toxic compounds, it should be clearly understood. (2) Where the operational focus is on the implementation of, e.g., single use/disposable technologies for defined unit operations, this should be clearly conveyed.

User Requirements Specification (URS)

The project technical scope may be documented in a User Requirement Specification (URS) focused on the technical/GxP/compliance requirements; this will form a subset of the overall Statement of Requirements. The URS should focus on:

- the Business requirements (e.g., production increase, operational cost reduction, regulatory adherence, safety enhancement, or security)
- the end user functional requirements (i.e., what must the facility be capable of achieving, e.g., must be able to run with both product A and product B)
- specific GxP/regulatory/compliance requirements

A URS is appropriate for use during several stages of a project and can be used to define either individual elements of the scope or the overall requirements, e.g., for key process equipment a URS summarizing regulatory/qualification requirements can be developed including a GxP risk assessment and a list of the critical process parameters (see Chapter 6 of this Guide).

At the end of the conceptual development stage, an approved project definition URS should be delivered by the Project Sponsor and End Users with QA expertise. Note that there may also be user requirements developed for specific systems.

Option Analysis

The list of options to be pursued during the conceptual development stage should be specified at the start of the stage to give the project team boundaries and to help define the time and effort that will be required.

The options may be:

- Very high level (e.g., make or buy?)
- High level (e.g., build in Ireland or Shanghai?)
- Medium (e.g., expand facility A or build a new facility B?)
- Low level (e.g., build the tank farm to the north or to the east of the production line?)

Other than the low level options, criteria other than capital cost can have a significant bearing on the business case (e.g., tax regimes, operating costs, etc.). Responsibilities for making those non capital costs comparisons should be defined in discussion with the Project Sponsor.

4.5.6 Conceptual Development Stage Activities and Deliverables

This section provides an overview of the key activities and outputs from the conceptual development stage.

List of Deliverables

The checklist provided in electronic form as (see Appendix 1) can be used as a guide from which to develop the outline deliverables list.

Project Delivery Strategy

An overall Project Delivery Strategy for the selected option should be developed as an output from the conceptual development stage. This should cover the overall project from start of project delivery planning through to commercial production/benefits realization; this will be at a strategic level. It should include:

- Introduction/Purpose
- General Project Information (Business Objectives, Project Objectives, Scope Description Overview, Schedule Milestones, etc.)
- Organization Chart and Roles and Responsibilities
- Project Governance
- Critical Issues
- Relevant “Lessons” from Past Projects
- Procurement and Contracting Strategy (high level)
- Commissioning and Validation Strategy (high level)

- Handover Strategy (high level)

For information on design and technical aspects and external approvals and permits, see Chapter 6 of this Guide.

Health, Safety, Environmental (HSE)

The HSE strategy for the project should be defined in the conceptual development stage report highlighting specific challenges/risks that need to be addressed or investigated; many companies are focusing on meeting “green” design requirements, such as Leadership in Energy and Environmental Design (LEED).

End User

The key operability and maintainability needs should be defined highlighting any key challenges, e.g., process containment.

Contract and Procurement Strategy

The overall procurement and contracting strategy for the project should be developed to include:

- The overall project contracting strategy options, focusing on the “high level” approach to contracts.
- The material and equipment procurement strategy, particularly for long-lead items or items that have a significant impact on the design.

For further information, see Chapter 7 of this Guide.

Construction

The constructability of the various options should be assessed in the conceptual development stage. The assessment should identify key strategies, assumptions, challenges, and items to be further investigated in the project delivery planning phase. The construction input should contribute to the development of the contract strategy for each option.

Validation

A thorough summary of the anticipated life cycle approach/validation strategy should be developed to support the project cost and schedule estimates. This requires commitment from both the regulatory/quality and validation groups to ensure the basis for the project is firm. Specific issues to address include:

- Overall philosophy – clarity on the approach being taken, i.e., verification or leveraged Commissioning and Qualification or traditional approach of full Commissioning followed by full Qualification.
- Life cycles for Equipment, Utility, Automation and Building systems showing pre-requisites and interface constraints for documentation, tests and sign offs, etc.
- Requirement and approach for compliant automated systems using, e.g., the GAMP approach.

A Validation Master Plan (VMP) will not typically be prepared at this stage, though a validation strategy may be defined.

Project Cost Estimate

Scope, cost, and schedule assessments should be performed, preferably using experienced personnel with access to good historic project data and benchmarks. This is a critical activity, if too conservative an estimate is prepared a good project will not be approved; too optimistic an estimate will result in wasted effort/risk for the business.

The project cost estimates will be based on the design information available. The development of this estimate is likely to be heavily “top down” requiring the use of parametric or factoring techniques that use the design information available supported by proven data from previous similar projects and published industry metrics.

Where the project involves process equipment the installed costs may be factored in, based on the major equipment costs. The equipment costs will typically be based on “budget pricing” from suppliers based on the preliminary equipment sizing and assumptions for materials of construction, automation configuration, and finishes, etc.

The estimate at this stage should be based on a preliminary project delivery strategy and master schedule allowing preliminary cash flows to be developed. Conceptual development estimates will normally have an accuracy level of 25 to 30%. The accuracy is a function of the design information available and of the experience of the team member leading the estimation effort and approach. Project estimates at this stage will also include a significant contingency.

For further information on project estimates, see Chapter 5 of this Guide.

Project Schedule

During the conceptual development stage, the project master schedule for the preferred option should be developed to cover project stages from Project Delivery Planning, through detailed engineering, procurement, construction, commissioning, validation, start-up, and licensing.

Previous project historic data and benchmarks should be referenced to assure that a realistic schedule basis is established.

Risks and Opportunities

The conceptual development stage report should identify the key risks and opportunities identified for the project. These should take into account all aspects of the investment, e.g., business case, technical aspects, location, and market forces.

4.5.7 Value Management Reviews

During both the Conceptual Development and the later Project Delivery Planning stages, certain reviews have been found to be particularly useful in developing a robust project delivery strategy/design package. Five of the typical review types are listed here. Each of these reviews should be carried out by a multidiscipline cross section of the team; they should not be carried out by one or two individuals in isolation. They should be considered an integrated part of project delivery throughout this and future stages.

Value Management

Value management should focus on the whole life cycle costs and benefits of the project rather than the initial “up front” capital investment. The value management review may add to the initial capital cost as the use of more energy efficient equipment may require a capital premium.

Investment guidelines which may be specific to an organization and address the issue of “value” and value management should be available to the project team.

Value management reviews should consider the organization’s sustainability goals and the initiatives/objectives to be addressed.

Value engineering is a technique which is used within pharmaceutical projects, but may not be part of a value management process. Value engineering looks at whether a particular step can be performed more cost effectively without adversely impacting achievement of the project objectives and business benefits, e.g.:

- Can we build these storage tanks from plastic instead of stainless steel?
- Do we need to insist that all pumps be painted in the company colors before delivery or can we accept the vendors standard paint scheme?

Lessons Learned

The design phase of a project should include a review of lessons learned from previous projects. For further information, see Chapter 10 of this Guide.

Issues that may be forgotten during the Conceptual Development and Project Delivery Planning stages include:

- Staff recruitment and training.
- Deciding on the format of handover documents that will be used in the future.
- Agreeing on the documentation requirements and format for Operating and Maintenance (O&M) manuals and remembering to ask for them as part of the quotation when enquiring equipment.
- Retrofit/expansion projects – the Customer organization may not be ready to provide existing as-built documentation; significant time can be lost waiting for facility drawings, load capacity data, etc. Identifying and collecting this information early for issue to the Design Team can be beneficial.
- Checking existing Piping and Instrumentation Diagrams (P&IDs) accuracy before starting the design of a new facility expansion.
- Doing a proper ground survey to check for obstructions in the locations of future foundations.
- Including delivery of equipment drawings as a networked and expeditable activity in the schedule – the Architect/Engineering (A/E) team will need the equipment drawings long before the construction team needs the actual equipment.
- As built drawings – ensuring these are planned for early and funded.

Process Simplification

Process simplification is an attempt to view a production process and see whether steps can be removed without upsetting the overall process e.g.:

- Can we use a filter/dryer instead of first filtering, then sending to a dryer?
- Can we use a top down material flow, thus removing the need for pump X?

Constructability

Constructability looks at the detail of how a facility will be constructed. These reviews should be held several times throughout the project and the reviews should include a wide cross section of disciplines to ensure cross fertilization of ideas. The review should consider the mechanics of construction (e.g., local custom and practice, stick build, or modular available construction machinery) and the logistics of site access and site safety. Aspects of having a large number of contract workers on site for a temporary period should be considered, e.g.:

- How will workers enter the site?
- Where will workers eat etc.?
- Where are the material laydown areas?
- Hot work welding areas?

Operability and Maintainability

The operability and maintainability review should be performed by operations and maintenance representatives. It should consider how the plant (facility, equipment, or IT system, for example) will be operated and maintained, and the strategic aspects of the concept design. It should address layout philosophy items such as:

- Can you safely access and operate the equipment?
- Can you clean around the equipment?
- Can you maintain the equipment?
- Are the design redundancies aligned with the maintenance and operational philosophies?
- Can you easily and cost effectively replace equipment in case of a failure?

4.5.8 The Gatekeeping Decision at this Gate

The decision to be made in the gate at the end of this stage includes:

- Is there agreement on a single option?
- Does this option meet the business objectives and URS?
- Is the business idea sufficiently viable and warrants spending money to go to the next stage?

The Project Manager should ensure that there has been formal approval or cancellation of the project by the Project Sponsor. Alterations/options/items for further investigation should be accurately defined and formally recorded for inclusion in the scope of the Project Delivery Planning stage. This process should result in a clearly communicated "Go/No Go" decision.

For an approved project, the Project Manager should ensure alignment of the business and project objectives via an updated and signed off Project Charter (which aligns to the Benefits or Business Case) circulated to all project stakeholders.

The Need for Bridging Funds

For high business impact capital projects that are under schedule pressure, the need for bridging or interim funding should be considered with the Project Sponsor. This allows for design activities to proceed with some degree of risk while the formal approval of final funding for the Project Delivery Planning stage is obtained.

Choosing a Project Delivery Planning Service Provider

Where in house resources are unavailable, a customer may engage outside assistance to support the execution of the Project Delivery Planning stage. The type of support required can include services such as:

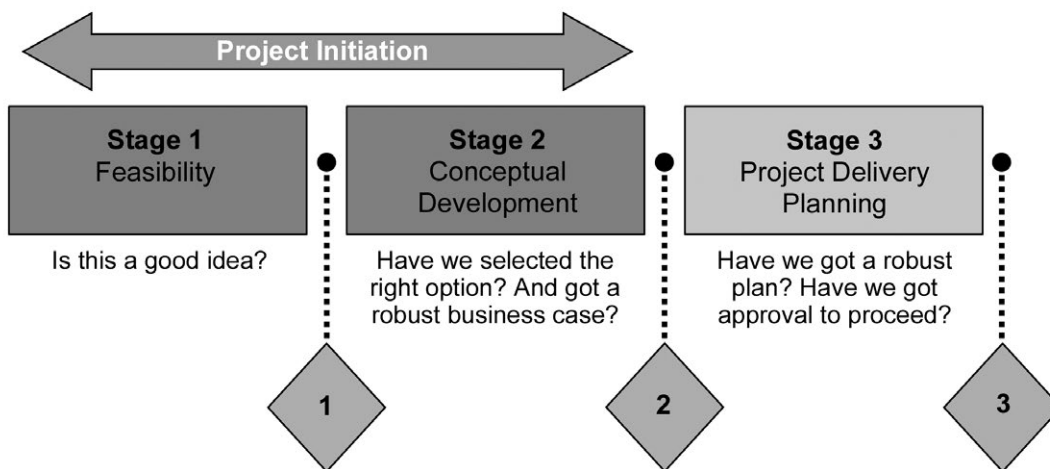
- Project Management
- Project Controls
- Architectural and Engineering Design
- Procurement and Contracting
- Pre-Construction, i.e., constructability cost estimating, scheduling, logistics planning, etc.
- Commissioning and Qualification

For further information, see Chapter 7 of this Guide.

5 Project Delivery Planning

This chapter discusses the third stage gate, Project Delivery Planning. It assumes the concept development work required to pass through Stage Gate 2 is complete (see Chapter 4 of this Guide) and that the project has been approved to proceed to the next stage of Project Delivery Planning (Figure 5.1).

Figure 5.1: Typical Project Life Cycle – Front-End Stage Gates



The success or failure of a project may be determined by the amount and type of planning. Extra time to effectively plan a project can be more than compensated for by a more cost-effective project delivery and earlier completion date. This links in to the concept of Front End Loading (FEL) (see Chapter 4 of this Guide). Where speed of implementation may be the primary consideration, a comprehensive plan can be highly beneficial.

This chapter uses a traditional facility capital project as an example.

5.1 Project Sponsor

The Project Sponsor should be connected to the project and business throughout and provide guidance and leadership as needed. Key areas of Project Sponsor activity include:

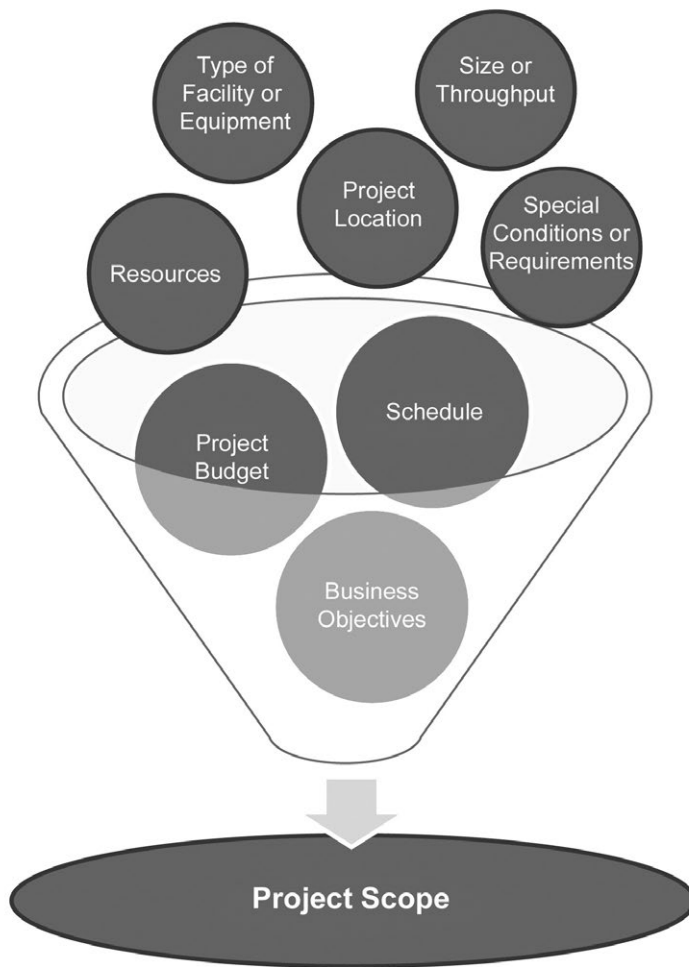
- Development of the benefits management plan:
 - Challenging the business benefits of a project to fully understand what is required and what may be the best approach or business solution.
 - Developing a benefits management plan. Typically, this would highlight how the benefits of the project would be measured in order to demonstrate that the business case has been achieved.
- Identification of stakeholders and development of the stakeholder management plan:
 - Discussion of the process of stakeholder identification and management is included later in this chapter (also see Chapter 2 of this Guide).
 - Project sponsors should support the Project Manager in identifying senior stakeholders and in planning how to manage their engagement throughout the project.

- Support in development of the Communication Plan:
 - The Project Sponsor should assist in developing the planned communications to key senior stakeholders. Communications should ensure that key senior stakeholders have an aligned, shared vision of project success.

For further information on the principles of communications, see Section 2.7 of this Guide.

5.2 Project Scope

Figure 5.2: Project Scope



5.2.1 Business Drivers and Objectives

The business justification already defined for the project will comprise one or more business drivers. These business drivers lead to a series of business objectives that form part of the Project Scope (Figure 5.2). Therefore, the business value of a project should be clearly identifiable within the project scope, as identified by the project objectives.

The business drivers will normally have associated objectives that are identified and detailed in a PDP and consistent with the Project Delivery Strategy outlined in Chapter 4 of this Guide. Elements of the strategy contained within the PDP may include:

- Introduction/Purpose
- General Project Information (Business Objectives, Project Objectives, Scope Description Overview, Schedule Milestones, etc.)
- Organization Chart and Roles and Responsibilities
- Project Governance
- Critical Issues
- Relevant “Lessons” from past projects
- Procurement and Contracting Strategy (high level)
- Commissioning and Qualification Strategy (high level)
- Handover Strategy (high level)

The PDP should identify how the project scope and business objectives align with the overall strategic plan for a site normally referred to as a Site Master Plan. For example, allowing management to review the interaction between projects and assess priorities.

5.2.2 Scope Detail and Definition

A project scope should define the work required to achieve a goal. The work should be defined in terms of the specified features and functions to which it should adhere. The definition of resources, tasks, time, and costs can be complex.

Example

An example of the complexity is the potential for major project modifications during design. While a new product manufacturing facility is being designed, it is normal for researchers to continue refining the production process. These refinements may result in large scale process changes requiring modifications to multiple elements of the design. While these changes are incorporated into the project, the design would need to be evaluated repeatedly for its future viability, e.g., its ability to achieve regulatory approval while accommodating the changes.

One technique is to identify what is not in scope. These and other lean six sigma “DEFINE” methodologies (Reference 18, Appendix 3) support clarity within the project team and provide a baseline from which to communicate to stakeholders.

5.2.3 Tools to Evaluate Project Definition

A project scope should be properly defined and supported by a valid business case.

There are several methods for evaluating the quality of a project definition by assessing the degree of a project's scope development. Commercially available tools can be used to analyze:

- level of technical definition as compared to external benchmarks
- specific scope criteria which is required at specified levels to achieve full funding
- gaps in scope definition

Organizations may have tools developed internally which can benchmark against similar projects within the organization and lean six sigma based improvement tools which challenge scope based on its contribution to the value required (as defined in the approved business case).

The assessment can be used as an objective assessment of a project's readiness for funding at any stage gate. It can also challenge the scope of a project. In most pharmaceutical projects, there is a lack of precise and accurate data at the early stages. This type of assessment can test the project justification in relation to how it may be affected by external influences at each stage gate.

The tools may be applied and used throughout the project life cycle. The tools are appropriate for both capital and non- capital projects.

Example

On-going clinical trials may alter projected product dosage volumes mandating changes to the project scope. Using these tools, the project can be evaluated in its present state of development in relation to the changes. The resulting score or assessment will provide the management with the justification to continue the project, alter the business objectives, or take other action.

5.2.4 Scope Change Management

Project scope change is a high risk factor and a plan to manage changes should be developed. Effectively monitoring the factors that create change and managing their impact to the original project scope requires a plan that is linked to the PDP. This management plan should monitor the project alteration requests as well as corrective measures required to address unforeseen changes. An effective scope change management plan should establish a culture of change factor identification, recognition, and evaluation to proactively manage changes. The change management plan should include the following principles to establish a proper correlation with the PDP:

- Change Identification – defines the change and identifies impacts to the project including cost and schedule.
- Technical Evaluation – formal technical evaluation of the change by key project team members.
- Regulatory Evaluation – appraisal of impact upon a project's ability to comply with regulations.
- Business Evaluation – review of the potential business and value impact.
- Risk-Based Approach Evaluation – should define how the risks associated to the scope change will be managed, identifies the risk factors, creates a risk probability and impact rating, details how change scope risk factors should be monitored and managed.
- The change process should be formal and documented, requiring sign-off and approval.

Changes to a project scope may be funded by means of a project contingency (see Section 5.4.3 of this Guide).

5.3 Project Schedule

5.3.1 Schedule

A project schedule starts with a baseline schedule that is expanded and updated throughout the Project Life Cycle. The schedule should be developed upon logical analysis of the scope components. Durations should be established for the tasks identified. Interdependences should be formed between tasks based on experience and historical data. Tasks should be organized in a sequential arrangement to satisfy project objectives and comply with project constraints.

At the PDP phase of a project, a schedule consisting of the detail associated with a Level 2 or 3 schedule is expected (Table 5.1). A Level 2 schedule expands upon an Executive Summary Level 1 schedule which details only major project milestones. A Level 2 schedule identifies the scope of work required to achieve the milestones identified in Level 1. This next level of detail involves a summary of the major components required for each milestone and the start of the development of the work breakdown structure (WBS). Critical dependencies between tasks should be identified so that the critical path may be analyzed and used to streamline the project delivery while identifying and managing scheduled risk appropriately.

Table 5.1: Levels of Schedule Development

Level	Key Components	Linkage	Typical Presentation
0 – Management	Key phases of a program	Dependency between projects in a program	Milestone Chart
1 – Project	Key phases in a project	Dependency between project phases or stages	Milestone Chart or Level 1 Gantt Chart (no resource loading)
2 – WBS	Key project work packages	Dependency between work packages	Level 2 Gantt Chart (preliminary resource loading per skill or function)
3 – Work Package	Sub contract or work package programs	Dependencies within the work package to develop an interim or final deliverable	Level 3 Gantt Chart (resource loaded)
4 – Task Detail	Individual tasks	Individual activities or deliverables within a work package	Activity Lists (resource allocated)

5.3.2 Resource Plan

Tasks identified in a schedule are defined by their duration and associated resources. As resources are identified for each task a resource plan should be developed. Resource allocations may be derived from previous project data or educated predictions and assumptions. The resource plan should identify the people, materials, and equipment necessary to complete a task, work package, stage, or entire project (see Figure 5.3).

The resource plan is used in a PDP to forecast resource expectations and the associated costs.

The resource plan is applicable to both capital and non-capital projects. In capital projects, resources may account for the majority of the costs expended by the project.

In addition to normal project team responsibilities, typical pharmaceutical projects have distinct components that require previous experience to complete a project, including:

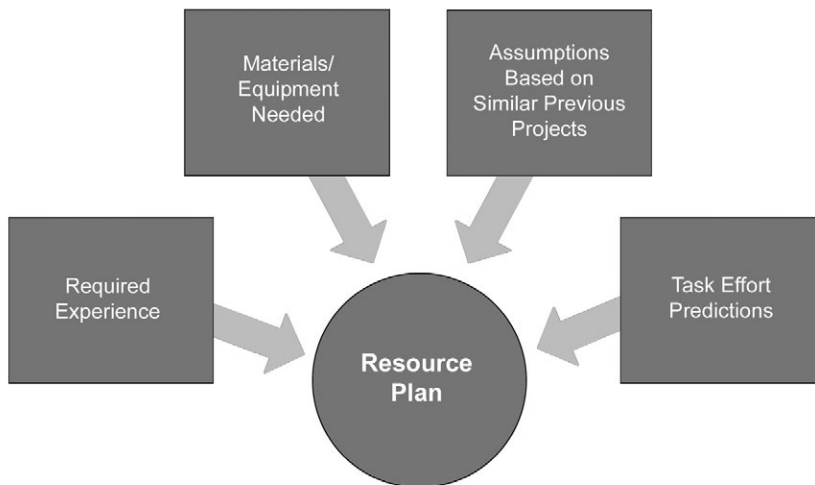
- Regulatory in-process design reviews – pharmaceutical product regulations examine aspects of a facility while it is being developed (e.g., process flow diagrams, area sterility approach).
- Module equipment assembly – modules comprised of several different manufacturer's equipment create challenges in testing equipment compatibility, ordering/shipping, monitoring assembly and final delivery.
- Factory Acceptance Testing procedures – the scheduling of FAT activities can have a significant impact on a schedule as they are near the end of a project.
- Equipment shipping/customs – requires identifying custom inspection durations and expediting inspection plans when needed.

- Commissioning – entails planning the resources and staging of the equipment start-up procedures.
- Validation – defining the activities necessary for the production process to be made operational.

The PDP should identify any specialized skills required, at what point in the project they will be required and have an initial plan on how to acquire them.

During project initiation, project planning should include a sufficient amount of funding to either hire specialized skills for the various stages of the project or provide backfills for existing and qualified employees of the organization.

Figure 5.3: Resource Plan



5.3.3 *Schedule Utilization*

A schedule should establish a common understanding among the project team in relation to the tasks, their durations, and the resources expected to achieve a project's objectives. The schedule should also support the business justification, e.g., by predicting the introduction of a product to the market.

Other uses of a project schedule within a PDP include the generation of resource planning as discussed and identify project constraints. Risks connected to the schedule can be monitored and utilized as a key element of the scope change management plan and the basis for project control measures. A well defined project schedule can provide a project with an effective plan for meeting the objectives.

5.3.4 *Schedule Management*

The project schedule is a dynamic undertaking that should be constantly reviewed and updated to maintain its accuracy and reliability as a project guide. Scope changes or uncompleted tasks require the schedule to be updated so the impact of each can be identified. Risks associated to these schedule changes should be identified and analyzed throughout the PDP, utilizing the scope change management plan.

5.4 Project Cost

5.4.1 Funding Strategy

Project costs follow a similar maturity pattern as a schedule (see Figure 5.4). The project costs are normally aligned with the Work Breakdown Structure (WBS) established for the project schedule. As a project develops through the stage gate process, the additional project detail enables a more comprehensive and accurate project cost estimate. During the Project Delivery Planning stage, the project funding typically transfers from expense to capital and will remain as capital unless the project is later stopped at a subsequent stage gate. However, some costs may always remain as expense costs such as spare parts, commissioning parts and consumables. It is important to understand the local accounting policy with respect to the treatment of capital and expense as it may differ from one organization to another and may differ over time. For example, the treatment of capital and expense may change as a result of a recent merger or acquisition. .

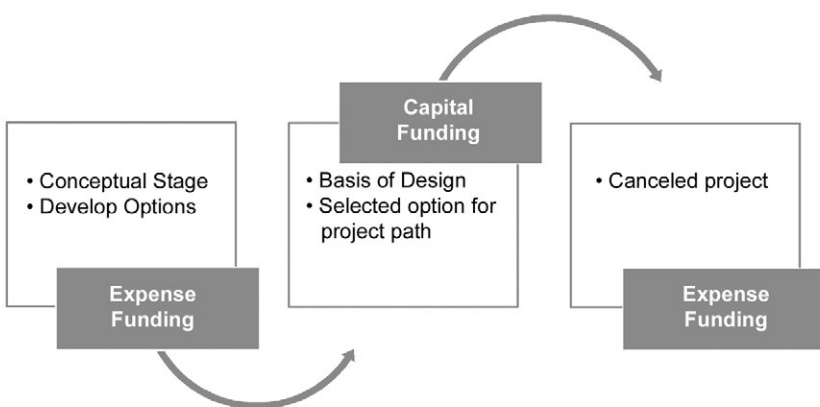
During the Project Delivery Planning stage, the project funding typically transfers from expense to capital and will remain as capital unless the project is later stopped at a subsequent stage gate.

The conceptual design effort (see Chapter 4 of this Guide) would normally lead to the development of a Basis of Design (BOD) during the Project Delivery Planning stage. The BOD is then used as the basis for justification of the funding for the final engineering design (see Chapter 6 of this Guide). The BOD may be used to justify the full funding of the project.

The funding strategy should be defined in the PDP to minimize the commitment in cost of the project at each project stage gate while at the same time meeting the objectives of the project. A well planned funding strategy will minimize the impact in the event of not proceeding with a project. Cancelling a project often results in the project costs being expensed and not capitalized; another reason why a funding strategy is important.

Fast track projects may include the detailed engineering for long lead items within the feasibility or conceptual development stage to expedite the schedule. Where a project is cancelled, the receiving site would be required to absorb expenses incurred.

Figure 5.4: Project Funding Flowchart



The estimate is a rough calculation of costs associated with the entire project or large grouping of tasks. As the project's detail is developed the cost estimate begins to itemize individual or smaller groupings of tasks creating a project budget. The budget will have an associated variance factor which will diminish as the project detail is developed. A well defined budget that accurately represents the level of scope detail provides the assurance necessary for obtaining a capital commitment. It is directly tied to the schedule and scope which together form the foundation for project controls (see Section 5.5 of this Guide).

Projects may not require the use of capital funding, e.g., demolition projects or business change projects. However, they will require a funding strategy so that final expense funding can be obtained.

5.4.2 Cost Estimation

To support the funding strategy, a variety of cost estimates are required of increasing cost estimation accuracy. This section describes the complete process of cost estimation through project stages 1, 2, and 3 when a control estimate is developed.

Feasibility and Conceptual Cost Estimating

Projects usually start with a high level estimate based on data from other projects as part of the Feasibility and Conceptual Development Stage Gates (see Chapter 4 of this Guide). These types of estimates are based on benchmarked data often referred to as a “Stochastic” method of calculation, e.g., cost per m2 for an Oral Solid Dosage facility, or cost per metric ton for a bulk API Facility.

Key points to consider when using benchmark data to develop this type of cost estimate (see Table 5.2) include:

- Comparisons – benchmark estimates are only accurate to the extent that the benchmark facilities resemble the new facility. Benchmark estimates for “standard” facilities such as office buildings, warehouses, and laboratories can be very accurate because there are not significant differences between these spaces. Process spaces and renovation work can be very different, as they are frequently unique. Along with facility type and age, the ratio of different types of space within a facility also drives the overall cost. For example, a “manufacturing” building that includes a significant amount of laboratory and office space will have a lower total cost per square foot than a facility that is predominantly process space.
- Inclusions – what is included in the benchmark numbers that are used to develop the estimate should be understood. The more that is known about the scope of the benchmark facilities and the content of the benchmark facility estimates, the more accurate the benchmark estimate. Examples of costs that may not be included in benchmark facility costs include:
 - Site Preparation – Clearing, Grading, Landscaping, Site Utilities
 - Utility Generation Equipment – Boilers, Chillers, Emergency Generators
 - Existing or Relocated Process Equipment
 - Furniture, Fixtures, and Equipment
 - Indirect Costs – Project Staffing, Capitalized Interest
 - Escalation, Exchange Rates, Regional Cost Adjustments
 - Completion Schedule
- Square Foot (SF) Estimates – when using Cost per SF metrics, the ratio of different types of space within the benchmark facility and corresponding ratios in the new facility should be known. The benchmark facility estimate should be a summation of different square foot costs for different types of space.
- Equipment Factors – equipment costs drive the overall cost of a process facility. In order to use equipment factors to estimate other facility costs, a comprehensive equipment list with estimated equipment costs is required. Most process facility estimates should start here. Facilities with similar equipment lists should be benchmarked to factor other related costs including process piping, automation, and electrical power. Existing or relocated equipment should be accounted for on both sides of the equation.

Table 5.2: Example Conceptual Estimate Summary

Preliminary Budgetary Assessment					
PRELIMINARY BUDGET ASSESSMENT					
A	BUILDING COST	25,250 GSF @	\$ 195	/GSF	\$ 4,917,386
	Office Space	4,160	\$ 133		\$ 553,695
	Class 100K Mfg	4,000	\$ 391		\$ 1,565,200
	Class 10K Mfg	2,250	\$ 497		\$ 1,118,250
	Lab and QC	400	\$ 374		\$ 149,520
	Warehouse	1,500	\$ 112		\$ 168,300
	Support Space	1,130	\$ 171		\$ 193,230
	HVAC/Utilities Area	11,180	\$ 99		\$ 1,169,190
B	FIXED EQUIPMENT	(2.00% of A)			\$ 98,348
C	SITE DEVELOPMENT	(5.00 % of A)			\$ 245,869
D	TOTAL CONSTRUCTION	(A + B + C)			\$ 5,261,603
E	SITE ACQUISITION/DEMO				\$ 0
Fa	MOVEABLE EQUIPMENT	(0.00% of A)			\$ 0
	Office Space	10.00%			
	Warehouse	1.00%			
	Labs	8.00%			
	Manufacturing	0.50%			
	Support	0.50%			
	HVAC/Utilities	0.50%			
Fb	PRODUCTION EQUIPMENT				\$ 2,097,600
Fc	PROCESS PIPING/ELECT/CONTROLS	(110% of Fb)			\$ 2,307,360
G	PROFESSIONAL FEES	(20.00% of D+F)			\$ 1,471,841
	Architecture/Engineering	12.00%			
	Construction Management	8.00%			
H	CONTINGENCIES	(20.00% of D+F)			
J	VALIDATION	(0.00% of D+F)			\$ 0
K	TOTAL BUDGET REQUIRED (D+E THROUGH J)				\$13,100,000

Example

If the cost of a benchmarked facility was 4X the cost of the equipment, it is important to know how much of the equipment was purchased new, how much of the equipment was existing equipment, and how the costs of the existing equipment were calculated in the benchmarked equipment estimate. Where the plan is to use this 4X factor as a data point in developing the cost estimate, the total cost of the equipment to be installed should be included. For example, if the cost of the existing equipment is not included in the baseline equipment estimate, the 4X factor may be too low.

Control Estimate

A control estimate should have sufficient detail to manage the scope, and therefore, the cost of the facility as it moves through the design phase and into construction. As a priority, the construction team should develop a comprehensive, itemized, estimate with quantities, labor rates, and unit prices. This control estimate becomes the baseline to control the scope, establish the control budget, and forecast cost at completion, manpower loading, and cash flow throughout

the life cycle of the project. A robust cost estimate can provide a foundation for other aspects of project execution and establishing a solid control estimate early in the project can be beneficial.

Control estimates should include an appropriate level of contingency to cover the cost of changes as a project progresses. The contingency account will typically be larger at the beginning of the project and decrease as funds are spent to cover changes or decreased as questions are answered and open issues are resolved.

Associated expense costs related to the project should be considered; projects may only require expense costs, e.g., demolitions and product transfers. Depending upon the accounting rules within which an organization operates, the individual budget cost items may be either capitalized or expensed. It is considered good practice to manage and take notice of expensed items such as the recruitment of staff and associated training costs.

Some of the more common expensed costs are End User start-up costs and staff, for example. As well as the cost of the design and engineering contractor(s), there will inevitably be the cost of the End User personnel assigned to the project. When building a new facility, staff will be needed to run the facility once the project is completed. These staff need to be either recruited or transferred from elsewhere in the organization (in which case their replacements in their previous roles will need to be recruited). The new staff will also need to be trained (or re-trained) for the new facility before they can assist with commissioning or operation.

At completion of the project delivery planning stage, the project should have a control estimate, used for project funding approval and for future cost management as the project is delivered.

Cost Management

Cost management involves monitoring the effectiveness of risk mitigations, obtaining agreement from parties involved in a cost change, and monitoring the actual changes to assure they track according to projections. It is the responsibility of the Project Manager. Several tools and techniques are available and are usually determined by the report data requirements of the end user organization.

Effective cost management usually relies upon accurate forecasting of a project's cost status. Forecasts may be based upon current data or assumptions and can help the Project Manager to assess the project's cost required for completion. The current project performance status can also be identified. Periodic project reviews can provide assessments of cost and schedule performance to reflect the current status and identification of performance trends.

A representative pharmaceutical PDP typically includes measuring techniques that produce the monitoring data, e.g.:

- **Planned Value** – projected amount of cost associated to a task or group of tasks.
- **Actual Cost** – total costs incurred to complete a task or group of tasks.
- **Earned Value** – projected cost of tasks actually or partially completed (e.g., typically linked to tangible evidence such as a deliverable).
- **Cost Performance Index** – cost-efficiency gauge, equal to the ratio of the Earned Value divided by the Actual Cost, a value of < 1 indicates a cost overrun while a value > 1 indicates a cost under run.
- **Schedule Performance Index** – forecast project completion date, value equals the ratio of the Earned Value divided by the Planned Value.
- **Estimate to Complete** – forecasting estimate for completing remaining activities being considered, value is usually calculated by subtracting the earned value from the cost budget.

Cost sampling should be conducted regularly as the project is being delivered. Cost sampling compares the activities underway to the cost estimate for those activities. This strategy may be used on project components that

have been identified as high risk. Early detection of deviations from the estimate basis can provide the project team with adequate time for correction, or provide early warning that costs have changed. The PDP should require this technique to be applied during project implementation.

Similar monitoring data can be obtained from non-capital projects; resource usage is considered key and usually tracked. In this case, the time spent delivering a task or activity can be checked against the estimate – as total hours worked on a task (the effort). Where organizations do not have systems to track what personnel spend their time on, the effort to generate the data should be balanced with the value of the data and its affect on team behaviors. If team members believe that their time is being closely tracked, it may have a negative impact (see Section 2.7 of this Guide).

For business change projects, a discussion on effort against deliverable progress can be sufficient to determine the validity of the original estimate.

Change Management

Due to the dynamic nature of the pharmaceutical industry, change plays a major role in most pharmaceutical projects. Facility requirements can be subject to change until the end of construction. For further information on the sources of change, see Chapter 1 of this Guide.

In order to manage change, the design and implementation team should identify, communicate, and manage assumptions on which a project is initiated. The project team should be made aware of assumptions to allow them to determine the most appropriate way to proceed, e.g., choose to wait until more information is available, or incorporate contingencies into a control estimate to accommodate changes

Example

It is usual practice to design manufacturing suites before the equipment in the suite has been fully designed or fabricated. In this case, the team should be aware that the design is based on assumptions related to the equipment, and that the design currently underway is subject to change when the equipment design is finalized.

Typically, Control Estimates include allowances specifically for different types of change, e.g., during the construction phase change needs to be managed in terms of scope, schedule, and cost.

The construction team should help to anticipate and implement changes from pre-construction through the completion of handover, with minimal impact to the overall delivery of the project. The construction team should be aware of assumptions made during cost estimation and plan construction accordingly. Changes during the construction phase should be limited to avoid impacts on the cost and schedule and in order to meet the baseline budget and schedule.

Example

The construction team may choose to sequence construction to start in areas where there are less assumptions or where effects of potential changes would be less costly. This may not be the most efficient way to complete the construction of the facility, but it may be the best approach in the overall context of the project. Once the project enters the construction phase, the cost and schedule impacts of changes can be overwhelming.

Changes:

- Can be mandatory; these changes are typically driven by market conditions, safety, or regulatory requirements.
- Substantially increase output or reduce operating costs; these changes can be justified by a cost/benefit analysis.
- May be preferential; these changes may not provide significant objective value to the project as a whole.

- May be additional scope; these changes are not part of the project's initial objectives.

The project team should minimize the number of changes that occur, incorporating only those changes that are essential to the project or that provide clear and substantial objective benefit to the project. An evaluation process should be used to evaluate potential changes against a set of specific criteria which is consistent with the business objectives of the project. Changes that do not meet the criteria should not be implemented.

Contingency

A contingency (or reserve) in the project cost can help to minimize the risk of cost uncertainty. Typically, the contingency is viewed as an allowance for unanticipated changes to the project scope. A contingency should have a clearly defined purpose and allocation and approval process. Reserves (Figure 5.5).and their intended purposes include:

- Management Reserve:
 - Allowance for unplanned scope changes and their cost impacts
 - Typically, this reserve is not viewed as part of the project cost budget until the funds are committed to the project.
 - Utilization controlled by Customer
- Project Reserve:
 - Allowance for unexpected events or omissions
 - Included as part of the project cost budget
 - Utilization controlled mutually by the Customer and Project Manager
- Construction Contingency:
 - Allowance for construction related issues
 - Included as part of project cost budget
 - Utilization controlled by Project Manager
- Allowances:
 - Appropriated funds for specific known or unknown project elements
 - Included as part of the project cost budget
 - Utilized as required by the scope of the assigned project elements

Figure 5.5: Reserves



The development of a robust contingency budget is linked to the cost estimation activities, the proposed delivery strategy, and the clarity of assumptions made. Project Managers should identify the assumptions under which they are working and evaluate the risk and potential cost and schedule impact associated with each assumption. Once the potential impacts have been assessed, the project team should assign reasonable cost and schedule contingencies to accommodate likely changes if the assumptions are erroneous.

During the delivery of the project, contingency may be managed by managing assumptions. Design assumptions that are not resolved when construction starts should be listed and tracked. As the project moves forward, assumptions will be replaced by actual data. At that time, the project team should revisit the assumptions and determine whether changes are required. As assumptions are resolved, contingency accounts set aside to address those specific assumptions can be reduced accordingly.

Projects can be confronted with an expense that exceeds risk reduction measures. The PDP should anticipate and establish a mechanism for handling major scope changes.

Example

A major expense example would be a project scope change to include an additional manufacturing line to accommodate revised production projections. This major scope change will require an increase in the project funding and should include a percentage of reserve funds commensurate with the scope change complexity. A reserve for an additional manufacturing line may include a much higher reserve percentage in comparison to the original project reserve amount. This is necessary as the complexity and risk associated to an individual manufacturing line is much higher than an all inclusive project which includes low risk factors such as foundations, steel, and the building envelope.

5.5 Project Controls

The PDP should identify the specialized project controls skills required to report, monitor, and forecast project status and outcome. The PDP should address the overall process of the data recorded, by which organization, and how it will be reported. The PDP should clarify the role of the owner, the designer, consultants, and sub-contractors in project controls. The resources to collect data and perform the required analysis will be required throughout a project and the PDP should establish the criteria for these resources and ensure funding will be allocated.

5.5.1 **Monitoring**

Project monitoring techniques are used to measure and evaluate a project's implementation to determine actual or potential discrepancies in a proactive approach. The evaluations indicate variances to the PDP and identify their sources. The Scope Change Management Plan is then utilized to identify corrective actions and control how the actions are incorporated into the PDP. Effective project monitoring is an on-going process throughout the project. Monitoring requires accurate data in order for the evaluations to effectively denote corrective actions.

This data should be collected periodically into a Project Controls Report as defined in the PDP. Project components that are normally measured and found in a Project Controls Report include:

- Approved Budget
- Current Project Activities
- Cost Expended to Date
- Percent of Work Scope Complete
- Estimated Final Cost
- Variation + or (-)

This data listed is used to generate customary metrics (see Section 5.4.2 of this Guide) from which the project is evaluated. These metrics determine the value of the work completed and forecast performance expectations for the project. The performance data generated by these metrics identifies and predicts trends allowing the project team to identify effectively the necessary corrective actions.

5.5.2 **Controls Techniques**

The PDP Scope Change Management Plan (see Section 5.2.4 of this Guide) should be used to control the implementation of corrective actions. The project team should identify possible corrective actions by evaluating the Project Controls Report. Input data should be checked before planning corrective actions. If the variance is confirmed, the project team should identify and determine which corrective actions best satisfy the project's technical, business, and risk factors.

The corrective actions implemented through the Scope Change Management Plan should identify the impact to associated tasks in order to continue to monitor accurately the revised PDP. Tracking the individual tasks can help to determine if the corrective actions taken were effective and as planned. Tracking individual tasks can be an effective means of determining if a variance is an event isolated to a specific group or a project team issue.

Example

Delayed tasks associated with the delivery of testing documents and equipment start-ups can negatively impact an otherwise well performing project. If evaluated as a whole, the project team could identify corrective actions for all team members rather than focusing them at the source of the variance. By viewing the project in total and by a breakdown of tasks, the project controls will be increasingly more effective.

5.5.3 **Cost Systems**

The costs linked to the corrective actions should be monitored, as they are usually supplied from a reserve. Monitoring project reserves can help with the project's financial success and can reduce the risk of exceeding financial expenditure. Factors which can cause major changes in pharmaceutical projects include:

- underground construction work scope
- equipment changes
- manufacturing criteria modifications
- regulatory modifications

The reserves and allowances should be regularly evaluated against the remaining project scope risk factors. This assessment should identify if the cost systems are satisfactory to support the remainder of the project. For example, a project having a scope of work that is 50% complete, with many high risk factors remaining to be complete, should have the large majority of its reserve budget remaining to offset potential changes.

Monitoring the reserve or contingency run-down can be used to review the status of the project and enables forecasting to occur until the end of the project. It is based on an interpretation of the risks still able to impact the project and those that are no longer an issue.

5.6 Project Team

5.6.1 *Project Manager*

The selection of the Project Manager may already have been decided prior to the project delivery planning stage and in preparation for feasibility or conceptual development work. If not, the selection of a Project Manager will need to be considered carefully (see Chapter 2 of this Guide). During the project delivery planning stage, the key roles and responsibilities of a Project Manager are:

- development of the key stakeholder relationships
- development of the PDP including Project Team selection
- engaging the project team in readiness for project delivery

5.6.2 *Selection of Project Team*

The general considerations that go into the selection of a Project Team are discussed in Chapter 2, Section 2.4 of this Guide. Considerations specific to the project delivery planning stage are:

- the availability of project team members who supported the previous project stage
- the requirement for additional SME linked to the challenges of this project stage
- any gaps in SME support from within the organization and therefore the need to source externally
- the need to engage with SME typically needed later in the project life cycle but whose input and engagement is needed early
- any appropriate supplier expertise required for effective project delivery

Example

During the project delivery stage for the installation of a new packaging line, the Project Team highlighted the need for an integrator that had the capability to fully integrate the packaging line. The team identified an SME resource within the organization located at a different site. The team discovered that several of the packaging suppliers can perform as integrators in addition to supplying one or more of the packaging machines. The decision to use a supplier's SME for the packaging line integration was found to be successful on a previous project while at the same time mitigating an important risk. After evaluating the options, the Project Team decided to appoint one of the suppliers when they discovered the internal SME was already committed to another project and unable to re-locate.

5.6.3 Roles and Responsibilities

During this stage and once a Project Team is formed, it is important to verify that the selection of team members is appropriate. This is typically achieved by developing a project team RACI Chart (see Chapter 2 of this Guide) within a Project Team launch meeting. Other key activities during this time include:

- establish project team ground rules
- evaluate whether the Project Team can provide the capacity and capability for their defined role
- develop engagement through early risk brainstorming so that the team engage with the project vision of success

Irrespective of the team make-up, the “forming,” “storming,” “norming,” and “performing” stages hold true for most teams (Reference 19, Appendix 3).

5.7 Communication Plan

Good communication can aid project management and provide benefits, e.g., a team that is more responsive to changes with a proactive decision making process due to a more inclusive environment. It can also reduce project risk.

5.7.1 Identification of Key Stakeholders

The first step of a communication plan is to identify the key stakeholders (see Section 2.3 of this Guide), e.g., End User.

Stakeholders may include the Project Sponsor, Project Team, and supervisors of the Project Team members. There may be additional stakeholders external to the organization e.g., end user of a manufactured product or project equipment or service provider.

5.7.2 Type and Frequency of Communication

Communication can take several forms from an informal conversation in person to a formal monthly report (see Appendix 1). Too much emphasis on communication can take up valuable resources and recipients may need to spend excessive amounts of time receiving updates on the project.

Suitable methods and levels of communication should be discussed with stakeholders. For example, some stakeholders may be content with just a written communication in the form of a monthly report for project updates (see Appendix 1). In contrast, Project Team meetings would normally require a higher level of interaction with a lot more verbal communication.

A communication plan (see Chapter 2 of this Guide) should define stakeholder communication requirements. Streamlining the communication can be beneficial, e.g., by combining the communication for different groups and communicating similar content to multiple stakeholders and groups. A large project may require several communication streams.

A communications plan typically contains:

- a segmentation of stakeholders into different “audiences”
- a division of the communications plan into key project phases which require distinct messages and what those messages are
- the types of communication vehicles to be used to convey different messages to the relevant audiences and responsibilities for their delivery
- how audience reaction or feedback will be tracked
- form and location of document stores

5.8 Design Management Strategy

For the purpose of the PDP, the planning associated with Design Management should focus on how Design Management will be managed at a high level, e.g.:

- Will it be handled internally with existing resource?
- Will an external design firm or contractor be used?

In business change projects, the design management is likely to be delivered by business change specialists such as those training in lean six sigma methodologies; these may or may not be internal to an organization.

Design Management of a project is discussed in Chapter 6 of this Guide.

The proposed design strategy of a project should be used to identify an appropriate level of detailed design based on an agreed upon level of risk. The design strategy can impact the cost and delivery of a project and may affect the final scope of a project. The design strategy should be outlined in the PDP.

The PDP should recognize the additional interfaces of a large project and establish how they will be managed, e.g., where work may be contracted to architects, designers, consultants, and engineers from different organizations.

Example

It is important to differentiate the delivery of a product transfer for a conventional dosage form that is not on a critical path with the fast track delivery of a new and complex technology for a new product launch. In this case, having an incorrect design strategy can prevent a product from being launched on time and from it realizing its projected sales revenue. In an industry that requires a disproportionately high level of research and development for a new product spread over many years, the failure of a new product launch can be catastrophic in terms of missed sales revenue and market share. Therefore, it is important to outline the design strategy in the PDP.

Considerations to be addressed in the PDP include:

- How will the scope and definition be developed and transmitted?

- What project controls will be established to monitor progress, cost of services, cost of the overall project, and design quality?
- What roles will the owner's project team and operating organization have in monitoring and reviewing the design?
- What specialized resources will be required from the operating organization to conduct these reviews, how much of their time will be required, and what is the process for freeing them from their day to day work?
- How will cost estimates and constructability reviews be conducted and will any other personnel/companies be required to interface with this group; if so what is the mechanism?

5.8.1 Collaborative Approach

A collaborative approach to the design of a project requires engagement with consultants, design and software suppliers, and contractors early in the project life cycle. Corresponding stakeholders should also be identified (see Section 2.3 of this Guide). The planning associated with a collaborative approach may be referred to as "integrated project delivery" is very different to the more conventional approach. The alternative approach involves more collaboration earlier on in the design phase of a project with corresponding stakeholders being identified much sooner. The open and more collaborative approach in theory lends itself to a higher degree of accountability, with the elimination of wasted time and effort, while resulting in a more desirable outcome in terms of cost, scope, and implementation (see Section 2.5 of this Guide).

A suitable partner for the design effort should be identified. The contractual agreement should be suitable for this method of execution. For more details on this approach, there is a Guide written by the "American Institute of Architects" entitled "Integrated Project Delivery"(Reference 20, Appendix 3).

The benefits of the collaborative approach are more apparent for non-conventional projects that contain a higher level of risk. The expansion of a conventional oral dosage facility based on an earlier recent expansion, e.g., is less likely to yield the same level of improvements when compared to the more traditional approach to Project Management.

5.8.2 Design Reviews

Design reviews should be planned, as they require preparation and may affect the schedule and cost of a project. Necessary participants, such as the End Users, specialist SMEs, and Project Sponsor should be listed. The number of design reviews depends on the type and complexity of a project.

Design reviews enable the design effort to be challenged against the original scope of the project and may be focused on specific aspects of a project such as safety, e.g., HAZOP, or more generally such as a value management session.

The PDP strategy should have included planning for a series of integrated project reviews which manage risk of all types and which make clear which aspects are to be reviewed.

To ensure the review strategy is robust, the Project Manager should evaluate:

- Review INPUTS – what data, documents, and personnel/skills are required for an effective review.
- Review PROCESS – what tools, techniques, and/or approaches are needed to conduct the review.
- Review OUTPUTS – what is the required outcome of the review.

For if one discipline's documents are not developed to a comparable level as those included in the review then the review could be unproductive and create a delay to the project. The key to innovative solutions is often derived from these reviews and the interaction that occurs, therefore being an essential and critical step in any project. Multiple

design reviews may be combined to save time and effort. This becomes more feasible when the same or similar group of participants is included in more than one type of design review. It is also beneficial if the design is being carried out in a location remote from the company location.

5.8.3 *Design Standards*

Design standards should be understood and can vary depending upon the owner, project type, location, and country. The approach to standards should be agreed in the PDP to avoid any confusion or non-compliance that could later cost the project valuable time and money, e.g.:

- Will the project only satisfy minimum local requirements to keep cost to a minimum?
- Are there additional corporate standards that need to apply over and above any local standards?
- Are there conflicting design standards that need to be managed?

The final project cost and schedule can be affected by the standards.

This area of the PDP may be called the Quality Plan or Quality Matrix as it defines which standards are applicable to which parts of the project. This definition while critical for capital facility projects has equal relevance for capital IT projects and also non-capital business change or improvement projects.

Within the pharmaceutical industry, the conceptual design of a project may be determined by the GxP regulatory standards governed by the specific markets served. There is usually less latitude with standards when dealing with safety and local building codes.

Regional markets and their regulatory requirements should be understood early in the project and before detailed design begins.

Example

For the Brazilian market, the ANVISA code requires much stricter separation of human and animal health products compared to other countries (Reference 21, Appendix 3). Lack of understanding of the regional regulatory requirements could, e.g., delay a product launch or prevent a site from being able to manufacture a product.

5.9 **Technology Strategy**

The PDP should address the project technology strategy at several levels. At the highest level, the PDP should address how far the project should “chase” new technology, e.g., should I buy my PC now or wait until the next generation is available? Generally, it is not practical to incorporate continuous technology upgrades in an on-going project. The PDP should establish the criteria for when a technology upgrade can be incorporated and what methodology the Customer will use to evaluate the cost and schedule consequences.

5.9.1 *Technology Trade Offs*

The PDP should evaluate the practicality of new technology for the project location. In low cost labor locations, the PDP should evaluate the trade-off between automated equipment and manual operations. There will usually be a trade-off between lower investment manually operated equipment and higher investment automated equipment. Factors such as quality and reproducibility of the product should be considered. Note: low labor cost may not mean lower cost.

The PDP should ensure that requirements are established for servicing higher technology at the project location.

5.9.2 Process Technology

Process Technology includes any technology required to convert raw materials into finished product and package the product for delivery. In pharmaceutical manufacturing, the process technology may be predetermined by Clinical Trials, R&D, or existing equipment on a manufacturing site. Where this is the case, it should be recognized early in the PDP and an appropriate procurement strategy developed to ensure the project gets competitive pricing.

5.9.3 Standardization

The opportunity to standardize on “supplier standards,” standard building components, and previously proven designs can shorten schedules and reduce costs. The PDP should address the standardization opportunities early in the project and develop an understanding of the costs and benefits of customization versus accepting standard equipment and designs. The PDP should establish a mechanism for technical personnel to justify “non standard” designs or modifications to suppliers’ “standard” offerings. The PDP should establish the Basis for Design of the project that defines the preference for and extent of customization. The PDP should also ensure a mechanism is established to identify when “non standard” equipment or designs are proposed for inclusion in the project.

5.9.4 “Green” Technology

Pharmaceutical companies may have established environmental goals and “green” guidelines. The PDP should incorporate requirements for renewable energy, waste treatment, noise, odors, light, and other impacts to the local environment. These requirements can have a significant and disruptive effect on the project cost, schedule, and morale if not addressed early in the project-planning phase. In some countries, implementing some “green” technologies can result in government grants or tax incentives that can help offset the additional capital investment.

5.9.5 IT and Security Technology

IT and Security infrastructure are considered essential to systems for projects; standardization and justification for investment should be developed. The PDP process should engage professionals from these areas and ensure that the requirements for their areas are specified in line with the overall project schedule and that the investment level is financially justified.

Examples of IT and security infrastructure considerations include:

- the use of electronic batch records
- the impact of continuous manufacturing processes on control systems
- the emergence of PAT and the role that process understanding and sophisticated instrumentation has in ensuring quality standards are achieved
- viruses designed to infect and interfere with process control systems leading to the need for security on IT and automation systems
- the need for security to protect Intellectual Property (IP) and to ensure document version controls are properly used

IT sub-projects may be needed within larger capital programs; in smaller capital or non capital projects, IT sub-projects may be one distinct work package to be delivered. For example, within a business change project on an R&D site, the changes to how material safety data is managed could require an IT solution as one work package although the focus of the business change could be how that data is used.

5.10 Procurement Plan

The PDP considerations for procurement will, generally, fall into the following categories:

- Scope of the Project, Timing, and Delivery Requirements
- Procurement Responsibilities and Resource Needs
- Strategy for Contracting
- Market Capability
- Market Competitiveness
- Expediting and Inspection
- Equipment Protection during Storage and Transport

The PDP should define the process of integration and interaction between the design and procurement phases. For example, the need to procure equipment/automation systems will be driven both by the physical “required onsite” date and by the need to have the selected and qualified supplier’s detailed design available to support and integrate with the facility design. If this award date assessment is not performed correctly, the project runs the risk of significant design changes (and associated construction works changes) due to this “late” supplier supplied information. It is important to reference and communicate the critical design documents and corresponding deadlines with the suppliers. The purchase orders should refer to the critical design documents and deadlines either directly or by reference to another approved contract or document.

For further information, see Chapter 7 of this Guide.

5.11 Construction Plan

Planning for the successful construction of a capital project should occur early in the project development.

Key aspects that should be addressed in the PDP fall into several categories, i.e.:

- Site Management
- Constructability
- Restraints on Construction
- Safety
- Construction Methodologies
- Equipment Procurement Strategy
- Quality Management
- Project Turnover

During project delivery planning, the construction plan should address compliance issues to ensure that the final outcome meets regulatory needs.

For further information, see Chapter 8 of this Guide.

5.12 Testing and Commissioning Strategy

For the majority of projects, there will be some requirement for testing and or commissioning. The Guide considers testing and commissioning as any activity which provides assurance that the project deliverable meets the required specifications, this includes:

- Verification that the installation meets the design specification.
- Verification that the materials used for construction meet the specification, e.g., there is adequate documentation to confirm pipework is 316L stainless steel, concrete has the specified strength.
- Conducting safety checks of installed mechanical/electrical and process systems prior to energizing them.
- Setting mechanical/electrical and process systems to work.
- Balancing HVAC systems.
- Balancing water systems.
- Verification that the systems perform to meet the design specification, for example confirming:
 - Sequence of operations.
 - Alarms and interlocks.
 - Operate to specification under worst case conditions, e.g., the full load on a standby generator.
- Confirming that a system produces product samples within specification.

Developing a testing strategy within the pharmaceutical environment involves:

- Definition of the documentation standards and deliverables.
- Definition of the performance levels – functional and regulatory.
- Determination of who and how – including the documentation requirements.
- Development of a testing program – when tests need to be done and how the results will be evaluated.
- This strategy has to be defined as a part of the organizational quality system.

For further information, see Chapter 9 of this Guide.

5.13 Project Start-Up Strategy

The start-up of a process, manufacturing operation, laboratory, or office is a critical step in the delivery of a project, requiring careful planning throughout the Project Delivery Process.

During the project initiation and planning phase, the Project Team should develop a clear approach to ensure the project start-up goes according to plan.

5.13.1 Accountabilities and Liabilities

During start-up, all systems will be powered and the potential for accidents, spills, or other damage to the project or surrounding facilities can occur. The PDP should address liabilities early and ensure that the contracting documents reflect the PDP intent. Where applicable, accountabilities for each organization working on the project should be clarified. For example, a contractor may supply labor and material under the direction of an owner for specific testing regimes, in such cases, the PDP should clarify the accountability of the contractor versus that of the owner. These arrangements should be considered early on and reflected in the contracting documents. This section should also stress the importance of not bypassing safety systems and avoiding shortcuts.

5.13.2 System Completion Planning

The PDP should establish the System Completion Plan. During construction, contractors will tend to achieve high rates of progress by installing bulk components, such as large bore piping, main cable runs, and steel erection. Small bore piping, cable terminations, and other labor-intensive operations required to fully complete systems may fall to a lower priority. This results in partial completion of many systems, but full completion of none, resulting in delays to testing and putting systems into service. The PDP should address the system completion and segregation requirements to ensure an efficient system completion and a safe and effective start-up. These requirements should be incorporated in the project contracting documents to ensure effective follow-through.

This is equally relevant in non-capital projects, such as manufacturing improvement projects where new standard operating procedures or manufacturing batch documents are generated, but not approved. An approval plan is usually required to get new business processes in use for each system.

5.13.3 Documentation of Testing

A complete set of testing and validation documents is usually required to ensure the facility or systems is designed, procured, constructed, and tested per specification. This includes testing performed at the supplier location. The PDP should establish the documentation requirements, timing of their delivery relative to project milestones, method for tracking/receiving, and incorporate these requirements in the project contracting documents.

5.13.4 System Interfaces

System interfaces can be within a single system or between systems. These interfaces are a significant source of risk during start-up and the PDP should ensure the start-up personnel are experienced in the systems they are required to start and that they are allocated the time required to analyze the consequence of multiple work fronts on interfacing systems, e.g., a Building Management System (BMS) that may have to be integrated with multiple systems from different suppliers.

5.13.5 The Start-Up Team

In general, the starting up of a new or renovated facility requires a higher level of technical skill than routine operations or construction. Supplier specialists, product specialists, and technical expertise from engineering disciplines will be required. In addition to the technical expertise, overall coordination, and following a planned start-up sequence will be required. The PDP should address the resource and organizational requirements and ensure the contracting documents reflect the requirements. Additionally, responsibility of the overall coordination of the start-up activities should be established and similar project management planning and control tools implemented to coordinate this phase of the project.

5.14 Project Close-Out and Handover Strategy

Project close-out and handover should be considered during the early stages of project initiation. Planning and developing close-out requirements in the PDP can prevent issues at project close-out. For example, understanding what turn over package documentation is required and when, with clear accountability and responsibility, can save time, cost, and effort later in the project. It is usually easier to develop these requirements during the planning stage. It can also enable suppliers to plan ahead and include any additional resource or other project requirements when submitting bid proposals.

As a minimum, the PDP should address:

- Financial and Contractual Close-Out
- Liability Transfers
- Retention Release and Final Payments
- Managing Warranties and Guarantees
- Handover Activities
- Planning for Partial Handover and Beneficial Use
- Owners Readiness to Accept the Facility
- Turnover Package Requirements and Documentation Deliverables
- Knowledge Management
- Knowledge Management during Project Delivery
- Knowledge Management after Project Completion
- Close-out Checklist

The project close-out is the final step before a project is fully operational. Within the pharmaceutical industry, the handover of a project typically requires a number of steps that have the potential to cause delays, e.g., a high level of testing and documentation. Having a rigorous project close-out strategy and plan can help to prevent unnecessary delays. It can also help secure the built-in float or buffer time to accommodate other delays that can occur and for which it is more difficult to plan.

For further information, see Chapter 10 of this Guide.

5.15 Completion of Project Delivery Planning

For the project delivery planning phase to be complete, the Project Sponsor should confirm that:

- The project is adequately scoped and is the right project.
- The project will deliver sustainable business benefits.
- Any changes in the business environment have been captured and do not affect the future viability of the project.

This chapter has been written with a traditional facility capital project as an example throughout; however, as shown by examples within the chapter, the principles, tools, and techniques discussed in this chapter are applicable to other types of project within the scope of this Guide (see Appendix 1).

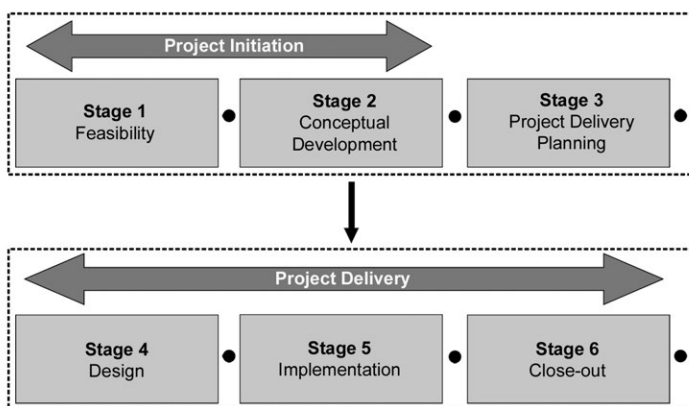
6 Design Planning and Delivery

6.1 Introduction

The planning and delivery of project design activities may involve many different skill sets and objectives. The Project Manager should balance these in a manner that meets project goals and objectives in terms of quality, budget, time, and regulatory compliance.

This chapter introduces the design process across the overall project life cycle (see Figure 6.1) and discusses the different elements of the process in terms of design planning and design delivery, focusing on meeting project scope needs, as well as tools used by the Project Manager.

Figure 6.1: A Typical Project Life Cycle



Before a project reached the detailed design stage (Stage 4), it usually progresses through earlier design phases as a part of project initiation (Chapter 4) and Project Delivery Planning (Chapter 5). This chapter will cover the project management of the design through these stages:

- Project Stage 1 Design Activities – Feasibility (evaluation of design options)
- Project Stage 2 Design Activities – Conceptual Development (development of design options)
- Project Stage 3 Design Activities – Project Delivery Planning (Basis of Design, also called Front End Design, Scheme Design, and Preliminary Design)
- Project Stage 4 Design Activities – Detailed Design

Design planning and delivery in the early stages of the project is extremely important in ensuring that the aims and risk areas are clearly identified. The Project Manager's role is to ensure that the design process is consistently managed across the stages of the project so that appropriate decisions can be taken at each of the stage gates and so that the implemented project meets the intent of the stakeholders.

In each stage within the project design, the concept of integrated validation and integrated risk management applies (see Chapter 1 of this Guide). Assessing and meeting the regulatory requirements of the project and mitigating critical risks through robust design (where possible) are part of the Design process.

6.1.1 Design Quality Management; Good Engineering Practice

Good Engineering Practice (GEP) should be the foundation for design activities, including drawing and specification development, protocol development, system testing, and verification. Design activities should take into account regulatory requirements, including GxP, safety, health, and environmental components. GEP is an integral aspect of the entire project delivery process (See Chapter 3 of this Guide). The design process should include time and resource allowances to properly implement GEP activities. Also see ISPE GEP GPG Reference 16, Appendix 3).

6.2 Project Stage 1 Feasibility – Design Activities

Generally, there is little original design completed at this early stage in a project. Typically, design solutions are reviewed from other similar projects and selected to support the business case and associated early scope definition. If an original solution is required, its feasibility in terms of the design outcomes as well as the business case should be assessed.

6.3 Project Stage 2 Conceptual Development – Design Activities

Formal design activities start within the conceptual development stage (see Chapter 4 of this Guide) and form a key part of identifying the project scope and objectives to feed into the planning process.

The first step in forming the project design activities should be the development of a comprehensible, detailed definition of the project scope and objectives. This definition should be clearly communicated to project participants and understood by members of the project team as the lack of a clear project definition may be a contributing factor to project failure.

6.3.1 Project Definition

Project Managers should consider technical, operational, regulatory attributes, and business risks when defining a project in order to ensure that the design meets all project objectives. Business elements that should be addressed include:

- Capital Costs
- Operation and Maintenance Costs
- Process and Technology Issues
- Financing
- Definition of the Regulations the Project must comply with

Project definition should have objectives that are measurable. Vague or misleading language, e.g., “use of cutting edge technology” or “implementation of current best industry practices” should be avoided. The project goals should be defined (measurable) and focused on corporate business objectives, e.g., “product output of 5 million doses annually” or “roll-out a new email system to 90,000 users by Q4 next year.”

In the project definition, the scope of the technology proposed and operational philosophy should be explicit

Example

Where a design focuses on ensuring product and environmental safety related to the handling of toxic compounds, this should be clearly understood. Where the operational focus will be on the replacement of a paper batch record with an electronic solution, then the impact on End Users should be clearly defined.

6.3.2 Functional Objectives

Functional objectives for concept design delivery require planning, and the project goals should be understood. Questions relating to functional objectives include:

- What is the facility supposed to provide?
- How much material or product is to be manufactured?
- What is the expected number of orders to be processed in the Enterprise Resource Planning (ERP) system?

The project design should address the functional objectives, through (for example) the definition of the use of the IT system, the formulation of the product, the manufacturing process, the stages of product development to be served, and the range of activities to be performed.

Questions to help to ensure that function is conveyed correctly and understood by project participants, include:

- Is the project focused on producing clinical materials or commercial product?
- Will the facility be a single product or multi-product platform operation?
- Is the IT system a replacement for an existing system or brand new?
- Are new hazardous or toxic materials required as part of the product transfer?
- Will the facility need to meet heightened energy efficiency requirements?

For facility or product transfer projects, functional objectives require scientific and engineering information related to the:

- Product Attributes
- Process Unit Operations
- Relevant Regulatory Data
- Local and State/Regional Ordinance Data
- Site Planning

This information can be compiled in preliminary engineering documents that may include site plans, conceptual layouts, and high-level process descriptions.

For IT and business focused projects, functional objectives require business process mapping and infrastructure knowledge which can be related to current practices, IT systems, and data. This information can be compiled into business requirements documents that may include “to-be” and “as-is” process descriptions, and IT performance requirements (capacity, availability, etc.).

Establishing the functional objectives of the project at this stage should be complementary to developing or refining the User Requirements Specification (URS) for the project or facility. For further information on the approach to developing requirements, see Section 6.5.3 of this Guide.

Design planning should include a preliminary scope of work document that includes known requirements, and addresses areas of potential risk. It should include the technical requirements that will form the basis of design, an initial consideration of project attributes, and should outline the project funding, schedule, and regulatory requirements. Figure 6.2 provides an example of the contents of a preliminary scope of work typical for facility projects.

Figure 6.2: Example Preliminary Scope of Work

Section 1 Project Overview a. General Project Description b. Project Approach c. Schedule d. Project Funding Section 2 Technical Description Process Description	Section 3 Design Criteria a. Civil b. Architectural c. Structural d. Mechanical e. Piping f. Electrical g. Utilities h. HVAC i. Environmental j. Process k. Equipment	Section 4 Execution a. Organization b. Reporting c. Project Security d. Regulatory e. Validation f. CAD g. Document Control h. Document Distribution i. Document Review Section 5 Scope of Services a. Phase I Preliminary Design b. Phase II Detailed Design c. Phase III Construction Liaison
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Note for Figure 6.2: Documentation produced at this stage of the design process (e.g., process descriptions) may form the basis of future documents. Generating multiple documents with the same or similar content should be avoided as it will significantly increase the document management burden.

6.4 Budget and Schedule Objectives

As the Project Conceptual Development is completed (Stage 2), and Project Delivery Planning (Stage 3) is to be addressed, an important task for the Project Manager is to maximize the benefits of the available resources for the design activities. In many projects, establishing the budget, schedule, and resources for design tends to bridge Stage 2 and Stage 3 as it is often necessary to identify and plan (or even) commit to key resources at an early stage.

This requires an understanding of:

- What those resources are.
- How the resources will be utilized.
- When the resources will be called upon for deliverables.
- When the resources will be removed from the project team.
- The time required to produce the deliverables necessary to meet project goals.

6.4.1 **Budget Objectives**

The design budget is normally integrated into the overall project budget. This budget will be dynamic as the scope definition progresses and further detail is developed for the design information required to complete the project. The budget should be communicated to and understood by the design coordinators.

Available technical solutions can have different levels of associated cost, which should be balanced with the budget and technical quality and innovation.

Example

Product protection and contamination control can be accomplished through a combination of procedural and environmental controls, the implementation of various physical segregation approaches, or the use of more advanced equipment technology, e.g., RABS or isolators. Each option may meet project objectives and regulatory requirements, but with a different level of cost to the project.

During the conceptual development stage, the development of the design budget is usually based on a broad definition of the project scope. As more defined engineering information is developed, the design budget can be better defined. As the design progresses, assumptions and allowances in the conceptual estimate should be revised to reflect the increased definition of the design information. The budget should be monitored. Project functional objectives should be reviewed to ensure that they continue to be addressed, and therefore, correctly valued in the budget.

Design changes should be identified and the changes approved in a timely manner. Change control should be applied to both technical design and budget increases/decreases as part of the overall control of the project.

6.4.2 **Schedule Objectives**

Design activities on the project schedule should include clearly defined milestone dates for each design deliverable and where milestone dates lie on the critical path of the project, this should be identified. Although this is true for any schedule, design activities tend to have some unique challenges for the Project Manager. Often, design can be intangible until the final deliverable appears, and because of this, it is much harder to measure progress in a meaningful way. Designs are often subject to review, approval, revision, and re-review – occasionally repeatedly. As a result of this, the design activities within the project schedule should be:

- Short (typically a two to three week “package” specific activity, rather than a two to three month “design” one).
- Measureable (have a defined deliverable at the end).
- Incorporate time for review, approval, and rework.
- Highlight the point at which the project will consider the design “frozen.”

Design schedules should support the project goals, e.g., product launch, technology transfer to support manufacturing, or regulatory submission. The design schedule normally occupies only a small portion of the overall project scope; it should be ensured that key design milestones align with overall project goals.

Facility project design schedules should support the construction delivery approach that has been selected for the project. This will vary in terms of construction implementation needs; design information for critical (often long-lead or specialist) equipment deliveries may become the main design milestone. The schedule should also consider requirements for review and approval of documents and data, both for technical content and regulatory compliance.

The design schedule should be evaluated against the:

- list of deliverables required to complete the project scope
- activities defined in project scope
- resources available to the project

Finally, the schedule (and associated resource allocations) should be reviewed throughout the project design activities, as changes to the design activities and resource allocation can increase (or decrease) required man hours to levels that will not support the budget and cash flow objectives of the project, and therefore, impact the design budget.

6.5 Project Stage 3 Project Delivery Planning – Design Activities

6.5.1 Scope Definition

Defining the project scope and ensuring that all members of the project team understand the scope definition is the responsibility of the Project Manager. As design elements of the project are confirmed and the scope is written in the form of a Basis of Design (BOD) document (see Chapter 5 of this Guide), the design will become “locked” in order to allow for management and control of the design budget and schedule. Changes to the scope of work should be formally managed and tracked as part of the project control system. It is usual to have key design concepts “frozen” as early as the conceptual development stage (concept design) as they are fundamental principles which underpin the detailed design process, e.g., the rationale for materials of construction, which are usually selected within an API Facility based on quality risk (if contacting the product) or safety, in addition to cost.

It may be beneficial to hold a formal “kick-off” meeting with the design team, customer, and key suppliers to ensure that everyone understands and is aligned with regard to the:

- Project Goals
- Project Objectives
- Project Scope
- Project Timelines
- “Frozen” Design Concepts

The project BOD is a written narrative of the project scope in terms of design attributes, project goals, and the business needs. Figure 6.3 provides an example of the contents of a “typical” BOD for a facility project.

Figure 6.3: Example BOD Contents – Facility Project

Project Goals and Objectives Process Narrative Process Description Process Flow Diagrams Equipment Summary Automation Control Philosophy Architectural Narrative General Description Production and Production Support Areas Laboratory and Office Areas Code requirements Room Data Sheets IT infrastructure/Controls Philosophy	Mechanical Narrative HVAC Systems Zone and Classification Diagrams Pressurization Diagrams Piping Systems Production Areas Support Utilities 4. Electrical Narrative Building Electrical Service Distribution System Back-up Power Grounding and Lighting Special Systems 5. Attachments
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The scope definition should answer the question, “What is the work required to deliver the objectives of the project?”

6.5.2 **Process Description**

A process description is normally required in pharmaceutical projects. It should define the process operations as they are understood at the time of issue. Examples of process descriptions include:

- For product transfer or facility projects, a process description will define process steps by unit operation, the raw materials required to support manufacturing, process and facility support utility requirements, and identification of the equipment necessary to support the process.
- For IT and business change projects, the process description will outline the details of the business process, its key stages, and the data handled or generated at each of those stages.

For facility projects, this information will be used to develop or enhance the Process Flow Diagrams (PFDs), the initial project equipment list and equipment descriptions, mass balance information, energy balances, the first set of drawings used to define the project. For IT and business change projects, this information will allow the development of the use cases and requirements for the future state.

6.5.3 **User Requirements Specification**

The User Requirements Specification (URS) is the responsibility of the customer, but may be written by a third party during the design phase of the project. The URS needs to be a written description of what should be done (or happen), but not how it should be done. The URS should be written by designated Subject Matter Experts (SMEs) and reviewed and approved by the customer (e.g., Process Owner). The URS should be clear in its definition of the system requirements and it will form the contract between the project and the customer.

During the development of the URS, project management should ensure that the proper resources are involved, that the process description is clear and understood, and that the contents of the URS are clearly defined and testable. The URS should not contain any commercial discussions. The URS typically includes:

- Operational Requirements (e.g., who and how will the system be used)
- Functional Requirements (e.g., those functions that the system must perform)
- Data Requirements

- Technical Requirements (e.g., the specification limits that the system must meet)
- Interface Requirements (e.g., what existing systems need to be interfaced to)
- Performance Requirements (e.g., the systems performance limits should perform)
- Security Requirements
- Maintenance Requirements
- Regulatory Requirements
- Life-Cycle Requirements

Where relevant, the URS should address the migration of electronic data and any regulatory constraints that may have been identified. Requirements should address the applicable GxP regulations and should highlight those aspects that are critical to patient safety, product quality, and data integrity.

Ownership of the user requirements lies with the regulated organization. URS development can be facilitated by the Project Manager through the development of use cases (defined scenarios) and by using user workshops to challenge the requirements. The requirements defined in the URS should be specific, measurable, and testable during the project. The requirements in the URS should be traceable through the design to the verification activities.

Note that there may be a project URS as well as system specific user or process requirements.

6.5.4 *Supplier Request for Proposal/Selection*

At the completion of Stage 3 Design – Basis of Design (BOD), it is likely that suppliers for the supply of equipment and/or services will need to be engaged to proceed to the detailed design stage. For further information on the procurement process, see Chapter 7 of this Guide.

6.6 Project Stage 4 – Detailed Design Activities

6.6.1 *Design for GxP Compliance*

Project Design Attributes

Project Managers should be aware of the GxP requirements and expectations defined within regulatory guidelines as they apply to the project.

Project design requires a clear understanding of the project attributes, i.e., what are those elements critical to completing a compliant project successfully and what level of risk is associated with each? For example, to properly execute and manage a manufacturing facility design effort, understanding Critical Quality Attributes (CQAs) of the product and the Critical Process Parameters (CPPs) of the manufacturing process is necessary to allow definition of equipment attributes, quality inspection and verification requirements, and regulatory requirements.

Product and process information, as it relates to product quality and patient safety, should be used as the basis for making science- and risk-based decisions that ensure that the manufacturing systems are designed and verified to be fit for their intended use. This is a critical aspect of ICH Q9 (Reference 7, Appendix 3) as well as the ASTM E2500-07 (Reference 12, Appendix 3)(see Chapter 3 of this Guide).

The project team should define the critical aspects of all manufacturing systems; these are typically the functions, features, abilities, and performance characteristics necessary for the manufacturing/process systems to provide consistent product quality. During design, these should be defined based on product and process understanding.

Product – Process Synergy

Process understanding is associated with product knowledge. The CQAs of a drug product will be critical in process definition and design. The process description (see Section 6.5.2 of this Guide) should include product information related to:

- process design/unit operation needs
 - production output requirements
 - detailed descriptions of each process unit operation (formulation, fermentation, filling, etc.)
 - a description of the services required for the process (glass wash, CIP/SIP, inactivation)
 - the utilities necessary to support the process (WFI, clean steam, gases)
 - control system philosophy (control system architecture)
- There should also be an operational analysis completed if the manufacturing operation involves multiple products to ensure that adequate time is provided for each unit operation making up the process.

System Design Approach

The CQAs and CPPs will define many of the system design criteria. Management of the system design approach requires understanding regulatory expectations for proper design, including:

- proper separation of manufacturing and testing activities
- proper material, personnel, and product flows to minimize contamination
- adequate space and layout to support manufacturing and maintenance
- good plant systems for Heating, Ventilation and Air Conditioning (HVAC), water, sterilization, cleaning, and waste treatment
- proper protection of product via open or closed systems
- proper protection of employees via containment of hazardous/toxic materials
- effective program for qualification/verification of all critical manufacturing systems

Establishment Licensing

For facility projects, where the end result of the design efforts will be the manufacture of therapeutic drug products, the facility must receive a license from the regional regulatory agency, e.g., FDA.

Where design information will be used as part of the overall regulatory filing, it is considered good management practice (which can potentially reduce or omit risk leading up to the completion of the design activities) to discuss design options with the regional regulatory agency.

6.6.2 Design Scope Management

Project Managers should manage scope during the design phase. Changes to scope usually arise through two routes:

- externally through the customer or supplier
- internally through the project team

Changes to scope usually become apparent as:

- a change in cost (deliver for less)
- a change in requirements (the business needs to do something other than the approved project)
- a change in design

Project Managers should manage both the formal change control process (where a change is clearly identified) and the delivery of value for the project (where the change is less apparent).

Scope Creep

Scope creep occurs where the original objectives of the project are added to in a progressive way until the cost or schedule is affected. Because of its scientific, technical, and regulatory complexity, scope creep is a particular issue in the pharmaceutical industry and can take several forms, e.g.:

- Feature or function creep – frequently associated with technology led activities - where the project team adds functions which were not explicitly requested, but which are seen as “useful” or “will be needed” or “just in case.” Function creep can also occur when different design teams or members try to re-work original designs.
- Requirements creep – usually where the initial requirements are added to in a piecemeal way - where the customer (e.g., End User or Process Owner) tends to “fill-in-the-blanks” with additional requirements that were not clear in the original project scope definition.
- Instruction creep – can be widespread in large organizations – where processes and procedures are progressively layered and complexity is added to what started as a simple objective. Particular attention should be paid to business change projects where the initial simplification of business instructions becomes more complex to provide for unforeseen eventualities.
- Validation creep – unique to regulated industries and associated with several project types - where validation activities seem to overwhelm and drive the project activities and where validation is viewed as a layer on top of the conventional design activities, rather than as part of the project methodology.

Project Manager should also be aware of the potential ratchet effect in technology projects: when project scope or complexity increases the way the technological solution will be used making it almost impossible to successfully de-scope it.

Project Managers usually have the most impact on creep and the ratchet effect the Project Manager needs to have the authority to prevent scope changes.

Dealing with Scope Creep

Tools for Project Managers to deal with scope creep include the:

- stakeholders
- project brief/objectives/requirements
- project organization

Informed and engaged stakeholders, a comprehensive understanding of why the project is being executed, identified roles and responsibilities within the project organization, and a documented and agreed cost/benefit statement for each change can be beneficial. Illustrating scope changes as a percentage of budget or schedule can be used to drive clarity around decisions.

Requirement and instruction creep can be handled through the selective use of stakeholder influence and a clear set of objectives and requirements. It can be beneficial for the stakeholders to be clearly aligned with the project objectives and for the stakeholders to challenge additions to requirements/scope against those objectives

Project Managers should ensure that the requirements generate measurable results that can be challenged from the outset against the objectives. This can help to avoid additions being made on the basis of “clarifying” requirements.

Where multiple solutions can meet requirements, Project Managers should be able to select the option that most effectively meets the project cost and/or schedule.

For feature and function creep, change can be controlled through the objectives and requirements, questions to ask include:

- Does the feature add value to the objectives or not?
- Does it align with a requirement? If not, should the requirement/objective change?

If the requirement or objective is not changed, the function is not required.

For validation creep, the Project Manager can use the risk assessment process to align the activities and define the design deliverables and verification processes that need to be undertaken. Integrated risk and validation management should be the goal. The concept of Quality by Design should be seen as a tool to define the scope of validation (by defining the critical quality attributes of the project – see Chapter 3 of this Guide).

6.6.3 Design Review

In accordance with GEP and an effective risk management program, formal design reviews should be a part of the management of the design process. Project Managers should ensure that an appropriate number of design reviews are scheduled, and that adequate time is incorporated into the project plan to accommodate those reviews (see Section 5.8.2 of this Guide). In terms of a streamlined project process, the scheduling of integrated design reviews can mitigate a number of risks through considering aspects which impact the design.

The design review/design freeze process can be a useful project control tool. A formal design review can be used to align stakeholders and achieve agreement.

The review process should include consideration of:

- Adequate Design (has there been consideration of constructability, cleaning, maintenance, calibration, etc.?)
- Verifiability (can the design be tested and demonstrated to meet specific requirements?)

These concepts support the ultimate validation of the project deliverables.

For the Project Manager, the focus should be on ensuring that there are measurable acceptance criteria for the design review activities. Typically, these will reference the traceability from the requirements, through the detailed design documentation to the acceptance test criteria and should reference the GxP requirements for the project.

6.6.4 Design Qualification

Eudralex Annex 15 (Reference 22, Appendix 3) describes design qualification as follows:

“9. The first element of the validation of new facilities, systems or equipment could be design qualification (DQ). 10. The compliance of the design with GMP should be demonstrated and documented.”

Where required (usually for GxP facilities, (though it should be noted that approaches vary depending on the company philosophy)) the design may also be qualified.

The process of reviewing and documenting the approval of the design for “compliance with GMP” may be integrated into the GEP design review process or conducted in a separate focused design review.

6.6.5 Design Organization

Internal Resources

Resources assigned to a project’s design phase from the customer’s organization (e.g., process engineers) may be required to perform some or all of their “normal day-to-day” job responsibilities in addition to their new project assignment; this can be detrimental to the project. In addition, it can also be detrimental if insufficient resources are assigned to a project to adequately address the scope of work and the schedule requirements necessary to support the project design milestones.

When making internal resource assignments, the Project Manager should understand elements of the project such as:

- project scope of work
- deliverables, by functional area and discipline
- document review roles and responsibilities
- project design schedule milestones
- change control procedures
- any inspection and testing requirements to support the project procurement
- skill sets necessary to provide discipline support
- corporate business needs for ongoing operations

The project schedule and the duration of the resource commitment should be understood when assigning internal resources. The movement of resources into and out of the project during its delivery can add to the risk level of information being incorrectly developed and reviewed; to avoid this, where possible, internal resources should be dedicated to the project.

External Resources

The project scope, contractual format, internal design capabilities, and schedule will have a determining factor in how external resources are applied to a project design organization. External resources may need to be assigned in order to complete the project design scope of work.

Where applicable, external resources should be qualified (as required by National Standards or regulatory agencies) regardless of cost, schedule availability, or previous work history. The design scope roles and responsibilities should be clearly defined in the scope of work and the contract deliverables language. Assignment of resources, resource utilization, and commitment based on schedule needs should also be clearly understood. Resources deemed as "key" or "critical" to the project design, such as Subject Matter Experts (SMEs) or Discipline Leads (DLs) should be interviewed and selected based on the key factors of similar project experience, project scope understanding, availability and commitment to the proposed design schedule, and recommendations from previous clients.

The assignment of key individuals should include an assessment of their compatibility and synergy with the rest of the project team, including the internal resources assigned to the project. Where resources are obtained from an external organization, that organization should be audited in respect to its project and GxP capabilities.

Roles and Responsibilities

Individual resources assigned to the project design team, both internal and external, should understand their roles and responsibilities during design phase delivery. A RACI may be used to assist in defining the expectations and needs of resource assignment (see in Chapter 2 of this Guide). Table 6.1 shows an extract of an example RACI Chart for a Project Design Team.

Table 6.1: Example Design Stage RACI Chart

Role →	Project Manager	Finance	Engineering	Compliance	Process Owner	Vendors
Activity ↓						
Establish Production Requirements	I		C		AR	
Define Production Process	C		AR		C	C
Define Production Control System			AR	C	C	
Identify Process Requirements			AR		C	
Prepare Validation Master Plan	C		C	AR	C	
Environmental Impact Report	I		AR	C	I	
Prepare Schematic Drawings			AR			C
Prepare Specifications			AR			C
Approve Design Criteria			AR	C	C	
Develop Summary Schedule	AR		C	C	C	C
Project Budget Estimate	AR	C	C	C	C	C
R = Responsible – who does the work to complete an activity or task A = Accountable – who is ultimately accountable for the correct completion of the activity or task; approval C = Consulted – whose opinion is sought during the completion of the task; consulted by R I = Informed – who is kept up to date about the progress of a task and/or its completion; informed by R						

Project Managers should ensure that external resources have a clear definition of their roles and responsibilities related to design deliverables, both from a design delivery viewpoint and in terms of contractual scope and obligations. Requirements for document submittals to support design, permitting, start-up, qualification, and validation should be clearly defined. A document matrix can be checked and maintained in a dynamic manner throughout the design phase to ensure good engineering practice and regulatory expectations are integrated into the design team's ways of working and then met (Table 6.2).

Table 6.2: Example Document Matrix

	Engineering			Manufacturing			QA/Technical Services		
	A	A/N	R	A	R	I	A	R	I
Conceptual Design									
Process Flow Diagrams		X		X				X	
Process Description		X						X	
Mass Balance		X						X	
Yield Balance		X						X	
Architectural Layouts	X							X	
P&IDs		X						X	
Room Criteria Sheets	X							X	
Validation Documentation									
Master Plan			X	X			X		
Turnover Packages			X		X		X		
SOPs				X			X		
Protocols			X	X			X		
GMP Checklists			X		X		X		
A = Approved, A/N = Approved as Noted, R = Review only, I = Information only									

6.6.6 Design Risk Management

Understanding and managing the risks at the design stage is the best way to avoid those becoming issues on the project. Chapter 3 of this Guide provides comprehensive details on the risk management process for the project. Design Risk Management should be considered in exactly the same way; as part of an integrated risk management approach. In terms of design, specific risks tend to reflect choices about technology, operational and regulatory constraints and include;

- Incomplete or imprecise requirements – these can drive change as the details of the project emerge and the customer understanding develops. Piloting/prototyping or walking through the design at an early stage can help to refine the requirements. Use cases or scenarios may be used to extract and challenge the requirements.
- Incomplete or changing scope (see Section 6.5.1 of this Guide (scope creep)).
- Technical risk – new or unproven technology and its initial implementation. Risk management should prioritize the design of novel elements and establishing clear decision criteria to ensure that there is time to resolve problems prior to commissioning.

Design Risk Assessment

For further information on a typical generic risk process, (see Chapter 3 of this Guide). Design risk assessment should be integral to design activities and a project manager should:

1. *Ask the right questions.*

- This requires a clear understanding of the CQAs and CPPs.
- What are the risks in the process?
- Which suppliers pose the most risk?
- What level of control is needed?

2. *Understand the process.*

- The Team should have a common understanding of the process, both in terms of manufacturing and quality.
- Develop and “lock in” process flow diagrams.

3. *Use real data.*

- While there will always be a need for some assumptions to be made during a risk assessment, where feasible, realistic and applicable data is needed to ensure that the risk assessment provides meaningful results.

4. *Understand that risk assessment depends on people.*

- Assessing risk involves personal opinions as well as facts. The involvement of SMEs is critical to this process.
- Make sure that the tools and scales used are realistic (see comments on heuristics in Chapter 3 of this Guide).

5. *There may be more than one answer.*

- Risk reduction and control methods can be numerous. During design, it is important to assess the impact of the risk against project goals and attributes such as regulatory compliance, cost, and schedule.
- Allow for flexibility and insist that common sense is a key element of the evaluation process.

6. *Document.*

- Risk assessment activities during design should be captured in a formal Risk Register that can be used during the verification and validation activities.
- The documentation of design risk evaluation will be key element of change management. The Project Manager should describe the reasoning so that others that were not involved in the process can understand how and why you reached the assessment.
- Note that critical risks should form part of regular reporting to stakeholders and also be a component of any stage-gate approval process.

Examples of risk assessment application during design include:

- open (exposed) versus closed (not exposed) systems
- implementation of single use technology
- area classification
- process control requirements
- data archiving requirements

6.7 Completion of Design

The design review marks the end of the formal design process and the design review should be a check of the design against the requirements to ensure that the intent is either met or alternatives agreed. It is important to note though that the design can be completely frozen at this stage and during the implementation stage, there may be a need to address specific issues that arise by revisiting the design.

The Project Manager should ensure robust change control to avoid compromises in the design that introduce risk or reduce the delivery of the project objectives.

7 Implementation: Procurement

7.1 Introduction

7.1.1 *Procurement in the Pharmaceutical Environment*

The role of Procurement in the pharmaceutical industry has become recognized as a key resource in ensuring value, driving savings, and increasing efficiency in the procurement process while maintaining the highest expectations of quality.

The industry has increased focus on improving profit through many measures including streamlining (“Leaning out”) operating costs as well as optimizing capital expenditures. The procurement function can add value to a project by:

- obtaining best value from the supply base
- incorporating sustainability into the procurement process
- improving the ability to execute faster with fewer resources
- mitigating risk
- ensuring compliance with the specifications
- optimizing life cycle costs (total cost of ownership)

As part of cost control measures, there has been a higher utilization of contracted services; with this, the supply base has evolved and grown to meet this shift in resource demand for pharmaceutical expertise.

Owners should assure these resources meet the regulatory requirements, assuring that resources are qualified to provide the services they have been contracted for, e.g., 21 CFR 210 and 211 references – 211.34 Consultants (References 23 and 24, Appendix 3). Procurement has a role in helping to assure these requirements through the Supplier Qualification Process and agreements establishing terms under which suppliers understand and comply with GxP (supplier quality agreements).

As the role of procurement has grown in supporting capital projects so has the need for greater agility and speed in delivery. The timeline in the tender and selection process for suppliers may be improved by the development of strategic alliances for specific types of highly utilized goods or services. This strategy is a process outside specific project delivery through the development of long term strategic alliance agreements.

This strategy establishes the early supplier engagement activities such as:

- execution of non-disclosure agreements
- pre-qualification for financial viability
- insurability and acceptable safety record
- completion of any regulatory and corporate engagement policy requirements
execution of agreed terms and conditions

Aspects of the commercial terms defined in an agreement may be derived by conducting a Request for Information (RFI) and Request for Proposal (RFP) process. This strategy may be beneficial for both services and goods and can yield delivery efficiencies and cost savings. Suppliers may benefit from this process as it can put them in a better position to be awarded more predictable and consistent levels of work which allows for improved resource planning and pricing opportunities.

The decision to align strategically with a single organization or to establish several organizations for a particular service or goods that are competitively bid at the project level should be considered. Aspects to consider include the geography, timing, volume of work, and required skills. In addition, the longer term considerations of the dynamics of economic conditions and globalization of the types of goods and services used by the pharmaceutical industry can significantly impact the market forces that drive quality, service, and value.

Good supplier alliance programs include relationship management or relationship monitoring led by procurement. Alliances with a single or multiple organizations for critical or high value goods or services should include monitoring and continuous improvement metrics. The monitoring process should include appropriate stakeholders at all levels in the organization to ensure a complete assessment and identification of opportunities in the relationship.

Procurement and the controllers of planning for capital expenditures from a corporate perspective (usually engineering), should work together in developing a strategic alliance program to ensure that the strategic focus of procurement for the supply base needs is aligned to the direction of the capital spend for the company.

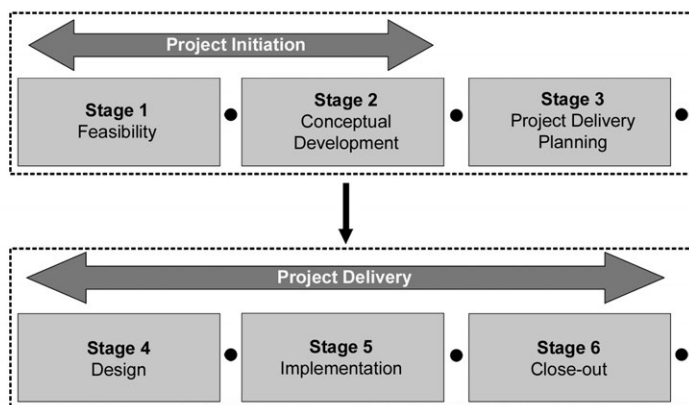
The procurement resource support for a particular project will vary depending upon the size and complexity of the project. Smaller, less complex projects may be supported with the basic up front strategic delivery planning and may need minimal Procurement support if the supply base needs are already established. The Procurement function should be engaged early to establish an understanding of the overall needs and strategy setting for delivery of the project.

The principles in identifying and the procuring the right external support discussed in this chapter may also apply to non-capital projects where project procurement is concerned with the purchase of expertise e.g., SMEs, and other expense items.

7.1.2 Project Life Cycle Considerations

Figure 7.1 shows a typical stage gate process (see Chapter 1 of this Guide).

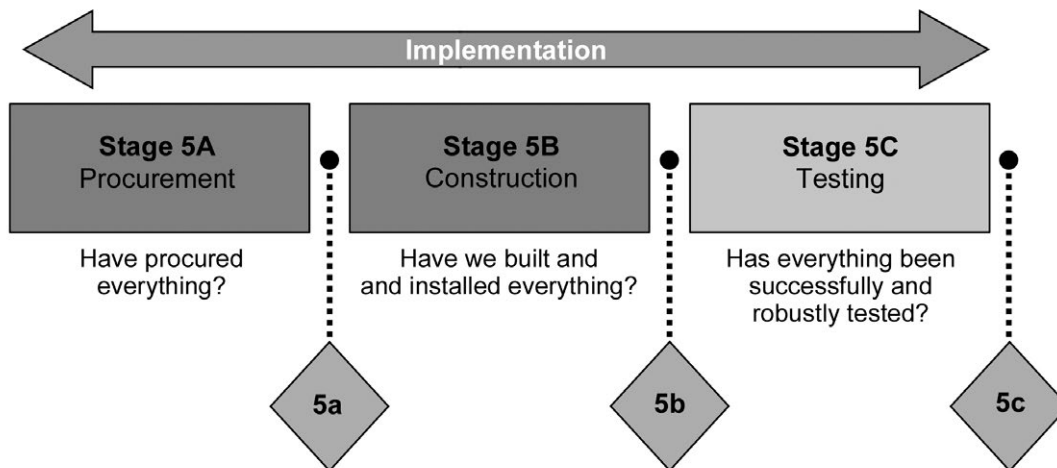
Figure 7.1: Typical Project Life Cycle



Procurement is a consideration in all project life cycle stages, i.e.:

- **Stages 1 and 2** – Project Initiation (see Chapter 4 of this Guide) – the procurement strategy is started during Feasibility and Conceptual Development. Items requiring extended delivery times (long lead items) are identified as the basis of the technical design is clarified. These could be goods (equipment) or services; typically it is the goods.
- **Stage 3** – Project Delivery Planning (see Chapter 5 of this Guide) – the Procurement Plan is developed (see Section 7.3). In addition to defining the Procurement Plan, the activities typically performed include:
 - Selection of overall contract type for the project (see Section 7.3 of this Guide) and main managing external resource (see Section 7.3 of this Guide).
 - Selection of long lead items that need to be procured before Stage 4 is complete.
 - Identification of the items which need to be procured so that they can provide final design details to the project team and the timing of this.
- **Stage 4** – Design (see Chapter 6 of this Guide) – typically the delivery of the Procurement Plan starts as long lead item suppliers are sourced, selected, and purchase orders placed.
- **Stage 5** – Implementation (see Chapters 7, 8, and 9 of this Guide) – the majority of procurement activities commence and/or continues during project Implementation (see Chapter 7 of this Guide). While there are micro-stage gates between individual items, there are typically no true stage gates between the three implementation stages of procurement, construction, and testing in a capital project (Figure 7.2). It is normal for there to be a great deal of crossover between the micro-stages within Implementation and likelihood that the close-out of all procurement activities will be completed long after the handover of a project for beneficial use. This may be particularly true in the case where retentions or guarantees have been provided which may be based on performance during Performance Qualification (PQ). Management of these issues should be considered in the project planning stage along with consideration for who will have responsibility for final release of funds and full financial close-out for the project.
 - A micro-stage gate is where each item should be considered: each item should be designed, procured, installed, and then tested in that order.
 - Construction and installation do not usually require the completion of all procurement activities to commence; therefore, there is no proper stage gate between these phases.
 - A review gate (such as 5a, 5b, and 5c) can be used as a final check that a stage is completed, e.g., review gate 5a should check whether all items been procured. This can mean their purchase or delivery, but usually delivery is more technically correct as procurement is the management of the full life cycle in purchasing goods or services.

Figure 7.2: Typical Capital Project Implementation Life Cycle with Review Points



- **Stage 6** – Close-Out (see Chapter 10 of this Guide) – where procurement is finally closed-out (see Section 7.5 of this Guide).

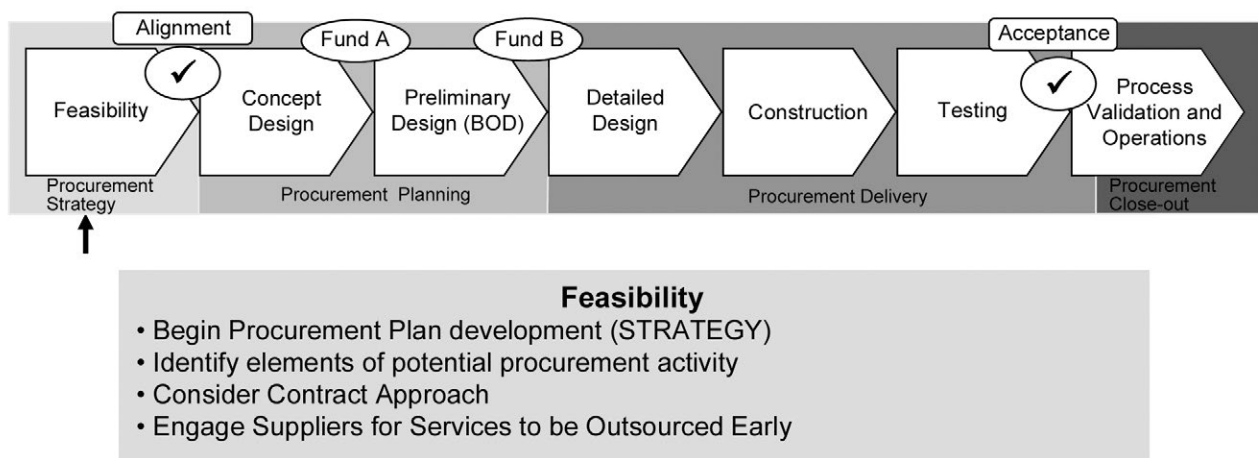
Business change or small projects which use expense funds also spend money and therefore follow the procurement process.

7.2 Procurement Strategy

The principles of the Procurement Strategy should be developed during Project Initiation (see Chapter 4 of this Guide) based on the level of definition and schedule established in the Feasibility stage (Figure 7.3).

Project Managers should engage procurement during the feasibility stage to help assure that the resource needs of the project for both goods and services are in place when required. Additionally, procurement professionals may be aware of parallel activities occurring within or outside the organization that may provide timing or cost benefit or that could become a resource constraint for the project. Unique delivery requirements should be considered in this stage, e.g., developmental technology or extremely short schedule items that may require a non-typical approach in order to meet the project needs.

Figure 7.3: Typical Capital Project Process – Procurement Strategy



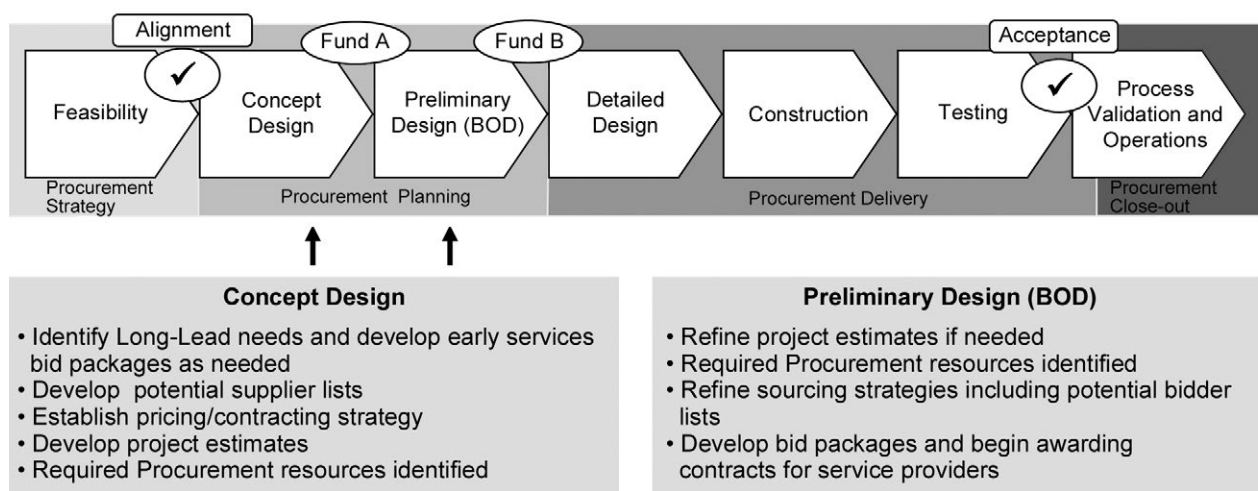
The Procurement Strategy should be further developed as part of the Project Delivery Plan (PDP) (see Chapter 5 of this Guide) and is the basis for the Procurement Plan.

7.3 Procurement Planning

7.3.1 Introduction

As outlined in Chapter 5, the Procurement Plan is a part of the Project Delivery Plan (PDP) and should provide a more comprehensive look at the procurement needs and timing for the project. Figure 7.4 illustrates the timing and key considerations in the development of the Procurement Plan.

Figure 7.4: Typical Capital Project Process – Procurement Planning



Depending on the scale of the project and the extent of in house resources, an owner may need to engage outside assistance to support the completion of the project delivery planning stage. The type of support required can include services, such as:

- Project Management
- Project Controls
- Architectural and Engineering Design
- Procurement and Contracting
- Constructability
- Commissioning and Qualification

A key consideration in setting out the scope of these services is the overall procurement approach/project delivery philosophy of the End User, i.e.,

- Is there a panel of pre-qualified/approved/pre-selected service providers for these services?
- Will the services be negotiated with a pre-qualified supplier?
- Will there be a need for this type of service in the follow on phases of the project life cycle?

- Should the selected service provider be expected to run through the full project life cycle of the project?
- Will the services be re-bid at the end of the PDP phase?

7.3.2 Considerations for Procurement Plan Development

In support of developing the Project Delivery Plan (PDP), the Project Manager should be supported by procurement professionals to create the Procurement Plan (see Section 7.3.4 of this Guide). Activities usually fall into the following categories and should be considered before creating the procurement plan:

- Scope of the Project, Timing, and Delivery Requirements
- Procurement Responsibilities and resource Needs
- Strategy for Contracting
- Market Capability
- Market Competitiveness
- Expediting and Inspection
- Equipment Protection during Storage and transport

Scope of the Project, Timing, and Delivery Requirements

The first item to address in developing the procurement plan is to understand the overall scope of the project, the construction schedule, and when equipment and materials need to be available for installation. The Procurement Plan should include, for each subcontract, the equipment item, bulk material purchase, and a schedule to ensure that:

- Contract and purchase orders are awarded on time.
- Equipment and materials are delivered on time.

Typical milestones, as a minimum, should include:

- Specifications completed.
- Request for proposal prepared and issued.
- Bids received.
- Purchase orders or contracts awarded.
- Key documentation deliverables/schedules.
- Factory Acceptance Tests completed (if required).
- Shipping date.
- Site arrival.

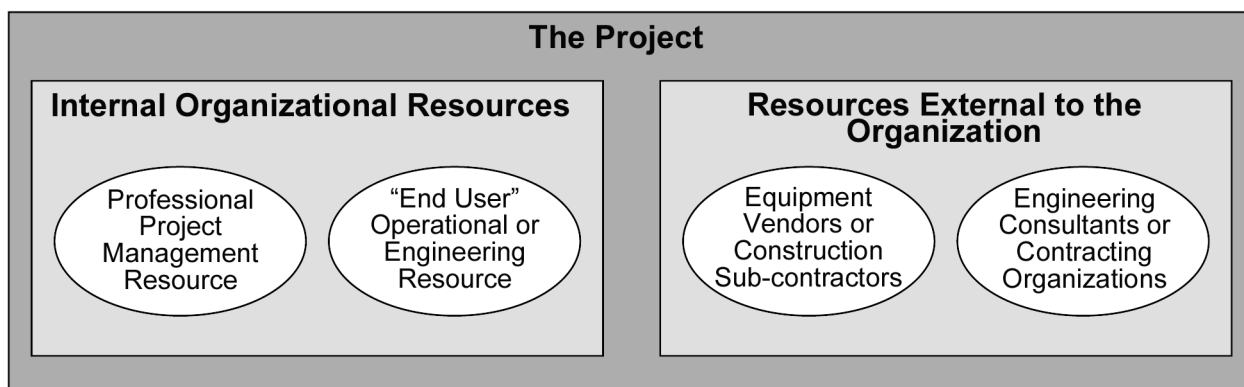
The PDP should establish these timing requirements and ensure that the dates required for specifications are confirmed and fed back to the Project Team. This will usually require several iterations to complete and time should be allocated to ensure that this is correct. The detailed procurement plan will generally not be fully developed in the PDP, but these requirements should be established in the PDP and included in the contracting documents so that project team can complete the details.

Procurement Responsibilities and Resource Needs

Procurement of equipment, materials, and services can and should be allocated to multiple Suppliers. The procurement options should be worked through in the Procurement Plan and a responsibility matrix for the project should be developed. Procurement may affect design and construction and the responsibilities should be established before these contracts are awarded. When established, these responsibilities should be included in the contracting documents for the project.

Generally, procurement groups from a Customer organization are not structured to conduct the intensive procurement activity required for a large capital project. In addition, their experience from procuring bulk construction materials may be limited, and the resources required to negotiate and award a large number of individual purchase orders or sub contracts in a concentrated time can become a limiting factor. Because of these limitations, the Procurement Plan should be clear on the role of a Customer organization procurement group (Figure 7.5).

Figure 7.5: Procurement Resource Planning



Where the selected architect or engineering organization does not have full procurement capability, they generally provide a duty specification for major equipment and bulk materials, and the construction contractor or sub-contractor procures the equipment and material. The Architect or Engineering Organization usually reviews the purchases, and in principle, gives approval or comments. On less complex building projects this method can be successful; however, on more complex projects, such as pharmaceutical R&D or API manufacturing facilities, more equipment may need to be installed in tighter spaces and the risk of dimensional conflicts increases. To minimize this risk, the Architect or Engineering Company, and the construction contractor or subcontractor, should ensure that the equipment selected is dimensionally coordinated with the building structure. This is a substantial activity and should be conducted effectively to ensure that a coordinated installation occurs. The Procurement Plan portion of the PDP should ensure the responsibility for coordination of contractor/subcontractor procured equipment is defined in the contracting documents and also ensure that there is a mechanism to check the quality of this co-ordination work. Within the Project Team, there is typically a space coordinator responsible for these types of issues.

One option is to select full service contractors that provide design, engineering, procurement, Construction Management (CM), and other services. In this case, the full service provider will organize equipment and material purchases to deliver the detailed design (and therefore, coordinate space management) and will issue detailed and coordinated construction documents. This route minimizes interfaces and usually results in fewer installation clashes. The PDP should evaluate the availability of full service contractors and determine if this contracting method is suitable for the project. The Customer should incorporate a higher level of controls, incentives, and monitoring when using this

method as construction management and procurement services mark-up and subcontractor mark-up on equipment can be a significant cost factor.

7.3.3 **Strategy for Contracting**

The overall procurement and contracting procedures and strategies for the project should be developed and included. (These may vary for different options, but they should nevertheless be defined as part of the conceptual development phase). The material and equipment procurement plan requires consideration of issues such as:

- What are the critical long lead items of equipment?
- What are the possibilities to source from low cost countries?
- What are the existing procurement agreements for valves and other bulk items?
- Which items will be single sourced?
- Can e suppliers who have existing items on site be used?
- Is there a possibility of “Bundling” orders for different items via a wholesale supplier or go direct to the manufacturer?
- The procurement plan (a register showing the critical items to be procured and the approximate procurement durations used in the project master schedule).

The contracting strategy focuses on the “high level” approach to contracts:

- How will we divide up the work, e.g., in-house? Design (D) then Engineering Procurement and Construction Management (EPCM), Design rolling into detailed engineering, Full DEPCM, Design Build, or Design-Assist?
- Will construction be split into different packages or will there be one main construction contractor to do everything?
- What contract remuneration form will we used (e.g., reimbursable, lump sum)? Will we use incentives or penalties?
- What form of contract will we use (e.g., in-house general conditions plus specific conditions or FIDIC or IChemE (see Section 7.3.5 of this Guide))?
- The procedure for raising a prequalification request for information, confidentiality agreements, a full request for quotation, evaluating bids, and placing a contract. This should include signature authority levels and signature requirements (i.e., who has to sign what).
- The criteria for evaluating bids (technical capability, commercial evaluation, total cost of ownership).
- The approved list of contractors that will be approached for each contract.
- The contract plan (a register showing all contracts to be placed and the approximate dates for raising enquiries, etc., linked to the overall project schedule).

The enquiry package for the service provider required to support the Project Delivery Planning phase should be produced before the end of the conceptual design phase. Bulk material such as piping, cable, concrete, and other material that does not require physical coordination may be supplied by sub-contractors at minimum risk to the project, i.e.:

- Typically, a schedule of rates is agreed with the contractor.
- A bill of quantities would usually be developed in advance of the purchase order.

The PDP should ensure that if this route is chosen, a mechanism is established to ensure the specified quality is purchased and installed. Other considerations are outlined in this section.

Market Capability

The Procurement Plan should establish criteria for the selection of design companies, contractors, construction managers, and their respective teams and the procedure for deciding supplier lists, award recommendations, and contract signing. The selection process may require several face to face visits and interviews with potential suppliers of material and services. The PDP should ensure adequate time and funding are allocated for this activity. Typical selection criteria include:

- experience in similar size and type of project
- experience on owners past projects
- experience at project location
- size of companies work force compared to requirements of project
- experience of the proposed project team (size, project type, location) and fit with overall project team

Market Competitiveness

Market competitiveness may affect pricing conditions and availability of experienced and capable teams. The Procurement Plan should assess the level of activity in the market and identify sectors that are operating close to maximum capacity and that may have difficulty in performing at the required level. If this situation exists, the Procurement Plan should identify a mitigation strategy that may require a higher level of management supervision for these sectors, or a different contracting strategy. The potential for service providers to share market and project specific information should also be considered and mitigation strategies developed before approaching Suppliers in the market. Mitigation strategies for this risk should be locally developed with specific knowledge of the market conditions.

Expediting and Inspection

Expediting equipment and material purchases provides an important source of information to the project team on vendor and sub-contractor performance. Updated and verified delivery information of critical path deliveries should permit the Project Team to adjust schedules to allow for schedule slippages or to engage early on with the supplier to avoid delays. Where possible, expediting should be a physical “at the supplier” review. Typical expediting activities will include review and verification of:

- equipment design and engineering schedule
- vendor or contractor procurement schedule
- fabrication schedule
- testing and shipments schedule

The PDP should establish criteria for what should be expedited, how often, and who will conduct the reviews. There may be local organizations that can conduct these reviews for a reasonable cost. Alternatively, there may be an affiliate from within the organization in the locality that may be able to assist. These requirements should be estimated and included in the project budget and contracting documents.

Inspection of equipment and materials should ensure compliance with specifications and delivery of quality products. A typical inspection process includes:

- Early visit to supplier to review and confirm understanding of specifications and Purchase Order (PO) requirements.
- Review of material purchases to ensure compliance with specifications.
- Review of fabrication process to ensure quality of sub-systems and material.
- Attendance at acceptance test.

The PDP should establish what should be inspected, how often, and who will perform the inspection. As with expediting, there may be local organizations and sometimes local affiliates that can provide this service. For specialized equipment that may be required for pharmaceutical applications; however, specialized skills may be required. The PDP should ensure these requirements are defined and included in the project budget and contracting documents.

Equipment Protection and Storage

The PDP should ensure that there is a plan to store, secure, and maintain specialized or weather sensitive equipment that may be delivered before facilities are complete or ready for the equipment to be installed. The plan should include a definition of any specific requirements, e.g., storage conditions maintenance requirements. It is considered good practice that the equipment arrives at the site on time to be installed. This should be coordinated between the procurement team and the project team. There may be pressure to move this equipment directly into non-weather tight buildings at the risk of damage to the equipment. Providing a secure storage location for equipment can avoid damage, theft, and help to ensure quality is not compromised. Secure locations can include lock and key storage from which sensitive items and instruments are checked in and out. In addition, particularly on long duration projects, provision for maintenance on equipment before it is put into service may be required. The PDP should identify equipment that may need special handling during construction and ensure requirements are included in the budget.

7.3.4 Procurement Plan Development

The detailed breakdown of how, what, when, and where each package in the Work Breakdown Structure (WBS) is to be procured (whether goods or services) in an activity called procurement planning. This is usually completed in two stages:

- Stage 1 – Procurement Package Definition
- Stage 2 – Procurement Package Delivery Planning

Together the two stages are collated into the Procurement Plan.

Stage 1 – Procurement Package Definition

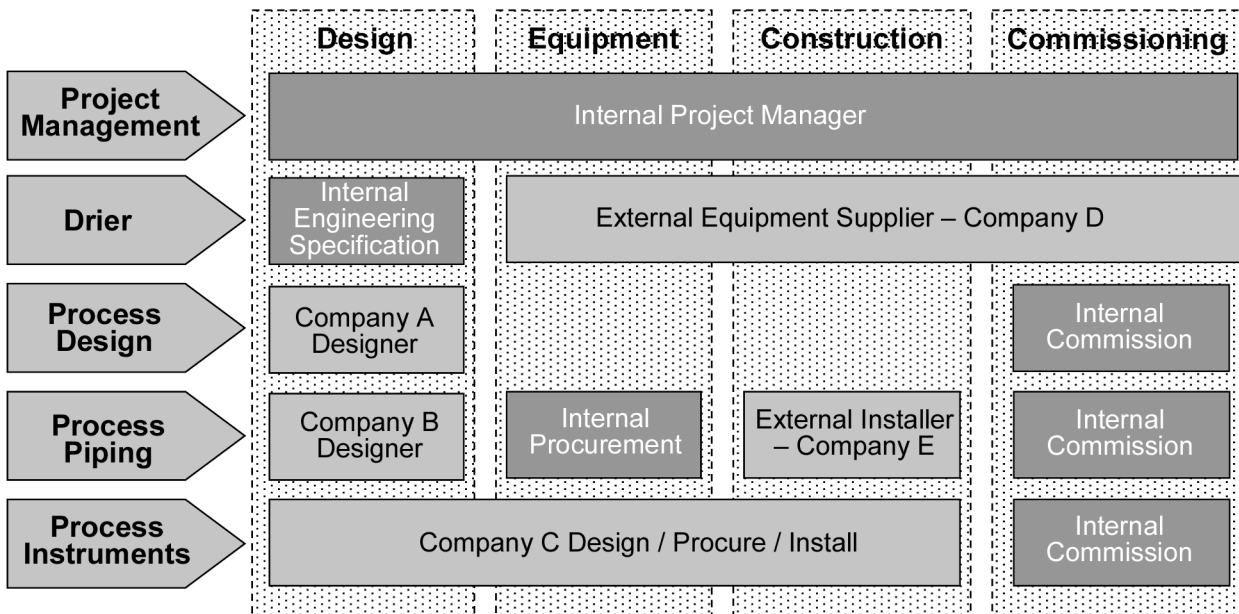
The work packages which fully describe the scope of a project should be divided into discrete, non –overlapping procurement packages. A procurement package for goods, services, or a combination of both should be defined based on several considerations. Within a pharmaceutical project, there are specific considerations in dividing packages (see Table 7.1).

Table 7.1: Procurement Package Definition Considerations

	Technical Ability to Deliver Quality which Meets GxP	Ability to Meet Qualification and/or Verification Needs
Strategy	Risk has been placed within the procurement package which is most able to manage the risk	Division of procurement packages aligns with the qualification or verification plan and systems breakdown
Pre-Qualification	Select suppliers that have the appropriate skills and experience to supply the procurement package	Select suppliers that have the appropriate quality systems in place to generate evidence to support qualification and/or verification Examples include: • Do they understand GxP? • Do suppliers follow the GAMP 5 (Reference 5, Appendix 3) approach? • Do they understand FAT may be part of the wider validation/verification process? • Do they understand the needs for materials certification/certificates of conformity? • Do they have appropriate design and change control processes in place?
Selection	Suppliers proven via bid return that they understand the specific GxP issues associated with this procurement package	Suppliers proven via bid return that they understand the specific qualification or verification issues associated with this procurement package including all documentation requirements
Management	Build in the ability to perform quality audits and performance reviews during the contract delivery	Ensure review of documentation packages is built into the contract management with final packages required to close-out the contract and ensure the contract identifies the quality requirements and deliverables including that appropriate checks/balances are in place?

As a part of the definition typically a matrix is developed to identify contractual boundaries. In the example of an API Drier Upgrade project (Figure 7.6), the four work packages are divided into separate procurement packages requiring the engagement of four external companies plus an internal team.

Figure 7.6: Example Procurement Package Matrix



The procurement matrix allows a review of the boundaries of each procurement package and typically the pharmaceutical considerations are reviewed to check for the placement of GxP and compliance risk. General considerations at this stage, include:

- Ability to get the full procurement package scope from the market:
 - If the packages are not traditionally available in the market, there will be issues in terms of the availability of suppliers to deliver a compliant bid.
- The pricing strategy for the project:
 - The division of the work packages can impact the overall cost: expecting a supplier to take more risk or a non-traditional work scope can cost more.
- The schedule requirements:
 - Packages may be made more bounded to match with design progress and the supply lead time.
- Contractual considerations:
 - Existing supply contracts may be in place, particularly for consultancy, management, or on site installation services and this may drive the boundary of specific packages.

Stage 2 – Procurement Package Delivery Planning

Once the packages are clearly defined, it is usual for some form of procurement milestone plan to be developed as shown in the example provided in Table 7.2.

Table 7.2: Example Procurement Milestone Plan

Package	System Category	Contract Style	Planned Milestone Dates				
			Supplier List	Tender Issued	Supplier Selected	Order Placed	On-site
1. Drier	Direct	Lump Sum	Date x1	Date x2	Date x3	Date x4	Date x5
2. Pumps	Direct	Lump Sum	Date y1	Date y2	Date y3	Date y4	Date x5
3. Control System	Direct	Lump Sum	N/a - Preferred Supplier	Date x2	Date x3	Date x4	Date x6
4. Civil Works	Some Direct but most Indirect or non-impacting	Bill of Quantities	Date z1	Date z2	Date z3	Date z4	Date x4
5. Mechanical Works		Schedule of Rates	N/a - Tender to both site based suppliers	Date z4	Date z5	Date z6	Date x5

The milestone plan links the procurement package to the schedule needs of the project giving the Project Manager a tool to track progress. The shipping method, required duration, as well as any specific customs requirements need to be defined and incorporated into the plan. In the example (Table 7.2), target dates are assigned to each stage of the procurement process for each package. Some packages may be dependent on others and this type of detailed plan can take this into account.

The Procurement Plan

The typical content of a procurement plan is:

- Introduction – detailing key aspects of the strategy and project objectives which are driving the procurement plan
- Procurement Package Matrix – as per Figure 7.6
- Procurement Milestone Plan – as per Table 7.2
- Procurement Plan RACI Chart – detailing the key person to manage the package to completion
- Contractual Considerations – as outlined in Section 7.3.5 of this Guide
- Design Link – the defined flow of information to and from design and in particular any long lead items which may start the procurement process with earlier design information
- Procurement Process to be followed (as outlined in Chapter 7 of this Guide)

The Procurement Plan is a part of the overall Project Delivery Plan (PDP) as defined in Chapter 5 of this Guide.

7.3.5 **Contractual Considerations**

In the procuring of goods or services, the supplier may retain overall responsibility for performance of the service up to the point of transfer of ownership to the Customer. In this respect, it is important that the contract conditions and scope of services clearly define this requirement to avoid any subsequent dispute. If this is not the case, the responsibility for operation, maintenance, and monitoring of equipment that has been set to work needs to be addressed contractually. To ensure that the supplier complies with the required obligations, it is considered good practice to have clauses included in the contract conditions that ensure the supplier is focused on attaining these obligations. Some of the methods used are described in this section of this Guide:

Liquidated Damages

Liquidated damages are a specified sum of monies that the owner can deduct from the supplier for a genuine failure to meet a specific milestone as defined in the contract conditions.

Liquidated damages should be a genuine pre-estimate of costs determined at the time of issuing the enquiry and not at the time the clause is invoked. Liquidated damages may be expressed as a sum of monies due to the Customer for each day or week of delay by the supplier in reaching a specified milestone.

The use of so called “penalty clauses” may not be enforceable in some jurisdictions, and professional legal advice should be sought if applicable.

Performance Bond

A performance bond is a mechanism whereby the Customer is entitled to a specific sum of monies; usually a percentage of the contract sum, for the failure of the Supplier to properly perform the contract or if the Supplier becomes insolvent.

A performance bond will generally incur a cost premium which should be identified at bid stage so an informed decision can be made as to whether a bond should be included.

The bond will generally be provided by a third party surety.

The owner can only get the benefit of the performance bond by demonstrating to the surety that the Supplier has failed in their obligations under the bond.

On Demand Bond

An on demand bond is an entitlement by the owner to draw down a specific sum of monies for the failure of the Supplier to properly perform the contract.

The difference between this form of bond and a Performance Bond is that there may be no requirement for the owner to prove the Supplier failed to perform their duties.

Suppliers can sometimes resist providing Demand Bonds as they may be perceived as another form of discount if invoked without cause by the owner.

Collaborative Working

More recently, the industry has been utilizing more collaborative methods and incentivizing approaches to contracting with good success. Some of these include:

- Shared Savings and Incentives:

- There are several ways to execute a shared savings program, but the principle of the methodology is that a budget or target cost is agreed between the parties for a defined deliverable and any savings on that budget cost is shared between the parties at an agreed percentage. It is critically important that these programs should be enacted to assure that Suppliers are not incentivized to sacrifice safety or quality for cost savings.
- Another more innovative Shared Savings program involves establishing a “fund” separate from the budget to cover unexpected occurrences within the scope of the project. Owner driven changes in scope or schedule are excluded. Any unspent portion of the “fund” is shared. With this program, the incentive is to deliver within the original budget and minimize the use of the “fund.” The Supplier has control of the “fund” with monitoring by the Owner and approval required over certain spending thresholds.
- Incentive programs are quite common in the construction environment, especially with government projects for infrastructure such as highway projects. These programs are often driven by meeting or beating schedule and provide a financial award tied to meeting or beating a particular completion date; usually, the earlier the delivery to higher the award.
- Shared Savings or Incentive programs should be established with Key Performance Indicators to assure that the Supplier delivers with an impeccable safety record, on schedule, and under well managed and maintained change management systems. This will be key to a successful dispute free program.
- Key Performance Indicators (KPIs)
 - For complex process systems, the use of Key Performance Indicators (KPIs) associated with payment milestones is a method to ensure the plant or equipment operates to its specified capacity over a specified period.
 - The contract should be managed (see Section 7.3.5 of this Guide). Record keeping is fundamental to the proper initiation or defense of claims and disputes. The conditions should be understood and a claim should be initiated and defended in accordance with the specific conditions.

Documents for a Procurement Package

Documents forming part of a procurement package Request for Proposal (RFP) usually fall into the following general categories:

- Terms and Conditions
- URS including all relevant technical drawings or specifications
- Commercial Pricing Documents, if applicable
- Confidentiality Agreement, if applicable
- Other documents as necessary to support the enquiry which if not issued may subsequently have a cost or schedule impact

These categories should be used to manage document flow contractually. The conditions or technical documents should stipulate the format, quality, and quantity of documents to be submitted. They should also indicate the time frame required by owner to review and comment on submittals.

Terms and Conditions

Terms and conditions should address key issues to help to eliminate subsequent disputes. Table 7.3 provides a list of some examples.

Table 7.3: Example Terms and Conditions Considerations

Key Issue	Benefit	Risks
Order of Precedence of Contract Documents	Critical to avoiding or minimizing disputes between documents.	Dispute arises over which commercial or technical document takes precedence resulting in potential additional cost.
Confidentiality and Publicity	Protects owner propriety design information. Reduces unnecessary publicity.	Key owner information passed to third parties. Project kept from the public domain if deemed necessary.
Intellectual Property	Propriety design, trade secrets, copyrights, patents, etc, developed as parts of the project are vested in owner.	Owner loses benefit.
Indemnity and Insurances	Specified insurances like: • Employer and Public • Product and Professional are in place with Supplier or Owner as appropriate.	Supplier under insured exposing owner to claim from third parties. Owner unable to pursue Supplier for design negligence.
Payment and Invoicing	Clearly defines mechanism for making payment	Dispute arising due to late or non-payment.
Warranties and Guarantees	Owner knows that the equipment is fit for purpose and has a mechanism for recourse to the Supplier if defective or non-performing.	Replacing defective parts or equipment at own cost.
Cancellation	Establish pre-agreed mechanism for establishing costs if contract cancelled. Particularly important.	Exposure to unreasonable costs that can often be hard to validate.
Law and Dispute Resolution	Eliminate jurisdiction confusion and agree how disputes are resolved.	Protracted and costly.

Forms of Contract

There are various forms of contract used within the industry. These can be owner bespoke forms of contract or industry standard forms. The decision on which form of contract to be used is dependent on the procurement strategy being chosen. Examples of some typical contract options include:

- Owner Led Contract
- Construction Management Contract
- Management Contract
- Design Build Contract
- Lump Sum Turnkey Contract

Legal advice should be sought whenever amending standard forms of contract or adding special conditions to ensure the amendment does not invalidate the contract or contract condition, or cause conflict with another clause

The selected contract must deliver the Procurement Strategy. It needs to be considered early in the Procurement Strategy stage and should take account of design, construction, operation, and maintenance.

Figure 7.7 highlights some typical procurement routes which are defined as follows.

Figure 7.7: Typical Procurement Routes

Procurement Route	Early Completion	Financial Certainty	Quality
Prime Cost and Prime Cost + Fixed Fee	✓	✗	✓
Management Contract	✓	✗	✓
Construction Management	✓	✗	✓
Two Stage Tender	✓	✓	✓
Approximate Quantities	✓	✗	✓
Firm Quantities	✗	✓	✓
Specification and Drawings	✗	✓	✓
Design and Build	?	✓	?
Turnkey	?	✓	✓

Notes for Figure 7.7:

- “?” indicates the activity may be at risk depending on when the activity starts or the quality of the Employers Requirements.
- *Prime Cost /Prime Cost + Fixed Fee* – this is a cost plus form of contract whereby the contractor gets an agreed mark-up on the base cost of labour and materials.
- *Management Contract* – agreement between client and a management company engaged for coordinating and overseeing a contract for a project. It spells out the conditions and duration of the agreement and the method of computing management fees. The Managing Contractor in turn engages and manages all the necessary trade contracts/sub-contracts.
- *Construction Management* – while all contracts will be held directly by the Customer, the construction management organization will tender, award, manage, and coordinate all the contracts on behalf of the client.
- *Two Stage Tender* – a contract is tendered at an early stage of design to select a preferred bidder and the scope is then re-tendered once design is complete based on the original tendered rates.
- *Approximate Quantities* – a contract is tendered based on a schedule of approximate quantities developed by the Project Team or Supplier. Final quantities are generally only determined after they are installed on site or in some instances on the issue of construction drawings.
- *Firm Quantities* – a contract is tendered based on a schedule of firm quantities developed by the engineer. Design will have to be well advanced for this route to be effective. In this context firm refers to an accurate but not fixed schedule of quantities.

- *Specifications and Drawings* – a contract is tendered based on specifications and drawings developed by the engineer. Design will have to be advanced for this route to be effective. Changes post tender to specifications and drawings will incur additional costs.
- *Design and Build* – a contract whereby a contractor takes responsibility for design and construction based on an Employer's Requirements brief. The Employers Requirements have to be very specific as items overlooked are not included in the contract price and may become an extra. Quality may often be priced to meet the minimum requirement of the Employer's Requirements so special emphasis should be given to this area.
- *Turnkey* – a contract where one party takes full responsibility for the design, construction and commissioning of plant, delivering the plant (facility or equipment within a facility) in full working order to the Customer based on the Customers' Requirements.

Examples of available standard forms of contract include:

- Federation Internationale des Ingenieurs Conseils (FIDIC) International Forms of Contract:
 - The Red Book – Design by Employer
 - The Yellow Book – Plant and Design-Build
 - The Silver Book – EPC Turnkey
 - The Green Book – Short form contract for small capital works
- Institute of Chemical Engineers
 - Green Form of Contract – Reimbursable
 - Red Form of Contract – Lump Sum
 - Orange Form of Contract – Small Works
 - Burgundy Form of Contract – Target Cost
- International Chambers of Commerce (ICC)
 - Turnkey Supply of an Industrial Plant Contract
 - Major Project Turnkey Contract
- New Engineering Contract NEC Form of Contract

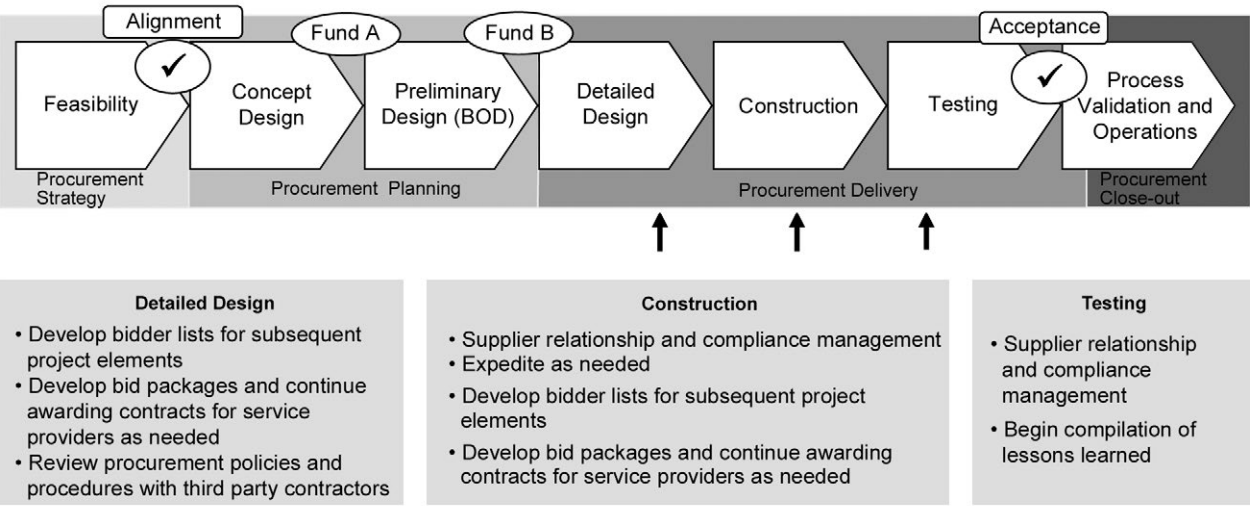
Caution should be taken in using a standard form of contract or owner bespoke contracts outside of their normal jurisdiction as changes will generally have to be made to area of law, safety, insurance, etc.

7.4 Procurement Delivery

7.4.1 Introduction

Upon completion of the Procurement Plan, it is likely that the project will be entering the detailed design phase. This is typically when procurement starts delivery and continues throughout the project (Figure 7.8).

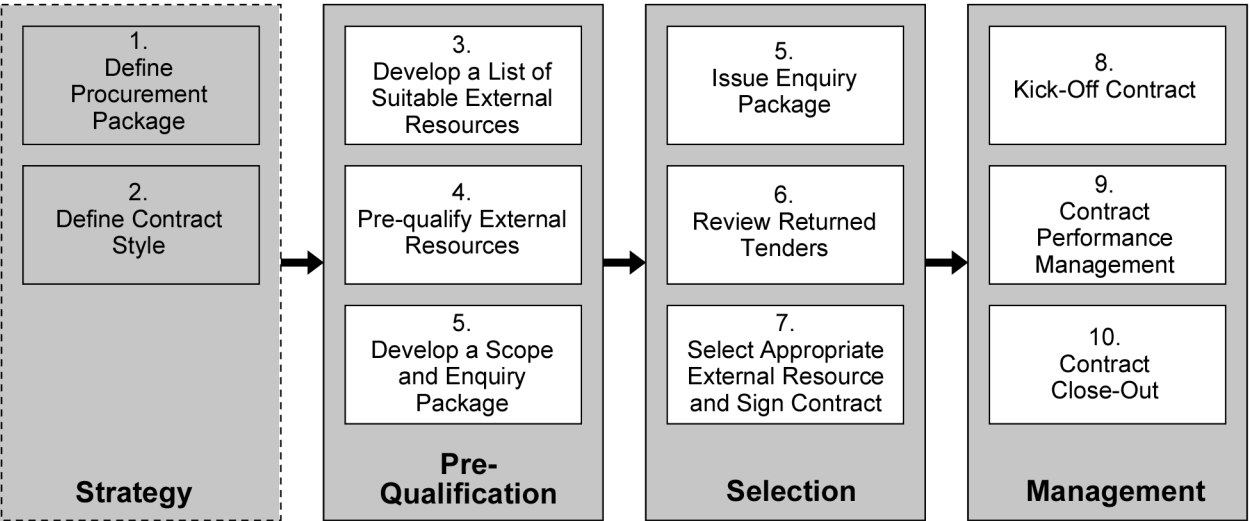
Figure 7.8: Typical Capital Project Process – Procurement Delivery



There are typically three stages (see Figure 7.9) of procurement delivery following development of the strategy:

1. Pre-Qualification
2. Selection
3. Management

Figure 7.9: Typical Procurement Delivery Process



The Project Manager should engage with the appropriate procurement professionals during the initial stages of the procurement delivery process to ensure that the strategy, plan, and objectives of the project are not compromised.

7.4.2 *Pre-Qualification*

Developing a List of Suitable External Resources

The project objectives and the procurement strategy will define whether goods and services will be obtained by a single/sole source or competitively tendered. Within the pharmaceutical industry, the overhead of qualifying and managing suppliers for GxP critical services and equipment coupled with the significant life-cycle costs of maintaining the compliance of critical equipment should not be under-estimated, particularly for specialist areas. Initially, Project Managers should consider the organization's preferred list of suppliers. This should usually enable a suitable list of external resources to be established for the project.

Where novel technologies or equipment are necessary, particularly during the definition and design stages of the project, the approach to procurement may be more collaborative with more potential for sharing of risk between the parties involved. If the project includes a new technology, it could be a critical issue for the current products (developed with other technologies). At this stage, it is recommended to test the feasibility of new equipment (technology) with a pilot batch of product to assure proof of concept at a scale close to that of production.

Pre-Qualify External Resources

It is considered good business practice to pre-qualify potential suppliers down to a small group, e.g., three or less, for the project.

The effort required for pre-qualification can depend on:

- the size of the list of potential suppliers
- the complexity (or novelty) of the project
- the time-scale
- the costs
- risk to the project

In many cases, the financial stability of a supplier will be verified prior to defining a bid list. For example, a small, low-cost project would not be suitable for an extended list of suppliers to be led through several weeks of pre-qualification exercises. In this case, the Project Manager usually pre-selects a supplier from a list of previous contracts and enters scope and formal enquiry discussions immediately.

For more complex or more expensive projects, the use of a more formal process for the pre-qualification may be appropriate. Typically, the pre-qualification process is used to answer the following questions:

- Can the supplier deliver the equipment and/or services required?
- Do they have adequate available capacity?
- Is the anticipated cost within the budget for the project?
- Does the supplier understand the validation life cycle and has the supplier accounted for the necessary documentation and qualification or verification steps? Can the supplier meet necessary GxP requirements for the project, e.g., construction material traceability, generation of production/revision records, pre-delivery cleaning, and prevention of contamination during delivery?
- Is the supplier financially viable?

Current workload and current overtime being worked are data points which may be used to help confirm capacity constraints or raise discussions points.

The most effective way to establish the answer to these questions is to use a Request for Information (RFI). This is a formal enquiry which may contain:

- The outline of the requirements for supply from the supplier, typically expressed in terms of overall project objectives, e.g., supply of an air handling unit capable of “x” cubic meters per hour or a process control system with 500 I/O.
- Appropriate project requirements and standards and a request that the supplier confirm their ability to meet the requirements or not.
- Validation requirements of the project, potentially expressed in terms of the qualification or verification activities expected. This should be led by the risk assessment performed on the project scope and ensure that the focus is in line with the risk.
- Request for information on the supplier’s financial status (unless this is available from external sources).
- Request for information on the supplier’s proposed approach to deliver the project (project organization, control processes, etc.)
- Request for a budget estimate of the costs (to a defined level) and schedule for delivery.
- Request for a response against the anticipated commercial terms and conditions for the project.
- For specialized equipment, the supplier’s ability to provide suitable support and ongoing maintenance requirements, as required.

Where a new supplier is to be used, it may also be necessary for an audit of the supplier to be performed to confirm that the required levels of quality for the project can be met. Sufficient time and effort should be allowed for and the Project Manager should work during this pre-qualification stage to address any audit issues that might arise.

RFI responses should be evaluated through separate technical and commercial rankings. Typically, the technical review will score against the requirements while the commercial review will “standardize” the costs from all responders to ensure that a like-for-like comparison can be made.

The Project Manager should be looking at the pre-qualification stage for up-to-three suppliers to progress. Lack of suitability of a supplier or suppliers may be indicated if the evaluation shows:

- significant differences in cost (> 25%) and/or schedule
- major exceptions to the project requirements
- issues arising from audits
- specific GxP concerns, where a supplier has either limited or no experience and their existing internal procedures will not easily support such requirements
- major exceptions to commercial terms and conditions

Either or both of the first two indications would tend to imply unclear or inadequate requirements. Major cost differences for the same scope should be investigated to understand whether the difference is “real” or as a result of aggressive initial costing.

Either of the third or fourth indications would suggest that while a supplier may be able to supply the required scope, they may represent an unacceptable risk to the overall completion and handover of the project.

Significant exceptions to the commercial terms and conditions are likely to lead to extended discussions between the supplier and the Project Manager's legal team that could significantly impact the time to agreement. At this point, the Project Manager should be deciding on the short-list of up-to-three suppliers for the formal enquiry stage of the project.

Development of a Scope and Enquiry Package

The formal enquiry process is an extension of the RFI used for pre-qualification. The major difference is in the technical and commercial detail sent to the supplier and expected back.

The enquiry or Request for Proposal (RFP) package represents a significant effort, as it will almost certainly result from design activities being undertaken in the project. The Procurement Plan should be used to define the outline of each major RFP package, including the appropriate terms and conditions, technical documents such as specifications, standards, as well as those relating to project scope.

The Request for Proposal is intended to obtain a response from the supplier against which an order can be placed. As such, the RFP should contain specific requirements and a clear list of services and/or deliverables required (with adequate technical details where appropriate). The response from the supplier should contain:

- a statement of acceptance of the requirements
- a statement of acceptance of the commercial terms and conditions
- a clear list of services and deliverables
- a clear and itemized list of costs for the services and deliverables
- a clear statement of cost for change

7.4.3 Selection

Issue Enquiry Package

Having pulled together the package for the enquiry, the Project Manager should ensure that a robust process exists for the enquiry and selection process.

An equitable and clear approach to dealing with the package, queries, and responses should be maintained. Initially, the package should be issued to the appropriate people in an organization with clear instructions to cover:

- The bid-period – ensuring that there is a clearly defined date and time by which the bid should be returned.
- Clearly defined format of the response – typically involves the separation of commercial and technical responses, the delivery point and person.
- The contact for bid submission and queries – nominating one person to act as the contact point for queries, both commercial, and technical. The procurement person on the project may be suitable and they can route queries to the correct source.
- Establishing the approach to dealing with queries – a usual approaches is that the query (once made anonymous) and the response are copied to all bidders to ensure no advantage.

The bid-period should be fair and reasonable. The Project Manager should make a considered decision as to the length of time it will take to respond to an enquiry. There may be a temptation to take as long as possible to produce the enquiry package and expect the supplier to respond rapidly to maintain the schedule. The project manager should be realistic and flexible; a quality response to an enquiry is required to make a considered decision.

Increasingly, electronic procurement methods are being used to handle the enquiry and proposals process. Using electronic procurement approaches will still require the same attention to detail as for the traditional process.

For some items of equipment or services, reverse auctions (where suppliers compete to obtain business) may be appropriate. The nature and limitations of the reverse auction approach should be understood. Typically, these types of auctions are useful for commodity or well defined and understood items. These types of auctions may not be appropriate for complex proprietary items.

Review Returned Tenders

The response from the enquiry process is the tender; contractually, this is an offer for services and/or equipment and its acceptance leads to a contract. The evaluation of the tenders is, therefore, considered a critical step in the procurement process. To ensure objectivity, the project team should establish the selection criteria and selection process steps in advance of opening tenders. It may be useful to share appropriate aspects of the selection criteria and process as part of the enquiry package. The review process will generally go through the steps described in this Section of the Guide.

Technical Evaluation

The technical team should review the content of the tenders to determine:

- Whether the offer meets the critical technical requirements and are there any unacceptable exceptions?
- What does the project delivery model look like and what are the deliverables from the supplier? Do they meet the project requirements and will the approach fit?
- Can the supplier meet GxP requirements appropriate to the project scope and deliverables? Have prequalification considerations been confirmed as acceptable?

The intention of this stage is to rank the suppliers in terms of technical capability and identify whether any should be eliminated at this stage on technical grounds.

Commercial Evaluation

The commercial team, a part of the project team plus procurement, should work with the supplier to ensure that adequate detail is contained in the proposal to allow standardized costs to be established for each supplier. Lump-sum costs from a supplier may not be suitable, as the exact scope of supply for each supplier will be different. The commercial team should consider:

- Whether all requested costs are included?
- Whether the detail provided will allow the cost of change to be adequately managed?
- Whether the commercial terms and conditions will be met?

The intention of this stage is to rank the suppliers in terms of the commercial offer and identify whether any should be eliminated on commercial grounds.

Post-Bid Presentations

For more complex or critical components of the project, suppliers may be invited to present their bid to the Project Team. Typically, these will be technical rather than commercial proposals and may include demonstrations of how specific requirements will be met. Post-bid presentations require significant effort both from the suppliers and the Project Team (most (if not all) of the suppliers should be invited), so this activity should be limited to critical elements of the project.

Selection

Following the initial RFI and RFP process, the Project Team will be presented with a choice of suppliers (ideally two or three suppliers) for key project elements.

At this stage, the selection process should extend from the “will it do it” and “is the price right” stage to a consideration of wider factors, in effect a procurement risk review:

- What is the supplier's previous experience, either in the pharmaceutical industry or with the organization?
- What is the total cost of ownership of the equipment?
- For major investments, the life cycle may extend beyond 10 to 15 years. Are there costs associated with routine maintenance or software support/upgrades? These life-cycle costs should be considered and may exceed the capital project spend by an order of magnitude.
- How well does each Supplier fit the culture of the Owner's Organization?
- How well and at what cost can each candidate provide after the purchase support in both service and parts? This is particularly important in foreign markets where some suppliers will have less support capability.
- Are there any specific opportunities presented by one supplier above another? These could include:
 - Diversity – some companies have obligations to provide a proportion of business to Suppliers that meet certain diversity criteria.
 - Increase the pool of qualified suppliers available for future business. This might be an advantage where one Supplier has a disproportionate share of business and there is a desire to increase competition.

Once the selection decision has been made and documented, the next stage is to finalize the contract with the selected supplier. At this stage, it is considered desirable to have an alternative available, both as a commercial lever and as a fall-back in the event of a failure to close the negotiations.

Select Appropriate Resource and Sign Contract**Contract Negotiations**

Negotiation is the process of discussion in order to reach an agreement. Negotiation is not the application of power to achieve an end. At this stage of the procurement process, contract negotiations should be used to clarify points in the proposal and look for opportunities to establish cost savings.

The Project Manager with procurement support should approach the negotiation process with a realistic assessment of what is achievable (often gained through experience). Entering into a contract negotiation to dramatically reduce the cost of a piece of equipment or significantly increase the scope of supply for the same cost can be difficult. If this is required, it may reflect that fact that the requirements, pre-qualification process, or budget are inadequate. Incorporating incentives and defining the incentive program may be considered at this point in the process.

Contract

The contract is the end result of the enquiry, proposal, and negotiation process. It needs to accurately reflect the agreed scope of work, schedule, costs (including any penalties or performance bonuses), and terms and conditions. These details should be captured in the contract to avoid later discussions for the inclusion of items that were considered agreed.

Finally, and most importantly, remember to raise the purchase order! It is surprising how many projects have floundered through the omission of this vital step. The length of time that this process can sometimes take should not be underestimated and especially for large contracts or equipment items where multiple and sometimes off site approvals are required. Such considerations should be made during planning for stakeholder management and engagement with the project sponsor. Advances in e-procurement have made this final step a natural progression from negotiation.

7.4.4 Management

Kick-Off Contract:

Kick-Off Meeting

Once orders have been raised and contracts launched, it is recommended, subject to the order/contract size and complexity, to hold a kick-off meeting with the supplier and Project Team. Some key items to be addressed at the kick-off meeting are:

- Safety
- Communications – responsibilities, contact details, response times
- Contract Administration
- Management Structure
- Documentation and Deliverables
- Risk Summary

Notwithstanding the size of the Order/Contract, regular progress meetings/teleconferences should be held to monitor the progress of the Order/Contract. Examples of issues that may be discussed are noted in Table 7.4.

Table 7.4: Example of Kick-off Meeting Topic Items

Discussion Topic	Owner	Supplier
Safety	- Confirm safety objective of the project. - Confirm all design and construction related safety requirements. - Initiate any statutory safety obligations.	- Safety induction requirements established. - Statutory safety obligation confirmed. - Safety representative, if applicable, confirmed.
Communications	- Confirm communications flow process. - Confirm formal method of communication. - Document collaboration Web site, email, etc. - Confirm meeting requirements and frequency. - Provide decisions with agreed timescale – track GxP critical decisions. - Agree single point of contact for technical and commercial issues.	- Submit FAT and SAT schedule. - Submit manufacturing and delivery schedule including critical sub-suppliers. - Provide design information as per agreed timelines.
Contract Administration	- Confirm and adhere to change order procedure as per PO/Contract conditions. - Confirm invoicing procedure. - Confirm all necessary insurances, bonds, guarantees, etc., are in place. - Management of change within agreed procedures – linked to overall compliance control process.	- Notify cost or schedule impact variations in accordance with PO/Contract conditions. - Submit invoices as per agreed time and payment milestone schedule. - Submit copies of insurance policies. - Review and assess impact of change requests within agreed timescale.
Management Structure	- Confirm management team. - Identify roles and responsibilities of team.	- Submit project organization chart. - Notify any proposed changed to team, if allowed.
Documentation/Deliverables	- Confirm documentation requirements as per User Requirements Specification (URS), noting critical parameters and GxPcritical aspects. - Review and comment on submittals in accordance with agreed timelines.	- Confirm FAT and SAT procedures. - Submit documentation as per agreed timelines. - Submittal and approval process to be followed at design, fabrication and commissioning stages.
Risk Review	Review of risks within the area of scope covered by the contractual scope.	Risks as viewed by the supplier and proposed mitigation strategies.

Contract Management

Contract Administration – Variations/Change Management

Purchase Order and/or Contract conditions should address how variations/change orders are to be managed. If not properly addressed, the Supplier/Contractor can hold the owner/project effectively at ransom, by delaying manufacturing/construction until costs are agreed.

Commercial conditions should ideally have a time barring clause for variations, e.g., “the Supplier/Contractor must notify the owner in writing within a certain number of days of becoming aware of a variation” otherwise they lose

their entitlement to that variation. A requirement that the works progress while the variation is being agreed may be considered prudent, and can avoid manufacturing and schedule delays.

Assessment and approval of variations/change orders should be performed in a timely manner to help to maintain good relations with Suppliers/Contractors.

Contract Administration – Contractual Issues

During the course of an Order/Contract, a contractual issue can arise; in order to defend against a claim from a Supplier/Contractor the project team should follow simple guidelines, e.g.:

- Maintaining records of all correspondence; both hard and soft copies.
- All correspondence in writing, or confirmed in writing.
- Proper filing of hard and soft copy correspondence.
- Make no commitments outside of owner team's remit.
- Seek professional procurement or legal advice at an early stage if unsure on course of action.
- Do not commit to paper or email anything that may harm the defense of a claim if the correspondence subsequently becomes the subject of a discovery order, e.g., if legal proceedings are initiated.

Contractual claims and disputes should be dealt fully in accordance with the Order/Contract conditions.

Documentation Management

Proper document management should be used to ensure successful Order/Contract close-out and project start-up. Without some form of proper document management system, it may not be possible to:

- Confirm a document deliverable milestone has taken place; hence delaying payments.
- Defend a claim against late owner approval impacting on late delivery.
- Start the IQ stage of the project and/or progress IQ successfully.

The document management system should link into the document deliverables requirement of the URS/Order. Documentation should be tracked on a regular basis to ensure:

- Documentation is received on schedule.
- Specified copies are received.
- When collated, comments are returned to the Supplier/Contractor.
- Record of pre-Factory Acceptance Testing (FAT), if applicable.
- Record of FAT.
- Record of Commissioning/Site Acceptance Testing (SAT).
- When handover documentation packs are received.

- Qualification/commissioning documentation received on schedule.

Roles and Responsibilities

In the management of the procurement process key Customer team members, applicable Architect/Engineering organizations and the Suppliers/Contractors, should clearly understand their roles and responsibilities within the project. This should help to prevent delayed decision making and poor communications which may delay delivery of key deliverables, equipment, or services.

Depending on the selected procurement strategy, the roles and responsibilities of the team members may change from one project to another and especially the input requirements of Suppliers/Contractors. This can be particularly important where there is early Supplier/Contractor involvement in the procurement process. The development of a responsibility matrix or RACI Chart can be a useful tool to aid in the successful delivery of a project. It can cover all the stages of the procurement process such as the:

- Planning Stage
- Pre-Bid Stage
- Fabrication and Delivery Stage
- Commissioning, Start-Up, and Close-Out Stage

Alternatively, it can focus on one or two critical stages as deemed appropriate by the Project Team.

At contract close-out, all Supplier/Contractor deliverables should have been received and all tests should have been performed, witnessed, and accepted by the owner. Risk of advance or over payment may result from failure of a proper close-out process. It may also result in a greater risk of a delay to equipment or facility start-up. Some key items are identified in Table 7.5.

Table 7.5: Typical Contract Close-Out Checklist

Discussion Topic	Owner	Supplier
O and M Manuals	Specified quantity and format received.	Impact on maintenance and operation.
Material Certificates	All certification as specified in URS is received.	Delay or Failure of IQ/OQ/PQ stages of project.
FAT Certificates	All certificates received.	Delay to SAT.
SAT Certificates	All certificates received.	Delay to OQ/PQ.
Spare Parts	Specified spare parts received.	Delay to commissioning and start-up.
Material Guarantees and Warranties	All specified guarantees and warranties received in accordance with terms and conditions.	Dispute on warranty period. Failure by Supplier to replace products under guarantee.
Performance/On Demand Bond or Guarantees	Specified Bond or Guarantee is in place as per conditions of contract.	Owner incurs additional cost for non performance of Supplier/Contractor.
Final Account Agreement	Signed off agreement on value of final account.	Unforeseen commercial issues arising on orders/contracts deemed closed out.

Table 7.5: Typical Contract Close-Out Checklist (continued)

Discussion Topic	Owner	Supplier
Retention	Reduction/Releasing of retention monies in line with contract conditions.	Monies release too early which may impact on timely remedying of defects by Supplier/ Contractor.
Back Charges	Any relevant back charge to the Supplier/ contractor has been notified to them and their account adjusted accordingly.	Genuine back charges to Supplier/ Contractor have been passed on hence reducing costs.
Supplier/Contractor Evaluation	Evaluation of Suppliers/Contractors performance by project team.	Inadvertent re-use of poor performing Supplier/Contractor.

On completion tests should be correctly signed off and witnessed by the Owner to ensure that equipment/systems meet the requirements of the URS and to prevent delay or rejection at Operational Qualification and Operational Qualification stages. Delegation of sign off or witnessing authority should be recorded on an individual basis and should be by exception only. Pro-forma test and acceptance forms should be used wherever possible which record all relevant testing and acceptance parameters.

Supplier/Contractor Evaluation

Supplier/Contractor performance evaluation should be used to maintain an up to date Supplier/Contractor database and to ensure poorly performing suppliers are identified. At order/contract close-out, some form of performance evaluation should be undertaken; typical contents for evaluation can include:

- Safety
- Documentation
- Quality
- Cost/Financial
- Schedule
- Management Systems

A simplified rating system may be more effective than complex scoring systems, e.g.:

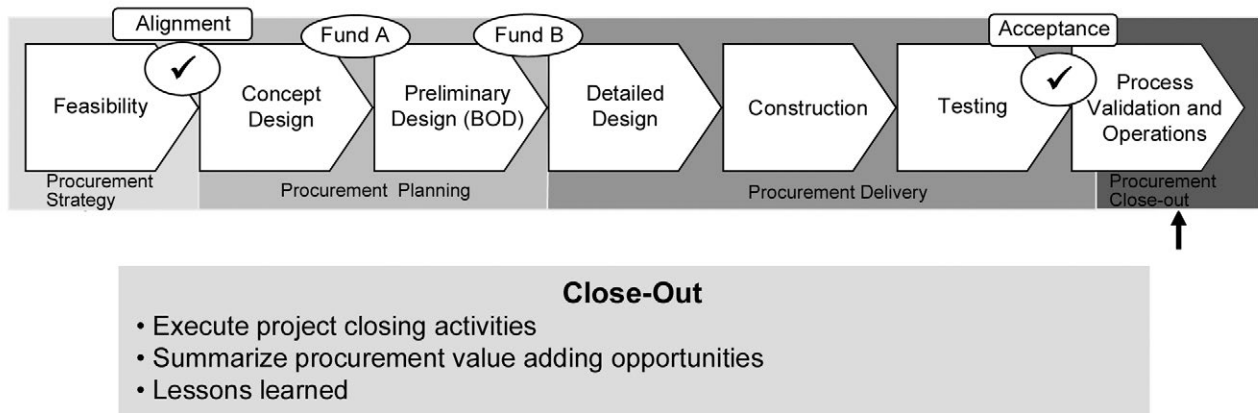
- Exceeding Expectations
- Meeting Expectations
- Below Expectations

The results of the evaluation process should be communicated with the Supplier/Contractor and the Supplier/ Contractor should be allowed the opportunity to discuss and revise the evaluation if deemed necessary.

7.5 Procurement Completion

In addition to closing the individual contracts, there are Procurement considerations and involvement, depending on the size of the project and accounting rules, for the capitalization of the assets being put in to operation (see Figure 7.10). For further information on aspects related to project close-out, see Chapter 10 of this Guide.

Figure 7.10: Typical Capital Project Process – Procurement Close-Out



Procurement related project closing activities should be considered in the Procurement Plan and PDP, including:

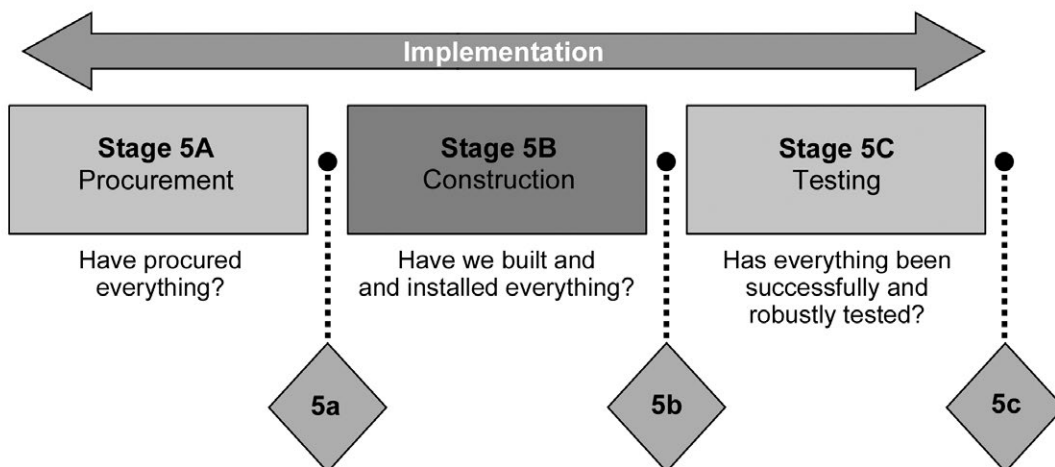
- Purchase orders fully invoiced, paid and closed (including taxes and freight).
- Procurement files are up to date and complete for all purchase orders on the project with signed RFP, PO, signed contract, bids or sole source justification as appropriate and final Lien waivers on file for all subcontracts.
- Any procurement value adding/cost savings are recorded as appropriate.
- All commercial issues closed (i.e., tax and legal issues, service agreements, punch list).
- Participate with the project core team in Lessons Learned activities and be prepared to discuss the success and opportunities experienced with the execution of the Procurement Plan.

8 Implementation: Construction

8.1 Introduction

Pharmaceutical construction projects typically encounter a variety of challenges that include meeting GxP requirements, constructing within operating pharmaceutical facilities, accelerating construction prior to design completion, changing business drivers, updated regulatory requirements and on-going process development. The construction team's goal is always to provide a successful turnover of the project to the Testing Teams achieving a smooth hand over of systems, areas, and documentation to an agreed sequence that supports the ultimate success of the project. This chapter focuses on how the construction team can successfully address and overcome unique challenges presented by pharmaceutical construction projects.

Figure 8.1: Typical Project Life Cycle – Implementation



While the focus of this chapter is on facility projects, the key concepts are applicable to other project types within the pharmaceutical industry that require some form of construction or installation, e.g., IT projects.

8.2 Who Provides the Construction Input?

Given the technical complexity, quality, and schedule demands, experienced construction personnel should provide early input to the project design and implementation planning. The responsibility for this construction input will vary depending on the project contracting strategy and the project stage; however, typical responsibilities are shown in Table 8.1.

Table 8.1: Construction Input Responsibilities

	Project Stage			
Contract Strategy	Initiation	PDP	Design	Implementation
EP and Separate CM	Owner	CM	CM	CM
EPCM	Owner	EPCM	EPCM	EPCM
Design and Build	Owner	Designer or Consultant CM	D and B	D and B
General Contractor	Owner	Designer or Consultant CM	Designer	GC

The Project Manager should arrange for the appropriate construction expertise during each project stage. Particular attention should be given to the Initiation and PDP stages or those situations where the construction team are not yet engaged (and therefore not yet a part of the Project Team). References to the “construction manager” in this chapter should be understood in the context of who is providing that input at that particular stage of the project.

8.3 Preconstruction

The importance of planning should be considered. Allowing the amount of time needed to effectively plan a project can be compensated for by providing a more cost-effective project delivery and earlier completion date. Having a comprehensive plan is considered a pre-requisite. Preconstruction is the term given to the initial construction strategy development and planning; it is typically performed during the PDP and Design stages of the project. (See Appendix 1).

On complex projects, preconstruction is considered the most critical phase of construction. During this time, the Customer, Architect/Engineer (A/E), and other Project Team members such as the Construction and Testing leaders should collaborate closely to produce an agreed construction execution strategy that will be essential to the success of the project.

The core components of a construction plan include:

- Site Considerations
 - Site Layout and Management
 - Path of Construction
 - Constructability
 - Restraints on Construction
 - Responsibilities for Obtaining the Necessary Permits
 - Safety
 - Provision of Site Power and Lighting
 - Fire Detection/Protection

- Environmental
- Drainage
- Construction Methodologies
 - Project Objectives
 - Project Delivery Approach
 - Project Team Organization and Contracting
 - Construction Objectives
- Equipment Procurement Strategy
 - Equipment Procurement Strategy
 - Issues Resolution/Change Management
 - Performance Monitoring Procedures
 - Schedule and Cost
- Quality Management
 - Quality Control and Assurance Procedures
- Project Turnover Procedures

Effective preconstruction planning and communication during the construction phase allow the project team to focus on other important issues later in the project.

8.3.1 Site Considerations

Site Layout and Management

On new or existing sites, construction activities can cause significant disruption to surrounding neighbors, businesses, or operating facilities, and also affect construction productivity. The PDP should include a detailed plan to create access for construction equipment, material, and personnel that will minimize the impact on surrounding areas. In addition to access, in some locations, a wider site infrastructure may be required. This could include changing rooms, food service, and first aid or medical services, as well as road cleaning of neighboring roads. Security, particularly on an operating pharmaceutical facility, should be reviewed early and the results included in the PDP. In general, Site Management issues will result in a cost to the project and early planning can ensure that the costs are correctly estimated and included in the project budget.

Path of Construction

The term “path of construction” refers to the direction and sequence in which the facility build progresses onsite; it is a key decision for the project team as it can drive aspects such as the facility design concept and the sequence of design production.

Constructability

Constructability Reviews of the facility design before construction starts are considered an essential part of construction planning. The PDP should establish the goals of Constructability Reviews and at what points in the project they will be conducted. Constructability should be a part of the integrated approach to managing design risk within the project. Senior construction staff should be required to be involved in these reviews. The PDP should identify where the required resources for these reviews will come from and ensure that any costs required to conduct these reviews are included in the project budget. The PDP should also establish a dispute resolution mechanism to quickly resolve differences of opinions (i.e., designer versus builder) during these reviews. The PDP should also identify any follow-up reviews to ensure recommendations are implemented.

Restraints on Construction

The PDP should identify restraints on construction due to site location and/or project complexity.

- Site restraints could be caused by noise, restricted working hours, overhead obstructions, vibration (proximity to rail networks), or other local issues that could impact construction.
- Restraints due to complexity could result from high-density piping and equipment areas that limit the number of operators that can progress the work.

Both of these types of restraints could impact total cost and schedule and should be identified in a PDP and included in the cost and schedule estimates.

Safety

Construction safety should be considered a high priority. The PDP should establish the project's Construction Safety goals and define what steps should be taken to achieve them. These steps may include Safety and GxP Induction programs for workers before they are allowed on site, sub contractor/contractor safety history performance as a qualification for selection, and when and if Safety Incentive programs are required. These items should be identified and costs for these programs included in the project budget.

Equipment Procurement Strategy

This should be considered when planning construction. See Chapter 7 of this Guide.

Quality Management

Construction should integrate quality risk management into its ways of working to ensure that risk to patient is not affected by construction activities or outcomes (see Sections 8.3.6 and 8.4.5 of this Guide)

Project Turnover Procedures

Preconstruction planning including the planning of construction completion and handover for testing (see Section 8.5 of this Guide).

8.3.2 Project Team Organization and Contracting

Members of a construction team should be selected and integrated into the overall Project Team early in the PDP and design stages. The preconstruction or construction planning activities should establish key project management tools to ensure the successful implementation of the project. This can be accomplished through the preparation of delivery and quality plans, schedules, cost estimates, and design/constructability reviews.

The selection of a construction management organization is typically accomplished in two steps:

1. Request for Information – (RFI)
2. Request for Proposal – (RFP)

For further information on the selection of a construction management organization, see Chapter 7 of this Guide. Key points to note from a construction perspective are the importance of:

- Relevant construction experience – both in terms of size and type of project.
- The determination of construction capability – technical, quality, and project management.
- Meeting a potential construction partner beforehand.

8.3.3 Project Staffing Requirements

The staffing requirements for pharmaceutical project differs from most other industries due to the unique nature of the technology involved in the project and the regulatory requirements applied to the industry. The staffing knowledge level should be appropriate to the project's requirements. Subject Matter Experts (SMEs) may be necessary to provide the project with the required expert knowledge focused on one area, e.g., sterility or containment, or specific knowledge of equipment, containment strategies, and water purity. In addition, the client may have specific requirements while the type of pharmaceutical project can also have specific requirements. For further information on the composition and roles of a project team, see Chapter 2 of this Guide.

Client Requirements

Client requirements could result in additional safety personnel, field personnel, equipment expeditors, or management. In the pharmaceutical industry, clients usually have more reporting requirements than considered standard for the construction industry as a whole. These extra requirements can require additional project schedulers and planners, additional cost controllers, or even computer programming personnel to build systems for the automation of these reporting requirements.

- Project Requirements
- Pharmaceutical projects can be classified into the main categories:
 - Bulk Manufacturing
 - Fill/Finish
 - Laboratory

Each of these categories has different personnel requirements. Categories may be more equipment intensive, involve some form of modular build such as super-skids or are simpler, based on the scale. These could result in additional equipment expediting personnel, who could come from either the engineering group or the construction group. In addition, a bulk manufacturing facility could require additional mechanical and instrumentation engineers due to the complexity of the API processing. Fast-track schedule requirements can result in additional field personnel, safety personnel, and office personnel. The requirements for the turnover of a pharmaceutical project are usually more elaborate than other industries due to the regulatory requirements. The more complex the facility is, the more extensive the turnover package required.

Staffing solutions vary dependent on the client and project and each situation should be analyzed and addressed accordingly.

8.3.4 **Construction Objectives**

Construction objectives should initially be established by the owner during the development of the overall project objectives. The construction objectives should support the business needs of the project. It briefly identifies what needs to be accomplished from the construction effort, goals and objectives, high-level requirements, success criteria, risk areas, and any assumptions and constraints.

The initial construction objectives document should be refined, when the construction team is formed, and incorporated into a construction delivery plan. The construction delivery plan should focus on the planning aspects to establish the foundation for efficient execution during the procurement, construction, start-up, and turnover phases. This plan is a part of the Project Delivery Plan, but typically, the plan presents a summary description of the people, systems, and tasks that need to be accomplished and provides a general overview of what needs to be executed. The following are the typical sections of a Construction Execution Plan (a deliverable coming out of the PDP phase, a sub-set of the PDP):

- Introduction
- Goals and Objectives
- Project Description
- Engineering Plan
- Permitting Plan
- Procurement Plan
- Safety Plan
- Construction Plan
- Quality Plan
- Start-Up Plan
- Factory Acceptance Testing Plan
- Equipment System Training Plan
- Document Management and ETOP Plan
- Commissioning and Turnover Plan
- Validation Plan
- Project Communication and Reporting Plan
- Project Organization/Staffing Plan
- Project Controls Plan

The Construction Execution Plan should be produced through the joint effort of the project team. The construction manager or general contractor should own the plan and be responsible for leading this effort. The plan should be clear on how compliance with regulations will be achieved. The construction manager should finalize the Construction Execution Plan at the end of the conceptual design phase and get it approved by the key project team members.

8.3.5 Construction Methodologies

Innovative methods for completing projects should be employed. Each of the various methodologies has benefits and limitations. The analysis of these solutions should find the correct fit for a project. The methodologies should be evaluated and direction chosen in the preconstruction phase. The construction approach should be incorporated into the detailed design documents, the project schedule, and the Project Delivery Plan. Alternative construction methodologies can be used to accelerate design as well as construction by outsourcing detailed design activities and allowing multiple groups to work in parallel under the supervision and direction of the A/E. This overview focuses on Greenfield types of facilities, but similar strategies can be employed for renovations or fit-outs.

Traditional Build

By definition, this is the traditional way of building a facility from the ground up. Through this method, everything is built on-site and in place. While the greatest benefit of this is that all work happens in an environment that can be controlled by the Client or Construction Manager, there are limited options for acceleration of the project schedule other than working multiple shifts or expending overtime. These have limitations in their abilities to complete a project more quickly. Studies have been performed on the effectiveness of overtime, analyzing the duration of overtime, based on the amount of hours worked resulting in various losses of efficiency. In addition, depending on where the project is being delivered, working multiple shifts may be limited to the size of the local work force or the ability to pay premium rates to bring in staff from other geographic areas.

Modular Approach

This term is commonly used for what is really “Off-Site Construction,” but there are applications where a Modular Approach can be utilized. Such applications are for facilities where there are multiple installations of the same process repeatedly. Through this approach, “modules” can be built in one location, be it at another site, or even on another part of the project site, and “plugged” into place. The repetitive nature of building and installing modules can see efficiencies in terms of speed from being able to execute work in multiple, overlapping steps. “Modules” could be as small as individual 5L reactors or as large as portions or rooms of a building. The key factor is the ability to build the same thing, repeatedly.

Off-Site Construction

Portions of the construction or installations are completed at a different site than the project site, and then brought to the project site for installation. These assemblies could be process skids or super skids, (more frequent in this industry), or could be portions of a facility. There are several benefits of this type of execution, e.g., schedule acceleration, on congested project sites, it reduces the amount of personnel required to be there, reducing the amount of general conditions types of expenses associated with them. This can also be particularly useful when a project is being executed in an area that does not support a deep or well qualified work force. Foundations can be going in on the project site while major portions of the facility are being built elsewhere.

8.3.6 Quality Planning

For the purpose of this chapter, construction quality is defined as compliance with the construction documents and the project requirements. This includes:

- Installing the work in full compliance with the plans and specifications.
- Installing the work with an acceptable level of craftsmanship, including fit and finish, and within stated tolerances.
- Verifying and documenting that the work has been installed correctly.
- Providing test and inspection documents that are comprehensive, legible, complete, and accurate.

A construction quality plan should be developed to identify the quality control procedures and documentation requirements for the project. These requirements are intended to provide sufficient quality of installation and ensure that commissioning and qualification activities may be completed in a timely fashion. In addition, this plan ensures that other good engineering practices related to construction are documented in a consistent manner. Construction activities can have a profound impact on the critical operating systems in the facility. Unresolved construction issues, which are usually identified during subsequent commissioning and qualification activities, can result in major delays to the project schedule. In some cases, these construction issues, if not identified, could impact product quality.

The Construction Manager is responsible for the quality of the construction, and the engineering and validation teams are responsible for verifying this quality. The Construction Manager typically is responsible for the development and maintenance of the construction quality control plan. The construction quality program should outline the construction quality requirements and procedures that will be followed to:

- Identify testing, inspection, and documentation requirements for vendors and subcontractors, and include these requirements in subcontracts and purchase orders.
- Verify that construction complies with the project plans and specifications throughout construction and start-up.
- Collect and organize operation and maintenance manuals and other relevant information to facilitate development of Standard Operating Procedures (SOPs) and maintenance plans for facility equipment and systems.
- Collect and organize submittals, test data and other documentation to support commissioning and validation activities.

The construction quality plan should include design reviews, tests, inspections, and documentation performed and collected during the preconstruction, construction, and start-up phases of the project. The following topics are usually defined in a construction quality plan:

- Constructability Reviews
- Value Engineering
- Contractor Selection
- Subcontractor Responsibilities
- Interdisciplinary Coordination
- Submittals
- Mock-Ups and Benchmark Installations
- Third Party Inspections
- Off-Site Inspections
- Factory Acceptance Testing
- Equipment and Material Receiving
- Rolling Completion List/Punch List
- Non-Conformance Reports

- Construction Change Management
- Document Control
- Project Turnover
- Project Close-out

In order to develop a successful construction quality plan, it should be integrated with the design/engineering and commissioning/qualification or verification plans. This integration should be viewed as a customer-supplier relationship. Construction is the customer for the design/engineering process and commissioning/qualification or verification is the customer for the construction process. Successful customer-supplier relationships can be developed through highly effective communication and well defined customer requirements.

8.3.7 Planning and Scheduling

Integrated Project Delivery

For the purposes of this chapter, “Integrated Project Delivery” is not a form of contract, but delivery strategy that starts at the inception of the project. It is the delivery of a project where the Client, the A/E, and the Construction Manager (CM), including subcontractors and material vendors are in partnership for the duration of the project from the very start of the design. Delivering a project this way allows the specific knowledge and skills each party brings to be leveraged and utilized for the success of the project.

Schedule acceleration is a benefit that can be realized utilizing this strategy. An example of this schedule saving could be the elimination of the bidding process for subcontractors. In this strategy, the contractor is selected not by a bidding phase that requires contract drawings, but by a selection process based off of parameters including quality programs, past performance and experience, and safety records and programs. This selection can happen sooner than the traditional bidding process and save time once design starts to be issued.

The American Institute of Architects, among other organizations, has published multiple papers on this topic for a more in-depth explanation (References 20, Appendix 3). Although contracting strategies may be addressed in these documents, the operating principles are more important than the form of contract. Integrated project delivery can be accomplished using a variety of different contract formats.

Scheduling Strategy

Construction schedules for complex pharmaceutical projects should integrate design, procurement, construction, and handover to support the overall objectives of the project. Construction planning should start at the required endpoint and work backward. By developing the construction plan to meet the handover goals for the facility, the construction team can in turn define for the design group what deliverables are required and when, in order to complete their phase of the work. The end result is a construction schedule that serves as a conduit from design to commissioning and qualification or verification.

Planning Sessions

Projects should be started with interactive planning sessions, as there are numerous interfaces and handoffs between engineering, procurement, construction, and commissioning. In these sessions, the project stakeholders should clearly communicate their needs and expectations to the rest of the project team. Once all the project requirements have been identified, the team will work together to build a high level milestone schedule for the project. This approach gives the team an overview of the entire project and helps them execute their piece of the project more effectively in support of the overall goals of the project.

Pull Planning

Project planning can be accomplished using one of two basic methods; “pull” planning or “push” planning. Pull occurs when each group defines what and when it will need deliverables from its predecessor group. For example, on a pharmaceutical construction project, the validation group should define what it needs from the commissioning group in terms of data, documentation, and physical handover of systems in the facility, including the sequence and timing of each. The commissioning group then structures the commissioning plan to meet these requirements, and by doing so defines what and when it will need corresponding deliverables from the construction team. Pull planning results in a smooth transition between phases of the project and eliminates wasted effort and delays. The project stakeholders know what to expect and when to expect it. This allows them to be ready to accept deliverables from predecessor groups when they are completed.

The converse of pull planning is push planning, where the predecessor group delivers elements of the project to the next team based on what is most convenient for them. With a push style transition, the deliverables may lack the information required by the successor or are delivered in the wrong sequence, too early or too late, for the follow on group to effectively execute their work. Follow on groups may not need or may not be ready to accept deliverables when they are delivered. Push planning can result in delays, wasted effort, and general frustration for the project team.

Baseline Construction Schedule

The planning and scheduling effort should ultimately produce a clear baseline schedule that clearly states major construction milestones. The milestones should be carefully selected to be simple, clear, and relevant to the progress of construction. Throughout construction, the construction team should report progress against the baseline schedule to monitor schedule performance. The level of detail for the baseline schedule may be tiered, with a handful of high level milestones for executive level reporting, and larger number of intermediate milestones for reporting to other team members, such as engineering and commissioning. The baseline schedule should be constant. Reporting against “old” milestones where there have been significant changes to the project scope should be avoided.

Construction

Projects pass through several stages with hand-offs between each phase. Construction occurs between the design phase and the commissioning phase. On a fast track projects, construction starts before design is complete and commissioning starts before construction is complete. Construction of the facility is not the end of the project. The construction team should understand that they are turning the facility over for commissioning and qualification. Following the concept of pull planning, the construction team should complete and handover systems and areas in the sequence defined by the commissioning and qualification group. The handover schedule will strongly influence the sequence of construction activities during the construction phase.

Equipment

Equipment drives the schedule of most pharmaceutical projects. The construction schedule should account for the procurement, design, fabrication, testing, and ultimately delivery and installation of long lead equipment. Construction documents may be issued for construction with assumptions around equipment that has not been fully designed. The construction team should be aware of these areas and plan construction activities to mitigate potential delays when equipment details are flushed out and the facility design changes as a result. Portions of the building should be left out to allow for installation of late arriving equipment. Temporary construction may be required to allow commissioning to start before all of the equipment is installed. This can affect multiple trades and should be accounted for in the construction schedule.

Turnover

The construction schedule should clearly communicate how and when systems and areas will be completed and turned over to the commissioning group. This section of the schedule should address substantial completion,

inspections and acceptance, punchlist completion, and final completion. The criteria for each of these stages should be well defined early in the project and outside of the project schedule. System and area boundaries should be clearly defined to prevent misunderstandings during the critical turnover stage of the project.

8.4 Construction Delivery

8.4.1 Purpose

This section focuses on the specific materials, techniques, and considerations that are unique to pharmaceutical projects, as well as how and when “traditional” construction techniques must be modified in a pharmaceutical construction environment.

8.4.2 Safety

Caring about people’s well being, including the workers that arrive on site to build new facilities, is usually considered throughout pharmaceutical construction projects. Construction projects are inherently dangerous and safety is a challenge on all construction projects; there are a few areas that are unique to pharmaceutical projects.

Ongoing Operations

Most pharmaceutical projects are built in or around ongoing operations. This exposes both the construction workers and operations staff to hazards to which they are unaccustomed. Construction workers may risk exposure to chemical and biological hazards on pharmaceutical sites. Detailed logistics and communications plans should be used. Construction traffic and work activities should be segregated from ongoing operations to the greatest extent possible. Work permits and Lock Out Tag Out (LOTO) procedures should be used. Teams should communicate constantly so everyone involved in the project knows what to expect when they enter the work area.

Commissioning

The handover period is considered a very dangerous phase of the project. Systems are being energized for the first time. Systems may be temporarily modified and partially energized to facilitate early start-up and commissioning of equipment. Electrical panels that are de-energized one day may be live the next day. The construction team may have care and custody of some systems and the commissioning team may have care and custody of others. New people will be working in the facility for the first time to test and qualify systems and equipment. LOTO and effective communications should be used during this phase of the project. The safety plan for a project should specifically address how the project team will communicate in order to mitigate risk during this stage of the project. Visual techniques to effectively communicate area and system responsibility either on site and/or at the site entrance are typical ways to reinforce these issues.

Emergency Response

Construction workers are susceptible to the hazards of fires, chemical releases, and dangerous weather conditions. The increased number of people on site during the construction phase of the project can put a strain on existing safety procedures and infrastructure. Emergency response plans for the construction team may be independent of existing plant protocols or construction workers may follow the existing procedures. Projects usually require a combination of both. The project safety plan should address how construction personnel will be protected in emergency situations. The construction team should work with plant EH&S departments to ensure that these procedures are integrated.

8.4.3 Security

Effective security prevents unauthorized personnel, vehicles, and equipment from entering or leaving a work site along with preventing theft and vandalism. It is also part of the safety plan. Limiting access to the work site prevents

unauthorized personnel from wandering onto the job and hurting themselves. Controls should be placed on what personnel, vehicles, and equipment can enter the site. Sites with secure site perimeters should create a secondary security perimeter around the construction site. Site security personnel should participate in the security of the construction site, even if they are not permitted to physically enter the work site. Personnel leaving the site should be controlled and monitored. This can help to discourage theft. From a safety standpoint, everyone on site should be accounted for in emergency situations.

8.4.4 Special Considerations

High Purity System Construction

High purity systems can include product flow lines, gas systems, or clean water systems. Each of these systems comes with their own requirements for installation, testing or inspections, cleaning and passivation, and these requirements should be built into the construction execution plan in the planning stages of the project. For example, the requirements of power and purge gas required for orbital welding; on a bulk type project, there could be 15 to 30 welding machines working at any given time. The electrical requirements for this added load should be built into the temporary electrical plan and included in the execution strategy. Also, to put a Dewar or tank of purge gas with each one of these welding stations could become cost prohibitive and time consuming to exchange throughout the life of the project. A bulk system could be a good solution and would need to be included in the execution strategy.

Construction of Classified Spaces

The construction is different from and the level of detail required is significantly higher to build a pharmaceutical cleanroom rather than building an office building.

While some of the materials could be the same, such as metal stud framing and gypsum wall board, others are not, such as cleanroom wall panels (which are available in a variety of materials), walkable ceilings, epoxy floors, and chemical resistant finishes. In addition to these differences in materials, the way that these types of system are built and sequenced is also different. Instead of a gypsum board or suspended ceiling going in last, a walkable ceiling is installed more toward the middle of the overall sequence. Also, depending on the type of wall system used, the finished product could be installed sooner than when would be considered normal on a traditional build. In addition, the stopping and sealing of air movement is necessary to the successful start-up and qualification of a classified space. Air can leak through electrical wall boxes and subsequently, through the conduit attached to those electrical boxes and could affect the ability to achieve the proper pressure differentials required.

Equipment Installation

For a pharmaceutical project, there may be a need to build the facility and then install the equipment later due to long lead times. Ideally, this is planned for within the design process to build in accommodations for bringing in the equipment at a later date. This could include the addition of roof hatches, roll-up doors, removable wall panels, modifications to the structural framing to allow portions of it to be left out, final locations of the equipment being closer to exterior walls, etc. Questions that the team should address include:

- How will I get it into the building?
- Once in the building, do I have a clear path to get it there?
- How will it be moved? What will the riggers need to get it in place?
- If I need to leave piping and ductwork out to get the equipment into position, does that affect my ability to start-up and turn over any other systems?

Additionally, the required infrastructure for the equipment including water services, compressed air, vacuum, power supply AC/DC, purified water, steam, process air, etc., should be well coordinated for the equipment to perform as

expected. Environmental requirements, including positive/negative air pressure, temperature, humidity, etc., should be given proper consideration so the proper environmental conditions are maintained.

Working within Classified Spaces

These types of considerations usually occur during the end of a construction project after an area has been qualified or during a renovation. When work needs to be completed inside of a classified area, there are special precautions that should be taken. Construction personnel should be trained on how to enter and exit from these spaces, the proper gowning procedures for these areas, and the proper way in which to complete their work to avoid negatively impacting the classified area.

The materials and tools brought into these areas should be cleaned and prepared. If the work will continue in a classified area for an extended period of time, new tools would be bought and dedicated to only be used in a classified area. Otherwise, they would need to be wiped down and cleaned before being brought into the space. In addition, materials should be wiped down and cleaned. For example, metal materials such as piping, conduit, or metal stud framing have some machining oil residue that would need to be removed.

Limitations on Materials

Pharmaceutical cleanrooms are concerned with the growth of micro-organisms, so more aggressive cleaning agents are used which limits the materials that can be used, in particular, limitations on metals. Most metals will oxidize when treated with these cleaners. Organic materials such as wood and cellulose based products can introduce or attract insects to a facility and should not be used or limited to minimal use only. In addition to the limitations of what materials can be used in the construction of GxP cleanrooms, there are also limitations of what materials can be stored with other materials in preparation of being used for construction. Stainless steel should be segregated from other metals or risk contamination of the materials.

8.4.5 Quality Management

During construction, the deliverables of the quality plan should be monitored for adherence to the plan and to ensure that the appropriate level of progress is being made to satisfy the schedule requirements. A systemic quality issue could be discovered due to the progress monitoring of the quality plan activities and so monitoring progress against the following quality plan objectives will help to ensure an efficient transition from construction to commissioning.

Third Party Inspections

These independent inspections should ensure that specialized tests and inspections are being both conducted by the subcontractor and witnessed by the construction management company.

Off-Site Inspections

Off-site inspections should ensure fabrication is progressing in a manner that satisfies the quality requirements. These inspections typically verify that:

1. The vendor is working from the most current construction documents.
2. Materials are compliant and properly controlled.
3. Vendors quality control program is being followed.
4. Documentation is being generated and organized as the work progresses.
5. Corrective actions are being addressed.

Equipment and Material Receiving

These procedures should ensure receiving inspections are being completed and documented against the plans, specifications, and approved submittals. The construction team is responsible for checking for damage when material and equipment arrives on site, in addition, checks should be made to ensure operating manuals and spare parts list are included. Leveraging the construction team to collect or verify other data at the same time to support commissioning and qualification (or verification) can be effective in reducing the testing timeline. In order for this to be effective, however, the testing group should specify the data that they need and the forms and procedures that should be used to collect the data. The testing group should then monitor equipment receiving reports in real time so that discrepancies can be corrected immediately, rather than waiting until the end of the project.

Rolling Completion List/Punch List

These lists are utilized to ensure walk downs are being completed and all corrective actions are identified on the punch list. The punch list should be closely monitored by frequently reviewing the number of punch list items being generated and closed by subcontractor and in total.

Construction Change Management

A change management plan should ensure that changes are implemented with the approval of the Engineer using the Request for Information (RFI) system. The change management plan should also take into account the impact on the testing documents. The number of RFIs generated and closed should be reviewed frequently.

Document Control

Document control procedures should ensure documentation is being generated and organized as the work progresses. The speed of modern communication can also make managing and controlling important information difficult. Document control procedures should be applied to the process of requesting, providing, and distributing data to the project team.

8.5 Construction Completion

8.5.1 What Does Construction Completion Mean?

The fast track nature of most pharmaceutical construction projects usually results in a phased transfer of care and custody from the construction team to commissioning, maintenance, and operations. Handover can be accomplished in a variety of ways and is usually determined by the makeup of the project team and the roles and responsibilities that have been assigned to each participant. What constitutes “construction completion” should be defined and exactly who will accept each element of the work should be clarified. This should happen early in the project so that the people responsible for operating and maintaining the facility have time to prepare for this additional responsibility and work load. A completed project should not be forced on a group that is not ready to accept care and custody of the work.

8.5.2 Facility Turnover

Project turnover is an orderly transition of care, custody, and control of the facility, equipment, and systems from the construction team to the commissioning, maintenance, and operations groups. The turnover process should include the:

- Transfer of equipment/system control to the commissioning team.
- Transfer for maintenance responsibility to the owner’s maintenance department.

- Transfer of custody of building areas (i.e., security control, access, cleaning, etc.) to the appropriate owner's operations departments.
- Transmittal of the final turnover documentation to the owner's engineering department.

A detailed turnover plan should have been developed that outlines the priority and sequence of the turnover of building areas and systems. System Turnover typically occurs through a two step process:

- **Step 1 – Interim System Turnover** – interim turnover allows the owner's engineering and operations groups to begin routine maintenance and monitoring of equipment and systems based on a conditional acceptance of the equipment/system. This usually occurs when the equipment/system start-up activities, punch list walk down and training have been completed.
- **Step 2 – Final System Turnover or Care and Custody** – at Final Turnover, the owner's engineering and operations groups assume full responsibility for the equipment/system. This typically occurs when all construction punch list items, commissioning and transmittal of the final turnover documentation are complete.

A clearly documented plan, agreed to by all interested parties that outlines the specific requirements for these turnover steps should be used when turning over a facility. If there is any ambiguity, the resulting schedule delays can negatively impact the project's overall success.

Facility Turnover by Area

In addition to turning over facilities by system to facilitate the testing schedules and plans, parts of the facility may need to be turned over to allow the user groups to move in and begin work. Usually these parties are involved in the qualification or verification process and want to be located where the work is to be performed. To accommodate this, a Partial Certificate of Occupancy, or its equivalent, is needed from the Authorities Having Jurisdiction (AHJ). Aside from this permission being granted, the building should operate properly to accommodate people working in it. As a result, special considerations are usually needed to ensure that the systems that are brought up to accommodate the user groups' need to remain in operation and not be turned off unless coordinated through a shutdown.

Operations Hand-off

- **System Familiarization** – the first step in turning a system over to the Operations Personnel is that they should be walked through the entire system and trained as to its operational intent, operational limitations, and operating parameters. From an operations and a qualification or verification standpoint, this should prevent the system being made to perform beyond its capabilities. Making this error could slow down the testing process or damage the system or injure its operator. Where possible, this walk-through is led by the engineer responsible for the system's design prior to the system being started up.
- **Safety Reviews** – prior to a system being turned over to the operations personnel, the system should be deemed safe to operate. To do so, a walk-through of the system should be completed with the operations personnel with the purpose to ensure that it can be operated, maintained, and worked on in a safe manner. This safety review can be completed in conjunction with the Installation Verification testing completed during the commissioning phase, in advance of the formal start-up of the systems.
- **System Operational Training** – once a system has been verified, started, and tested to ensure proper operation, the operations personnel will should be educated on how the system functions and operates. This training should cover:
 - How the system functions.
 - Its operational SOPs.

- Its alarms, and the reactionary steps to those alarms.
- The required preventive maintenance.
- Formal start-up and power down steps.
- The LOTO procedures for the equipment.

If possible, the more involvement of the operations team in the testing phase of the project, the more streamlined the training process, e.g., using the system “live” and seeing how it reacts.

8.5.3 Acceptance of the Facility

The orderly and efficient transition from construction to testing is considered a critical aspect of the overall project success. The construction-testing transition is a complex process for many pharmaceutical projects as the transition typically occurs in many steps and primarily occurs at the equipment/system level and not at the building level. Two conditions are usually required for a successful transition from construction to commissioning:

- The construction manager is committed to completing the project by addressing all reasonable deficiencies.
- The owner has applied the appropriate resources to accept the equipment/systems.

These two conditions are mainly responsible for producing an environment of trust between the owner and the construction management company. This environment of trust creates a push-pull situation, where the owner helps the project move from construction to testing.

9 Implementation: Testing and Commissioning

9.1 Introduction

Project Managers should be aware of the strategic issues for planning and delivering the testing scope of a project. Projects usually have some level of testing, required to verify that the project meets the design specifications. The method of testing may be based on a risk-based approach with increasing reliance on Good Engineering Practices (GEPs). The fundamental aspects of testing, and the Project Management of those aspects, form the main focus of this chapter.

Management of the testing stage should use proven project management tools and methodologies and go through the same process as any other part of the implementation of a project: plan, deliver, complete. The tools and methodologies referenced and presented within this chapter are scalable to projects of different sizes and the principles are applicable to a wide variety of projects.

Testing activities should be planned and the plan should be followed. The plan should have sponsorship and be communicated to and enforced within the entire project team, including team members that perform activities prior to the testing phase, as well as the ultimate system owner that will employ the systems tested and maintain those systems to the defined level of compliance.

9.1.1 Terminology

In this Guide, testing is understood to be a defined and planned approach, through assorted methods of documented challenges and evaluations to verify that requirements are met. Terminology used in support of this chapter is for the purpose of illustration of topics and concepts only.

Project Managers working within the pharmaceutical industry should be familiar with industry good practices, current trends, and the applicable governing regulatory agency guidance, as well as the operating organization's internal regulatory affairs, quality assurance, quality control, and engineering group procedures.

This chapter is not intended to define technical requirements or specific methodologies for testing or to redefine the term "Testing." It is not within the scope of this chapter to address any differences in industry terminology (e.g., validation, commissioning, qualification, or verification, see the Glossary, Appendix 4).

9.1.2 Planning for the full Project Life Cycle

This chapter mainly refers to facility projects; the principles may be relevant for other project types. Testing requirements should be adequately defined as early in the project life cycle as possible, and managed closely throughout subsequent stages. Key factors that can help to meet the project quality expectations include:

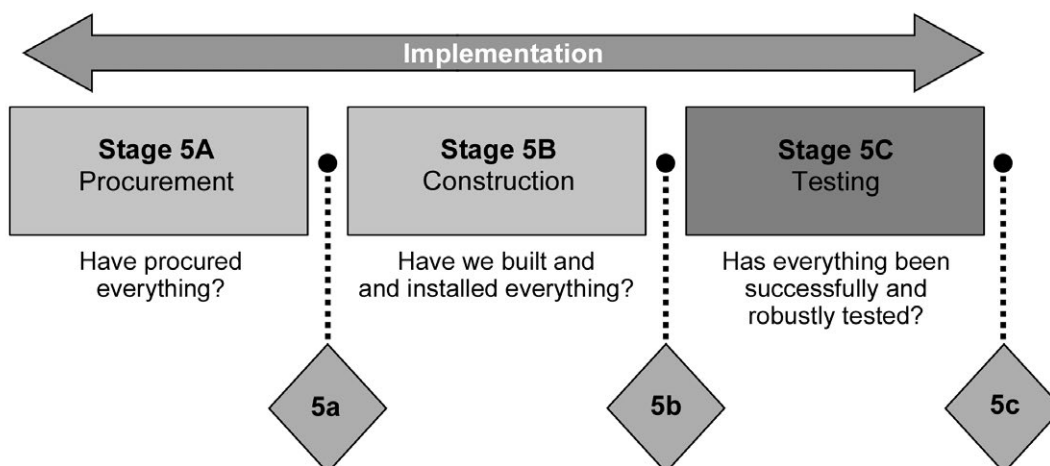
- Defining the scope of testing at the early stage of a project.
- Estimating the level of effort required to develop and execute the scope of work.
- Developing, documenting, communicating, and tracking the testing budget.
- Developing robust safety plans for the testing phase.
- Maintaining the testing schedule in the face of upstream delays and fixed end dates.

The testing phase of a project is usually more complex and critical to projects in the pharmaceutical industry that are subject to high levels of regulatory supervision. Testing typically appears almost at the end of the stage-gated project life cycle within project implementation; it is the culmination of a series of well-planned, defined, and documented quality activities integrated into previous project stages. Early life cycle approved documentation (e.g., specifications, drawings, data sheets) and test records should be maintained as a current view of actual project conditions. A Project Manager should incorporate this approach within the Project Delivery Plan (PDP). The benefits of an integrated life cycle approach to testing include:

- no repeated tests
- reduced deviations and/or discrepancies during the actual testing stage, etc.

If the initiation, planning, design, procurement, and construction phases are delivered without adequate consideration toward quality and testability, the project may exceed cost and schedule at the testing phase. The Testing phase is considered the third stage of project Implementation (see Figure 9.1) and should be considered the delivery window for testing activities rather than the beginning of testing activities.

Figure 9.1: The Project Life Cycle – Testing



The success of the testing delivery phase depends on the quality of the planning effort expended in the earlier project phases from conceptual development through to construction completion. Project Manager should obtain discussion, agreement, and sign off on the testing approach at the start of a project.

Testing should provide assurance that the project is installed and operates to meet the design specifications. Additionally, projects may require quality testing and challenges for the repeatability, reproducibility, and robustness of operations. Examples of testing include:

- Engineering System Operation
- Environmental Monitoring
- Software Functionality
- Product or Process Samples
- Supplier Materials
- Batch Record Use

Developing a testing strategy within the pharmaceutical environment involves:

- Definition of the performance levels – functional and regulatory.
- Determination of who and how – including the documentation requirements.
- Development of a testing program – when tests need to be done and how the results will be evaluated.

This strategy has to be defined as a part of the organizational quality system.

9.2 Pre-Requisites for Testing Success

The same project management tools are required for managing a testing project or the testing stage of a larger project. These involve planning, communication, monitoring, implementing, controlling, and completing.

In planning for the testing stage of a project during earlier phase, special consideration should be given to:

- Development of the Quality Requirements and Expectations
- Development of the Scope of Testing
- Development of the Schedule of Testing
- Development of the Budget for Testing
- Development of the Safety Requirements and Expectations
- Adapting Project Processes and Procedures to suit the Testing Phase

The subsequent sections of this chapter discuss each of these pre-requisites in more detail.

9.2.1 *Establish the Quality Requirements and Expectations*

Focus should be maintained on quality management. The testing phase of a project should support the regulatory requirements of product development, trial, manufacture or testing, or the business requirements of a project.

Once defined during planning, quality should not be negotiated, whereas negotiations can be made against schedule scope and budget. Quality means conformance to requirements. Defects are any deficiencies or errors that are passed on to the customer. Zero defects can be a quality requirement or a quality goal, although careful consideration should be taken to analyze the impact to project budget and project schedule if a zero fault tolerance requirement is placed on the project.

Testing is the final, documented check that the installation operates to meet the specifications. In planning the testing phase, the Project Manager should have a clear understanding of the requirements for the project and be satisfied that those requirements are:

- Testable – a requirement that is quantifiable and measurable that can be unambiguously tested. For example, a room air change rate of “X” number of changes per “Y” time period can be measured, a statement that the room air quality should be adequate for the intended purpose cannot.
- Realistic – a requirement that can be achieved. For example, a computer system with a down-time of less than “X” hours/year can be tested, a requirement that it should never fail cannot.

- **Traceable** – a requirement that can be tied to a specification, procedure, or guidance can be traced through design and tested, requirements that are not found in approved project documentation or corporate designated reference cannot.

This analysis should be done prior to the delivery of the testing stage. If not, the probability of failure to achieve requirements can increase, and consequently put the project's schedule and budget objectives at risk.

Refining the requirements should occur during the design stage of the project. The project quality culture should ensure that the quality requirements of the project are maintained during these phases.

During the design, procurement, and construction of a project, the testing phase should provide objective evidence that project requirements have been successfully met. Project Managers should understand the importance of quality and aim to develop a quality culture where quality is seen as everyone's responsibility. Quality should have quantitative measurement; the testing phase should provide this measurement.

Testing activity is the sum result of numerous earlier activities. This statement is applicable to the pharmaceutical industry where an integrated project delivery approach is demonstrating the value of integrated risk-reviews, e.g., which focus on mitigating risk to patient throughout the project's life. The regulatory requirements related to the manufacture of pharmaceuticals and medical devices require that a quality culture be established. This culture should be implemented throughout the entire project life cycle. By implementing a quality culture early in the project life cycle, and utilizing quality tools such as flowcharts, run charts, check sheets, histograms, and Pareto diagrams, a quality culture can be established.

Then, by understanding the quality needs of a project, whether regulatory driven or other, a testing scope can be developed to meet those needs.

9.2.2 *Develop the Scope of Testing*

This section defines a typical project management approach to scope development and control, and how these methodologies can be applied to the testing phase of the project life cycle or directly to a stand-alone testing project.

After the quality requirements of a project are established, the Project Manager should determine and document the Testing Scope, by asking the team:

- "What is and what is not in the testing scope?"

This simple question should be followed by three additional detailed questions:

1. What testing is **REQUIRED** to be included as part of the scope, in order to meet the **REGULATORY** requirements of the project? What is the appropriate **AMOUNT** of testing to assure that the requirement is not being over-challenged, with risk to the clarity of data generated?
2. What testing is **DESIRED** to be included as part of the scope, in order to meet the **BUSINESS** requirements of the project? What is the appropriate **AMOUNT** of testing to assure that the requirement is not being over-challenged, with risk to the clarity of data generated?
3. What team suggested, company dictated, or similar project type testing is **NOT TO BE INCLUDED** as part of the scope of the current project, either due to changes in the **REGULATORY** expectations or **BUSINESS** driver expectations?

Question 3 should be part of determining a project's testing scope. All three questions should be documented and agreed to by the entire project organization (Project Team and Senior Stakeholders) early in the project life cycle, to prevent testing scope expansion that is neither scheduled nor budgeted, and to identify testing scope that is required for success. The testing and inspection requirements should be incorporated into the project specifications.

The level of effort required to determine the testing scope depends on the project. For simple projects, the testing scope could be determined through verbal discussions with the Project Manager, system owner, and other applicable stakeholders. A testing scope may also be developed from project documents or combination of project documents such as the:

- Basis of Design (BOD)
- Testing Master Plans
- Project Delivery Plan
- Standard Operating Procedures (SOPs)
- Validation Master Plan
- Operation Manuals
- Piping and Instrumentation Diagrams

For more complex projects, the development of a clear testing scope should be developed using a combination of stakeholder meetings and documentation reviews; this may include updating or developing documents that take into account project specific criteria.

Typically, more experienced team members (testing professionals) will be tasked with the testing scope development to help provide an accurate testing scope that will meet the project team's and customer's expectations. Project stakeholders (e.g., engineering, production, validation, QC/QA, consultant) with applicable qualifying knowledge and experience may participate in the development of the testing scope. If the testing scope is defined and agreed early in the project life cycle, it will allow personnel involved at earlier project phases to support the testing activities; therefore, maintaining knowledge gained in earlier project stages. Tools are available to support the development and communication of the testing scope, e.g.:

- Industry standards, e.g., NEBB, AABC.
- A vision document.
- A testing requirement document.
- Work breakdown structures.
- A list of tasks with start and end dates.

The testing scope should be communicated throughout the project team and be championed by the Project Sponsor.

Where testing scope elements from similar previous projects are applied, care should be taken to ensure that these past approaches are applicable to the current project. Documenting what is also not in the testing scope, therefore, can help to mitigate unclear objectives, and reduce or prevent over-testing. This clear can save both time and costs, and allow team members to focus effort appropriately. This is considered a streamlined approach to testing scope definition.

Where changes and schedule requirements or budget change the project scope, the testing scope may also change; however, the quality objectives of the project should remain unchanged.

Where testing requirements are not defined or agreed early enough in the project life cycle, changes may be required to meet expectations. Again project management methodologies should be used to manage scope. These include:

- Planning – deciding how the testing scope will be defined verified and controlled. A scope management plan should include the testing scope change control process: the approval of additional scope or removal of scope.
- WBS – subdividing the project into tasks and milestones. Often the early WBS sets the testing sub divisions and is the foundation for the testing plan.
- Verification and Control – acceptance of the testing scope and process to control scope. A process to manage change should be defined to minimize testing scope creep (for information on scope creep, see Section 6.5.1 of this Guide). Scope control can be obtained by focusing on robust change management processes that challenge, approve, and track changes.

9.2.3 Develop the Schedule for Testing Activities

The defined quality requirements for testing determine and categorize the scope of testing activity. The next task is to determine the time required for testing and to produce the testing schedule. In developing the schedule, Project Managers should recognize the two significant phases of activity to be planned, resourced, and scheduled:

1. Documentation – Test Plan preparation, review, and approval in readiness for field execution.
2. Field execution – Test Plan execution, witnessing, review and approval.

Unique Testing Challenges in the Pharmaceutical Industry

Scheduling the testing elements of a project requires careful consideration of the sequencing and duration estimation associated with test plan documentation review and approval. Testing plans and procedures will need various levels of pre-approval from many functional areas of the organization, e.g., EH&S, engineering, manufacturing, operations, quality assurance, and regulatory affairs. The availability of individuals with the signature authority to review and approve the testing scope at the appropriate time should be identified and monitored continuously. The level of impact that this item has on a project is wholly dependent on several items, including:

- Definition of the authorizer's roles and responsibilities, and communication on a regular basis with each of them to determine external forces that will prevent them from performing those authorizations.
- Continuous defined communications that are intended to assure that all information needed for review and approval is available.
- Document preliminary peer reviews to assure simple or overlooked errors and omissions are captured before signature for approval is requested.
- Strong Document Control measures in place to assure that the routing of documentation is efficient and effective.
- Assurance that modifications are captured and tracked as incorporated in an efficient and productive manner. Consider having a central resource absorb all edit responsibilities and use original authors only for technical input.
- Use templates or software programs as much as possible to assure standardization of deliverables.
- Track lessons learned and communicate immediately and continuously to the project team to keep the same mistakes from derailing the review and approval momentum.

Testing usually has activities of fixed durations (cycles, loads, fill times, sanitization, etc.) that cannot be accelerated by adding resources or by extending working hours in a daily schedule. These should be identified.

Test activities may need to be “right-timed” to the project testing sequence, and any inherited delay or precursory failures will shift those activities. As the project schedule is developed, Project Managers should recognize and understand the need for pre-requisite or predecessor activities to be completed before a test can be progressed or signed-off. Studying the scope and required sequence can allow the Project Manager to recognize the high risk activities, i.e., those that if delayed will have a significant and disproportionate effect on subsequent activities. Project Managers should understand the project schedule critical path and within that the parts of the testing (planning, preparation, or execution) that are on the critical path.

External or third party elements on the test schedule should be carefully planned and managed. Such tests can require scheduling of outside testing entities (e.g., sending samples to a lab and turnaround time), availability and suitability of test equipment (e.g., calibrated data loggers for temperature mapping), and scheduling specialist resources to come in for specific tests. The Project Manager should have an understanding of the need for these resources and the ability to engage them at the right time for the testing process. Contingency should be allowed for in the testing schedule; this is typically seen as a defined buffer developed from a consideration of schedule risk.

Tests can fail or result in discrepancies, especially when new or previously unproven processes, equipment, methods or controls are being challenged. A test that does not meet its expected results should be appropriately evaluated immediately by the correct resources before a failure impacts schedule, budget, and quality, as well as team morale. The risk of test failure should be analyzed beforehand and contingencies put in place to manage that risk – both in term of obtaining the appropriate test result and also the impact on the schedule.

Testing requires project contingency (cost and schedule). A Project Manager should have a contingency plan to cope with test failures and manage a project culture that supports the inclusion of the risk management culture (see Chapters 2 and 3 of this Guide). Potential failures during testing are one of the main drivers of the need for contingency in the test phase (both Schedule and Budget) and it is important to make such a connection visible to the Project Sponsor and the project team. It is very hard to estimate time for failure resolution because there are so many unknowns (unless this project is very similar to a previous one). Critical failures could result in a stoppage of testing, re-execution of some testing activities, and possibly a full stoppage to a project. Test failure should be anticipated and the response to that failure pre-defined. Note that the designer has the contractual responsibility for the performance of a system and will be involved in review of test results, and the development of any remedial actions. Risk tools such as Fault Tree Analysis (FTA) and FMEA (see Chapter 3 of this Guide) may be used to support testing risk management.

Testing can require the use of automated test tools and in line data collection devices. The use of such tools can impact the project both in a positive (by allowing for the ability to have the right tool for the right task) and negative ways (by their own individual testing process giving rise to problems or delays) Use of these tools will require planning, training, and effort prior to execution of the test phase they are targeted to support, including considerations such as implementing and configuring the tool, qualifying the tool itself, and getting personnel trained on its use. Where these tools are new to the company as well as to the project, they may require implementation activity not under the project’s control. Careful consideration should be given in the analysis of schedule (as well as cost, quality and safety) impact when the project team is defining the requirements for the testing phase.

Test Schedule Preparation

Development of the testing plan and development of testing documentation should occur as early as feasible in a project life cycle. The testing activity to challenge the design intent and regulatory requirements can only occur after a system, process, or method have all infrastructure and platforms for operation in place and reviewed and verified to have been properly installed and able to operate in a safe and consistent manner.

Planned projects run the risk of taking longer to deliver than scheduled and schedule contingency is often used before the testing stage commences. Although there may be opportunities to decrease the testing durations by this point in a project, if effective preliminary efforts are well executed and documented, it is usual to try to maintain the project end date by shortening the testing period. The level of risk in this approach is considered to be extremely high. If a Project Manager is presented with this challenge, it should be remembered that quality cannot be sacrificed. Only

a modification in scope will mitigate this risk, by evaluating what activity can potentially be delayed and removed from the project. Adding resources may not provide a solution, and if explored, it should be reminded that an increase in cost will occur.

Project Managers should be aware of the risks associated with the testing schedule. As with almost any activity, involving the right resources to participate in the schedule development as early as possible, and building the right level of contingency into this project phase is important. A team of experienced professionals and consultants who have previously developed similar testing phase schedules are usually the most qualified to develop the testing phase schedule.” The major components of developing a test schedule include the following:

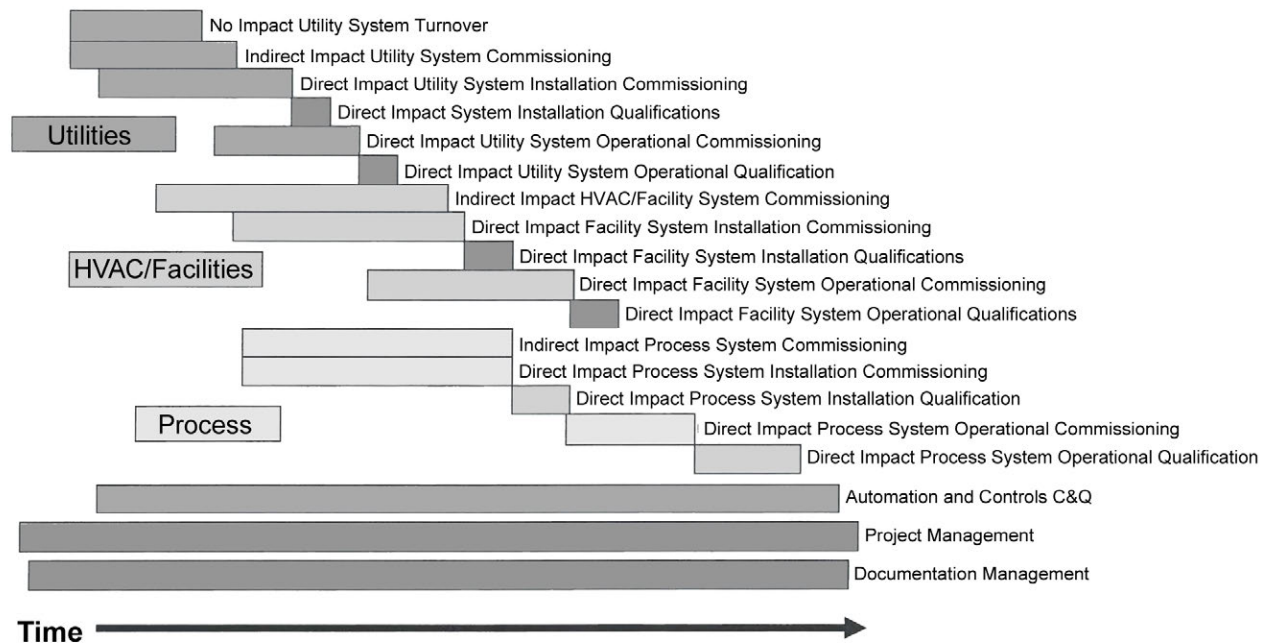
- Testing Scope
- Testing Sequence
- Testing Complexity
- Testing Labor hours
- Testing Duration
- Testing Schedule
- Testing Resource Competency
- Testing Preliminary Budget Estimate (see Section 9.2.4)

The testing scope should have been summarized in some form of approved Testing Plan. Testing Sequence is the logical and ordered timing of the testing activities in relation to the other deliverables of a project. For example;

- In a traditional approach to testing on a facility project: commissioning testing (if applicable and appropriate to the project) precedes qualification testing for Direct Impact Systems.
- Factory testing precedes site testing (which may or may not be part of commissioning testing).
- Utility systems may need to be tested before process systems that require the utilities, etc.

An example of testing activities being sequenced may be very complex or as simple as shown in Figure 9.2. Note again that any terminology, e.g., Direct Impact, Commissioning and Qualification are still currently commonplace in the industry, but are referenced here for illustration purposes only to aid a Project Manager. Specification and verification terminology, as defined in ASTM E2500-07 (Reference 12, Appendix 3), is however, becoming increasingly widely adopted. This Guide does not attempt to define what philosophy for testing methods is best or what terminology is correct or current. It is the Project Managers guide to assure their project identifies those items (References 15 and 16, Appendix 3).

Figure 9.2: Example Testing Schedule



Different customers have different requirements that may change the logic applied to effective sequencing. Project drivers and constraints may often not allow for a logical sequence for the project. Projects with rolling shutdowns, staggered manufacturing windows, or activities leveraged against seasonal constraints may have sequences that do not represent in a linear or linear overlapping manner. However, by effectively communicating with the customer, the Project Manager can work to plan considering those unique challenges. The areas of a project that have scope, schedule, budget, or quality nuances that prevent a logical sequencing require direct mitigation and planning to determine the best way to execute the project or project components within the customer organization.

Testing Complexity is an evaluation of the effort and amount of activity required to fulfill testing requirements based on some established method of evaluation (Figure 9.3). Typically, the more instrumentation and automation installed within a system boundary, the more complex the system will be to test. Also, systems that require laboratory testing may be more complex. Generally, estimated effort hours can be categorized against system complexity. It is often beneficial to build reserve schedule and budget for preliminary “ad-hoc” testing of complex system to “shake out” issues at different stages of the project. This testing may not be able to be classified to satisfy requirements, but will expose potential weaknesses in the project plan, potentially with enough time to have those issues resolved prior to the seriously impacting the schedule.

Testing labor hours are estimated based either on the scope, sequence, and complexity evaluation above. Additionally, testing labor hours by system may be determined from a history of previous projects that were similarly completed as much as reasonably possible. For example, if one executed a type of testing for an autoclave in 100 labor hours, it may be a reasonable to assume 100 labor hours when estimating the labor hours for new, similar-type autoclave that needs to be tested in the future. This method relies on documented project histories, and must be assessed against the current project design intent and requirements, and not be blindly assigned. Also, labor hours should be assigned to accommodate training and schedule management activities, meetings, etc. These are often overlooked in a schedule planning activity that focuses solely on labor hours that can be capitalized or assigned to a system to be tested.

Testing duration is the window of time that the testing needs to be completed within. It is important to consult with management regarding the desired testing duration, options, and flexibility. For example, management may want the testing to take between 30 and 60 days. This flexibility of completing the testing within 60 days could allow the testing scheduler to avoid having resources work overtime, which most likely impacts project costs. Conversely, in

some instances, management may have a business goal to start and complete the testing within 30 days or less, which may drive up the project costs by requiring overtime work and hiring more costly experienced professionals to perform the work in the shortest period of time possible. Understanding the drivers behind the end of testing target date is important to challenge the specified duration.

The competency of those who execute the testing needs to be understood. Usually, the organization requires the one performing the testing to have a resume on file, and required training documented. It is typically expected that someone with applicable education and experience would take shorter time to complete the testing than other alternatives, assuming no testing duration constraints.

Quality may be placed at risk if resource plans are prepared in line with a preliminary budget before adequate project planning has been completed to properly estimate the actual resource requirements for the project. The preliminary testing budget estimate plays an important factor in scheduling. Obviously, with a larger testing budget, the Project Manager has more flexibility, e.g., more skilled resources, ability to use overtime and other expenses such as airfare and lodging associated with importing experienced SMEs based elsewhere. However, as referenced in the Team section of the People (Chapter 2 of this Guide), an experienced Project Manager must recognize that there should be a manageable blend of Senior and less experienced resources. An All-Star team does not always win against a team that is better managed and trained, and who are chartered and committed to execute the project game plan without deviation.

These test scheduling components must be balanced: testing scope, sequence, labor hours, duration, expertise, and budget against the testing schedule. For example, increasing the scope, duration, and/or labor hours, will most likely increase the testing schedule, whereas increasing the budget and project team expertise would mostly likely yield a shorter schedule. The key is to find the strategic mix that yields a testing phase schedule that suits your project and organization.

Remember, throwing together a haphazard “wishful thinking” testing schedule may lead to over-promising and frustration. A team of experienced professionals and a balanced team of stakeholders (e.g., Engineering, Production, Validation, QC/QA, Maintenance, etc.) can develop a testing schedule that both achieves the overall business goals along with aligning available resources to complete the work in the most effective and desirable manner.

Figure 9.3: Example System Complexity Assessment Tool

Level of Complexity		1	2	3	4	5
General Category Classification		Non-Critical Utilities/Miscellaneous Equipment	Indirect Impact/Low Level of Automation	HVAC/Non Classified Facility Areas	Critical Utilities/Classified Environmental Areas	Critical Processes
System Category		No Impact Systems	Indirect Impact Systems	Indirect/Direct Impact	Direct Impact	Direct Impact
System Classification		Calibration Only (Simple stand alone equipment e.g., pH Meter)	Low Level of Automation (Complex Instruments (programmable) and field buses)	Medium Level of Automation (Automated equipment with local control)	High Level of Automation (Central controlled plant (DCS, etc.))	Very High Level of Automation (Full automated plant with integration into business systems)
Level of Automation		Minimal Instrumentation and Controls	Minimal Instrumentation and Controls	Medium Amount of Instrumentation and Controls	High Amount of Instrumentation and Controls	High Amount of Instrumentation and Controls
Amount of Instrumentation and Controls		Local Use	Distribution Only	Supports other critical systems/processes	Storage and Distribution (Product Contact)	Storage and Distribution (Product Component)
Extent of Utility Supply		Minimal or No QC tests	Minimal QC test	Minimal QC test	QC tests moderate	QC test extensive
Amount of QC Testing Required		Vendor supplied testing/documentation only	extensive vendor supplied test script	Minimal Amount of Custom Test Script	Moderate Amount of Custom Test Script	Extensive Amount of Custom Test Script
Testing Documentation Requirements		Low	Medium	High	Very High	Process Critical
Risk to Product		Low	Low	Medium	High (Temp/RH or Environmental Monitoring, Empty Chamber Mapping, POU Verification, Diversity Studies, Maximum Capacity Studies, etc.)	Process Critical (CIP/ISIP, Cleaning, Integration of Controls, Temperature Mapping, Sterility, Mixing Studies, etc.)
Complexity of Testing		Low	Medium	High	Very High	Process Critical
Amount of Safety Interlocks and Alarming		Low	Medium	High	Very High	Extremely High
Amount of Specifications and Requirements		Low	Medium	High	Very High	

Note: The table above offers guidance to determine a Complexity Level of 1 to 5. This ranking is then used as the baseline to estimate labor hours associated with execution of that scope from a Complexity Hours Estimate Worksheet that assigns an estimated total hours required to complete task. Hours Estimate may not equal schedule duration. That estimate may be further adjusted based on variables (schedule constraints, review schedules, system sequencing requirements, etc.) that are not defined above.

9.2.4 Develop the Budget for Testing

When developing a budget for the testing stage (Stage 5C) of the project, a Project Manager must first start with the end in mind. Whether the project is to create a new pharmaceutical product, renovate a facility, or bring new analytical instrumentation on line, the team must first understand the impact to the product or service that is being provided. It is also important to keep in mind that testing is not only done for product quality reasons, but also performed to mitigate business risk as well. A Project Manager may employ various methods, and if there are proven alternative methods to the following, they may be employed. Two methods of developing a testing stage budget are presented here. One method develops the testing budget from the “Bottom Up.” The other method develops the testing budget from “Top Down.”

Cost Estimation – Type 1 – Top Down

This method is typically used to develop testing budgets at the conceptual development phase of projects or when obtaining a general funding for a project when the accuracy can range +/- 30% (Chapter 4 of this Guide). At this early stage of a project, a “rule of thumb” approach is implemented based upon the overall project estimate, historical costing information, and the level of regulatory compliance that is needed. As a point of reference, a common rule of thumb that can be utilized is that the Testing stage of the project can range from 4% to 10% of the overall project cost depending on the amount of regulatory compliance that is required and/or the complexity of the systems being tested. For example, a product or project that deals with a sterile injectable medicine will have more testing costs associated with it than a product that is an excipient or a raw material

Cost Estimation – Type 2 – Bottom Up

This method generally provides a more accurate budgetary number and is typically utilized to provide a testing budget to support a full funding request during the Project Delivery Planning phase (Chapter 5 of this Guide). As with all cost estimating at the PDP phase of a project, significant project scope definition is needed: this includes the testing scope definition. Typically, the WBS will be developed to include the testing scope. Specific considerations when developing this level of estimate include:

- Available schedule and testing delivery plan complexity.
- Contract strategy for testing (mix of Client and suppliers).
- Contingency budget linked to testing risk assessment.
- Typically, the costs associated with conducting testing can be categorized:
 - Project direct costs (capitalized and reported under the project budget).
 - Project indirect costs (capitalized and reported under the project budget).
 - Operating costs (not capitalized and reported under the annual plant operating budget).

The split between Project Direct/Indirect and Operating costs should be defined in the project budget. The following are typical project direct costs estimated and tracked against delivery of individual items in the project WBS):

- Labor hours (time) for the:
 - development of system specific testing documents
 - execution of system specific testing documents
 - development of system specific specifications
 - development of system specific procedures
 - system specific metrology activities (labor)
 - testing phase maintenance activities (labor)
 - meetings required specific to a system
- Material costs for the:
 - testing phase spare parts by system

- testing phase disposables by system
- testing phase product manufacturing materials by system
- Other costs for the:
 - travel to fabrication facilities for audits and/or factory testing
 - testing requirements (materials, instrumentation, laboratory costs) to assure quality
 - testing requirements (material verification, pressure tests, test and balance, passivation, etc.) to assure adherence to specification
 - system specific materials needed to assure safety during the testing phase

The following items may be categorized as a project direct cost only if a specific WBS has been developed for each category. If hours for the following are simply “spread across” the project, they will be estimated as an indirect cost. The project management team can evaluate if those costs can then be spread against the other WBS as a percentage at project close-out. Project indirect costs that are incurred to execute the program will typically be capitalized. Examples of these indirect costs include:

- Training Hours (company/site specific, GxP, Safety, task based, etc.)
- Project Management Hours
- Project Reporting Hours
- Project meeting Hours (general)
- Project Team Building Activity Costs
- Project Driven Software Licensing Requirements
- Project Program Management Costs (metrology infrastructure, project specific engineering and maintenance infrastructure, etc.)

The following costs are typically not specifically identified in early project budgets, and are usually estimated as part of the project indirect costs. However, these costs may be significant and should be estimated and documented as early in the project life cycle as possible. These include:

- Temporary Project Workspace (space, utilities, custodial, etc.)
- Temporary Project IT and Communications Infrastructure
- Project Office Supplies
- Project Small Tools
- Project Furnishing
- Safety and First Aid Supplies
- Project Awards and Team Building Supplies
- Project “Petty cash” budget for non-categorized small items

In established operating facilities, employees of the facility are often tasked with supporting the project, either in a full time or part time role. As many projects require contract or consultant support, the project budget scope may be limited to those external contract costs with internal costs being tracked internally as “normal” operating costs. If possible, the time input required under the Roles and Responsibilities agreement made during the development of the project scope should be scheduled and budgeted against the project.

The above items are not all-inclusive, and may not be applicable to every project type, or applicable to every WBS within a specific project. They are presented to provide Project Managers a starting point to develop an accurate project budget and to agree the split of Direct/Indirect/Operating costs with the project cost management team.

Although some of these items may be repeats of items presented in Chapter 5 of this Guide, they should be considered against the testing phase budget separately, as projects may face turnover of critical personnel and shift in project focus at this stage.

9.2.5 *Develop the Safety Requirements and Expectations*

The testing phase of a project offers unique safety risks. Testing activities may take place around energized systems and also often test systems against Out Of Specification (OOS) scenarios. Facility infrastructure may still be in construction around the system being tested. Also, the system controls and safety infrastructure are in a state of flux as design intent is being verified. Stress levels are high, work hours are long, and team members are operating in a work environment that is often reactive against project interpersonal issues. Numerous examples are historically evident and can be referenced from many sources where accidents, including those that result in loss of life, occur under these conditions. Quite simply, safety of personnel during the testing phase is the only Project Management concern that is more important than quality.

Examples of the additional safety risks associated with the testing delivery phase are:

- Use of external support for short-term testing activities – these suppliers may not have been on the site before and to mitigate any risks they should be inducted into the project safety culture which may mean given critical induction information and then be accompanied around the site.
- Use of operations personnel to support testing as a part of their training in a new system – although the operations environment will be familiar to these groups, the testing is effectively being conducted within a construction environment and so risk mitigation through identifying areas of the facility that are RED (no go for anyone other than specified); AMBER (general construction access); and GREEN (general access for all project team including testing team). For example, specific testing activities may be identified within a RED area to prevent others accessing the area during testing.

Project Managers should encourage Project Team members to be responsible for theirs and others safety as well as for the task execution. A Project Manager should be prepared and capable of promoting and assuring that a safety culture is part of the project.

9.2.6 *Adapting Existing Project Processes for Testing Phase Delivery*

Critical areas of a Project Delivery Plan that should be re-evaluated include:

- Communications Management
- Knowledge Management
- Documentation Management

The continuity of established systems should be maintained.

Communication Management

An efficient communications infrastructure should be established, especially when the field testing stage of a project overlaps other prior stage to accommodate a fast track project schedule. Work may be scheduled on an hour by hour basis, particularly if resources are committed in support of testing delivery on multiple systems, and deviations or discrepancies need immediate resolution. System status can require constant monitoring, e.g., if there are issues with the start-up of a supplied utility system, other tests may not be able to happen as scheduled.

The status of activities, issues uncovered during testing, and the plans for resolution of those issues should be communicated to the entire project team, either directly or otherwise.

Delays or overages (time not used) in duration estimates can have a substantial impact on project schedules and budgets because of the high complexity of testing. These may require modifications to scope and put the quality of the project at risk. Project Managers should plan and deliver an effective communication program during testing.

Knowledge Management

The field testing stage commencement is a period of transition for many project team personnel. Methods or policies should be established to ensure that the knowledge possessed by early design and construction professionals who demobilize from the project (and may not be involved in the testing stage), is captured and made available to the testing professionals. Ultimately, this knowledge should be placed within the Customer organization team. The Project Team members involved in testing should have knowledge of any issues or changes that were made, so that the current design specification and operational parameters can be challenged. Where changes to the testing approach were negotiated, the testing team should assure that revision was made to testing project plans. Project Managers should recognize that knowledge management is a required activity as the testing stage commences, is delivered and closed out to turn over to the Customer.

Documentation Management

Information Management is the documented capture and communication of knowledge. This information may be captured, shared, reviewed, and approved as part of several different documentation packages.

Project Managers should encourage a system where information is managed and project documentation is controlled. A documentation management plan should be developed; a system selected and project team members trained on the system. Early stage documentation that has been designated to be updated, redlined, or retired should be treated as planned. During early project stages when the system is being defined the needs of the testing stage should be considered.

The documentation management plan should also be reviewed for improvement as the testing stage commences. Documentation should prove that testing activities occurred and that the project met the requirements designated; this is fundamental to project success. The documentation of a project provides proof that the quality requirements were met. A misplaced, corrupted, or incorrect document can counteract the activities that supported development of that document. This can lead to schedule and budget overruns.

The quantity of documentation on a project can overload available resources; the team should be supported by documentation control specialists. A small team of trained professionals that are responsible for the documentation can better serve a project than spreading responsibilities across the entire project team.

Project Managers should ensure that all project team members have appropriate access to the documentation needed to perform their job function. Documentation should be made available to avoid delays to the project schedule because a project team member is waiting for document from a repository with excessive control.

A documentation transition plan should be developed for the transfer of project documentation into the normal organization documentation control systems at the end of the project.

9.3 Delivery of the Testing Phase

A project presents many challenges throughout its life cycle, and more importantly in terms of delivering a successful testing stage, is subject to great amounts of change. A project may be completed and testing stage activities finalized, but that does not in itself make a project successful. Project Managers responsible for the testing stage should deliver the project's quality requirements first and foremost, as it has been stressed that these requirements are not negotiable. Secondly, a Project Manager must constantly manage and maintain the project's scope, schedule, and budget. Thirdly, the Project Manager must manage people chosen to support the project (See Chapter 2 of this Guide).

The testing stage can be subject to significant change; typically, there can be:

- delays in delivery of equipment
- resource allocation mix-ups
- personnel turnover
- missing documentation
- testing failures

These occurrences may result in significant re-engineering of established and installed systems. These delays are widespread and require management. The Project Manager, the testing team, and the customer should manage the change.

The solution to controlling the project testing stage is to manage against the original plan, which was set to manage known project components. Changes should be supported only after thorough evaluation of the impact of those changes.

During testing, the Project Manager will normally use project management controls to track progress, e.g.:

- Schedule and budget reviews against plan; tracking of contingency, and schedule buffer use.
- Risk reviews – looking at quality, safety, project and business risks, etc and tracking mitigation plans.
- Visual reporting on site – using visual methods to engage the testing team and give them the information needed to do their work on a day-to-day basis.
- Management reporting – using a one-pager approach to communicate key messages to stakeholders.

At the end of a testing stage, the project team should provide appropriate personnel with the training opportunities present at the turnover phase, as part of the pre-operations management support.

These items (e.g., Standard Operating Procedures, Preventive Maintenance Procedures, Operation Guidelines, etc.) have been referenced throughout this chapter and throughout this Guide, but a testing stage is not successful until these items are accepted and integrated into the non-project structure. The technical staff on a project is adept at developing technical procedures to support equipment operation, IT system administration, mechanical maintenance, instrument calibration, etc. They are also best to provide training on these procedures. This should be planned and budgeted early in the project and scheduled and communicated to assure its occurrence. The issue of project close-out is detailed in Chapter 10.

When the testing stage is completed, the Project Manager should document lessons learned from the project, and thank the entire project team for the role they played in the successful implementation and delivery of the testing program.

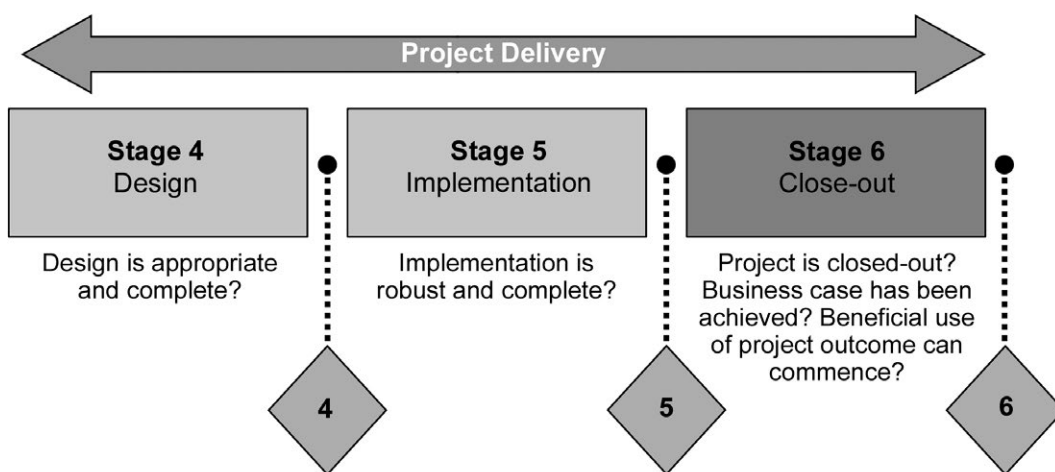
10 Project Close-Out

10.1 Introduction

Project close-out is the finalization of several activities that began before the end of a project. For further information on the need for a clear strategy and plan for project close-out, see Chapter 5 of this Guide.

Leaving the requirements of project close-out to the end of a project can result in unnecessary delays and cost. This chapter explains the elements of project close-out, what is meant by each element, and why it is important to plan for the elements of project close-out (see Figure 10.1).

Figure 10.1: Typical Project Life Cycle – Close-Out Stage Gate



Within pharmaceutical projects, the close-out activities can be divided into the following main categories:

1. Handover Activities
2. Financial and Contractual Close-Out
3. Knowledge Management

Projects usually require a formal close-out policy with similar elements to these main categories. The increased complexity of a project in the pharmaceutical industry can make the close-out more challenging. A well prepared plan, good communications, and a clear overview of the business benefits should be developed.

10.2 Handover Activities

10.2.1 Planning for Partial Handover and Beneficial Use

As projects with multiple operating units approach completion, there will typically be phased completions, handovers, and beneficial use of individual operating units. In addition to the technical and safety considerations cited in other parts of the PDP, plans should be developed for how depreciation for each operating unit will be phased into the organization's financial system. The PDP should address this early in the project, as it will more than likely impact the project cost estimating approach and project accounting systems. The PDP should identify the most likely operating units for phased completion and with corporate finance, establish the requirements to separate capital costs for these units during project delivery. This should ensure costs can be readily segregated to permit separate depreciation schedules as phased completion occurs.

In addition to the financial considerations, the PDP should address early occupancy of operating units to ensure that organization's personnel have appropriate access, training, safety support (i.e., personal protective equipment, emergency systems, egress, emergency response plans, safety programs encompassing a partially occupied facility or site, etc.) and infrastructure needs to enable effective beneficial use of phased operating unit completion. The PDP should also address the unique effects that partial occupancy has on security, logistics, safety, and maintenance of shared systems and/or utilities.

10.2.2 Owner's Readiness to Accept the Facility

The expansion of an existing facility or a new facility may require a significant change to the owner's organization. If the owner is not ready to accept the facility when it is complete, there can be delays in handover and likely additional costs. The PDP should address the Owner's plan to prepare for accepting the facility. This should include budgeting for:

- The additional staff required to manage a new operation, e.g., operators, technicians, supervisors and managers.
- When and how hiring will be performed.
- Training of staff before assuming duties.
- Involvement of staff in qualification/verification activities.
- Identifying the location of their work station.

Establishing clear criteria for the Facility/System Acceptance can help facilitate a clean hand-off from the project team to the owner. The owner's acceptance usually does not happen as a single event. From delivery of documents to new assets, it is the responsibility of the project team to assure that the owner is aware of expectations, time requirements, and key milestone dates for requirements to satisfy facility acceptance.

In addition to the standard documentation and training for new assets and systems, preparation should be made for an efficient and effective operation. For example, all new assets need to go through some form of criticality assessment with failure modes identified when appropriate. A reliability program should be developed to maximize uptime and Overall Equipment Effectiveness (OEE). The organization, systems, and procedures should be developed to enable and promote streamlined practices that can enhance the operation over time. An efficient and effective operation that can continually deliver should be handed over, including environmental factors such as waste management and the supply of energy resources. Focus should be on continuously reducing any form of waste while at the same time reducing the carbon footprint for the operation.

10.3 Financial and Contractual Close-Out

10.3.1 Liability Transfers

The Project Delivery Plan (PDP), along with supporting procurement contracts should specify when liability for safety, damage, and operations shift from one party to another. Typically, there will be a point defined in the contracting documents for the liability transfers to take place, but the contract will need clarification in regard to specific project requirements. This needs to be fully developed in the PDP with questions such as:

- Will all systems be energized and brought on line before liability transfers?
- Will there be partial transfer of completed systems to an owner organization, and if so, how will the dual liability be handled during the interim?
- When will the warranty period begin and who is responsible for damage, repairs, and maintenance at the different stages of ownership?

- Will there be a formal review and signature approval before systems, equipment, facilities, and supporting documents are accepted?

Project documents including the Project Charter, procurement agreements, and possibly organizational SOPs should be considered when assuring a successful PDP. The contracting documents should reflect the PDP decisions.

10.3.2 Retention Release and Final Payments

A proper acceptance of services should be assured before final payments are made to contractors and service providers. Final payments to contractors can be a cause of concern. The PDP should clarify the parameters for final payment and retention release and ensure these are either incorporated into, or consistent with, the contracting documents. Typically, the issues of concern at this stage of the project are:

- *Incomplete Documentation:* the PDP and project contracting documents should specify which documents the owner requires to accept the facility and what happens if documentation is incomplete or not to the required standard. Documentation logs and check lists are recommended. How will this judgment be made? It is important that the documentation meets the requirements for GxP and facility operation.
- *Punch Lists:* there are typically two main concerns to address. The first is contractor non-performance on clearing the punch lists. The PDP should address how this will be handled either through delay in final payment or other remedies. The second concern arises when the contractor is performing well, but there may be long delivery items holding up final completion. In this case, some accommodation may be appropriate and the PDP should provide guidance.
- *Payments to a Primary Contractor or Construction Manager, Versus Payments to Subcontractors:* if a subcontractor has completed its work, perhaps well in advance of final completion, how will warranties be handled? When will final payments be made to the subcontractor? What responsibility will the subcontractor have in the interim after completion of its work and final compensation? Lien waiver requirements should be understood and enforced before issuance of any progress payments.
- *Final Payments:* how will final payments be tied to:
 1. mechanical completion
 2. operable without product
 3. operable with product
 4. operating at specified conditions

Will there be a maximum time for final payment if operations at specified conditions cannot be demonstrated due to owner restraints?

The PDP should give consideration to the concerns raised in the following sections, recognizing that achieving specified performance may not occur for a significant period of time. The PDP should describe how each handover condition will be addressed and then incorporated into contracting documents.

10.3.3 Managing Warranties and Guarantees

Warranties are intended to increase the quality of a product by giving the contractor responsibility for replacement or repair of deficiencies. Warranties have been successfully used to protect investments from early failure and to improve overall construction quality. Express warranties can set limits on project risks, establish clear boundaries on project scope, ensure the collection of payments for each deliverable, minimize unnecessary costs to the project, and most importantly, facilitate proper project closure.

Successful project management of warranties starts well before any equipment is even installed. Participation from both the Owners Representative and the actual employee responsible for the project once turned over should be part of the project installation and testing stages. A clear definition of when the Warranty Period starts for each “system” should be provided, and should be aligned with the formal contractual liability transfers. Particular attention should be paid to subcontractor warranty periods that may begin before the full project is completed. This could result in shortened warranty periods or warranties expiring before the project is put into service. Sub-contracting documents should address this issue as well as the maintenance of installed equipment before start-up to ensure warranties are not voided. Effective Project Close-Out Planning should include a system for handling any questions and call backs during the warranty period. This Warranty Management System should include preparing a complete, accurate set of “as built” construction drawings and specifications, and ensuring the proper End User representatives have access to these. In addition, a binder with all the cut sheets on equipment and materials (including a copy of equipment warranty certificates) should serve team members during the time of “turnover” and move-in.

Summary Points:

- Not all warranties are one year – some are more, such as roofs and other large equipment.
- Warranty period commencement dates should be planned and clearly communicated.
- Warranties can be easily invalidated due to lack of maintenance or misuse/abuse by the End User.
- A clear plan of how to quickly and effectively call on Warranty Service should be developed and abided with by all parties.
- A log of all warranty requests received should be kept, including: request date, actions taken, completion date or pending.

10.4 Knowledge Management

In Chapter 2, the concept of knowledge management is introduced. The transfer of knowledge should be planned. There are basically two types of knowledge transfer that occur. The first happens during the delivery of a project and often referred to as a “Peer Review.” The second type of knowledge transfer, often referred to as “Lessons Learned,” occurs at the end of a project and links back to the original objectives or business benefit established for the project.

A Peer Review is a means to provide assurance that projects are progressing as reported and have adequate mechanisms and controls in place to ensure the delivered project meets business expectations.

Lessons Learned describes the process of eliciting, capturing, and disseminating the successes and learning points from specific projects. The lessons learned process involves an investment of time by the project team, sponsor, and customers/key stakeholders.

Both these activities have the potential to drive continuous improvement within a specific project and into the wider organization. The knowledge transfer process may be performed just at the close of a project; however, benefit can be derived from the application at key points throughout the life cycle of a project as well.

10.4.1 Knowledge Management during Project Delivery

Formal Peer Reviews

Peer reviews may be performed at key points throughout the project life cycle per the following:

- prior to starting (or at the close of) a phase that commits significant resources or financial investment
- at around 50% completion of the design activities to ascertain if the project is on track as reported

- at around 20% through construction to ensure that the build has been started in line with expectations
- at around 75 to 80% through construction to confirm that the build is on target for completion in line with expectations
- at around 50% through verification to confirm that the delivered project will meet User Requirements and fulfill business expectations

Formal Peer Reviews may also be initiated at any point where a problem is perceived to warrant closer inspection. The depth and duration of the review will be determined by a number of factors, including, for example; project complexity, financial investment, the current stage in the project life cycle.

Peer Reviews are typically conducted by a team of senior project management professionals. The team will include people with sound experience across all areas of project management practice (e.g., cost and schedule predictive capability, team dynamics, contracting, changes, engineering and construction quality systems), as well as specific knowledge of the type of project to be reviewed. The Peer Review team must be independent of the project under review to ensure the results are not biased; hence, it should not include members of the project team under review. Funding of the Peer Review activity (items such as travel costs, support costs, resource charging, etc.) should be provided from a budget unconnected to the functional reporting lines of the project, to preserve the independence of the review.

Formal Peer Reviews should be sponsored by a senior manager with the motivation and authority to take action on the recommendations that arise

Projects involving financial investments of less than (for example) \$10 million, may warrant a Peer Review team of one or two people, taking two or three days to execute the review. Larger projects will require more people to cover the areas in a reasonable time frame, such as 10 to 12 days.

Informal Peer Reviews

An informal review, especially during the initiation and closing phases of a project, can be invaluable in providing an independent critique, from other Project Managers on the strategic planning, scope, requirements, Work Breakdown Structure, charter, accountabilities, team assignments, and project schedule. This can benefit the project by leveraging the thinking and experience of peers involved in similar work. The review is most effective when kept at the project management level, focusing on whether:

- The right project has been addressed.
- The business need is met.
- The planned control process is appropriate to deliver against.
- The business expectations are adequately fulfilled with the resources available.

The review process should consider appropriate lessons learned and best practices identified from other (similar) projects across the organization.

10.4.2 Knowledge Management after Project Completion

Business Benefits Delivery

Delivery of the business benefits captured during the project initiation phase in Chapter 4 of this Guide and later developed in the PDP stage in Chapter 5 of this Guide, are critical to a project's success. Performance metrics around project delivery such as budget, schedule adherence, safety record, etc., are important, but are not the

ultimate objective of the project. The true gauge of project success will be whether the business goals of the project were realized. It is surprising across the industry how many companies do not perform a post-completion analysis to verify and report whether or not a project met expectations with regard to its benefit to the business. Introducing a formal review of business benefits post-completion not only helps encourage the proper discipline and set of behaviors in planning and executing the project, but also provides historical data on how well the business objectives were met and what could be improved upon in future projects to better achieve those objectives. A post-completion review process should be built into a company's corporate policies and procedures, including a reporting structure that, for larger projects, would communicate as high as the CFO to add importance and meaning to the exercise.

Business drivers for a project can vary widely, and include any number of the following aspects:

- Capacity Change
- Regulatory Compliance, including Quality, Health and Safety, or Environmental
- Equipment/Technology Upgrade
- Molecule Development
- Process Improvement
- Productivity Improvement

As is the case with many aspects of the project close-out phase, the verification of business benefits has its roots in the planning phase of the PDP. The PDP should establish quantifiable and measurable business goals for the project, such as:

- number of units produced per shift/per week or percent increase
- reject rate
- equipment reliability, as measured by percentage of equipment uptime vs. unplanned downtime
- operating expenses, including energy consumption

The desired business benefits should be agreed upon and documented early in the project so that they can be measured and analyzed after the project is implemented, and so that they can be incorporated into the requirements definition for each piece of major equipment, system, utility, or facility. The PDP should lay the groundwork for how business needs will be defined and by whom, though this is typically performed by a cross-functional team that includes Operations, Science, Technology, Engineering, Maintenance, Quality Assurance, and Finance.

Business Needs should be established with a "top down" approach, starting at the macro level, e.g., the impacted business process(es), then working down to the facility or production line(s) that support delivery of these processes, the major equipment items, etc. If established as part of the user requirements for a piece of equipment, the business benefits would be measured as part of the testing process by means of a productivity study, reliability analysis, operational cost study, etc. Taken as a whole, a more holistic analysis of the business benefits may be necessary. Again, the PDP should describe what is to be measured, when it should be measured, and how it should be reported. The timing of a business benefit review may require a data collection period of anywhere from 6 to 12 months after start-up, with the formal review session following thereafter.

Lessons Learned

Capturing "lessons learned" at the end of a project may deliver some outcomes, but the timing can present a number of challenges to eliciting and capturing many of the most valuable lessons and challenges such as:

- Team members may already be thinking about their next project or indeed have moved on.
- At the end of a project, much of what should be captured has been forgotten.
- The perspective is clouded by recent successes and challenges that the team has experienced.

This may benefit future projects. It can be more effective and efficient to capture lessons as they occur during the project life cycle, when situations arise such as, risks that require mitigation, quality defects, supplier issues, change requests. Review of the development of project deliverables, such as User Requirements, Design Specifications, Verification tests and their execution can reveal what worked well and where improvements can be made. A review of lessons learned from similar projects can be a valuable exercise at the start of a new project when those previous experiences and lessons can be incorporated into the PDP.

An effective way to address Lessons Learned includes:

- Description of the situation, why it occurred (it would be usual to conduct some form of root cause analysis), what actions were taken, what alternatives were considered to resolve the issue, what worked well, where improvements can be made, advice to other project teams.
- Capturing these lessons, so that they can be shared, recognizing that a lesson can be learned from both positive and negative experiences if analyzed appropriately.
- Making the lessons available in a readily accessible form for reference by other project teams and the organization as a whole, particularly to inform the start of another project. Knowledge repositories can be made accessible on organization intranet or databases that can be widely accessed within the organization.
- With maturity in knowledge management, best practices for project management (and for specific project types) can be derived from a growing body of lessons learned. Best practices can inform the evolution of a project methodology and should be made readily available within the organization.

Capturing and leveraging the knowledge and experience gained through project delivery can substantially reduce the impact of employee attrition on an organization's intellectual assets.

10.5 Summary – Example Close-Out Checklist

A project close-out checklist should include all aspects of the project: financial results, schedule compliance, contractor/vendor performance, project documentation and drawings (turnover package), stakeholder satisfaction survey, and lessons learned from the project.

Below is an example of a simple checklist that contains a lot of the key requirements when closing-out a project.

Financial Close-Out Requirements

- Confirm accuracy of all cost tracking accounts.
- Make sure all invoices have cleared the financial payment system.
- Set up assets and close project with Finance.

Project Management Database Close-Out

Update all fields below in Project Management Database if applicable:

- Actual Completion/Closed Date
- Actual Hours
- Spent to Date

Contractor/Vendor Performance Evaluation

- Document Contractor Performance for internal use
- Send information to Purchasing for their vendor/contractor database if not automatically captured

Project Drawing and Documentation Turnover Package

- P&IDs (As-Built)
- Drawings, including General Arrangements (As-Built)
- Building Permits or similar approvals
- Approved Safety Documents, e.g., PHA, HAZOP, and Corporate Risk Insurance
- Receipt of all Lien Waivers for sub-contractors
- Operations and Maintenance Manuals (Received prior to installation)
- Warranty Information
- Maintenance Service Contracts
- Vendor Equipment Drawings
- HVAC Drawings and Balancing Reports
- Spare Parts List and Prices (e.g., as suggested by the equipment supplier)
- Identified Purchased Spare Parts
- Preventative Maintenance Schedule (written prior to verification)
- Calibration Procedures and Certificates
- P&ID Specification Sheets, Drawings, and Process Definitions
- Complete Instrument Listing
- Process Descriptions and Control Points
- Lock Out/Tag Out Procedures
- List of Lubricants
- Verification Reports (as required)

- Maintenance Training (as required)
- FAT Documentation
- Commissioning Documentation

Stakeholder Satisfaction Survey and Lessons Learned Discussion

A meeting should be arranged between the Project Team and stakeholders to discuss lessons learned and project satisfaction. The Project Team should document the feedback from this discussion. The feedback should be used by the Project Team and the relevant organization to improve future project management performance.

Appendix 1

Supplementary Material

11 Appendix 1 – Supplementary Material

11.1 Web Resources

This section describes useful supplementary resources available in electronic format on the ISPE Web site (www.ispe.org).

These resources and other such information and examples may be added to, enhanced, and updated over time by the ISPE Project Management Community of Practice (COP).

Project Type Matrix

This Guide is specific to Project Management within the global pharmaceutical industry and to projects typical within that environment. The main focus of the Guide is facility and engineering projects. The concepts, principles, approaches, and tools are, however, also relevant to a range of other project types. Typically, these will include:

- Facility Construction
- Product Transfer
- Product or Process Improvement
- Automation
- Business Change
- Information Technology (IT)

The specific terminology of each type of project may differ, but their defining characteristic is that they each have a specific duration and an expected benefit to the business: They are projects, have the same type of life cycle, and the methods discussed in this Guide are applicable.

To assist in understanding specific terminology, a Project Type Matrix, showing key activities per life cycle phase, is available on the ISPE Web site (www.ispe.org). This provides examples of key activities within projects for a range of project types.

Sample Checklists

Sample checklists with specific guidance and topics to consider at various stages of a project are available on www.ispe.org.

- Topics covered include:
 - Project Initiation – Feasibility
 - Project Initiation – Conceptual Development
 - Pre-Construction Considerations

11.2 Testing Phase Supplementary Guidance

11.2.1 Integration

The following information has been provided by industry Subject Matter Experts (SME) as guidance to a Project Manager tasked with the delivery of a testing phase of a project that includes Integration. It should be noted that this guidance looks at the project life cycle phases leading to testing as well as operations after the testing phase is completed. Additionally, reference appropriate GAMP guidance (Reference 5, Appendix 3) and applicable ISPE guidance on verification and testing (References 15 and 16, Appendix 3).

Integration of automation and control systems is an area of a project that often presents high risk to the scope, schedule, and budget of a project. This is primarily through the failure to fully understand the start-up, installation, operation, and performance requirements of the systems early in the project life cycle, and the failure to effectively challenge those requirements during the testing. Lessons learned on projects confirm that the earlier and the more exhaustive the testing of the integration at the factory the smoother the start-up and the commissioning will go, thus minimizing impact to the schedule and the budget. A high quality FAT is the best tool for reducing risk during testing at the site of installation. A PM must make sure that the all parties review and APPROVE testing philosophy, methodology, and final test plans prior to the commencement of testing (pre-approval). This assures that at the end of the testing phase, there are no serious issues that could have been mitigated against earlier. Additionally, the earlier in the project testing is performed, the less expensive it is as compared to cost impact at later project phases. Some key considerations include:

- There is evident need from surveyed project history to specify function block level testing and apply formal change management for function blocks once tested.
- The project should always push to have a complete FAT that included all applicable hardware and software in a functioning final state. It is critical that the testing team at the FAT, test every I/O point and HMI tag, every operator input, and every system output. Additionally, they should simulate and test sequencing.
- The project should always conduct Site Acceptance Testing (SAT). The team should test everything that WAS NOT tested at the FAT, as well as test a statistical sampling of everything that WAS tested during FAT. This SAT should include a re-test of all automated sequencing, as live events are different than simulated ones.

Testing of integration needs to take a building block approach. All Input/Output (I/O) needs to be verified and all graphics need to be verified to assure the I/O points are tied in correctly and that control signals between the Human Machine Interface (HMI) and the controller are linked properly. These activities must be performed in sequence to establish that what you see and what you do are truly what is occurring in the field and that activity and response is as defined in applicable system specifications. Once this installation verification foundation is set, then alarms, sequences, trending, etc. can be tested. The following list is in a generally accepted order. Some tests may be concurrently tested; however, it is not recommended to alter the order of testing seen below.

Generally, the testing that relates to Integration includes, or may include:

1. Required Documentation (Preliminary)
2. Discrete Inputs
3. Discrete Outputs
4. Analog Inputs
5. Analog Output
6. Remote Networked I/O

7. Communications – i.e., inter-controller, inter-system, etc.
8. Graphic Tags
9. Alarm Tags
10. Alarm Control Logic
11. Alarm Annunciation
12. Trend Functions
13. Manual Control Operations
14. Automatic Control Functions
15. Automated Sequencing of Control Functions
16. Report Generation
17. System Security
18. Required Documentation (Final)

The following individuals or groups should be consulted and involved in developing the scope surrounding Integration testing:

Automation/Integration Company

- Is most familiar with the system and the requirements; the onus should be on them to develop a thorough and complete test plan.
- Reduces cost risk in attaining a comprehensive test plan secondarily reduces risk in commissioning schedule.

Owner's Operations Group

- Should have involvement to provide direction and insight on operational preferences and sequences.
- Reduces risk during OQ and PQ that operators can't use system or system creates confusion.

Process Engineer

- Should have involvement to verify proper testing of critical process control sequences and process parameter values.
- Reduces operational risk.

Owner Validation/Quality Groups and Validation Service Providers

- Provides insight on how documents should be structured, formatted, and executed to meet requirements; especially important if trying to leverage against qualification testing.
- Reduces cost and schedule risk for redevelopment/reformatting of documents.

This group should address the following questions in order to develop appropriate and accurate scope:

1. Can the tests be organized in a building block fashion?
2. Can the tests be executed in a building block fashion?
3. Is the test plan based on the requirements (FRS and DS)?
4. Are all the specifications tested? Should they be?
5. Have all parties bought into the level of testing required and approved the test plans?
6. Does the testing plan cover the entire system?

The selected Integrator is in the best position to guide the above development of Scope related to testing. Test plans should be developed from the URS, FRS, and DDS. The URS should be approved and included in the RFQ for the final scope of the integration. The FRS should be the first deliverable the automation company provides. The DDS should be developed once the FRS is approved. Only after the DDS is done should the test plans be developed. Ideally, the test plans are being written in parallel to the development directly from the specifications. The purpose of the test plans are to verify the system functions as the specifications states, not that the test plan is written to match the system. When lesson learned data on projects that have had significant unplanned changes in scope, schedule, or budget are evaluated, there is a direct correlation to the lack of timely approval of typical GAMP life cycle documents. The "documentation can catch up later" attitude leads to higher risk to these projects.

From a scheduling perspective, the worst time to find a problem is during PQ, where the time to recover from that problem is not available. Primarily, a PM should assure that the project invest time in early testing. Automation isn't a construction activity. Automation is more of an engineering function. Involvement of the automation company early in the project schedule allows the inclusion of automation input into the scheduling process and the scope development.

A PM should assure the scheduling of time to perform factory acceptance tests; this will generally require travel time as well as time to execute the tests. Expect that issues will be identified. Allow time to evaluate, correct those issues, and RE-TEST them prior to moving to the start-up/commissioning phase. Additionally, the PM should schedule time, resources, utilities, production supplies, and support personnel to execute the site acceptance test. With correct and approved testing accomplished from FAT and SAT, this is an area that can be done to GxP standards and leveraged for formal qualification. To aid in this effort, have the test plan place the system under a formal change management system at the onset of the test activity.

As related to budget, again, the most expensive time to find a problem is during PQ, where the budget to recover from that problem is not available. A project should invest budget in early testing. To avoid budget overruns, the PM should advocate for a structured programming approach (identified as Function Block here for simplicity not as a method necessarily). Specify function block level testing and formal change management for function blocks where/when possible. Always have a full FAT. Assure the team does not just test the hardware; the majority of the problems in the field that impact budget (and schedule) are software issues. Invest the time to estimate and budget for the FAT, including travel expenses. Insist that the system owner (or their representative) be present. The automation system is that small portion of the project that the owner will spend the majority of their time with once the project is completed. The engineering company should be involved to assist in verifying sequences and operations of the process. The construction company should be represented to monitor and record scope change and witness the testing. Additionally, budget for a SAT, including production supplies, utilities, and support personnel (maintenance, operations, quality, etc.).

In conclusion, lessons learned from past projects promote that the PM:

- Involve the automation company early to assist in developing scope and schedule.

- Create a testing philosophy very early in the project; get EVERYONE to buy into it and APPROVE it.
- Keep everyone involved through the project to avoid miscommunication or philosophy changes.
- Test in a building block fashion; make sure the test plans set a good foundation and test upward.
- Test everything.
- Test early.
- Allow time to correct issues identified in testing.

Testing should be approached like communications. It is not a single event, it is a process. It must be approached in a methodical manner and should occur throughout the project.

11.2.2 **Cleanroom**

The following information has been provided by industry Subject Matter Experts (SME) as guidance to a Project Manager tasked with the delivery of a testing phase of a project that includes cleanroom testing. It should be noted that this guidance looks at the project life cycle phases leading to testing as well as operations after the testing phase is completed.

Most Project Managers and many clients (end users) are inexperienced, unclear, and often times simply misinformed on the procedure and directives surrounding the requirements for the certification of the performance of newly constructed HEPA/ULPA filtered production areas. Often, the time frame and experience of the testing personnel are the two most important areas overlooked.

Generally, the testing that relates to cleanroom verification includes or may include:

- Testing that must be performed:
 - Non-Viable Particle Count Monitoring
 - HEPA/ULPA Integrity Testing
 - Differential Pressure Testing
 - Airflow (Velocity/Volume) Verification
 - Airflow Pattern (ISO 5 (Reference 25, Appendix 3) and cleaner) Testing
- Possible additional testing:
 - Room Recovery Rate
 - Lighting Level Verification
 - Noise Level Monitoring
 - Vibration Testing
 - Particle Deposition Studies
 - Temperature Verification

- Relative Humidity Verification

The following (if applicable and/or available) should be consulted in developing the scope around cleanroom testing:

- Project Manager – they will authorize the final invoice and sign off on the project.
- End User HVAC Engineer – they will need to be aware of the access and demand on their equipment. Additionally, they assure availability of that equipment.
- End User Validation –this group will supervise the certification process for the client and also provide the necessary SOPs.
- End User QA/QC – this group has the final say in compliance and usually is “late” to the process and that leads to the risk that there will be an attempt to try to “re-engineer” what has already been done.
- Supplier owner – this individual is ultimately responsible for meeting the schedule and needs to be aware of the demands placed on their organization.
- Supplier site supervisor – this individual needs to be aware of expectations and concerns of the client and PM.
- Plant Manager – as a mitigation in case they invite themselves into the process at a later date.

Specifically, the Owner/Owners Representative should state the “Objectives” for the project in the specifications and/or project plans that will describe the system development, process requirements, user requirements, documentation requirements, and Turnover Package (TOP) requirements. All of these items impact the scope, schedule, and budget of any project. A User Requirements Specification (URS) is helpful for the customer to provide to the certification supplier in order to communicate the requirements, qualifications, and specifications and to better define the process involved. Specifically, every attempt should be made to answer the following questions:

1. Are there end user supplied HVAC/cleanroom performance SOPs?
2. Are there specific requirements in the SOPs that must be met (such as 0.01% penetration)?
3. True “drop dead” time frame that testing and certification must be accomplished within?
4. Who will be responsible for repairs and adjustments identified during testing?
5. Who will keep the originals of the raw data generated during testing?
6. What are the owners specified reporting requirements?

The cleanroom certification supplier needs to have clear guidance as to the actual performance specifications the end user is expecting. Most often Validation will supervise the data collection, but QA/QC will have the final authorization of the work performed.

In order to get a clear estimate of cost and schedule, a PM should assure that if at all possible, an HVAC/cleanroom performance SOP is available at the time the Request for Quotation is supplied to Certification service providers and cleanroom equipment suppliers. Additionally, a PM should be aware of these common risks associated with the project schedule and cleanroom test activity:

- If the Construction timeline has extended to the point that the end user is uncomfortable with any additional “problems” or delays, zero tolerance for failures or discrepancies is considered “critical” at this point.
- There must be a clear distinction as to who is authorized by the end user to accept and/or establish deviations from the scope.

- End user must have a clear understanding of the complexity of gathering data for their proposed requirements; therefore, they are able to adequately evaluate suggested deviations.

The following individuals or groups must be consulted in the development of this applicable portion of the project schedule:

- Project Manager – ultimately responsible for the schedule.
- End User Engineering – they control the equipment and other contractors.
- User Validation – responsible from the end user's perspective to meet the schedule.
- Supplier Owner – must agree to meet the personnel and equipment requirements.
- Supplier Supervisor – must understand the time line.
- Plant Manager – feels they have the most at stake in meeting a corporate imposed deadline.

The following general statements should be evaluated in regard to the project budget:

- If a Request For Quotation (RFQ) was issued, most likely the final criteria for acceptance will be lowest cost, without attempting to discriminate between the vendors as to understanding, education, experience and industry qualifications.
- The established time line not only does not allow for delays, but the estimate may not account for the additional costs associated with delays (the RFP was based on ideal circumstances to allow for lowest price).
- The cleanroom performance vendor is the “caboose on a very long train” and as a result all issues culminate to the fore-front of this project phase and must be resolved before moving forward.
- End user may not have the project experience to fully understand the issues associated with any delays and therefore does not understand the reason for potential delays nor the additional costs required in resolving the issues discovered.

In order to mitigate against budget impacts, the following should always be involved in identifying the project estimate, final budget, or response to RFQ around cleanroom testing, as applicable:

- Supplier owner – will best understand the costs associated with.
- Supplier site supervisor – will be the first to know when the vendor approaches the allotted budget levels.
- Project Manager – has the best “big picture” view of the project budget.
- End user validation – would be the first representative of the end user to be informed of looming overruns.
- End user QA/QC - need to be aware of the costs associated with the requests they make.

There are certain Safety considerations that must be planned in relation to cleanroom testing activity. These include but are not limited to:

- Safety concerns of the use of Dioctyl Phthalate (DOP) or Poly Alpha Olefin (PAO) as an alternative must be communicated and approved.

- HEPA/ULPA integrity testing will set off smoke alarms in the HVAC system and may result in building evacuation if proper arrangements have not been made.
- Airflow pattern visualization testing can also set off the smoke alarms and must be planned and communicated appropriately.

Quality concerns should be addressed as early as possible in the cleanroom test planning. An open communication with the project team will uncover areas of concern. For example, the use of Poly Alpha Olefin (PAO) can speed up the degradation of silicone (and urethane) based gel seals for the HEPA/ULPA filters causing the filter frames to “leak” into the production area. Additional items should be openly communicated.

In conclusion, the testing activities related to cleanroom verification and certification present some unique issues that will impact the project testing phase scope, schedule, budget, safety, and quality if not addressed. Clear objectives and informed directives coupled with reasonable expectations will yield on time and on budget delivery of the project scope and successfully certified production areas.

11.2.3 Calibration

The following information has been provided by industry Subject Matter Experts (SME) as guidance to a Project Manager tasked with the delivery of a testing phase of a project that includes Calibration. It should be noted that this guidance looks at the project life cycle phases leading to testing as well as operations after the testing phase is completed. Additionally, reference GAMP Good Practice Guide: Calibration Management (2nd Edition 11/2010) (Reference 26, Appendix 3).

Calibration is performed for all instrumentation used to monitor and control utility systems, process equipment, lab equipment, and test standards. Calibration is a GxP requirement (21 CFR 211.68 (Pharmaceuticals) (Reference 24, Appendix 3) and 21 CFR 820.72 (Medical Devices) (Reference 27, Appendix 3)) and is a high visibility area during audits and inspections. Calibrations must be performed and documented by trained and qualified personnel with suitably ranged and accurate test standards traceable to nationally recognized standards (i.e., NIST). Most of the items listed below have effect on schedule, budget, and quality.

1. How will instruments (and equipment) be uniquely identified? Not all instruments have PID tag numbers (i.e., QC laboratory instruments and calibration test standards) and not all instruments have serial numbers. Skid mounted equipment and duplicate systems may have identical PID tag numbers. This is a seemingly small issue that leads to delays and significant rework. A PM should make sure a systematic numbering scheme is established and communicated (if necessary, even to suppliers on purchase).
2. A PM should assure that Instrument specifications for calibration range must coincide (and be purchased) with the scaling programmed in the computer system code (PLC, DCS). A PM should keep the personnel responsible for these areas in communication.
3. A PM should determine if calibration testing will be part of a formal instrument qualification process (see ISA Automation Book of Knowledge, Chapter 30 on Checkout, System Testing, and Start-up (Reference 28, Appendix 3)). These activities will help define the scope and reduce risk if implemented properly.
4. A PM must assess if Criticality Assessments (see to GAMP Good Practice Guide: Calibration Management (Reference 26, Appendix 3)) be performed during Design phase (ideal), Testing phase, or operational phase (or are they not applicable)? This will require additional resources and involve system owner representation and quality group input at a minimum.
5. Quality/Testing Group will need to provide input and approval of any additional calibration requirements, such as pre/post system testing calibrations which could dramatically affect cost and schedule.

6. The use of the in-house Calibration Department vs. use of an out-sourced calibration firm will affect cost, quality, and schedule. In house resources cannot typically handle the increased workload during peak testing times. Unqualified contractors performing calibrations leads to rework. Additional resources, personnel, and test standards will likely be required to meet schedule demands.
7. A PM should determine project requirements for Supplier provided calibrations (with purchase order), Bench Calibrations, and Field Calibrations. Recommendation: Typically calibration data is provided with new instruments, so put a system in place to maintain this documentation along with the vendor manuals when received. If Field Calibrations will be performed, there is not a need for bench calibrations except to reduce the risk and detect calibration failures long lead, high value instruments.
8. The impact of not performing loop checks should be addressed before the testing phase. Loop checks are a must for all I/O and must include the entire loop from field devices to/from control system/HMIs. If nothing else, loop checks can be efficiently performed concurrently with field calibrations, but expect problems and delays if this approach is taken.
9. A PM should address issues surrounding Calibration Management Software. Ideally, the End-User CMS System is in place for data loading and calibration documentation during the initial calibrations. If not, a PM should determine how calibration documentation will be controlled and maintained.
10. A PM should consider what calibration procedures will be used during the testing phase (in-house, third party vendor, etc). Do they need to be developed? If so, what is the format and who is responsible for approval?
11. A PM should recognize that Fieldbus installations reduce overall installed cost and testing time, but changes documentation, specification, and purchase requirements. If Fieldbus instrumentation is implemented, the project plan will need to address how this the areas listed above will be addressed.

Generally, the testing that relates to Calibration includes or may include:

1. Vendor, Bench, Field Calibrations:
 - Vendor (Supplier) Calibration – calibration parameters are specified with purchase order and the instrument is provided with an NIST traceable calibration certificate with data (calibration certificates without data are of no value).
 - Bench Calibration – Instrument calibration is performed on the bench upon receipt prior to installation in the field.
 - Field Calibration – Calibration is performed in-situ after final installation in the field.
2. Initial Calibration:
 - The first calibration performed after receipt from the supplier. This may be performed as a bench or field calibration. Additionally, may be used as a basis for setup of periodic scheduled calibrations, but this is not always necessarily.
3. Pre and/or Post System Testing Calibrations:
 - “On Demand” calibrations required by Testing Group to verify instrumentation is within calibration tolerance throughout specified range before and/or after system testing.
4. Interval – Based Periodic Calibration:
 - Scheduled calibration performed as required based on established calibration interval.

5. Loop Check:

- Testing performed for each Input/Output device to verify each instrument loop is connected properly, indications are properly scaled, alarms are functioning properly, and fail positions are properly configured.

The following individuals or groups should be consulted and involved in developing the scope surrounding Calibration:

Calibration Supervisor or Instrument Engineer – this is the person that is going to end up dealing with the system that is established during testing phase. If established company, this person will already have the established calibration program requirements.

Engineering Manager – overall approval of calibration program and areas that affect other engineering groups such as tagging.

Validation Manager – validation needs to communicate any additional needs for calibration (pre/post testing calibrations) and agree to the calibration plan so calibration requirements can be appropriately addressed in testing documents.

Quality Manager – quality needs to be involved in the discussions and buy-in to the calibration plan. If quality requirements are not agreed to up front, the changes that inevitably occur from later involvement will add cost and delay schedule.

Automation/Control System Representative – needs to understand the calibration plan during testing, how it fits into the schedule for control system integration testing. For scheduling purposes, needs to ensure control loops, PLC code, and HMIs are ready for loop testing and loop calibrations. Provide input on any Fieldbus testing requirements and plan.

Construction Manager Representative (Electrical or Instrumentation) – needs to understand the calibration plan during testing phase, communicate any safety requirements (lockout/tagout), and what involvement electrical contractors will play to ensure calibrations can be performed on schedule (for example, panels/instrumentation energized and turned over for calibration testing).

This group should address the following questions in order to develop appropriate and accurate scope:

1. How will instruments be tagged uniquely?
2. Do instrument specifications for calibration range coincide with the scaling programmed in the computer system code? How are changes communicated?
3. Will calibration testing be part of a formal instrument qualification process?
4. Will GAMP Criticality Assessments be performed? When in relation to testing phase?
5. Will pre/post system testing calibrations be required?
6. Who will be performing calibrations during testing phase (in-house, out-sourced, hybrid)?
7. What instruments will require calibration documentation provided with instrument? Which will require bench calibrations or field calibrations?
8. Who is responsible for loop checks? When and how will they be performed and documented?
9. What software will be used for Calibration Management and what is the implementation plan?

10. What calibration procedures will be used?

11. Is Fieldbus implementation applicable to the project?

Additionally, the following statements should be evaluated by the project team:

- Not all instruments have PID tag numbers (i.e., QC lab instruments and calibration test standards) and not all instruments have serial numbers. Skid mounted equipment and duplicate systems have identical PID tag numbers. This is a seemingly small issue that leads to huge delays and rework. Make sure a systematic numbering scheme is established and communicated (if necessary, even to suppliers on purchase).
- Mismatched instrument vs. programmed scaling is a common error that leads to rework, scheduling delays, and if undetected, hidden control failures.
- You can't decide to formalize the process after it has already begun and everyone must be on board from the beginning to make it efficient.
- This is a significant effort requiring time from multiple resources during an already chaotic time.
- If not planned for, will cause significant testing delays and cost overruns.
- Need to determine resources and plan accordingly to avoid schedule delays and account for costs.
- Changes to bench vs. field calibrations, in addition to requiring supplier calibration will change costs.
- Determining who is responsible for performing loop checks correctly will alleviate many problems that almost always occur during control system start-ups.
- Incorporating testing phase calibrations into an established calibration management program or making plans to efficiently migrate the data will lead to a smoother transition to the end user. Ideally, everyone working in the same database from design through operation is most efficient and eliminates duplication/data mismatches.
- If calibration procedures do not exist when testing phase starts, delays will occur to develop procedures.
- Fieldbus changes the control system implementation strategy for instruments on the Fieldbus. The basic Calibration process doesn't change much, but needs to be addressed to avoid scheduling delays.

The Project Plan should document all decisions made so that all areas are addressed, agreed to, and accounted for in schedule and budget. If resources change mid-stream, all early project phase program decisions are documented. The applicable sections of the Project Plan should be available prior to budget/schedule definition. If the same software can be utilized during design, through construction, testing, and final delivery to end user, project data can be best controlled. Otherwise, the final software needs to be available in sufficient time to load (migrate) data for calibration testing.

Calibration programming presents many risks to the project scope. Specifically:

- Adequate resources need to be available when calibration activities are scheduled. Consideration must be given to ensuring all necessary information is available to perform the calibrations prior to the calibration activities. This information includes technical manuals, correct calibration parameters organized and available in paper or electronic form, and assurance instruments are properly installed and powered up when scheduled for calibration. These are the typical issues that cause schedule delays.
- Loop checks from/to device/remote displays must be performed and deficiencies corrected prior to calibration testing. This leads to significant delays on most projects. Scaling issues, addressing, polarity, termination, and ground loops are common issues that do not get uncovered by a simple continuity test.

- Additional, unscheduled calibration requirements added by the testing group, such as pre/post test calibrations, affect schedule if not considered ahead of time.

The following individuals or groups, at a minimum, shall be involved in developing schedule requirements for calibration:

- Calibration Supervisor and/or Instrument Engineer – a calibration person experienced in start-ups will have a realistic expectation of scheduling calibration activities and the dependencies between activities.
- Engineering Manager – to ask the right questions when coordinating with other engineering groups.
- Scheduler – to properly implement a realistic schedule in the scheduling tool.
- Project Manager – overall responsibility for project schedule.

Calibration programming presents many risks to the project budget. Specifically:

- The resources used for calibration during the testing phase should be experienced with start-ups, quality documentation, in addition to the instrumentation technology utilized and its associations with the remote control system displays.
- The approach using supplier calibrations, bench calibrations, and field calibrations will need to be determined and built into the budget. The least expensive option with the highest risk is to only require “no additional cost” supplier calibrations and perform 100% field calibrations (with no supplier calibrations that add cost and no bench calibrations). This can be a manageable risk if combined with performing supplier calibrations /bench calibrations on high cost/long lead time instrumentation (i.e., large control valves).
- Utilizing a computer based calibration software system that is paperless will require a certain infrastructure in place vs. paper based calibrations. Depending on the methodology determined, if the chosen system is not in place when needed, there will be budget risks.

The following individuals or groups, at a minimum, shall be involved in developing budget requirements for calibration:

- Calibration Supervisor and/or Instrument Engineer – a calibration person experienced in start-ups will have a realistic expectation of budgeting calibration activities.
- Engineering Manager – to ask the right questions and realistic budget numbers for the resources required.
- Scheduler – to properly implement a realistic schedule in the budgeting tool.
- Project Manager – overall responsibility for project budget.

Calibration resources must be trained on all applicable site and system specific safety requirements. It should be determined what lockout/tagout procedures will be required to perform calibrations during the testing phase. Constant communication is required during the delivery of these activities to assure all personnel are kept informed and safe.

The project must obtain quality buy-in on the items addressed in this appendix and document those decisions in a project plan approved by quality management. Change in management mid-project tends to lead to the application of some quality requirements that are other than those agreed to during project inception and will lead to schedule delays and cost overruns. Specifically,

- Calibration requirements should be built in to the overall testing documentation.
- Requirement for Pre and or Post Testing calibrations should be established.

- Calibration procedures to be used during the testing phase must be documented and approved.
- If the project requires Paper Records of calibration specifications and calibration testing, this may require custom report(s) from Calibration Management System, and these must be approved in form.

The areas identified throughout this appendix are common deficiencies seen during testing phase of new facility start-ups or expansions. New facility start-ups for companies that do not have a calibration department in place tend to end up with calibration documentation that is unacceptable to quality and that does not fully test the entire instrument loop. These deficiencies lead to rework and systems that do not operate properly. Properly addressing AND DOCUMENTING decisions in the Project Plan for each of the items identified will lead to fewer “surprises” for calibration during the Testing phase of the project. Fewer surprises mean the risk to schedule delays, cost overruns, and quality is minimized.

11.2.4 Process Equipment

The following information has been provided by industry Subject Matter Experts (SME) as guidance to a Project Manager tasked with the delivery of a testing phase of a project that includes Process Equipment. It should be noted that this guidance looks at the project life cycle phases leading to testing as well as operations after the testing phase is completed.

Generally, an inadequate or poorly planned testing phase for process equipment will detrimentally impact the scope, schedule, budget, and quality of a project by risking

1. Increased project costs – corrections made to the equipment in the field, after equipment has already been shipped from the fabrication shop, will always be more expensive than corrections made in the fabrication shop environment.
2. Increased time – corrections made to the equipment in the field, after equipment has already been shipped from the fabrication shop, will generally take more time than corrections made in the fabrication shop environment.
3. Corrections made in the field may in some cases (often) reduce overall quality.
4. An inadequate test may not make it known that some additional scope items may be necessary for the process equipment system to function as desired (i.e., a proper test may shed light on some things that should have been included in the initial URS).

As the industry shifts toward greater application of Verification methodologies, a Project Manager should work diligently to communicate with and align supplier standard offerings to the project's quality plan. Typically, a process equipment supplier understands the following as required testing.

1. Installation Qualification (IQ) – this typically consists of physical check outs of items such as slopes, mechanical assembly, documentation, etc.
2. Operational Qualification (OQ) – component level checkout ensuring that they each operate as intended (for example, putting air pressure to a pneumatic valve and making sure it actuates).
3. Dry Simulation/Functionality Test – component level items are powered up, and items are sequenced in the order they are supposed to be run.
4. Wet Simulation/Functionality Test – all utilities, including water and steam are supplied to all component level items and the system is run as per operational specification.

The following (if applicable and/or available) should be consulted in developing the scope around Process Equipment Testing:

- Owner – Process Engineer/Process Owner
- Owner – Equipment Operator
- Owner – Electrical/Instrument Engineer
- Owner – Project Manager or Engineering Manager
- Owners Representative (Engineering Company/CM) – Process Engineer
- Owners Representative (Engineering Company/CM) – Person Staffing the FAT
- Manufacturer of Equipment – Sales Manager
- Manufacturer of Equipment – Project Manager
- Manufacturer of Equipment – Electrical/Instrument Engineer
- Manufacturer of Equipment – Engineering Manager

Specifically, the Owner/Owners Representative should state the “Objectives” for the project in the specifications and/or project plans that will describe the system development, process requirements, user requirements, documentation requirements, and Turnover Package (TOP) requirements. All of these items impact the scope, schedule, and budget of any project. A User Requirements Specification (URS) is helpful for the customer to provide to the supplier in order to communicate the requirements, qualifications, and specifications and to better define the process involved.

The Equipment Manufacturer should identify the complete scope of testing requirements at the time of proposal. This allows the supplier to determine any special items or deliverables that will be necessary to perform the final testing. This includes any equipment or processes outside of the system boundary that may be included in the SAT or on-site integration. Having this knowledge up front allows the supplier to include all pricing items at this time in order to avoid change orders throughout the project. During the quotation phase, the supplier can begin to develop (and propose) an inspection and test plan for the project. This would define all of the necessary resources required for the final testing phase of the project. This would include utilities that will need to be available at the time of testing (clean steam, deionized water, electrical power, etc.) as well as personnel that would need to be available at the time of testing. Once resources are defined, the pricing, schedule, and budget can be determined for the testing phase and can be included in the proposed Gantt chart for review by the customer.

In planning the testing phase activities at the RFQ stage, a Project Manager should assure that the following questions are considered when managing the development of testing scope related to a Process Equipment Factory Acceptance Test (FAT):

- Does the process equipment require any other equipment or systems for it to run properly?
- If yes to #1, how will that be address at FAT (e.g., a simulation program)?
- What level of testing is desired for this particular equipment at the FAT (e.g., IQ, OQ, Dry Test, Wet Test)?
- Are there any end user corporate standards (e.g., safety, electrical, controls) that will impact the level of testing that can physically be done at FAT?
- Who is responsible for the software and controls system for this process equipment, and will that be made available for the tests?
- If yes to #6, who will be responsible for the integration; the end user project team or the equipment supplier?

- Who will be in charge of making changes to test protocols and equipment changes at FAT?
- Is there a plan in place to implement a quick change order process at FAT if the end user or owner's representative wants immediate changes to scope at FAT?

These and other questions should be documented in the Request For Quotation (RFQ) (in the URS section or an addendum to the URS). In most cases, the final test plan is not finalized until after a kick-off meeting, but as much detail as possible is required at RFQ in order to allow the supplier to properly quote the full scope of the required equipment supply and testing/operational support. It is critical that this detail be communicated and approved by the owner group. It is critical that the system owner develop the documents and take document ownership in order to ensure good communication and prevent misunderstandings. The equipment supplier cannot properly cost the project unless the testing and documentation requirements are included in the RFQ. The only exception to this may be if an owner's representative has extensive experience with the owner for the type of process equipment under consideration.

Process Equipment procurement, installation, start-up, testing, and turnover offer some common risks to a project. To help mitigate against those risks, all phases of the project should be incorporated into the project Gantt chart from the beginning, including the test phase, and these activities and durations should be challenged and agreed to by all interested parties. Also, there should be a FAT staffing plan established up front by the owners/owners rep team. It is not uncommon for the equipment manufacturer to be ready to conduct FAT, but have delays on the project occur because a person that is supposed to staff the FAT has been delayed or is unavailable. Also, there are cases where the equipment supplier is not properly prepared. The test plan at FAT should have already been run by the equipment supplier before the end user/owners representative team is scheduled to arrive. It is better to delay a test plan/FAT by a week or two than have the end user/owners representative team show up for a test/FAT that has not already been pre-performed by the equipment supplier. Good communication during the fabrication period is the most important thing to a project in maintaining budget and scope. The better the right test plan is captured at the RFQ stage, the best chance you have of eliminating scope and budget increases. Also, it is always less expensive to make changes in scope at the fabrication shop, than it is to make them in the field after equipment has shipped.

As with all project areas, process equipment offers some safety considerations. Just as all parties must agree upon a test plan, they must also agree on a safety plan, especially at FAT and equipment installation. A chain of command must be agreed to so that changes are not made on the equipment unless approvals are received and all project procedures followed.

In conclusion, there is no substitute for good communication to give a project the best chance of success.

11.2.5 Hygienic Piping

The following information has been provided by industry Subject Matter Experts (SME) as guidance to a Project Manager tasked with the delivery of a testing phase of a project that includes Hygienic Piping. It should be noted that this guidance looks at the project life cycle phases leading to testing as well as operations after the testing phase is completed. Additionally, reference the ISPE Baseline Guide on Water and Steam Systems (Reference 14, Appendix 3), as well as applicable guidance related to Commissioning and Qualification.

The verification activities surrounding Hygienic Piping is often complex, and that complexity will have potential impact on the project scope, schedule, and budget, especially when that complexity affects the quality of the projects installation and documentation. Early project communication, alignment, decision making, and definition of applicable and required specifications is critical to a successful delivery of the testing phase.

The approach to Hygienic Piping testing should be standardized across the project, independent of the methodologies employed to deliver the project scope. These methodologies may include specifically, or a combination of:

- Field Fabrication and Installation

- Shop Fabrication and Field Erection
- Skid Fabrication, Assembly, Delivery, and Installation
- Modular Construction and Delivery

Independent of the methodologies employed, the execution and documentation of certain activities is extremely critical in the verification of the design and construction of high purity piping (hygienic) systems. These include, but are not limited to:

- Material of Construction Verification (from receipt to installation)
- As-Built Drawing Verification
- In-Line Component Verification
- Weld Quality Testing and Installation Verification
- Cleaning, Flushing, and Passivation
- Pressure (Leak) Testing
- In-Service Testing

The scope around the testing of Hygienic Piping is clearly initiated during the design phase of the project and much of the final testing requirements should be integrated into the construction period. To effectively assure that all requirements are scoped, scheduled, and budgeted, the need for testing must be communicated in the Request for Quotation or Scope of Work provided to all responsible installation service organizations. Most importantly, the definition of the quality expectations and requirements must be transparent across all functional groups to assure that client expectations and regulatory requirements are acknowledged, understood and documented to have been met.

Materials of Construction Verification

Materials of Construction are required to undergo Materials Clearance. Materials Clearance is the process of evaluation and approval of raw materials and product contact materials for use in production. Materials are appropriately reviewed, tested, and cleared from safety and compatibility standpoints prior to use in the production process. Material clearance information is included in the record for each product contacting and spare part that meets the definition of product contact. If the materials used for Hygienic Piping Systems on a project are acceptable against an end-user approved list, the materials procured and installed require documentation that is traceable through manufacture, procurement, delivery, and installation. It is imperative that the systems in place to accomplish this activity are adequate and pre-approved by the end-user to assure compliance with quality requirements.

Of special note, the approval, traceability, and verification of elastomers (gaskets, seals, diaphragms, etc.) is an area of a project that has many unique pitfalls. A clear understanding of approved elastomers must be communicated to the Owner and Consulting Design teams, and details surrounding the approved elastomers must be communicated to all applicable Service and Equipment Suppliers, and all Construction Management and Testing personnel. An elastomer management plan should be part of the Project Delivery Plan.

As-Built Drawing Verification

Accurate As-Built drawings are usually an issue on most projects. The accuracy and completeness (in a timely fashion) of As-built drawings are often overlooked during the construction process and this leads to delays and discrepancy during the testing phase. As-built record drawings are required to provide a means of schematic verification that the intent of the approved engineering design has been met by the construction of the project.

Typically, the contract requires the Systems Contractor to prepare, maintain, and deliver to the owner or owner representative, a set of redlined, record drawings, which show the actual as-built conditions of the construction phases. The timing of this activity is system by system driven, and in most cases, the systems are sequenced to support downstream system activities and a rolling project turnover. These activities must be scheduled and tracked to assure they do not impact the project.

After owner review and approval, these marked-up drawings will be converted to electronic revisions labeled As-Built. This process is often complex and must be defined and the definition of that process followed throughout the project, by the entire project team. A critical tie between the field installation and applicable drawings are field tags, and in addition to the above, the process for verifying the traceability between PID tagging and field tagging must be in place. Additionally, as slope is critical to the system design and verification, and is often shown on project drawings, slope verification should be executed in conjunction with system walk downs that result in As-Built Drawings.

In-Line Component Verification

It is often the responsibility of the Piping Systems Contractor to procure and install In-Line Components (Valves, Instrumentation, Gauges, Pumps, etc.). All of these have specification verification, design traceability and documentation deliverables related to them. The requirements for Submittal Approval, Receipt Verification, and Turnover Documentation must be established and communicated to the Piping Systems Contractor, as early as the Request for Quotation phase of the project so that adequate response can be made and evaluated prior to award. The accuracy of these deliverables is critical to the success of the testing phase.

Weld Quality Testing and Installation Verification

The quality of installation of hygienic systems, and the accuracy and quality of the support documentation verifying the installation, is often critical to the approval and use of the system. Additionally, as most hygienic piping is process related, this topic has high project visibility. Therefore, the level of documentation that exists to support welded systems is expansive, and all documentation must be reviewed for accuracy, applicability, and completeness. This is a daunting task that often results in significant discrepancy and re-work that greatly impacts the project schedule and budget, and often delays start-up of systems. Typically, systems must be in place for the generation, review, and acceptance of documentation associated with, but not limited to:

- Welded Material Acceptance Testing
- Material Certification Traceability
- Welder Qualification
- Inspector Qualifications
- Weld Gas Certification
- Welding Process Verification
- Welding Procedure Acceptance and Approval
- Weld Coupon Inspection
- Field Weld Physical Inspection
- Boroscope (Fiberscope) Inspection and Frequency
- Weld Map (Isometric Drawing) Verification

Typically, much of this information is tied to line lists (single forms) issued as referenced to the project drawings. Developing this type of information (and offering verification data and approval) on a single form provides everyone involved with the basic information needed for each line. Having access to this line-by-line information in such a concise well organized manner reduces guess-work and errors during testing. Typically, these include, in all or in part:

1. Line Size
2. Fluid
3. Nominal Material of Construction
4. Pipe Spec
5. Insulation Spec
6. P&ID
7. Line Sequence Number
8. From and To Information
9. Pipe Code
10. Fluid Service Category
11. Heat Tracing
12. Operating Pressure
13. Design Pressure
14. Operating Temperature
15. Design Temperature
16. Type of Cleaning
17. Test Pressure
18. Test Fluid
19. Type of Test

It is extremely useful to develop procedures for the review and acceptance of the documentation in conjunction with the service provider. The availability of review focused activity flow charts and detailed acceptance requirements early in the project will allow for the streamlining of the documentation review process and minimize schedule requirements for these activities.

Cleaning, Flushing, and Passivation

It is a requirement that hygienic piping be suitable for the service specified and cleaned, flushed, and often passivated to assure that suitability.

- **Cleaning:** a process where cleaning solutions are flushed through a piping system to remove contaminants such as cutting oils, metal filings, weld spatter, dirt, and other unwanted debris.
- **Flushing:** a process by which water, air, or an inert gas is forced through a piping system either in preparation for chemical cleaning or as the only cleaning process. Flushing can be accomplished by using dynamic pressure head or released static pressure head, as in a fill-and-dump procedure. Blow-down can be considered as flushing with a gas.
- **Passivation:** a process by which a chemical solution, usually with a base of nitric, phosphoric, citric acid, or other mild oxidant, is used to promote or accelerate the formation of a thin (25 to 50 Angstroms) protective oxide layer (a passive layer) on the internal surface of pipe, fittings, and equipment. In stainless steels, the most commonly used alloy at present, it removes any free iron from the pipe surface to form a chromium-rich oxide layer to protect the metal surface from aggressive liquids such as high purity waters.

Each of these processes (and their verification requirements) should be defined by approved project procedures and these procedures, and associated test forms, should be established as early as possible in the project life cycle. Scheduled verification that these activities were completed successfully should be conducted.

Pressure (Leak) Testing

Pressure testing is a misnomer that is quite often used when referring to leak testing of piping systems. In a true sense, a pressure test is a test you perform on a relief valve to test its set point pressure. The intent, when pressure testing a relief valve, is not to check for leaks, but to test the pressure set point of the valve by gradually adding pressure to the relief valve until it lifts the valve off of the seat. A leak test, on the other hand, is performed to check the sealing integrity of a piping system by applying internal pressure to a pre-determined limit, based on design conditions, then checking joints and component seals for leaks. It is not intended that the allowable working pressure of an installed piped system be verified or validated, as that could be destructive to that system. There are different types of leak testing, including:

- Initial Service Leak Test
- Hydrostatic Leak Test
- Pneumatic Leak Test
- Sensitive Leak Test
- Alternative Leak Test

The pressures challenged (or alternative methods to be employed) are calculated by the design engineer, and testing additionally looks for the ability of a system to hold pressure, as a surrogate for the visual verification of leak points. The applicability of testing and the process, approved procedure, and documentation supporting these tests is extremely important to the successful delivery of the projects testing phase. Typically, test reports would include:

1. Test Circuit Number
2. P&ID Number(s)

3. Date of Test
4. Project Name and/or Number
5. Location within Facility
6. Line Number(s)
7. Design Pressure
8. Test Pressure
9. Test Fluid
10. Test Fluid Temperature
11. Time (Military) Recorded Test Begins
12. Pressure at Start of Test
13. Time (Military) Recorded Test Ends
14. Pressure at End of Test
15. Total Elapsed Time of Test
16. Total Pressure Differential (plus or minus) from beginning to end of Test Period
17. Comment Section (indicate if leaks were found and system was repaired and retested or if system passed)
18. Signatures and Dates

It is critical that any testing contractor provides current calibration logs of their test instruments, such as pressure gauges.

In-Service Testing

The final piped system testing is often combined with the system testing activities that boundary the piping being tested. This In-Service Testing is the final opportunity to assure that all design parameters have been effectively verified to be represented by the installation prior to the systems use.

The complexities surrounding the installation of hygienic piping within a project scope lead to risk associated with the project scope, schedule, and budget starting in the design phase. The adequate definition of all project requirements, effective development of requirements into procurement packages and contracts, and the control of testing and documentation at all project phases is critical to mitigate against those risks. A PM must assure that these activities are represented in the project plan, as well as realistically represented in the project schedule and staffing plan, and effectively budgeted to be executed in a safe, quality minded fashion.

11.3 Example Project Report

Figure 11.1: Individual Project Report

SUMMARY				Phase 2 Expansion of Building A		Project Schedule		2 YEARS	4 YEARS	2011 2012																							
Oct 2011	Site	Tampa, Florida	Type	Definitive	Project Activity	Start Date	End Date																										
Project Manager	Robert Ispe	Proj #	PROJ001																														
Project Description				Phase 2 Expansion of Building A to accommodate the projected increase in volume for Product B. Two new Production Lines will be installed in the existing Phase 1 Expansion Area as per the Site Master Plan.																													
Financial Summary [US\$000's]				UPDATE FINANCIALS		FX Rate	1.41																										
Month	Approved Funding	Committed	Spent to Date	Estimate to Complete	Expected Final Cost	Variance	Contingency																										
Month Reported	110,000	27,000	16,500	72,250	99,250	10,750	10,000																										
Previous Month	110,000	25,000	15,000	74,000	99,000	11,000	10,000																										
Financial Overview [Risk Allowances, Variances, Contingency Alerts, etc.]				Marketing has developed a new presentation that will require additional tooling. The control budget has been increased by \$250,000 to cover the cost of the tooling.																													
Procurement [Top 5 Main Contracts]				SET BASELINE DATA ● ■ Scheduled ■ Completed ■ Flag Overview of Schedule [Critical Path, Major Shutdowns, Delays, etc.] Hurricane Charlie has delayed the construction activities by 1 week. The delay does not impact the critical path of the project enabling the start-up to occur on schedule. The planned shutdown for 21st October to connect the main utilities to the new expansion area is confirmed and has been scheduled by Production.																													
Procurement Overview [Selection Criteria, Performance of Companies, etc.]				Safety Overview ■ Total Hrs 30,000 ■ LTA's 1 ■ Recordables 1 A lost time accident occurred on 11th September when a contractor slipped on an epoxy floor and broke a finger when landing on a section of pipework. After a Method 1 investigation the route cause was found to be due to a leaking valve on a CIP Skid during commissioning. All staff and contractors have been notified and all actions from the investigation completed.																													
Other Critical Issues [e.g. Quality or Regulatory Issues, Results of Risk Analysis, etc.]				The impact of another hurricane may delay the start-up of the facility. Contract Manufacturer C is preparing to import additional volumes of Product B as a back-up plan.																													

Figure 11.2: Summary of Projects

SUMMARY OF PROJECTS										
Site Name	Project Title	PROJ #	Total Hrs	LTA	Approved (\$000)	Forecast (\$000)	Start Date	Initial End Date	Revised End Date	
Tampa	Demolition of Building C	PROJ009	45,000	0	15,000	13,650	31-May-11	31-May-12	31-May-12	
Tampa	Product Transfer from Site B	PROJ003	250,000	0	25,000	22,750	1-Aug-10	31-Mar-12	31-Mar-12	
Tampa	New Boiler House	PROJ017	15,000	0	10,000	9,080	1-Jan-11	29-Feb-12	29-Feb-12	
Tampa	Wind Turbines	PROJ005	1,500	0	1,500	1,356	31-Jul-10	30-Jun-12	30-Jun-12	
Tampa	CHP Unit	PROJ006	1,000	0	35,000	30,567	31-Mar-11	30-Sep-12	30-Sep-12	
Tampa	Replacement Blister Packaging Line	PROJ007	200	0	3,000	2,700	1-Feb-11	31-Jan-12	31-Jan-12	
Tampa	CMMS	PROJ008	0	0	1,000	909	1-Oct-10	30-Apr-12	31-May-11	
Tampa	Phase 2 Expansion of Building A	PROJ001	30,000	1	110,000	99,250	1-Jan-11	1-Apr-12	1-Apr-12	
Tampa	Car Park Lighting	PROJ010	2,500	0	300	273	1-Nov-10	31-Oct-11	31-Oct-11	
Tampa	Warehouse LED Lighting	PROJ011	6,000	0	500	455	1-Mar-11	15-Dec-11	15-Dec-11	
Tampa	New Product Launch C	PROJ012	500,000	0	150,000	137,500	1-Aug-10	15-Aug-12	30-Sep-12	
Brussels	Replacement BMS	PROJ013	0	0	750	685	15-Jul-11	15-Jul-12	15-Jul-12	
Brussels	New Bio Reactors	PROJ014	300,000	0	80,000	72,800	1-Nov-10	31-May-12	31-May-12	
Brussels	LIMS	PROJ015	0	0	1,000	910	1-Feb-11	29-Feb-12	15-Mar-12	
Brussels	Upgrade Waste Water System	PROJ016	1,500	1	10,000	9,091	1-Jan-11	31-Mar-12	31-Mar-12	
Brussels	Photovoltaic Panels	PROJ004	1,500	0	5,000	4,600	1-Feb-11	15-Aug-12	15-Aug-12	
Brussels	Product Transfer from Site D	PROJ018	200,000	0	40,000	41,005	1-Aug-10	31-Aug-12	31-Aug-12	
Brussels	New Product Launch E	PROJ019	150,000	0	25,000	22,727	1-Jan-10	31-Jan-13	31-Jan-13	
Brussels	Consolidation of Packaging Operations	PROJ020	0	0	50,000	45,010	1-Sep-11	30-Nov-12	30-Nov-12	
Brussels	Solvent Recovery System	PROJ021	75,000	0	7,500	6,800	1-May-10	30-Nov-11	30-Nov-11	
Brussels	Site CCTV System	PROJ022	50,000	0	1,500	1,365	1-Jun-10	31-Dec-11	31-Dec-11	
Brussels	New Containment Suite	PROJ023	65,000	0	12,000	10,909	1-Feb-10	31-Mar-12	31-Mar-12	
Brussels	Warehouse Management System	PROJ024	1,500	0	2,400	2,200	1-Feb-11	30-Sep-12	30-Sep-12	

11.4 Example Project Charter

Program:	Product XYZ Launch	Project:	Manufacturing for XYZ
Program Manager:	Bob Smith	Date:	Year 1 Month 1
Project Description		Project Delivery	
Project Manager: Fred Jones		Project Team: Representatives from: Production, Maintenance, Project Engineering, Quality, Materials Management	
Sponsor: Mary White, VP Manufacturing Division		Additional Resources: - Access to external engineering company - Corporate procurement	
Project Aim: To successfully and sustainably manufacture launch and post launch stock of XYZ		Organizational Dependencies: Linked to three other critical packages in the product XYZ Launch (Product Development, Regulatory Package, Global Supply Chain)	
Project Objectives: - Tech Transfer of Product XYZ from Product development Team within agreed schedule - API Facility Development within approved CAPEX Budget and target life cycle cost - DP Facility Development within approved CAPEX Budget and target life cycle cost - Compliant sustainable manufacture		Critical Success Factors (CSF): - CSF1 – Technology selection - CSF2 – Flexible capacity design - CSF3 – Lean Value Stream - CSF4 – Facility development schedule - CSF5 – maintaining scope to align with overall program business case	
Benefits: - Delivery of launch and post launch stock of API and DP to meet market need - Life cycle cost of product maintained at previous levels - Improved operational processes across the manufacturing division (piloted during this project)		Risk Profile: - CSF1 – AMBER – concerns on most appropriate technology for purification - CSF2 – AMBER – team has developed scenarios for flexing up and down which appear practical - CSF3 – GREEN – value stream engaged - CSF4 – AMBER – reliant on external companies - CSF5 – GREEN – clear link to other critical packages	
Final Deliverable: - API Manufacture - Transfer of API to supply chain for secondary manufacture within market - Value Stream Strategy		Critical Milestones vs. Deliverables: - Technology Transfer Kaizen – DATE1 - Select technology for Package A – DATE2 - Appoint External Engineering Company – DATE3 - Manufacture Launch Product – DATE4 - Transfer to sustainable supply – DATE5	
Interim Deliverables: - API Facilities in two locations - DP Facilities in four locations - Packages to support regulatory process		Project Delivery Approach: - Link to overall virtual program team and associated ways of working - Use of lean six sigma methodology to drive improvements - Risk-based approach to all areas of the scope	

11.5 Additional QRM Background

The ICH Q8 (R2), Q9, and Q10 tripartite set of guidelines (References 4, 6, and 7, Appendix 3) contain several useful references to product life cycle considerations during QRM activities. ICH Q9 (Reference 7, Appendix 3) formally links QRM to the product life cycle. It states that quality risk management is a process for the assessment, control, communication, and review of risks to the quality of the drug (medicinal) product across the product life cycle, and it defines Product Life Cycle as all phases in the life of the product from the initial development through marketing until the product's discontinuation. This includes the development, manufacturing, distribution, and the inspection and submission/review processes throughout the life cycle of drug substances, drug (medicinal) products, biological and biotechnological products (including the use of raw materials, solvents, excipients, packaging and labeling materials in drug (medicinal) products, biological and biotechnological products).

The application of QRM across the product life cycle presents opportunities for organizations. ICH Q8 (R2) (Reference 6, Appendix 3) refers to the potential use of QRM at different stages, such as product and process development, and manufacturing implementation. It indicates that risk assessments can be used to guide and justify development decisions. It explains, for example, how material attributes and process parameters can be linked to product CQAs by risk analyses and an understanding of functional relationships. It also indicates that product quality can be linked to the design of the manufacturing process via the execution of risk analyses.

Life cycle considerations with respect to the application of QRM can result in enhanced process and product understanding. In the area of Pharmaceutical Development and life cycle management, for example, ICH Q8 (R2) (Reference 6, Appendix 3) states that changes in formulation and manufacturing processes should be looked upon as opportunities to gain additional knowledge and further support establishment of the design space. Opportunities for more flexible regulatory approaches are also envisaged.

ICH Q10 (Reference 4, Appendix 3), which concerns the Pharmaceutical Quality Management Systems, also contains life-cycle considerations for QRM activities. It states that quality risk management facilitates continual improvement of process performance and product quality throughout the product life cycle. It indicates that quality risk management can provide a proactive approach to identifying, scientifically evaluating and controlling potential risks to quality.

Appendix 2

Case Studies

12 Appendix 2 – Case Studies

12.1 Product Launch Project Case Study

Scenario

As a part of the strategy to respond to a change in the market, an organization had re-developed a drug which would significantly increase its market share for a therapeutic area whilst also extending patent life and therefore the threat of generic competition.

The project involved most areas of the product life cycle:

- Product development team (based in Europe) – to increase product efficacy and stability.
- Regulatory group (based in Europe and US) – to launch to all markets globally (working with the Marketing group to manage the market changes).
- Manufacturing Division (based in Europe and US) – to redevelop facilities, review value stream operations and transfer the redeveloped product into two locations.
- Global Supply chain (based in US) – to manage the supply chain changes.

So the project was actually a program of interconnected projects and therefore virtual teams each delivering a critical package.

Outcome

The Project Manager for the program reviewed the overall goals and challenges and then proposed a way of working to address any potential issues with the location of the teams and the criticality of the project.

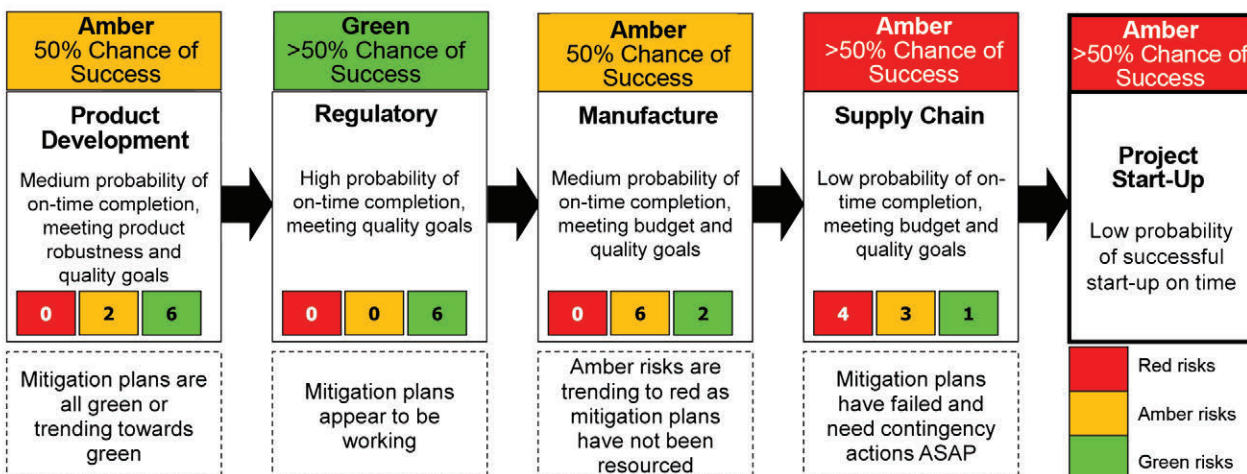
Virtual Ways of Working

- Set up a collaborative e-area to store and share project documents from each team.
- Internet meetings using collaborative tools which were working sessions as well as for information exchange.
- Virtual dashboard so that the large team would focus on the overall goal not just their part.

Risk-Based Approach

- The team for each critical package was required to report a risk rating with back-up data.
- The risk rating was collated into a critical path of risks (see figure) which was communicated to team and to executive board to back-up key decisions on pace and direction of the project.

Figure 12.1



The program progressed significantly before an anticipated risk occurred (related to the security of the supply chain for a key raw material). Because of the team communications in place and the way the risks were proactively managed, a delay to launch was approved without impacting the overall ability for the product to make its anticipated impact on the market. Once launched the product did indeed deliver its intended business case.

Lessons Learned

1. Virtual project teams need a way to effectively work together as face to face sessions are not always practical or indeed possible. Developing these early in the project generated a real team feeling as well as effective work practice
2. Managing a team across diverse groups requires tools to “bring the picture together” and the critical path of risks was highlighted as a way for groups to explain why something was or was not an issue at that time in a language that was accessible to others.
3. Allowing each team to select an appropriate risk tool for their critical package allowed each to own the risks identified and the way they needed to be controlled and managed.

12.2 API Capital Project – Project Initiation Case Study

Scenario

A \$10 million API capital facility project executed within a large multinational pharmaceutical company with extensive capital project experience and expertise. The purpose of the case study is to demonstrate some of the risks and pitfalls associated with project initiation/delivery planning and the need for mature and rational business case assessment and decision making.

The scope of the project was to increase the manufacturing capacity for a pharmaceutical product. A number of sites within the organization were manufacturing the product and were now competing for the capital investment to increase capacity.

Outcome

The project feasibility and concept study was carried out internally with an initial target cost provided by the Project Sponsor. The business case was very sensitive to capital cost with schedule also critical given the sales projections and the need to have the additional capacity online to avoid competitors gaining market share.

An EP contractor was awarded the PDP phase on a very tight fee. Given the revamp/retrofit nature of the project, the extent of site survey work and discussions with vendors was extensive. The scope of the project was developed technically and the capital cost estimate prepared to a +/-15% quality. The mid-point of this PDP cost estimate was in excess of both the internal feasibility and conceptual design estimates.

In parallel with capital funding approval, the EPCM contractor tendered and won the contract to engineer and construct the project. The project was kicked off and the design, procurement, and sub contracting activities began. Two months into the project the first sponsor meeting was held and the project metrics reviewed. The site general manager expressed extreme concern on viewing the EPCM contractor's projected capital cost forecast; this was 15% higher than the budget that had recently been approved.

Upon investigation it became clear that the capital funding submission had been prepared by the Client taking the very optimistic view of the capital cost estimate range; in fact, the figure had been "anchored" at the original internal cost estimate. This had not been communicated to the EPCM contractor who was still working to the cost estimate that had been submitted to the Client at the end of the PDP phase.

With the scope fixed and the schedule already fast tracked to meet the business demand, the instruction to the collective team was to "deliver to the budget" or else! After 12 months of recrimination and extreme stress for all project participants, the project was delivered at a capital cost 5% above the PDP cost estimate mid-point – this required an additional capital funding sanction which damaged careers, reputations, and relationships.

Lessons Learned

The initiation phase of a project is crucial to its eventual success or failure (see Chapters 4 and 5 of this Guide). The key learning points from this case are:

- Capital cost estimates in particular are prone to miscommunication and misunderstandings;
- Careful assessment is required of the cost estimate, what's included, what's excluded, its quality/accuracy, and the strategy for its conversion to a budget - companies have different policies for this.
- Remember, an Estimate is NOT a Budget.

12.3 Oral Solid Facility Project – Project Delivery Planning Case Study

Scenario

This case study is based on a fully automated \$60 million Oral Solid Dosage containment facility capable of manufacturing 1 billion tablets per year. The project was executed within a large multinational pharmaceutical company to support the launch of a new product that had previously been manufactured at a much smaller scale. The purpose of the case study is to demonstrate some of the key features associated with the project delivery planning that resulted in the project being so successful.

Outcome

Right from the early inception of the project, the scope of the project was always to go far beyond a traditional containment facility for high potency compounds. The scope of the project was extremely ambitious requiring careful planning and a well prepared Project Delivery Plan. Despite pressure to reduce the completion of the project to meet the projected volumes being forecast, the detailed design still took seven months after three months of conceptual Engineering during the Project Initiation phase.

The resulting project achieved its objective with a fully automated process that did not require manual intervention. A process simulation was developed to design a robust and streamlined manufacturing operation while taking full advantage of NIR technology for in-process testing. The final project met all the objectives and delivered a 40% cost reduction when compared to the previous small-scale operation. Below are some of the key features of the PDP that contributed to the success of the project.

- The Project Team was carefully selected with limited core team members that between them held most of the expertise needed to effectively manage the project.
- A flat project organization with timely and effective communication helped keep the project on track while meeting important timelines. The Project Sponsor was very supportive and the key stakeholders understood the challenges associated with the project.
- It was recognized that the scope of the project was extremely ambitious and required extensive planning. More time was allocated for the detailed Engineering to include the important process simulation used to further optimize the operation. All of this despite tremendous pressure to complete the project earlier.
- Through careful planning, the team was able to focus on the total cost of ownership by incorporating features that would reduce the cost of the operation, e.g., heat recovery from the HVAC exhaust, and the ability to collect statistical data for continuous process improvements.
- A technology review was included in the PDP and used to highlight key opportunities that would enable the proposed operation to realize significant advantages when related back to a very clear project scope and set of business drivers. The Project Team was extremely focused and did not waiver on their primary objective or purpose.

Lessons Learned

1. It is important to understand the business drivers and develop a scope that outlines the main objective of the project. By having the right scope, it is then possible to incorporate innovative and state of the art solutions that can provide a more competitive outcome.
2. Understanding the key stakeholders and managing their expectations and support via an effective communication plan is important, and not least when breaking new boundaries.
3. No matter how ambitious the project, provided there is a comprehensive Project Delivery Plan with an appropriate level of planning, almost all projects will succeed. This important step is often underestimated and the cause for most project failures.

12.4 Electronic Batch Record (EBR) Project – Design Case Study

Scenario

This case study is based on the implementation of an Electronic Batch Record (EBR) system for secondary manufacturing. The project was executed with a combined team of internal (end user) resource and external specialists; including the vendor of the software package selected for the project.

Outcome

The initiation of the project involved a detailed study with a three sites involved in oral solid dose manufacture to capture a generic set of requirements enabling the solution to be implemented across multiple sites with minimal reconfiguration. The output of this phase of the project was a functional design specification, cost estimates, and a prototype “proof-of-concept.” The suggested next step for the project was implementation at one (recommended) site to further establish the benefits and costs.

At the end of this phase of the project, there was a delay of several months in progressing and key members of the project team were re-deployed to other activities.

Following a review of the business requirements, a project was finally proposed to implement an EBR on two sites for packaging and one for oral solid dose. Costs (+/-10%) and time scales were based on the original project designs.

The project as sanctioned involved a set of new requirements, with a new team of people from within the end-user business to deliver a system to three geographically diverse sites. Since the original scoping exercise involved different people to the project implementation team, there was significant change generated as the new team gained an understanding of the solution capability. Most of these changes were fairly minor, but there were a lot.

The net result was that there was significant forecast overspend by the vendor and as a consequence, the project was halted while the scope, design, and commercial position was re-evaluated. The project was then restarted on the basis of a much more tightly established scope, fixed commercial framework, and ultimately, delivering less over a longer time-period.

Lessons Learned

- Sort out the scope at the beginning. Don't just absorb major changes because they seem "similar," especially if there is significant disparity between concept and implementation.
- For new technologies, start small, prototype, and get feedback as quickly as possible.
- Ensure that senior stakeholders are adequately informed, fully engaged, and have the power to say "no" to scope changes.
- Beware of clarifications or minor changes that can add up to significant impact on the project.
- Good design management (see Chapter 6 of this Guide) will support identification and management of the above.

12.5 Biotech Facility Project – Procurement Case Study

Scenario

A new \$30 million Biotech facility to manufacture a bulk antigen in a facility dedicated to Animal Health was being delivered. Prior to the start-up of this facility, the bulk antigen was being sourced externally at a much higher cost. The projected savings were considerable and the Project Team was under pressure to meet the project completion date previously communicated. One of the reasons for the facility being so cost-effective was the much larger scale of operation. Process trials were performed at one-tenth scale in a Pilot Lab, but never before at the proposed scale of operation. With this came some obvious risks.

Outcome

The new facility was an expansion to an existing building with several bio reactors, a Chromatography skid, and a couple of Tangential Flow Filtration (TFF) skids among other equipment and processes. The entire operation was controlled by a Distribution Control System (DCS). The DCS selected was from a reputable Supplier that the Owner had used almost exclusively for all its API operations. The Supplier was already pre-qualified and there was a global agreement in place. However, the site was not familiar with the selected system and the Owner had not used the system for a Biotech operation before.

During the pilot trials, a particular filter was found to work much better at the smaller scale. The Project Team decided to select this preferred filter for both skids. The main equipment Supplier had not been used before and the project was executed at a time when there was a tremendous demand for Bioreactors and skids within the industry. The Supplier was unable to supply the equipment as per the agreed schedule and was a relatively small company that had over-stretched itself in its ability to satisfy such a large order while busy manufacturing equipment for other clients.

In addition to the delays, integrating the DCS became a challenge. One of the reasons the project team had selected the DCS supplier was because they had an office nearby and were able to provide immediate support when needed. Part way through the project, it became apparent that all the technical work was being performed by an overseas office which delayed response time and made communication more challenging. The owner ended-up having to redeploy many internal subject matter experts from within the API organization to overcome the many challenges experienced. With the additional support came additional cost that the project had to carry. The project was eventually completed, but missed the critical start-up date and required more funding.

Lessons Learned

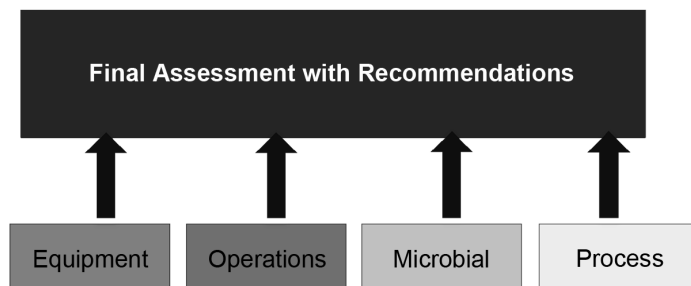
1. Gauging the market for Biotech equipment at that time would have raised a red flag of areas to be particularly careful, i.e., expect good Suppliers will be very busy and may be over-extending their capacity to meet schedules. A Procurement Strategy developed in advance to identify areas of risk and focus Pre-qualification discussions and Supplier visits in these areas would have mitigated delays.
 2. Pre-qualifying the selected supplier for biotech equipment would have raised some doubt on certain Supplier's capabilities, such as the ability to handle a project of this size.
 3. When engaging a Supplier, it is important to understand how that Supplier is organized. For example, is the technical support provided locally or from overseas? And how might this impact the project? Project specific Supplier Agreements could have specifically addressed these areas.
 4. When selecting a supplier, it is important to consider all the important factors that weigh into the decision, and not just one or two. For example, the filter type for the TFF skid forced the decision into using a supplier that was unable to deliver on time. When a decision or selection limits market options, it is critical that close attention be paid to deliverables associated with the item to minimize delays and ensure Supplier. As an alternative, the team may want to look for or develop secondary supply options.
- The integration of the DCS presented numerous unexpected challenges. A more comprehensive Procurement Plan that identified the supply needs and risks for Supplier selection would likely have highlighted the need for the additional support and expertise, while ensuring the required cost and resource is captured prior to committing to a budget and schedule.

12.6 Tech Transfer Project Case Study

Scenario

A global, cross-functional team was formed to evaluate current and historical bioreactor contamination data to determine where the highest risk areas/operations were being found and how risk mitigation strategies could be identified and transferred to sites based on these evaluations and assessments.

Figure 12.2



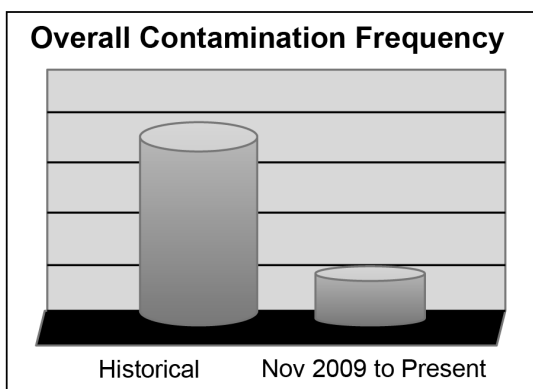
Outcome

The benchmark improvements focused on:

- Bioreactor Design Improvements
- Application of Industry Best Practices from Benchmarking and Consultant Input
- Investigation of New Sterile Connection Technology
- Means to Simplify the Current Process
- Analysis of Microbiological Data
- Microbial-Awareness Rraining

A key tool in this project involved the development and issue of a survey tool that captured data across companies with "similar" manufacturing platforms. This survey identified areas of potential focus that had not been previously identified.

Figure 12.3



Lessons Learned

The results of this project have resulted in key areas of knowledge management and development:

- Program to Update/Maintain Contamination Statistical Analysis/Review
- Process Improvement Program

- Updates to Contamination Response Protocols
- New Training in Microbial Awareness

12.7 Facility Project – Risk Management Case Study

Scenario

A Company was building a new “green field” facility at a cost in excess of \$400 million. The objective of the site was to double the capacity of US production for its main product which was one of several products available to consumers in a rapidly growing market. As such, time to market was critical for two reasons. First, the marketing campaign launch for the product had to be timed right such that demand can be satisfied once the marketing and sales efforts commence. Second, delays in launch would result in market share being lost to competitors.

Outcome

The project team conducted a risk management exercise to assess the high level risks to the overall success of the project. They conducted this assessment for several reasons:

- Identifying the risks allowed the team to then identify potential mitigating actions or contingency strategies to reduce the overall risk profile.
- Identification of the high-risk items allowed for site wide communication of priorities relative to project risk mitigation.
- The high-risk items were presented to the senior management team within the corporation. When resources were needed to mitigate a potential risk, this risk analysis provided the justification for the additional resources.

A five-step process was used:

Step 1: The site leadership team conducted risk identification sessions, with each functional leader gathering ideas from their respective departments. Each department was free to use whichever tool(s) they felt would help them identify potential risks. Some used Cause and Effect diagrams, some used brainstorming sessions, some used other techniques. Risks of most concern were those items that would impact overall schedule, overall project cost, ability to ramp up production, and those that would impact product quality. Each department was asked to present what they viewed to be the top 10 risks to the project.

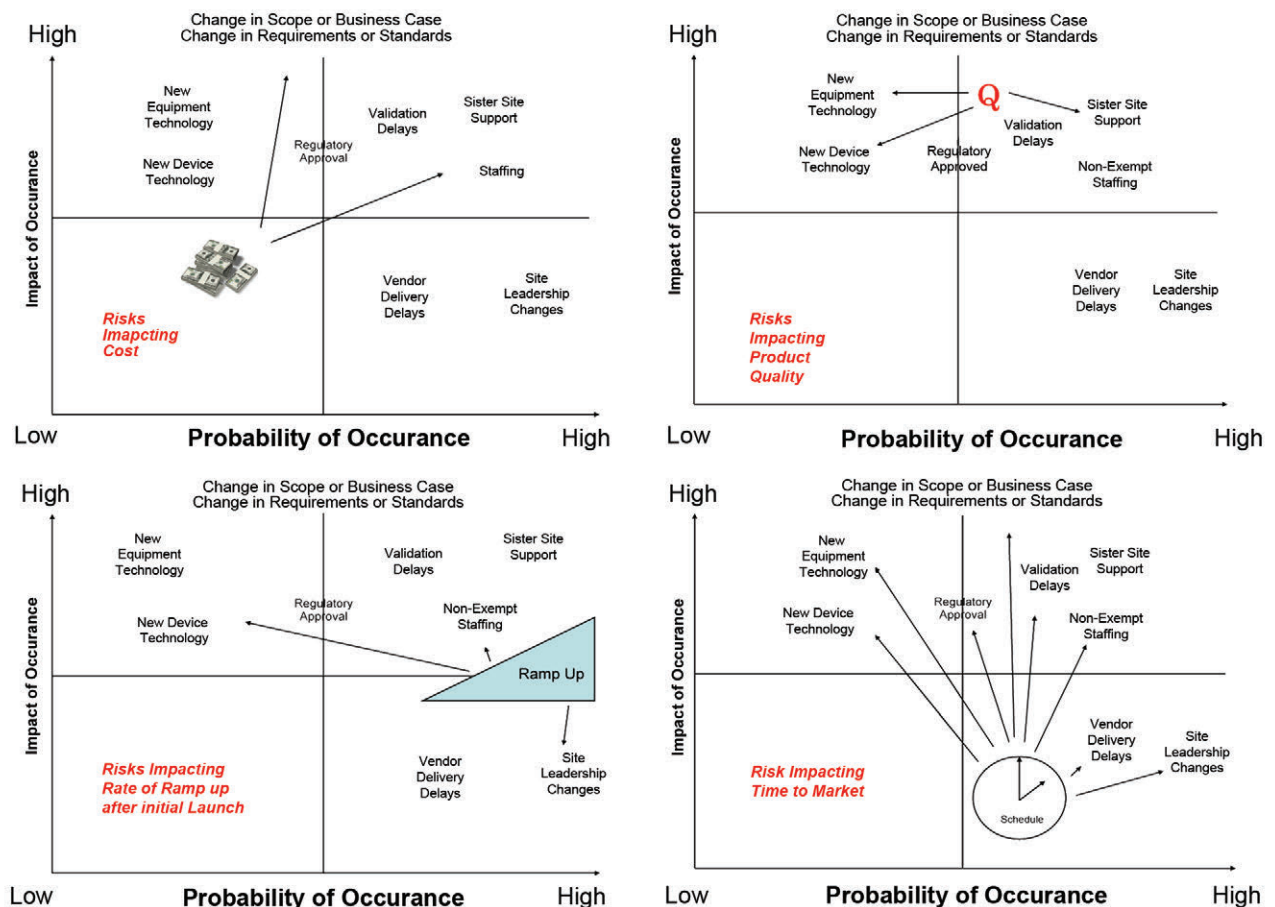
Step 2: Each department's output was combined to one list, which was then reviewed by the site leadership team. Each functional leader presented a brief comment about the items on his/her list, and answered questions regarding the items. Once all of the items were presented, each member of the leadership team voted for what they viewed to be the top 10 overall risks to the project. A pareto chart was used to identify the overall top 10.

Step 3: The top 10 list was “plotted” on a Boston Matrix with the x-axis being “Likely to Occur” and the y-axis being “Impact to Project.” In essence, a “severity” vs. “probability” was plotted for each item. The impact (or severity) to project was an overall assessment, rolling up the concerns identified in Step 1 above (Cost, Quality, Schedule, Ramp up). The chart looked like the diagram below.

Step 4: Once the top 10 was plotted on the Boston Matrix, the team set out to identify risk mitigation activities. In some cases, the only mitigation was to reduce the likelihood of occurrence (without being able to impact severity or impact to the project). In some cases, the opposite was true. In some instances, mitigation to both probability and severity were achievable. These mitigation activities were added to the project plan reviewed by the site lead team on a regular basis.

Step 5: For each of the top ten items on the Boston Matrix, each was assessed for impact to the four major areas of concern (Cost, Schedule, Ramp up Time, and Quality of Product). The major concern to the project as a result of this analysis was the project schedule. Each of the 10 items assessed had moderate to significant potential to impact the overall schedule (i.e., time to market). No more than three of the top 10 items had a moderate to significant impact on Cost, Ramp up time, or Product Quality. This data was presented to the project sponsors within the corporation, along with a request for the resources necessary to carry out the mitigating actions. All resources requested were granted, along with a challenge to keep the project on schedule.

Figure 12.4



Maintenance: Once a month, the progress of the mitigation activities was reviewed. Once a quarter, the Boston Matrix was reviewed to confirm that the risk profile was accurate. Over time, some items became less of a risk, some presented a higher risk to the project.

Lessons Learned

- Risk management requires stakeholder involvement, knowledge, and understanding.
- The risk process needs to be fully followed – which means ongoing review and communication (see Chapter 3 of this Guide).

12.8 IT Project – Construction Case Study

Scenario

This case study is based on the development of a standard deployment approach and installation kit for a process historian system to support multiple manufacturing and R&D sites for a global pharmaceutical manufacturer. The project was intended to replace the local site ad-hoc approach to implementation of the technology which had resulted in inconsistent installations and significant differences in the level of qualification activities undertaken.

Outcome

The project scope specified a standard system architecture (using company approved components) and a standard version of the software vendor's process historian. The project would carry out design and implementation of the system as well as standard functional and non-functional testing. This would deliver a standard installation and qualification process for local site use.

The planning for the project was fairly straightforward as it built on previous activities undertaken on specific sites and made use of a core team of experts. The project delivered a successful package for site use which resulted in a significant (>60%) reduction in the time spent on site implementations. Below are some of the key features of the implementation phase that contributed to the success of the project:

- The Project Team was carefully selected with dedicated core team members and vendor experts that between them held the expertise needed to effectively implement the project.
- The company above site Computer Validation group was involved in all aspects of the implementation, particularly in the detail design and test case production (not normally part of their remit). This was to ensure that the solution package could be re-used on sites with minimal additional testing.
- The vendor technology was well understood and had been widely deployed in the company in earlier versions.
- The approach to testing and associated record keeping was agreed very early in the planning, meaning that the testing process went smoothly and the scope did not extend at the late stage of the project.

Lessons Learned

- Implementation of a project, particularly one involving complex technologies requires dedicated expertise to be in place.
- To standardize deployments of IT systems requires that the technology being deployed is well understood (in use as well as in theory). Novel technologies and accelerated or standardized deployments do not mix well – they usually require a more iterative “pilot – review – refine – deploy” approaches.
- Understanding and agreeing the validation scope and purpose at the planning stage, and fully engaging with validation expertise is essential in successfully managing the delivery.

12.9 GAMP Inspection Readiness Project Case Study

Scenario

A computer systems inspection readiness program was being delivered using a GAMP 5 based approach: all GxP regulated computer systems were assessed for their compliance against current FDA and EU regulations. The result was to agree a project to ensure that applications as listed below had the appropriate level of verification documentation and procedures, and to review and update the existing site computer system validation policy if it was deemed necessary.

The scope of the project was to cover:

- All computer systems identified as GxP regulated (ERP, laboratory environment stability data collection, laboratory related software, stand-alone software (labeling)).
- All computer hardware and infrastructure (servers, networking).
- Procedures and records connected with operation and documentation of computer systems.
- Procedures and policies connected with the validation of the computer systems.

Outcome

The project was delivered in three phases where deliverables were given a timescale commensurate with risk.

- Immediate Start Tasks for Rapid Completion.
- Immediate Start Tasks for On-Going Completion
- Tasks for Completion towards End of Project

A task team, as shown below, was set up to ensure successful delivery of this high profile and important project within the organisation.

Quality Assurance Manager:

- Responsibility for all quality issues arising from the project and their potential impact on the business.
- Provide interface between existing and proposed systems.
- Provide QA final approval for all programme and project documents.
- Knowledge transfer and training as appropriate.

Quality Control:

- Inventory of all GxP equipment and software.
- Transfer of system knowledge and use.
- Provision of personnel during execution.

Commercial Supply and Logistics:

- Transfer of system knowledge and use.
- Provision of personnel during execution.

Information Technology:

- Provision of test environment to enable IQ/OQ, procedures and test scripts to be generated.
- Provision of documentation in support of validation activities
- Technical support for software and hardware systems
- Archiving of legacy system.

Lessons Learned

It was very encouraging that the company embraced the principles and concepts of GAMP 5 (Reference 5, Appendix 3), and to see how they integrated good project management with the application of GAMP.

They used a risk-based approach to focus the effort of their team on the areas and applications that need the most attention first, and created an action plan to ensure that there is no impact on patient safety, product quality, or the efficacy where computer systems touch the business process.

Appendix 3

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Appendix 4

Glossary

14 Appendix 4 – Glossary

14.1 Acronyms and Abbreviations

AABC	Associated Air Balance Council
ACS	Automated Commercial System (United States Customs)
A/E	Architect/Engineer
AIA	American Institute of Architects
ANVISA	Agência Nacional de Vigilância Sanitária (National Health Surveillance Agency Brazil)
API	Active Pharmaceutical Ingredient
BOD	Basis of Design
CAPA	Corrective and Preventative Action
C&Q	Commissioning and Qualification
CFR	Code of Federal Regulations
CIP	Clean in Place
CM	Construction Management
CPP	Critical Process Parameter
CQA	Critical Quality Attribute
DDS	Detailed Design Specification
DEPCM	Design Engineering, Procurement, and Construction Management
DL	Discipline Lead
DS	Design Specification
EPCM	Engineering, Procurement, and Construction Management
FAT	Factory Acceptance Testing
FDA	Food and Drug Administration
FEL	Front End Loading
FIDIC	Federation Internationale des Ingenieurs-Conseil
FMEA	Failure Mode and Effects Analysis

FRS	Functional Requirements Specification
FTA	Fault Tree Analysis
GAMP	Good Automated Manufacturing Practice
GDP	Good Distribution Practice
GEP	Good Engineering Practice
HACCP	Hazard Analysis and Critical Control Point
HAZOP	Hazard and Operability Study
HEPA	High Efficiency Particulate Air
HMI	Human Machine Interface
HSE	Health Safety and Environmental
HVAC	Heating, Ventilation, and Air Conditioning
ICH	International Conference on Harmonisation
IChemE	Institute of Chemical Engineers (United Kingdom)
IND	Investigational New Drug
I/O	Input/Output
IP	Intellectual Property
IPD	Integrated Project Delivery
IQ	Installation Qualification
IT	Information Technology
JPMA	Japan Pharmaceutical Manufacturers Association
KM	Knowledge Management
KPI	Key Performance Indicators
LEED	Leadership in Energy and Environmental Design
LOTO	Lock Out Tag Out
MHLW	Ministry of Health, Labour and Welfare
MHRA	Medicines and Healthcare products Regulatory Agency
NDA	Non-Disclosure Agreement

NEBB	National Environmental Balancing Bureau
NIST	National Institute of Standards and Technology
OEE	Overall Equipment Effectiveness
OOS	Out of Specification
P&ID	Process and Instrumentation Diagram
PAT	Process Analytical Technology
PDP	Project Delivery Plan
PFD	Process Flow Diagram
PHA	Process Hazard Analysis
PMO	Project Management Office
PO	Purchase Order
PQ	Performance Qualification
QA	Quality Assurance
QC	Quality Control
QRM	Quality Risk Management
RABS	Restricted Access Barrier System
RACI	Responsible, Accountable, Consulted, Informed
RFI	Request for Information
RFP	Request for Proposal
RFQ	Request for Quotation
SAT	Site Acceptance Testing
SIP	Steam in Place
SME	Subject Matter Expert
SOP	Standard Operating Procedure
SPC	Supplementary Protection Certificates
TOP	Turnover Package
ULPA	Ultra Low Penetration Air

URS User Requirements Specification

WBS Work Breakdown Structure

14.2 Definitions

Automated System

A broad range of systems including, but not limited to, automated manufacturing equipment, automated laboratory equipment, process control, manufacturing execution, laboratory information management, manufacturing resource planning, clinical trials data management, and document management systems.

The automated system consists of the hardware, software, and network components, together with the controlled functions and associated documentation. Automated systems are sometimes referred to as computerized systems.

Basis of Design

A design document that describes what the purpose of a given system is and how the system will accomplish its required task. This document is authored previous to the issuance of bid specifications and is often used to develop them. Until the system is developed this is a conceptual document.

Benefits Management Plan

Documentation as to how the project benefits of a project will be measured in order to demonstrate the business case has been achieved.

Bottom Up Estimate

Estimate derived from the analysis of specific project tasks utilizing historic comparison information, regulatory requirements, and owner policies to derive a value for each.

Bottom Up Project

Project initiated by an existing site which has identified a process improvement or new technology which can improve quality, yield, cycle time reduction, improve safety or just replace old assets.

Bridging Funds

Monies allocated to temporarily finance the progress of a project as it awaits stage gate approval for complete funding of the next stage.

Business Case

Purpose for the project and benefit to the owner.

Collaborative Approach

Project execution approach characterized by early and continued collaboration by all key project stakeholders.

Commissioning

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

Communication Plan

Defines key project stakeholders and the type and frequency of communication.

Conceptual Estimate

Estimate developed from the use of parametric or factoring techniques to account for the limited amount of design information available.

Constructability Review

Review of the detail as to how a project will be constructed for the purposes of assessing improved or value added alternatives for the delivery of the construction phase of the project.

Contingency

Monies predefined to support specific unforeseen project changes.

Contract Negotiations

Process by which the Owner and Supplier agree to the terms of a formal contract.

Cost Management

Monitoring the change risk factors, obtaining agreement from all parties involved in a cost change, and monitoring the actual changes to assure they track according to projections.

Critical Process Parameter (CPP)

A process parameter whose variability impacts a quality attribute and therefore needs to be controlled to ensure the process produces the desired quality. A critical process parameter remains critical even if it is controlled.

Critical Quality Attribute (CQA)

A physical, chemical, biological or microbiological property of characteristic that needs to be controlled (directly or indirectly) to ensure product quality.

Critical Step

Unit operation or processing step in which operation out of a specified range of controlled parameters could result in a product that is out of specification, but undetectable by routine measurement methods.

Customer

Process or facility owner who will use the project outcome to generate revenue for the business.

Customer Relationship Management

Process with four basic phases; Gaining Entry – making initial contact, Contracting – clarifying and agreeing roles and responsibilities, Engagement – meeting agreed roles and responsibilities, and Disengagement – agreeing that the contract is complete.

Design Management Strategy

Approach to monitor the design activities.

Design Qualification

Documented verification that the proposed design of the facilities, equipment, or systems is suitable for the intended purpose.

Design Review (IEEE)

A process or meeting during which a system, hardware, or software design is presented to project personnel, managers, users, customers, or other interested parties for comment or approval. Types include critical design review, preliminary design review, system design review.

Design Standards

Standards that describe the characteristics of a design or a design description of data or program components.

Documentation Management

System by which project documentation is issued, administered, distributed, and stored.

End User

A person whose occupation requires the use of an information system but does not require any knowledge of computers or computer programming.

Explicit Knowledge

Tangible information captured in documents, databases, websites, etc.

Fast Track Project

The method of overlapping project life cycle stages to reduce the overall project time line.

Fault Tree Analysis

The identification and analysis of conditions and factors which cause or contribute to the occurrence of a defined undesirable event, usually one which significantly affects system performance, economy, safety or other required characteristics.

Fishbone Diagram

Cause and effect diagram tool used to gain understanding of the root cause of an effect.

Failure Mode and Effects Analysis (FMEA) (IEC)

A method of reliability analysis intended to identify failures, at the basic component level, which have significant consequences affecting the system performance in the application considered.

Front End Loading

Increased extent of effort expanded at the start of a project to initiate, define, and scope a project.

Gantt Chart

Gantt charts illustrate the start and finish dates of the terminal elements and summary elements of a project. Terminal elements and summary elements comprise the work breakdown structure of the project. Some Gantt charts also show the dependency (i.e., precedence network) relationships between activities.

Good Engineering Practice (GEP)

Established engineering methods and standards that are applied throughout a project's life cycle to deliver appropriate, cost-effective solutions.

GxP

The underlying international pharmaceutical requirements, such as those set forth in the US FD&C Act, US PHS Act, FDA regulations, EU Directives, Japanese regulations, or other applicable national legislation or regulations under which a company operates. These include but are not limited to:

- Good Manufacturing Practice (GMP) (pharmaceutical, including Active Pharmaceutical Ingredient (API), veterinary, and blood)
- Good Clinical Practice (GCP)
- Good Laboratory Practice (GLP)
- Good Distribution Practice (GDP)
- Good Quality Practice (GQP)
- Good Pharmacovigilance Practice
- Medical Device Regulations
- Prescription Drug Marketing Act (PDMA)

Hazard Analysis and Critical Control Point (HACCP)

Method to identify potential hazard within critical risk areas of a project.

Hazard and Operability Study (HAZOP)

HAZOP is a structured and systematic examination of a planned or existing process or operation in order to identify and evaluate problems that may represent risks to personnel or equipment, or prevent efficient operation.

Heuristic (Merriam-Webster's)

Involving or serving as an aid to learning, discovery, or problem-solving by experiment and especially trial-and-error methods.

Ishikawa Diagram

Cause and effect diagram tool used to gain understanding of the root cause of an effect.

Isolators

A leak tight enclosure designed to protect operators from hazardous/potent processes or protect processes from people or detrimental external environments or both. A basic enclosure consists of a shell, viewing window, glove/sleeve assemblies, supply and exhaust filters, light(s), gauge(s), Input and Output openings (equipment door airlocks, Rapid Transfer Ports (RTPs), etc.), and various other penetrations.

Kaizen

The philosophy and practice of continuous improvement through the identification and elimination of waste throughout a value stream.

Kaizen Event

An improvement tool that brings together a team to review a situation, identify waste, and propose ways to remove it, and then implement the agreed changes.

Kano Analysis

Method of using terminology to understand the things a customer doesn't typically articulate.

Key Performance Indicators (KPIs)

Project specific milestones that are tied to payment terms.

Lang Factor Approach Estimate

Factor estimate for an entire facility derived solely from equipment costs.

Leaning Out

Refinement of operating costs or procedures to the least amount of effort required.

Lessons Learned

Review of challenges or opportunities from previous projects or a summation of those experienced within the current or future projects.

Lien Waivers

A document from a contractor, subcontractor, materials man, equipment leaser, or other party to the construction project (the claimant) stating they have received payment and waive any future lien rights to the property (of the owner).

Life Cycle Cost

Total cost of ownership over the life of an asset (building or equipment). Typical areas of expenditure which are included in calculating the whole-life cost include construction and acquisition, operations, maintenance, depreciation and cost of finance.

Liquidated Damages

Financial penalties an owner can incur to a supplier's contract for failure to meet a specific milestone as defined in the contract conditions.

Lock Out/Tag Out

Specific practices and procedures to safeguard employees from the unexpected energization or start-up of machinery and equipment, or the release of hazardous energy during service or maintenance activities.

Market Competitiveness

The degree to which competition exists in the market for a specific good or service. Higher levels of competitiveness tend to drive higher efficiencies amongst suppliers.

Master Agreement

A contract reached between parties, in which the parties agree to most of the terms that will govern future transactions or future agreements. A master agreement permits the parties to quickly negotiate future transactions or agreements, because they can rely on the terms of the master agreement, so that the same terms need not be repetitively negotiated, and to negotiate only the deal-specific terms.

Operation and Maintenance (O&M) Manuals

Manuals detailing the operational and maintenance requirements for equipment.

Overall Equipment Effectiveness (OEE)

OEE is a hierarchy of metrics which focus on how effectively a manufacturing operation is utilized. The results are stated in a generic form which allows comparison between manufacturing units in differing industries.

On Demand Bond

Entitlement by the owner to draw down a specific amount of money, without conditions, for the failure of a supplier to properly perform a contract.

Organizational Chart

Diagram which defines a project's team reporting structure and functional division of labor and responsibilities.

Orphan Drug

The FDA grants Orphan Drug status to one company for a drug that is believed to substantially increase the life expectancy of the treated patient for a particular disease. This excludes other companies from receiving an FDA license to produce a similar drug for a finite period (usually 7 years), thereby allowing the company producing the drug to recuperate their R&D expenses.

Pareto Diagrams

A Pareto diagram is related to Pareto's Law: 80 percent of the problems come from 20 percent of the issues (this is also known as the "80/20 rule"). A Pareto diagram illustrates problems by assigned cause, from smallest to largest.

Peer Review

Review of project related documents, equipment or construction by industry knowledgeable personnel who are not directly associated to the project.

Performance Bond

Mechanism whereby the owner is entitled to a specific sum of money for the failure of the supplier to properly perform the contract or becomes insolvent.

Performance Qualification (PQ)

Documented verification that the process and/or the total process related system performs as intended throughout all anticipated operating ranges.

Prequalification

Review and acceptance of a supplier as qualified to provide a formal proposal for services or goods for a project.

Prime Cost

Total of direct material cost, labor cost and expenses costs.

Process Safety

The extent to which the process operating conditions and raw materials can vary while continuing to assure the required product quality.

Process Simplification

An attempt to view any production process and identify if steps can be removed without negatively impacting the overall process.

Process Technology

Any technology required to convert raw materials into finished product and package the product for delivery.

Procurement Plan

A report to identify all bid packages and proposed pre-qualified bidders. The report should list the scope of each bid package along with the contract terms (e.g., lump sum, time, and material, not to exceed) .

Procurement Strategy

Overall strategy for execution of the Procurement related aspects of a Capital Project.

Product Life Cycle (ICH Q9)

All phases in the life of the product from the initial development through marketing until the product's discontinuation.

Program Manager

Project manager in large information technology projects.

Program

A group of related projects managed in a coordinated way to facilitate effective management and control.

Project Charter

Document that succinctly encapsulates the headlines of a project.

Project Controls

Control activities used to monitor, report and control cost, schedule, documentation and engineering changes – projects.

Project Delivery Strategy

Overall project summary that includes an introduction, business case, general project information, organizational chart, roles, responsibilities, project governance, critical issues, procurement and contracting strategy, commissioning and qualification, and handover strategy.

Project Director

Project manager in large capital engineering projects.

Project Initiation

Commencement of activities that begin to define a project.

Project Leader

Project manager for a research and development type project (or Product Leader).

Project Life Cycle

Complete duration of a project from the time it is first conceived as a viable business approach until it is fully operational.

Project Manager

Person responsible for delivering the successful project outcome.

Project Portfolio

A collection of programs and/or projects that are grouped together to facilitate effective management.

Project Sponsor

Person within an organization with the authority for the part of the organization being changed by the project.

Punch List

List detailing incomplete construction related items.

Qualification

The process of demonstrating whether an entity is capable of fulfilling specified requirements.

Quality Risk Management (ICH Q9/Q10)

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

Quality Systems

The organizational structure, procedures, processes, and resources needed to implement quality management.

RACI Chart

Matrix that defines who will do the work and be responsible for its completion (R), who will remain accountable for the completion of the work (A), who should be consulted as the work is being progressed (C), and who should be informed of the work upon completion (I).

Regulatory Approval

A project's satisfactory compliance with the regulations as required by the governing regulatory bodies.

Regulatory Bodies

Governmental or industry regulations that impose criteria upon a project which must be satisfied in order for the project to meet its business case.

Resource Plan

Allocation of people or materials required to complete a task as identified within a schedule.

Retention

Monies that are held by the Owner to assure all services and goods have been provided as per the contract.

Reverse Auction

Method by which suppliers compete to name their best price in a bid environment to be awarded a contract.

Request for Information (RFI)

A question generated by a party in relation to an issued documents - examples question concerning design drawing intent or clarification of a proposal parameter .

Request for Proposal (RFP)

A formal invitation to a service provider or equipment manufacturer to provide a contractual offer for the goods or services defined within.

Risk-Based Approach

Defines how the risks associated to the scope change will be managed, identifies the risk factors, creates a risk probability and impact rating details how change scope risk factors will be monitored and managed.

Risk Management (ICH Q9)

Systematic application of quality management policies, procedures, and practices to the tasks of assessing, controlling, communicating and reviewing risk.

Scope Change Management Plan

Strategy to monitor project alteration requests as well as corrective measures to address unforeseen changes.

Scope Creep

Result of added project requirements that increase the cost or schedule outside the original defined scope.

Standard Operating Procedure (SOP)

Written procedures (prescribing and describing the steps to be taken in normal and defined conditions) which are necessary to assure control of production and processes.

Stage Gate

Review period within a project where the project is analyzed to determine if it continues to satisfy its business case with a positive review resulting in additional project funding.

Stakeholder (ICH Q9)

Any individual, group or organization that can affect, be affected by, or perceive itself to be affected by a risk. Decision makers might also be stakeholders. For the purposes of ICH Q9, the primary stakeholders are the patient, healthcare professional, regulatory authority, and industry.

Statement of Requirements

Document that defines how the business will measure a successful project, at what capital cost the business case will no longer be viable, valid business reasons for expending additional funds to accelerate the project and project options to be assessed.

Stochastic Estimate

A “top down” estimate approach based on rough cost capacity benchmarks - example cost per sf factor or cost per ton of a product produced from a plant.

Strategic Alliances

Tactical relationships between a owner and its suppliers, service providers, or equipment manufacturers which benefit both parties by an agreement based on volume and price.

Subject Matter Expert (SME)

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

Tacit Knowledge

Information in people's heads, their experience, and personal learning which translate into insights and ideas.

Tech Transfer

The systematic procedure that is followed in order to pass the documented knowledge and experience gained during development and/or commercialization to an appropriate, responsible, and authorized party. Technology transfer embodies both the transfer of documentation and the demonstrated ability of a Receiving Unit to effectively perform the critical elements of transferred technology, to the satisfaction of all parties and any, or all, applicable regulatory bodies.

Technology Strategy

Defined approach outlining the use of technology within a project.

Tender

Response from a supplier to provide the services or goods defined in the proposal.

Testing Sequence

Logical and ordered timing of testing activities in relation to the other deliverables of a project.

Top Down Estimate

“Rule of Thumb” estimate based upon an overall project estimate using only one parameter to determine the value, (i.e., level of required regulatory compliance, square footage, similar building type, similar systems comparison).

Top Down Project

Project initiated by a business owner wanting a capability installed to discover or manufacture a product.

Turnkey

A contract where one party takes full responsibility for the construction, commissioning, and delivering of a project in full working order to the owner.

Two Stage Tender

Two-stage tendering is a procedure typically used to achieve an early appointment of a contractor to a lump-sum contract. For the first stage, the objective is to competitively appoint, on the basis of limited information, a preferred contractor for further negotiation.

User

The pharmaceutical customer or user organization contracting a supplier to provide a product.

User Requirements Specification (URS)

A requirement specification that describes what the equipment or system is supposed to do, thus containing at least a set of criteria or conditions that have to be met.

Validation

Establishing documented evidence that the system does what it purports to do.

Validation Cycle

Listing of a series of events within the life of a direct impact manufacturing system which are identified as important to create or maintain product quality over the life of the direct impact system.

Validation Master Plan

A high level document, which establishes an umbrella validation plan for the entire project and is used as guidance to the project team for resource and technical planning.

Value Management

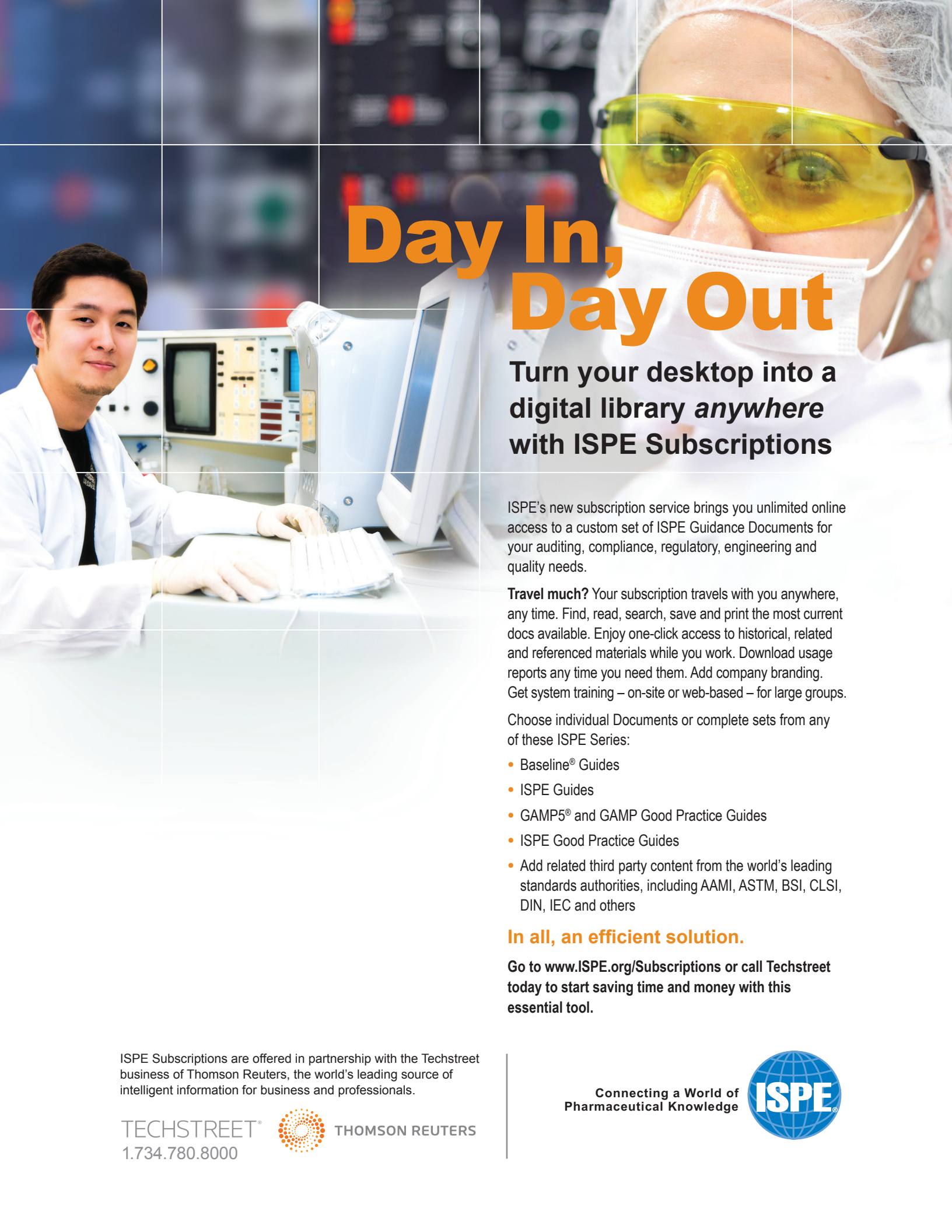
Focus on the entire project lifecycle costs and benefits of the project rather than just the initial “up front” capital investment.

Warranties

Product guaranties for a product to perform to a defined standard for a specified period of time.

Work Breakdown Structure (WBS)

A simplification of a project to list of tasks with start and end dates and milestones.



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Our teams deliver projects that help your teams deliver.

When our Life Sciences customers ask us to work on a new project, they can rely on our extensive and proven expertise of working within validated environments and delivering “best in class” results. Our dedicated Life Sciences project teams, based around the globe, are able to incorporate industry best practices and progressive solutions to deliver a wide range of quality-assured projects on time and on budget. We use our strong project management presence and resources to carefully align the right teams with our customers’ facility locations, wherever they are located.

When delivering validated projects within GxP space, we employ a robust, process-driven approach to project management. We employ a single platform approach utilizing ISO-certified processes, with consistent controls methodology and reporting formats, which helps to drive global consistency and efficiency across all projects, both large and small. Our teams can manage all project phases from planning, design, engineering, and construction, through to commissioning, qualification and closeout. We are then able to use our global integrated facilities management expertise to ensure that the project smoothly transitions to the ongoing operational phase.

We believe that when buildings work better...people work better. That’s why our teams work with our customers to create operationally efficient, validated, productive and sustainable environments, designed to help their teams achieve.

If you would like more information about how we could help you, visit: www.johnsoncontrols.com/lifesciences or, alternatively, contact: **Dennis Boles** by phone: +1 520 421 3114 or email: Dennis.R.Boles@jci.com