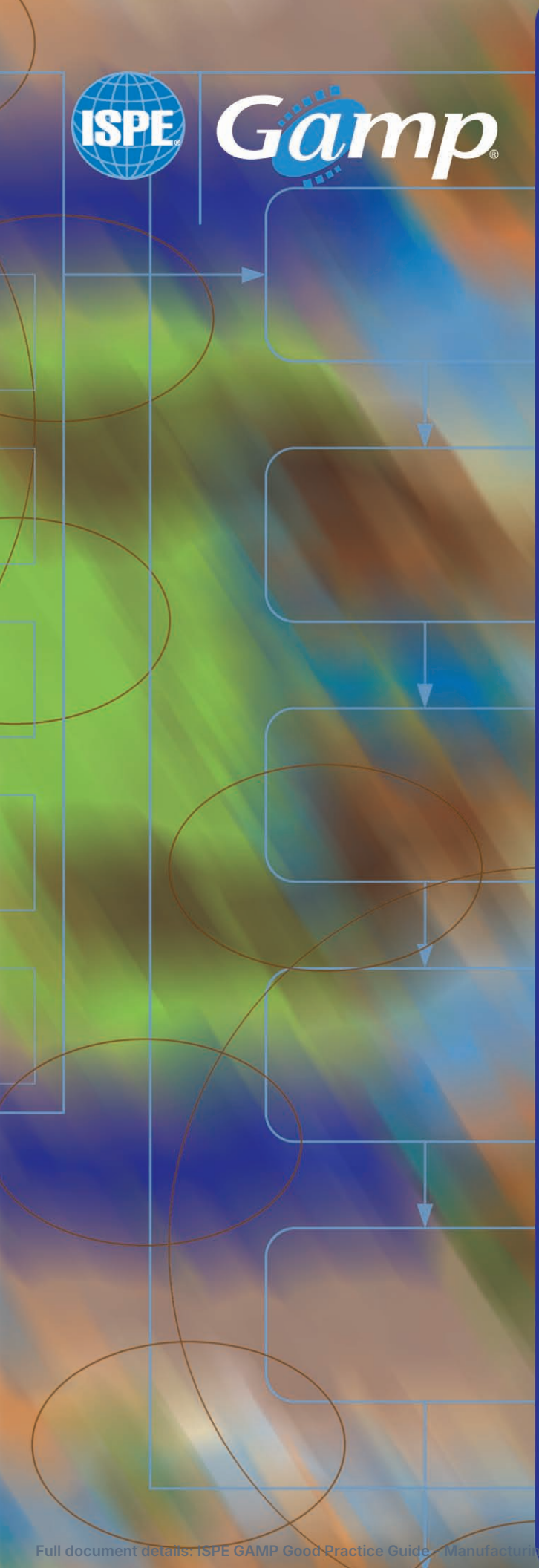

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Preface

The ISPE GAMP® Good Practice Guide: Manufacturing Execution Systems – A Strategic and Program Management Approach, was created to help to facilitate the planning, development, and testing of Manufacturing Execution Systems (MES) that may be used to support manufacturing in life sciences organizations.

This Guide is intended to help bridge the gap between the ISPE GAMP® Good Practice Guide: Global Information Systems Control and Compliance and the ISPE GAMP® Good Practice Guide: Validation of Process Control Systems for supporting and maintaining MES environments. The ISPE GAMP® Good Practice Guide: Manufacturing Execution Systems – A Strategic and Program Management Approach should be read in conjunction with these Guides.

GAMP® guidance aims to achieve computerized systems that are fit for intended use and meet current regulatory requirements, by building upon existing industry good practice in an efficient and effective manner. This Guide has been developed by pharmaceutical industry professionals to meet these goals and principles.

This Guide takes a life cycle approach to examining MES, not as an application, but as a collection or domain of manufacturing related functions that integrates business and process controls, information flow, and human interaction to facilitate the operation of an organization.

As individual systems evolve to become broader in scope, a system considered to be business-oriented may have functionality which connects to Manufacturing Operations and potentially affects product quality. Therefore, the integration of functions may require the application of testing principles for process control systems to a system considered to be business-oriented. The definition of a ‘business system’ may become difficult, and it may become necessary to create logical boundaries around functionality across systems to define categories of use and criticality.

The domain approach presented in this Guide provides an approach to manage life cycles for the integrated manufacturing environment.

The authors of this Guide have built upon ANSI/ISA 95.00.01-2000, Enterprise-Control System Integration, Part 1; Models and Terminology, an industry independent standard for improved integration of manufacturing through communication that defines common terminology and a consistent set of models that emphasize good practices for integration of control systems with other enterprise systems.

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Many other individuals reviewed and provided comments during the preparation of this Guide; although they are too numerous to list here, their input is greatly appreciated.

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Table of Contents

1 Introduction 9
1.1 Overview 9
1.2 Purpose 9
1.3 Scope 10
1.4 Benefits 10
1.5 Objectives 11
1.6 Key Concepts 12
1.7 Structure of Guidance 15

2 Approach to Achieving Control and Compliance 17
2.1 Strategy for MES 17
2.2 MES Life Cycle 19
2.3 Quality Risk Management 20

3 Project Phase 21
3.1 Introduction 21
3.2 Planning 23
3.3 Requirements Definition 28
3.4 Specification and Design 29
3.5 Configuration and Customization 30
3.6 Implementation 31
3.7 Verification 32
3.8 Data Migration 35
3.9 Reporting and Release 37
3.10 Supporting Processes 38

4 Operation Phase 43
4.1 Introduction 43
4.2 Operational Change Control and Configuration Management 43
4.3 Security 44
4.4 Performance Monitoring 44
4.5 Backup and Recovery of Software and Data 44
4.6 Record Retention, Archive, and Retrieval 44
4.7 Business Continuity and Contingency Planning 44
4.8 Periodic Review 45

5 Appendix 1 – Coordination of Compliance, Project, and Operations Activities for MES 47
5.1 Introduction 47
5.2 Structuring a Program 47
5.3 Program Responsibilities 48

Documents
Document Sharing Hub
Full document details: ISPE GAMP Good Practice Guide - Manufacturing Execution Systems - A Strategic and Program Management Approach 2010

6 Appendix 2 – MES Planning 51
6.1 Introduction 51
6.2 Challenges 52
6.3 Business Drivers 53
6.4 Program Planning 54
6.5 Strategic Planning 54
6.6 Functional Domains 58
6.7 Application Selection 58
6.8 MES Implementation Plan 58
6.9 Risk Considerations 58
6.10 Roles and Responsibilities 58
6.11 Regulatory 60
6.12 Data Management Planning 60
6.13 System Architecture 60
6.14 Funding 61

7 Appendix 3 – Domain Approach 63
7.1 Introduction 63
7.2 Applying Domains to Systems Design 64
7.3 Domain Impact on Risk Management and Verification 66
7.4 Domain Approach Implementation for Existing Systems 67
7.5 Summary of Domain Approach Benefits 67
7.6 Expanding the Genealogy Example 68

8 Appendix 4 – Developing an MES Implementation Strategy 69
8.1 Introduction 69
8.2 Considerations and Concepts for Strategy Development 69
8.3 Horizontal Implementation Strategy 70
8.4 Vertical Implementation Strategy 71
8.5 Application Control Strategies 72
8.6 Core Team Activities 74
8.7 Deployment of MES Core Functionality 75
8.8 Phased Deployment 76
8.9 System Controls during Deployments 77
8.10 Other Considerations 77
8.11 Life Cycle Phase Relationships 77

9 Appendix 5 – An Approach to Application and System Selection 79
9.1 Introduction 79
9.2 Development of the Tactical Approach 79
9.3 Scope and Justification 82

10 Appendix 6 – System Integration: Interfaces and Touch Points 85
10.1 Introduction 85
10.2 Data 85
10.3 Middleware 85
10.4 ERP Interface 86
10.5 Process Automation 87
10.6 Batch Systems 88
10.7 LIMS 88
10.8 Interface Issues for Electronic Records and Signatures 89

Documents
Document Sharing Hub

Full document details: ISPE GAMP Good Practice Guide - Manufacturing Execution Systems - A Strategic and Program Management Approach 2010

11 Appendix 7 – Electronic Production Record Systems 91
11.1 Introduction 91
11.2 Establishing Equivalent Electronic Functionality 92
11.3 Ancillary Records 94
11.4 Recipe Management and Testing 94
11.5 EPRS Base Functionality 96
11.6 EPR Modules 97
11.7 Supplemental EPR Processes 98
11.8 Streamlining the Process 98
11.9 EPRS Approaches 99
11.10 EPRS Advantages 101

12 Appendix 8 – Review by Exception 103
12.1 Definition and Justification 103
12.2 Production Report Content Considerations 103
12.3 Considerations for New or Upgraded Systems 105
12.4 Phased Deployment 106
12.5 Periodic Systems Reassessment 106

13 Appendix 9 – Logon, Identification, and Signature Methods 107
13.1 Introduction 107
13.2 Physical Aspects 107
13.3 Logical Aspects 108

14 Appendix 10 – Human and Workflow Considerations 111
14.1 Introduction 111
14.2 Standard Interface and Enforced Operational Sequences 111
14.3 Psychological and Cultural Aspects 112
14.4 User Interface Considerations 112

15 Appendix 11 – Compliant WIP Materials Management 115
15.1 Accounting versus GxP Methods 115
15.2 Managing Material Inventory and Status 115
15.3 Dispensing (Pharmacy) and Material Consumption Considerations 116

16 Appendix 12 – Configuration Management 117
16.1 Introduction 117
16.2 Operational Definitions and Key Aspects 117
16.3 MES Domain Ownership and Life Cycle 118
16.4 Functional and Product Configuration 119
16.5 Coordinated Systems Release Processes 119
16.6 Configuration Management in an MES Domain 120
16.7 System Identification and Nomenclature 121
16.8 Installation Based Nomenclature 124
16.9 Infrastructure Tracking 125
16.10 Establishing Rules for Configuration 125

Documents
Document Sharing Hub
Full document details: ISPE GAMP Good Practice Guide - Manufacturing Execution Systems - A Strategic and Program Management Approach 2010

17 Appendix 13 – Standards and Models for MES 127
17.1 Introduction 127
17.2 MES Functions Address Industry Profiles 128
17.3 ANSI/ISA-95 Enterprise-Control System Integration 128
17.4 XML and B2MML 131
17.5 ANSI/ISA-S88 131
17.6 The Supply Chain Council SCOR Model 131
17.7 MESA International 132

18 Appendix 14 – References 133
18.1 References 133
18.2 Bibliography 134

19 Appendix 15 – Glossary 135
19.1 Abbreviations and Acronyms 135
19.2 Definitions 137

Documents
Document Sharing Hub

Full document details: ISPE GAMP Good Practice Guide - Manufacturing Execution Systems - A Strategic and Program Management Approach 2010

1 Introduction

1.1 Overview

Computerized systems are used widely throughout healthcare manufacture as a result of the substantial automation of business processes and equipment that has occurred during the 1980s and 1990s. This automation typically has occurred in an incremental system-by-system approach, over an extended period of time, which has left many organizations with islands of automation and little or no strategy for systems integration.

A traditional view of Manufacturing Execution Systems (MES) is of computerized systems designed to integrate with and extend the capabilities of other systems, e.g., by providing Recipe Management for process control equipment. The true potential of manufacturing execution lies in the integration of capabilities and functionality of systems through a well designed MES Domain, which can provide benefits, such as reduced cost, faster turnaround, and improved quality, through elimination of redundant data entry, transcription errors, etc.

This Guide uses the framework of GAMP 5, (Reference 5, Appendix 14), as a complete life cycle approach to the development and use of MES for regulated manufacturing. GAMP 5 provides a framework to:

- facilitate interpretation of regulatory requirements based on good practices
- define the approach for planning and project activities
- apply Risk Management to all aspects of the life cycle activities
- identify roles and responsibilities to execute the life cycle
- integrate existing and new systems
- scale activities and documentation appropriately
- leverage existing documentation and knowledge
- identify boundaries and interfacing among the installed systems
- develop an appropriate strategy for MES

This Guide has been developed by the Manufacturing Execution Systems Special Interest Group (MES SIG) of the GAMP Community of Practice (COP), a technical subcommittee of ISPE, to provide project teams with practical information to address the complex challenges of MES.

1.2 Purpose

This Guide is intended to provide regulated pharmaceutical organizations with the information to assist in achieving and maintaining compliant MES appropriate to the needs and capabilities of an organization.

It collects and integrates information and knowledge from many disciplines and sources into a comprehensive guideline. Regulatory requirements, industry standards, and GAMP guidance are leveraged, and references to sources of additional information are provided.

The intended audience of this document includes:

- systems and process development staff

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- manufacturing technology staff
- information technology and engineering staff
- regulatory, compliance, and quality staff
- business process owners
- data owners
- suppliers of technology and systems to industry

1.3 Scope

This Guide focuses on regulated life science manufacturing industries, including:

- pharmaceuticals
- diagnostics
- biologics
- medical devices
- consumer products

It is intended to be applied to the development of new systems, to extensions of existing systems, and to the operation of systems.

Additional information about managing global IT systems may be found in the ISPE GAMP Good Practice Guide: Global Information Systems Control and Compliance (Reference 6, Appendix 14).

Although applications and examples in this document may refer to batch manufacture, the concepts, strategies, approach, and implementation presented in this Guide are applicable to manufacturing found in the medical device industry, consumer products, and packaging operations.

1.4 Benefits

The potential benefits of integrated manufacturing systems for recipe-driven operations include:

- improved scheduling and resource utilization
- improved manufacturing flexibility and process changeover
- reduced Work in Progress (WIP) and improved material tracking
- shorter production cycles
- enforced sequence of operations
- reduced production record errors, electronic or hybrid

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- improved visibility, accuracy and consistency of manufacturing data, enhancing decision support, Process Analytical Technology (PAT), and investigations capabilities
- minimized product recalls
- increased plant reliability
- realize paperless manufacturing
- automated Key Performance Indicator (KPI) generation and reporting, such as an Overall Equipment Efficiency (OEE) calculation
- support knowledge management and PAT
- reduce Quality Unit resources required for day to day operations by providing functionality, such as Electronic Production Records (EPR) and Review By Exception (RBE)

This Guide aims to enable organizations to:

- shorten development and implementation times by leveraging industry experience
- implement design and testing methods that improve life cycle activities
- build compliance into the process
- provide improved understanding and coordination of the complete manufacturing environment
- reduce the risk of project failure
- better balance costs of implementation and operation
- clarify Quality Unit resources required for ongoing system operational support

1.5 Objectives

This Guide aims to provide guidance for the effective and efficient development and operation of MES by:

- providing an understanding of MES
- providing a practical framework for applying the principles and concepts of GAMP 5 to MES
- identifying regulatory and compliance aspects of MES
- providing guidance for MES suppliers
- addressing MES technical considerations

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1.6 Key Concepts

1.6.1 MES Operational Definition

In this Guide, MES is considered to be the complete interactive system of human, electronic, and mechanized functionality to execute Manufacturing Operations. This includes the necessary business and manufacturing computer applications and systems to optimize operations, manage data, and control information flow.

This section further defines MES in the context of this Guide. These concepts have been developed from industry standards (see Appendix 13).

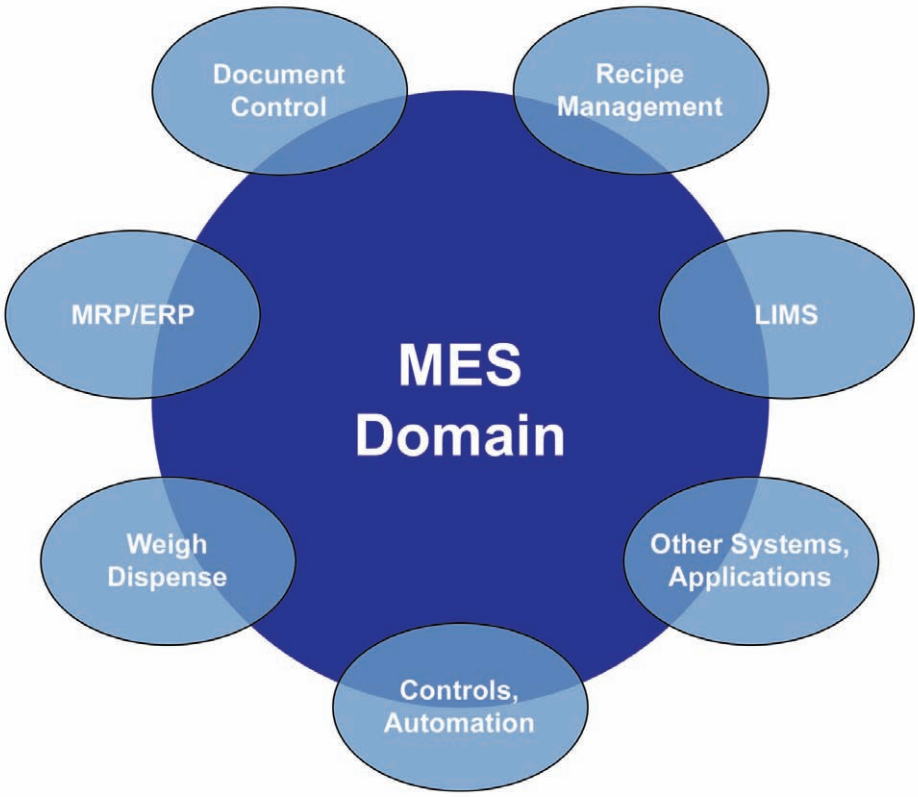
1.6.2 MES Domain Concept

This Guide considers the word 'domain' to be a method for organizing and documenting computerized systems and functions into groups or 'domains', based on common attributes, business and manufacturing goals, intended use, or risks.

The MES Domain is composed of computer systems, applications, and equipment functionality, along with any related data and information, which is used to produce desired intermediate results and final products.

The MES Domain is constructed by defining functionality necessary for production, then determining which existing or new systems or functionality are needed for implementation. An MES domain includes functionality relevant to the intended scope of manufacturing activities; this may incorporate only the necessary functionality from systems components or applications as necessary to support the domain defined by an organization. See Figure 1.1.

Figure 1.1: An Example View of MES Domain



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Systems or applications, e.g., Recipe Management, may have all their functionality within the MES Domain. Some systems, such as MRP and ERP, may have blocks of functionality within the MES Domain which impact manufacturing, and other blocks, such as financial management, outside the MES Domain.

For new systems, the MES Domain can be established during strategy and planning and further refined during implementation. For existing systems, the MES Domain can be defined prior to or during expansions or modifications in order to aid future implementations, testing, and system Configuration Management.

The MES Domain is a design tool, and a high-level indicator of which functionality within systems will need to be verified for GxP operations. The MES Domain also can be used to determine Risk Management activities, as the modular nature of systems can be a factor in determining risks at the functional level. Systems and applications may have differing risk levels for various functionalities or between base products and their configurable or customized modules. The domain concept is further developed below and in Appendix 3.

1.6.3 Functional Domain Concept

The term 'function' for this Guide is a group of tasks that can be classified as having a common objective (Reference ISA-95 (Part 1) (Reference 3, Appendix 14)).

A Functional Domain is a defined boundary around a set of system or application functions related to a common business process or function, including where the functionality resides in different systems or applications, see Material Genealogy Functional Domain example in Figure 1.2. The functions typically share common risks at the process level, but may have different risks based on other factors specific to the system in which that functionality resides, such as amount of customization verses standard equipment and software.

Functional Domains are a tool to aid in defining interaction of the four major components related to Manufacturing Operations, i.e.:

1. information
2. personnel
3. materials
4. equipment

This helps to identify both design requirements and testing activities based on processes, information flow, and regulatory compliance activities.

For further details on domains, see Appendix 3.

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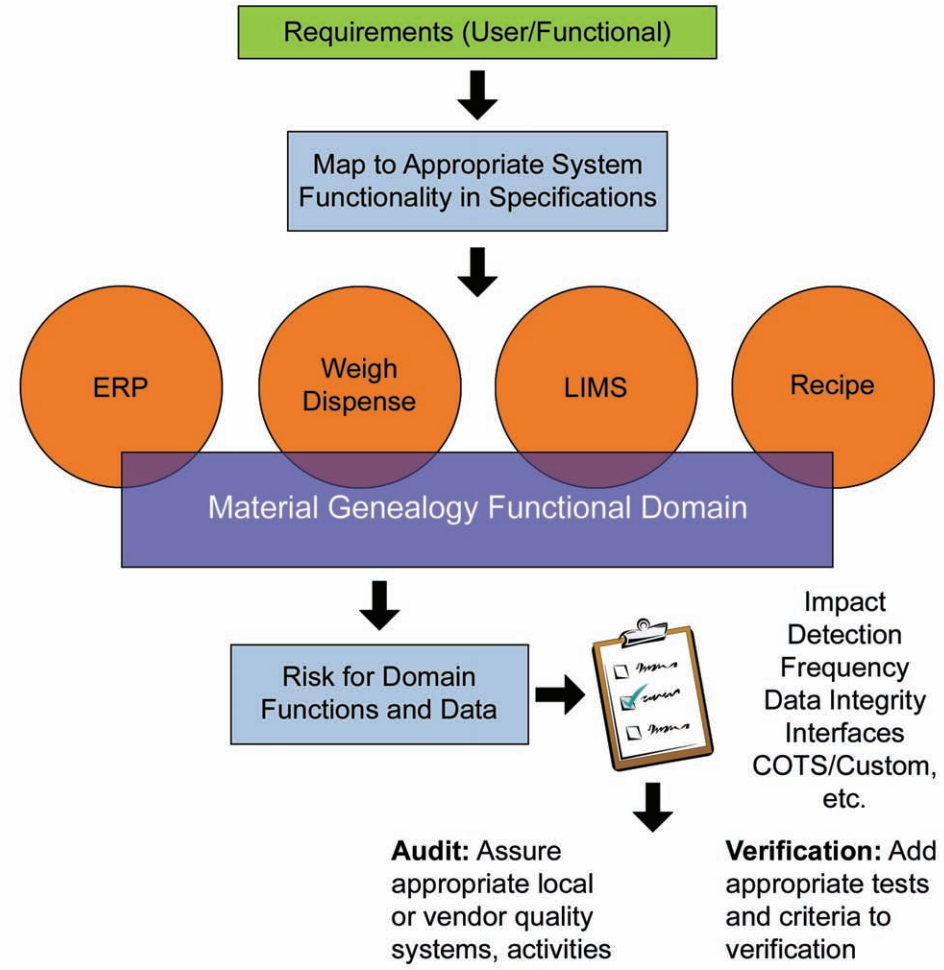
Figure 1.2: Example View of a Functional Domain for Design and Risk



1.6.4 GxP Regulation

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 an organization operates.

These include, but are not limited to:

- Good Manufacturing Practice (GMP)
- Good Clinical Practice (GCP)
- Good Laboratory Practice (GLP)
- Good Distribution Practice (GDP)
- Good Quality Practice (GQP)
- Good Pharmacovigilance Practice
- Medical Device Regulations

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- Prescription Drug Marketing Act (PDMA)

1.7 Structure of Guidance

This Guide comprises a Main Body and a set of supporting appendices.

The main body consists of three main sections:

1. Approach to Achieving Control and Compliance

    - This section applies the GAMP 5 key concepts and discusses the importance of developing a **strategy for MES**, following an **MES life cycle**, and applying **Quality Risk Management** throughout.

2. Project Life Cycle Phase

    - This section provides a **scaleable life cycle approach** to the Project Phase of an MES, from planning through to release. It also covers key **supporting processes**.

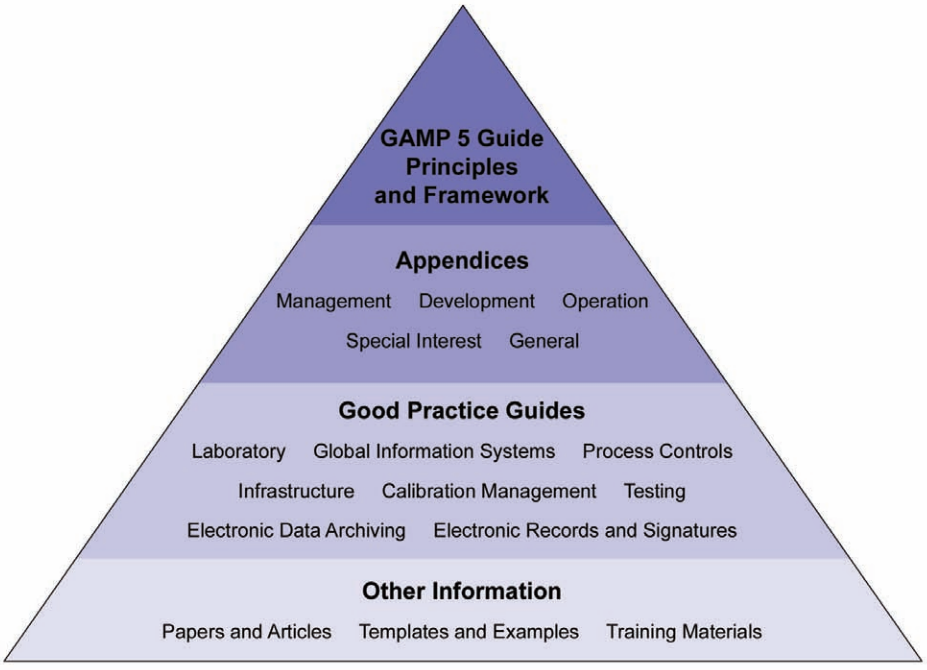
3. Operation Phase

    - This section covers the key processes that are needed in order to **maintain compliance and fitness for intended use** throughout the operational life of an MES. For further information, see the ISPE GAMP Good Practice Guide: A Risk-Based Approach to Operation of GxP Computerized Systems (Reference 6, Appendix 14).

The Appendices consider a range of relevant MES topics that support topics considered in the Main Body, along with references and supporting materials.

This Guide forms part of a family of documents that together provide a powerful and comprehensive body of knowledge covering all aspects of computerized systems good practice and compliance.

Figure 1.3: GAMP Document Structure



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2 Approach to Achieving Control and Compliance

The approach in this Guide is based on application of the following GAMP 5 key concepts:

- process understanding
- life cycle approach within a Quality Management System
- scaleable life cycle activities
- science-based Quality Risk Management
- leveraging supplier involvement

Business processes should be understood thoroughly in order to specify, design, and verify MES.

A computerized system life cycle approach, encompassing all activities from concept to retirement (see GAMP 5 (Reference 5, Appendix 14)), which embraces manufacturing, engineering, quality, and IT is considered a practical way of achieving and maintaining compliance. Required activities and documentation should be scaled commensurate with risk.

Existing documentation (including supplier documentation) should be assessed to determine which may be used. Subject Matter Experts (SMEs) from both the regulated organizations and suppliers should be involved, as required.

Application of Quality Risk Management as an integral part of the life cycle enables effort to be focused on critical aspects of MES in a controlled and justifiable manner.

Regulated organizations should seek to maximize supplier involvement throughout the system life cycle in order to leverage knowledge, experience, and documentation subject to satisfactory supplier assessment. For example, suppliers may assist with requirements gathering, risk assessments, the creation of functional and other specifications, system configuration, testing, support, and maintenance.

A practical framework for applying these concepts to an MES should include:

- developing a strategy for MES
- following a computerized system life cycle
- applying Quality Risk Management throughout

2.1 Strategy for MES

Adopting MES is a significant undertaking that should be carefully planned. Required activities and resources should be identified and funded. Implementation of MES also should be planned and managed appropriately.

2.1.1 Business Strategy

The business strategy for MES should identify the business need or drivers for MES, problems the MES should address, or business objectives MES are expected to achieve. A well defined business strategy is considered essential for gaining executive understanding, support, and funding approval.

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MES typically are linked with higher-order ERP systems that focus on the economic aspects of business processes and also link with PLCs on the automation level. This may result in the involvement of multiple groups, e.g. IT, engineering, production, and quality. Therefore, gaining management approval can be a complex and protracted process.

Appendix 2 describes Strategic Planning specifically related to MES. The GAMP 5 key concept of product and process understanding as it relates to an MES is also fundamental to developing an MES business strategy.

2.1.2 Globalization

To maximize business benefits, an MES may be implemented globally as part of the MES business strategy. This may involve taking into account a range of factors, including:

- definition of core and local needs for hardware, software, and infrastructure
- cultural issues (e.g., language, organization, geographical, legal)
- regulatory differences
- data management
- system architecture
- managing global processes and procedures
- verification approach
- operational management

For further information, see the ISPE GAMP Good Practice Guide: Global Information Systems Control and Compliance (Reference 6, Appendix 14). For further information on MES specific considerations in relation to global systems, see Appendix 4.

2.1.3 Implementation Strategy

Introduction of MES typically has significant impact on Manufacturing Operations and related personnel, from operators to management. Introducing MES requires careful planning to minimize production downtime and risks to Business Continuity. The development of an overall implementation strategy is outlined Appendix 4.

In addition to the defined strategy, the implementation also should address the introduction of new systems and processes into the manufacturing environment.

2.1.4 Implication of Change on an Organization

The introduction of new technology to a manufacturing environment may generate apprehension by many personnel within Operations, Management, and Quality; this should be considered within the strategy. There are several effective mechanisms to help address this apprehension, including:

- management approval of requirements
- Involvement by key stakeholders in requirements and functional data gathering activities. Stakeholders should include many levels of the organization, including manufacturing area personnel.
- communication throughout the planning, development, and implementation process

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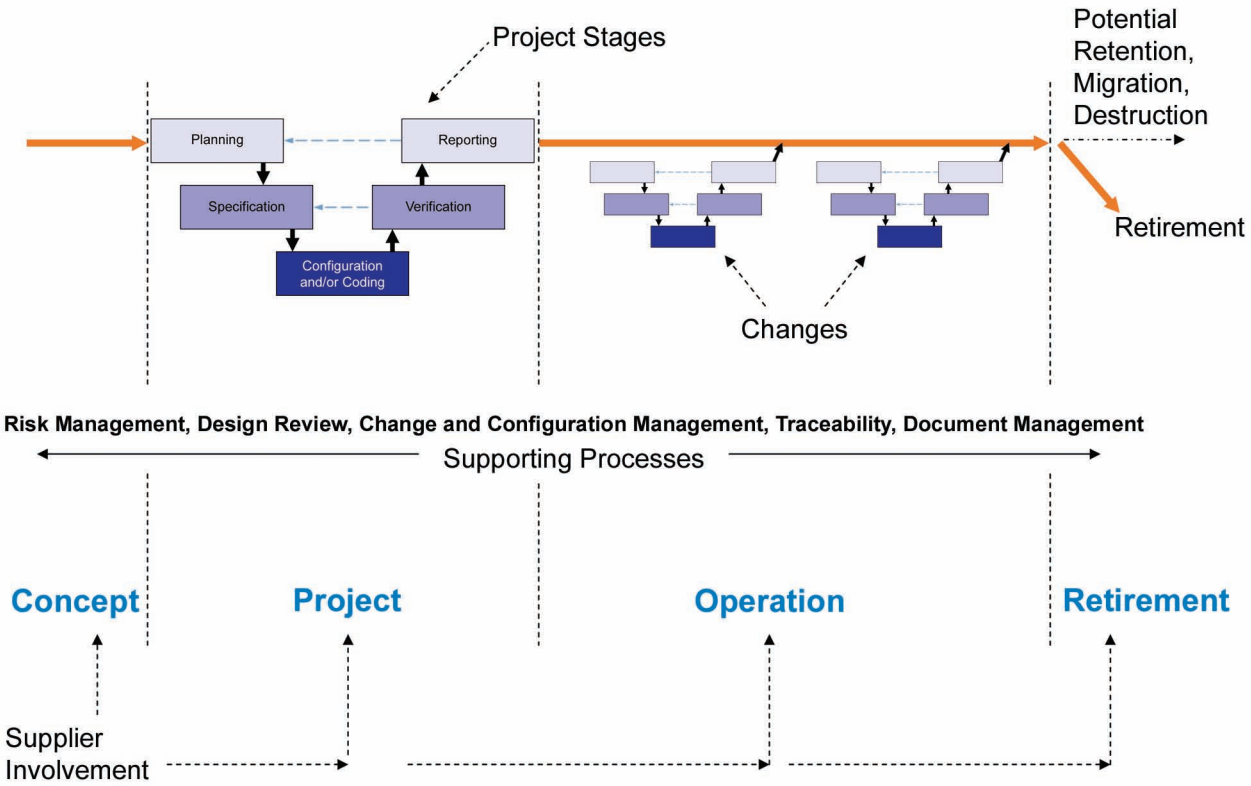
- participation in testing activities
- substantive support presence during initial use
- involvement by personnel in previous plant implementations
- effective, hands-on training programs

2.2 MES Life Cycle

This Guide provides a life cycle approach to MES based on the computerized system life cycle approach discussed in GAMP 5 (see Reference 5, Appendix 14). See Figure 2.1.

Figure 2.1: Project Stages and Supporting Processes within the Life Cycle



While the Project Phase consists of generally sequential stages, detailed activities may be performed in parallel or with some overlap. For example, verification activities may occur through several stages in the Project Phase.

In particular, an MES approach to manufacturing typically involves various levels of systems integration and activities, which can be implemented in stages or phases, as required and as resources allow. Within systems, functionality can be released as it is obtained and verified in a modular fashion if appropriate to systems, equipment, and application design. This may result in a significant overlap of activities. The application of the life cycle should take account of the potential for MES and Functional Domains to span multiple systems.

Two levels of life cycle can be applied to assure proper control of the manufacturing environment:

- **MES Domain life cycle**

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- **individual system life cycles within the MES Domain**

The MES Domain life cycle along with an appropriate management structure should coordinate the manufacturing environment with each system in the MES Domain controlled and tracked to a system life cycle. For further information, see Appendix 12.

To accommodate these types of approaches, the relationships between the life cycle activities and supporting processes become critical to success. Configuration Management and underlying processes for Change Control are particularly important for phased implementations to ensure control of release/gate points for systems, components, modules, equipment, and software versions.

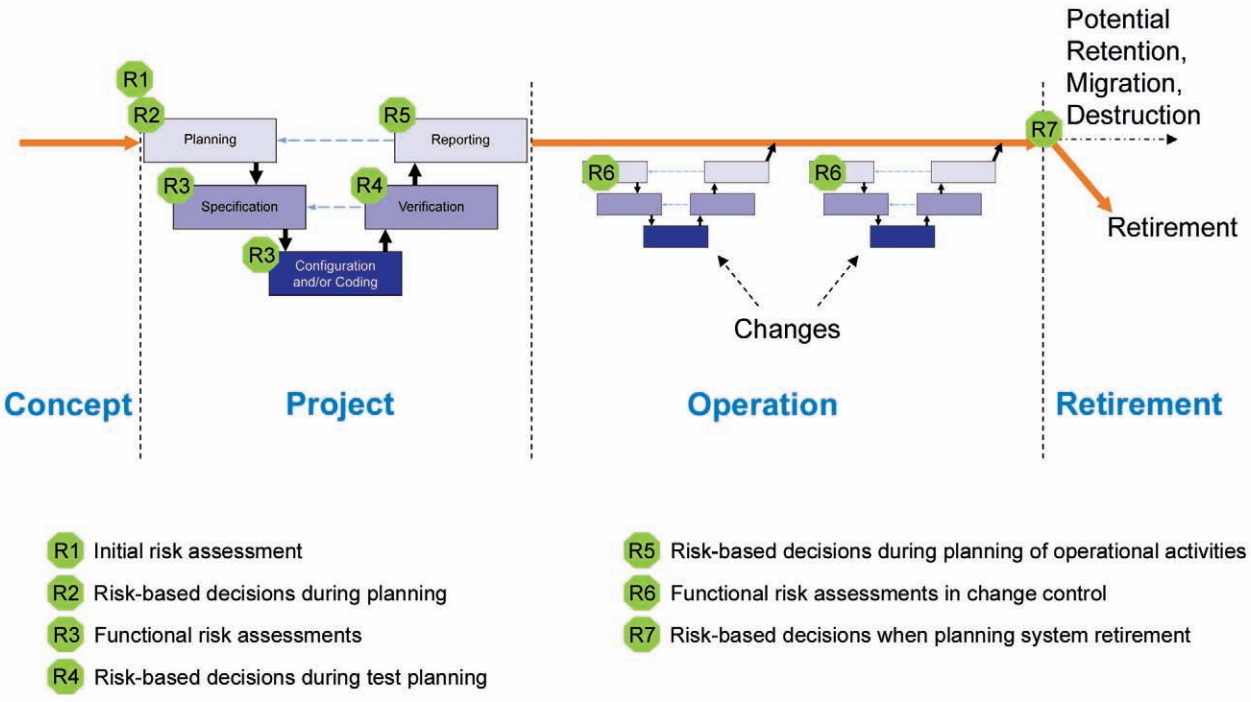
Further specific guidance on developing MES through the project stages is provided in Section 3 of this Guide. Further guidance on MES operation is provided in Section 4 of this Guide.

2.3 Quality Risk Management

Quality Risk Management is a systematic process for the assessment, control, communication, and review of risks. The evaluation of the risk to quality is based on scientific process knowledge linked to protection of the patient. It is an iterative process used throughout the entire computerized system life cycle from concept to retirement.

GAMP 5 describes a generic science based Quality Risk Management process applicable to the complete life cycle as shown in Figure 2.2.

Figure 2.2: Typical Use of Risk-Based Decision Making



For MES, Risk Management may be structured around defined MES Domains. For further information, see Section 3 of this Guide.

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3 Project Phase

3.1 Introduction

GAMP 5 provides a scaleable approach to projects using the systems life cycle based on the following software and hardware categories with increasing risk as the category number increases. Note that an application may have a combination of functions with different categories that may incur different levels of risk.

Software:

- Infrastructure Software (Category 1):
  - not considered in this Guide, reference GAMP 5 (Reference 5, Appendix 14)
- Non-Configured Products (Category 3):
  - This category should not be misinterpreted as having no user-set parameters. Category 3 specifically does not include configuring software to meet unique user business processes or practices, but can include parameters that select operations from among predetermined or programmed functionality, or parameters that allow software to perform the built-in functions in a specific organization IT or other technical environment, such as database aliases, network addresses, and communication with peripheral equipment.
- Configured Products (Category 4):
  - includes configuration of pre-existing modules or functionality to meet user business processes or practices
- Custom Applications (Category 5):
  - includes creation or addition of new or non-standard functionality

Hardware:

- Standard Hardware Components (Category 1)
- Custom-Built Hardware Components (Category 2)

Figure 3.1 shows the GAMP 5 project stages for a typical Configured Product (Category 4).

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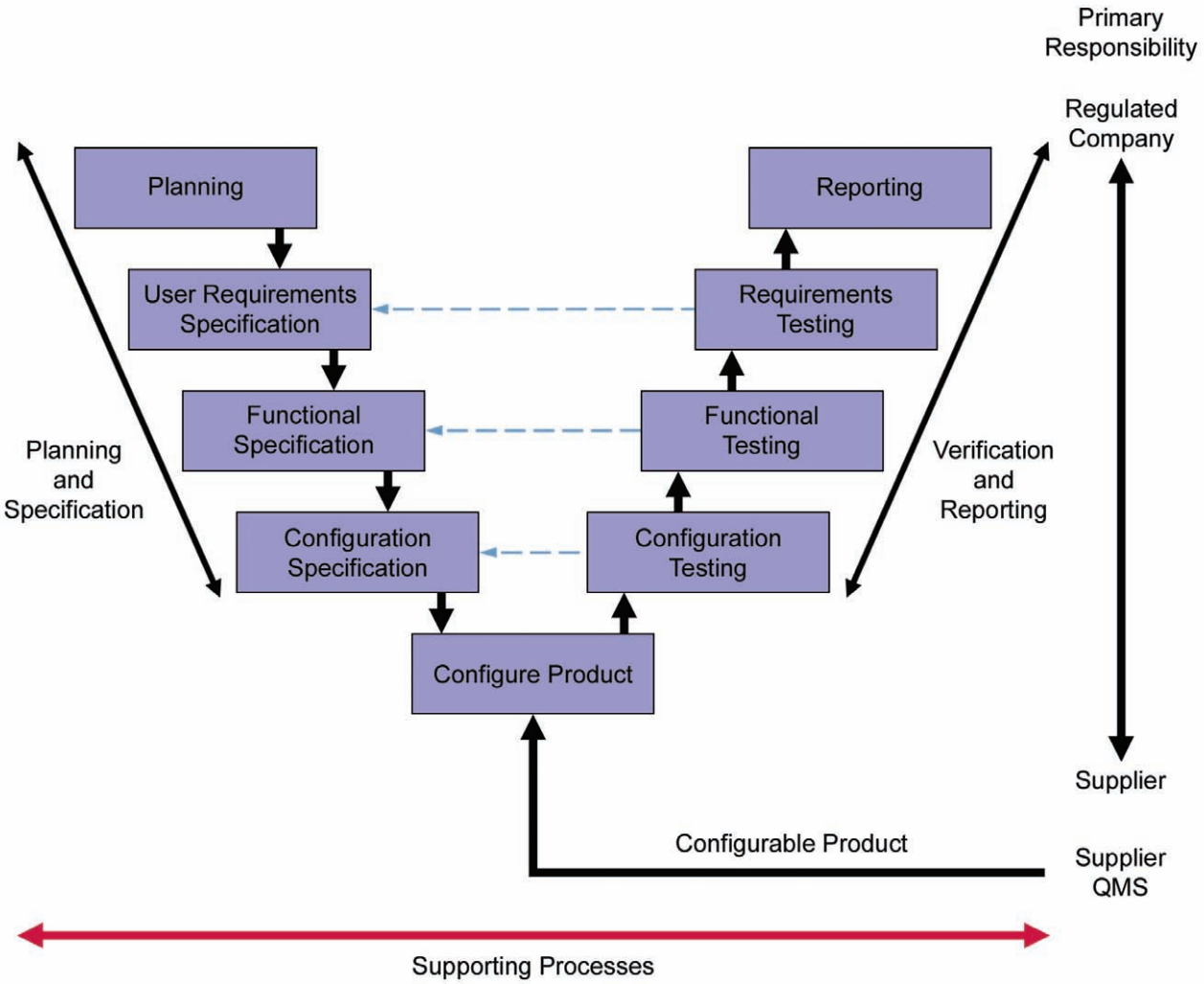
Figure 3.1: Typical Approach for a Configured Product



Note: the GAMP approach in Figure 3.1 defines a set of activities that support complex designs or implementations. Lower risk systems and equipment may not have all of the documentation and activities shown. Activities and documentation can be combined whenever appropriate. Assessed risk can determine the scope and rigor of life cycle activities, which in turn can determine the content and format of documentation (see ASTM 2500-07 (Reference 8, Appendix 14)). Integrated manufacturing environments often include equipment built into facilities production infrastructure that is driven by higher level Supervisory Control and Data Acquisition (SCADA) and recipes to coordinate equipment and operations. Risk assessments should examine the complete assembly of equipment and systems to determine the verification approach.

This section uses the typical approach for a configured model as the overall model for the Project Phase. Typical MES project implementations may include:

- self contained commercial applications that have Application Programming Interface (API) communications (Category 3)
- standalone modules that are integrated by manual data entry (Category 4)
- custom or bespoke software to address specific business processes (Category 5)
- kernel product applications that are supplied by a systems integrator (Category 3)

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- applications used to model business or manufacturing processes that could include all three categories (Category 3, 4, and 5)

- add-on configurable software packages, e.g., Historian, SCADA, batch/processing engines, or multivariate analytical tools that would be used to develop PAT enhancements (Category 3)

A single category for entire systems or applications may not be appropriate. Careful planning is required to ensure that an efficient and effective approach is taken for each component or module (see Section 3.2 for further details). The application of this general approach will vary widely depending on the risk, complexity, and novelty of individual systems. The specifications shown in the Figure 3.1 are not necessarily separate documents; thus, the life cycle activities and related documentation are adjusted to fit the determined risk of the subject system or component. For example, standard equipment is addressed with a simplified approach with high dependency on supplier documentation and quality systems.

3.2 Planning

Planning should focus on activities required to achieve compliant specification and verification during the Project Phase, which should form an integral part of project planning for the MES Domain.

Life cycle activities should be scaled in scope and rigor for factors such as:

- system impact on patient safety, product quality, and data integrity (initial risk assessment)

- system complexity and novelty (architecture and categorization of system components)

- outcome of supplier assessment (supplier capability)

Technical personnel should be capable of assessing risks of systems failing to meet requirements and specifications. Impact on patient safety and product quality requires cross functional Risk Management of which technical Risk Management is a part.

Planning should include appropriate activities to ensure that technical risks are properly addressed in overall safety and quality risk programs. The impact of technical failures should be understood and addressed by those quality risk programs. The risks to safety and quality are then factored back into design and implementation of systems to assure acceptable mitigation.

3.2.1 Initial Risk Assessment

As part of planning an MES Domain, an initial risk assessment should be performed based on:

- an understanding of business processes and business risk assessments

- user requirements

- regulatory requirements

- known functional areas

Either prior to, or as part of, the initial risk assessment, an analysis should be performed to determine which regulatory environments are associated with a system, such as life sciences (e.g., GxP), environmental, safety, and controlled substances and materials. Any relevant previous assessments may provide useful input that can be referenced in an updated document without repeating the activity if the information, data, and system context is still relevant.

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The results of this initial risk assessment should confirm whether the system is GxP regulated and which regulations apply. It should also include an overall assessment of system impact.

The level of effort, formality, and documentation of subsequent Risk Management activities should be determined based on level of risk and system impact. Stages at which risk assessment will be performed should be identified. Any specific Quality Risk Management procedures or standards to be followed should be defined.

3.2.2 GAMP Categorization

Where the default configuration is being used, applications may be considered as non-configured product (Category 3), e.g., where an Original Equipment Manufacturer (OEM) supplier has delivered a package that is not modified by the end user, such as equipment with an embedded control system. In these cases, risk mitigating factors, such as large user base and low complexity may help to determine the categorization.

Some applications, such as SCADA, require complex configuration activities and may be considered Category 4. Custom software, such as new interfaces, should be considered as Category 5, for which increased levels of specification and verification are required. However, the Functional Domain approach encourages examination of systems at a functional level to determine risks associated with system modules, components, or specific functionality. In this manner, GAMP categories can be applied directly to components of systems, preventing over estimating or underestimating risk for an entire system.

Functional Domains may contain different categories of software. For example, a supplied product may be considered Category 3, while additional customized or new software modules may be considered Category 4 or 5. These may be grouped together into higher risk Functional Domains. Additional testing and rigor can then be applied to the higher risk functionality without necessarily increasing the effort for the entire system. Care should be taken in specification and verification to understand how functions interact within a system, and whether functionality can be assessed individually, in groups, or simply as an entire system for GAMP categorization.

3.2.3 Supplier Assessment

The need for a supplier assessment is typically based on the category selected for the required functionality.

Planning should determine how best to use supplier documentation, including existing test documentation, to avoid wasted effort and duplication. Justification for the use of supplier documentation should be provided by the satisfactory outcome of supplier assessments, which may include a supplier audit based on risk factors such as complexity.

Supplier documentation should be assessed for suitability, accuracy, and completeness. There should be flexibility regarding acceptable format, structure, and documentation practices.

Large software and system suppliers may operate from multiple locations with a ‘base’ product being developed at a central location and regional centers working with end users to develop configuration and customizations. There may be multiple or different Quality Management Systems in each location. The supplier assessment should consider all pertinent locations and focus on how responsibilities are divided among the locations with a special emphasis on how patches and upgrades are assessed and tested against any prior end user customization.

Commercially available hardware, software, and documentation should be exploited to take advantage of reduced specification and verification activities. For further information, see GAMP 5, Appendix M2 (Reference 5, Appendix 14).

3.2.4 Validation Planning

A computerized system validation plan should be produced for the overall MES Domain, typically referencing individual plans for systems and processes within the MES Domain.

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Computerized system validation plans should define or reference documentation for:

- What activities are required?
- Methods for implementing and controlling activities and who is responsible. This includes how the system will be released for each stage of verification and for production use, such as any phased release or other techniques to be used. (See Appendix 12.)
- What are the outputs and results of activities and related deliverables, such as documentation?
- critical criteria

The level of detail in the validation plan should reflect the outcome of the initial risk assessment, GAMP categorization, and supplier assessment.

The MES Domain may comprise multi-site systems; thus, the location and Change Control strategy, including documentation, should be addressed early in the Project Phase.

When a central validation strategy is chosen for a standard configuration distributed by a central control organization, deployment sites should have access to supporting documentation for audits and inspections. Local representatives should be familiar with the documentation and document structure and interrelationships to support an internal or external audit. For further information, see the ISPE GAMP Good Practice Guide: Global Information Systems Control and Compliance (Reference 6, Appendix 14).

3.2.5 Key Roles and Responsibilities

The following are key roles and responsibilities when achieving MES compliance and should be assigned during validation planning. Designated individuals should have sufficient experience and training to perform the respective role.

Specific activities may be delegated to appropriate nominated representatives.

For further information, see GAMP 5, Section 6.2.3 (Reference 5, Appendix 14).

Process Owner

The owner of the business process or processes being managed should be identified. Where multiple process owners are responsible for the MES Domain, a Principle Process Owner should be identified. In addition to the responsibilities below, they also should have responsibility for appropriate consultation with the other business process owners. The process owner is ultimately responsible for ensuring that the MES and its operation is in compliance and fit for intended use in accordance with applicable Standard Operating Procedures (SOPs). The process owner also may be the system owner. Specific activities may include:

- approval of key documentation as defined by plans and SOPs
- providing adequate resources (personnel, including SMEs, and financial resources) to support development and operation of a system
- ensuring adequate training for end users
- ensuring that SOPs required for operation of the system exist, are followed, and are reviewed periodically
- ensuring changes are approved and managed

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- reviewing assessment and audit reports, responding to findings, and taking appropriate actions to ensure GxP compliance
- coordinating input from other groups (e.g., finance, information security, health, safety, and environment, legal)

System Owner

The system owner is responsible for the availability and support and maintenance of the MES and for the security of the data residing on that system. Where multiple systems make up the MES Domain, mechanisms should be established to coordinate the responsibilities and activities of the various system owners.

The system owner should act on behalf of the end users. Global MES may have a global system owner and local system owners to manage local implementation.

Specific activities may include:

- ensuring that SOPs required for maintenance of the system exist and are followed
- ensuring adequate training for maintenance and support staff
- ensuring changes are managed
- ensuring the availability of information for the system Inventory and Configuration Management
- providing adequate resources (personnel including SMEs and financial resources) to support the system
- reviewing audit reports, responding to findings, and taking appropriate actions to ensure GxP-compliance
- coordinating input from other groups (e.g., finance, information security, health, safety, and environment, legal)
- ensuring that governance structures exist to allow escalation of issues, decision making and drive business process harmonization

Quality Unit

The Quality Unit has a key role to play in successfully planning and managing the compliance and fitness for intended use of MES, and provides an independent role in the following:

- approval or audit of key documentation, such as policies, procedures, acceptance criteria, plans, reports
- focus on quality critical aspects
- approval of changes that potentially affect patient safety, product quality, or data integrity
- audit processes and supporting documentary evidence to verify that compliance activities are effective
- acts as the SME for GxP compliance aspects

Subject Matter Expert

Qualified and experienced SMEs have a key role in:

- defining the requirements of the MES

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- performing reviews and assessments
- taking technical decisions, using science- based process and product understanding, and sound engineering principles

Different SMEs may be involved with different activities, e.g., during specification and verification.

SMEs should take the lead role in the verification of MES. Responsibilities include planning and defining verification strategies, defining acceptance criteria, selection of appropriate test methods, execution of verification tests, and reviewing results. SMEs may come from a wide range of backgrounds as required, including business process, engineering, IT, supplier, quality, and testing disciplines.

Supplier

Suppliers (including internal suppliers, such as IT or engineering) should provide support for achieving and maintaining system compliance and fitness for intended use. Specific activities may include:

- provision of product documentation
- preparation and review of specific documentation
- acting as subject matter expert for technical aspects, such as configuration and design options
- performing and supporting testing
- change and Configuration Management
- supporting processes geared toward maintaining system compliance, e.g., by providing software patches, providing second tier support for problem resolution processes
- supporting requirements analysis for system customization
- supporting audits by customers to facilitate understanding of supplier quality systems

End User

In addition to using the system in accordance with approved procedures, end users also may be involved in the following activities throughout the life cycle:

- input to user requirements and specifications
- evaluation of prototypes
- testing
- acceptance of system and handover
- input to development of Standard Operating Procedures for use of system
- reporting defects (incidents and problem reporting)
- identifying opportunities for improvement

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3.2.6 Use of Prototype Systems

Projects involving integrated systems may make use of representative smaller versions of systems to facilitate development, as well as verification testing and other uses. In this Guide, the term 'prototype system' is used in place of 'pilot, development, or reference' system. The term 'test system' is used for the formal testing (or Quality Assurance) environment.

One or more prototype systems can be constructed on a small scale and used for verification of hardware, software, and integration functionality in a simulated production environment. Prototype systems may be maintained as training simulators provided that equivalent production system functionality and realistic master data are maintained.

Use of a common system for prototyping, training, and testing may help to justify the costs of maintenance over extended time periods. It should be noted that if testing is to be performed on a common system to support quality systems, such as Change Control, the common system needs to be maintained in a known, verified state that is an equivalent of the production system.

When a new facility or area is being constructed, the production system may be used for testing the complete set of functionality. However, once a production system is on-line for GxP use, testing of software fixes or upgrades prior to use in production becomes difficult without a separate system. This is particularly true where organizations run continuous processes without much down time, or with higher levels of integration where different applications require different shutdown schedules to meet business needs. In such cases, it is considered preferable to have representative test versions of interfaces and systems to perform verification activities away from the production environment. Where cost or complexity are prohibitive, verified and controlled simulations for interface input and output, such as SQL scripts or other tools, may be used instead of interfaces. For further information, see Appendix 4.

3.3 Requirements Definition

User requirements should be clearly and completely understood. The extent and detail of requirements gathering and specification should be sufficient to support risk assessment, further specification, and development of a system, and verification. Comparison of available solutions may result in refinement of the requirements.

For MES, a full understanding of relevant business processes and regulatory requirements is significant. The MES should be capable of complying with the organization's Quality Management System. Specific product process requirements and Critical Process Parameters (CPPs) should be addressed in the creation of the product recipes rather than system design.

User requirements are the responsibility of the user community and should be maintained and controlled.

Users of MES typically are not representative of a single business group. The MES Domain approach recognizes that usage may not be satisfied by a single application, but may be split across multiple applications and systems in the MES Domain. Identification of risks for specific processes or functions can be simplified by using the MES Domain approach. Trace matrices or other cross reference techniques should be used early in the requirements and design phases to ensure that gaps and overlaps are prevented.

A data flow design should be developed during requirements definition indicating data ownership and access and transfer requirements. Such information is a major factor in choosing applications and systems appropriate to the MES project, and will assist with subsequent specification and design.

Depending on the MES strategy and the scope, requirements should be compiled from across an organization under the guidance of an MES program. There may be more than one requirements document depending on the strategy chosen. In the case of multiple requirements documents, a high level document should provide a clear map of the scope and relationship of the various requirements documentation. Strategy documents may provide high-level requirements that are used to guide the development of detailed requirements. For further information, see GAMP 5 Appendix D1 (Reference 5, Appendix 14).

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Specific considerations for MES include:

- A key MES benefit is that it is an enabler of RBE (see Appendix 8).
- use of electronic records and signatures and compliance with relevant regulations (see Appendix 7), e.g.:
  - Security of logon and signature entries may use combinations of electronic, biometric, or manual methods for identifying an individual depending on system design.
  - confirmation of manual entry steps

For further information, see the ISPE GAMP Good Practice Guide: A Risk-Based Approach to Compliant Electronic Records and Signatures (Reference 6, Appendix 14).

- Data interfaces between different systems, e.g., transactional business systems may need to support continuous processing taking place in manufacturing area systems. Risk assessments should take into account loss of communications.

For further information, see Appendix 7 and Appendix 10.

3.3.1 Risk Assessments

Typically, high-level risk assessments alone are not adequate for the purchase of complex systems, as they do not reflect workflow details.

Further risk assessments, commencing during requirements definition, should address functional risks. These risk assessments should be based on the identified Functional Domains.

Each major user of the different functionality should be a principle contributor to defining risks and the resulting requirements.

3.4 Specification and Design

3.4.1 System Specification and Design

MES may be implemented using several approaches; therefore, the structure of the specifications may vary. As with requirements, multiple specifications may be required, and may trace to one or more requirements documents that cross business group, application, or system boundaries. Risk Management should take into account the structure of the requirements. Upon examining existing and new applications and systems, a functional map can be created so that risks may be assigned to required functions and various systems, taking into consideration the benefits for standard or customized integration.

Design documentation for MES should relate the application of the hardware and software to the manufacturing process. For further information on aspects of specification and design, see GAMP 5 Appendices D1 through D7 (Reference 5, Appendix 14).

Example of a System Specification Approach for MES

An example of a system specification approach that is hierarchical and traceable includes:

- The root specification describes and provides cross-references to individual systems and applications, integration, infrastructure, and equipment that comprise the MES implementation.

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- The root specification may include specifications for common functionality, such as user interface, data conventions across applications and systems, and self contained functionality from a supplier.
- Individual system specifications focus on each MES Domain component.
- Design and configuration specifications detail how the system is built and configured for use at each location.

How a system implements a requirement is important to Manufacturing Operations and often directly affects the required labor and systems integration related to unit operations. Time spent reworking specifications during implementation may reduce available resources and time required for adequate testing.

3.4.2 Design Review

System specification and design should be reviewed to confirm that proposed or ongoing designs will result in systems that are capable of executing the required business processes including Data Management. Design review may be performed once or in phased or cyclical approaches depending on the implementation methods and the level of risk and impact potential of the planned system. These activities involve reviewing the system specifications, and prototype if applicable, against the user requirements, design practices and guidelines, applicable regulatory requirements, and identified risks. The purpose is to ensure and document:

- the adequacy of the design and configuration specifications for development or purchase
- that the design will meet the intended use of the system and business process requirements
- that the system, as designed, will comply with GMP and other applicable regulations
- that identified risks are adequately controlled
- that adequate traceability among systems specifications and test documentation is established

For MES, which are based on Configured Products, a significant part of the design review activities should have been performed by the supplier during their development of the product. This should be verified during supplier assessment. User design review activities should focus on the configuration activities.

Design reviews should be performed by appropriate SMEs.

For further information, see GAMP 5, Appendix M5 (Reference 5, Appendix 14).

3.5 Configuration and Customization

3.5.1 System Build, Installation, and Configuration

System Build, Installation, and Configuration involves developing or procuring new hardware or software modules, configuring any hardware and software, and building the overall system. Decisions for the selection of hardware, infrastructure, and applications should be based on a Risk Management approach for the approved design.

For further information, see Appendix 12.

3.5.2 Configuration

Configuration typically involves setting system parameters to match an organization's business processes using standard system functionality, e.g.:

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- enabling or disabling a function
- that the design will meet the intended use of the system and business process requirements
- database queries
- hardware switch and jumper settings
- selecting options from embedded software in equipment

3.5.3 Customization

Customization involves altering or adding to standard or supplier delivered systems and equipment functionality. End users take on responsibility for added risk by requesting alterations or implementing their own changes.

Assessment of risks for customized software, infrastructure, or system hardware should determine the impact on production, as well as on systems functionality, including assessment of impact that may cross system boundaries.

Customized items can be grouped into one or more Functional Domains and the appropriate risk-based approaches applied to specification and verification based upon risk assessments for those Functional Domains, mitigated by individual function and hardware factors, such as lower complexity or impact.

Software examples include:

- software code changes
- new applications or programs
- new modules that link into applications
- complex scripting that modifies system functionality

Software customization is designated as software Category 5, requiring more extensive testing based on risk, and should be identified as part of the validation strategy. Customized hardware is designated as hardware Category 2.

3.6 Implementation

The approach to implementation of an MES Domain will affect the validation strategy and should be considered in advance. Factors to consider typically include:

- establishing control responsibilities for hardware and software environments
- determining single verses multiple process or site rollouts
- defining testing in controlled offline test environments verses production environments
- training
- future development

The following should be appropriately reviewed and resolved:

- how and when additional functionality is to be rolled out

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- how and when additional sites are to be rolled out
- how are phase and functionality additions going to be supported at both the new and existing sites
- ownership of the configuration, verification, and support at all the sites
- how to maintain validated systems when new functionality needs to be integrated and validated
- data management and migration, e.g., paper to electronic, existing system to new system, site to site

MES projects are typically deployed in one of the following ways:

- central control of applications
  - A central organization is responsible for specifying, developing, and controlling versions of applications in the MES Domain.
  - Changes requested by sites are implemented by the central organization.
- site control of applications
  - Sites are responsible for specifying, developing, and controlling versions of applications in the MES Domain.
- combination of central and site control
  - A central organization is responsible for core applications or functionality with sites responsible for the remainder.

For further information, see Appendix 4.

3.7 Verification

Verification confirms that specifications have been met and that systems are fit for the intended use. Verification encompasses Factory Acceptance Tests, Site Acceptance Tests, commissioning and testing, to identify defects, confirm installation, and demonstrate the system meets its requirements.

This section contains a summary of testing requirements for MES. For further information, including detailed checklists, see GAMP 5, Appendix D5 (Reference 5, Appendix 14) and the ISPE GAMP Good Practice Guide: Testing of GxP Systems (Reference 6, Appendix 14).

3.7.1 Test Strategy

An appropriate test strategy should be developed covering all required stages based on the risk, complexity, and novelty of systems. Supplier documentation should be assessed and used if suitable and the supplier is prepared to make the documentation available. The strategy should define which types of testing are required and the number and purpose of test specifications. The test strategy should be reviewed and approved by appropriate SMEs.

The test strategy should take into account the number of suppliers involved and whether suppliers are performing standard or specialized activities. For example, more rigorous testing may be required if a supplier is not following routine or well-established procedures.

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Since MES spans functionality between process control, operational control, and business systems, the test strategy should be defined to address all types of functionality. Business systems may tend to be transactional, maintained by an IT organization, and be enterprise or facility-wide. Process control systems tend to be real time, maintained by Operations or Engineering with designs based upon unit operations. The Functional Domain-based approach focuses the test strategy on the appropriate testing of functionality, regardless of the system or application within which the functionality resides.

3.7.2 Use of Traceability

The source and ownership of the data elements that are used within the MES Domain should be identified in order to define the scope of testing. A process should be established to link user requirements through functional specifications, design specifications, and configuration specifications to testing across the applications and systems, databases, and integration components that make up the defined MES Domain. Traceability should be confirmed during design review. Key parameters to consider include:

- identifying data or information elements as well as the source of the data (e.g., materials)
- defining the process that will convert the data or information (e.g., convert materials from ERP Inventory formats to shop-floor Work Order formats)
- identifying outputs from the conversion process, (e.g., material lots, production quantities, or other created information)
- defining the destination of the converted data or information
- defining the timing and delivery requirements

Within the MES Domain, the typical testing steps should then be applied as they relate to Functional Domain elements.

For further information, see Appendix 6.

3.7.3 Stages of Testing

MES typically involves the configuration of commercially available software products running on Standard Hardware Components. Software products which are configured for a specific business process are typically classified as GAMP Category 4.

In such cases, and based on satisfactory supplier and risk assessments, a testing approach based on the three levels of configuration, functionality, and requirements is typically applicable. The number of test documents required to cover these three levels will depend on the complexity and impact of the system.

Testing should focus on:

- Installation testing – tests should verify and document that system components are combined and installed in accordance with specifications, supplier documentation, and local and global requirements.
- Configuration testing – tests should verify that the package has been configured in accordance with the relevant specification. The tests may take the form of inspections or check of supplier documentation.
- Functional testing – functionality that supports the specific business process based on risk and supplier assessments (this is an area where supplier documentation may be leveraged).
- Requirements testing that demonstrate fitness for intended use; this may include testing the system holistically against requirements depending on risk.

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- Requirements testing should include delivery and acceptance of the final documentation set from the supplier, including specifications, manuals, and drawings, if not already covered.

- Any further or more rigorous tests as a result of risk and supplier assessments.

When working with suppliers, tests are often structured to allow contractual acceptance, e.g.:

- Factory Acceptance Tests (sometimes abbreviated to FATs) are performed at the supplier site before delivery to show that the system is working sufficiently well to be installed and tested on-site

- Site Acceptance Tests (sometimes abbreviated to SATs and sometimes called System Acceptance Testing) show that the system is working in its operational environment and that it interfaces correctly with other systems and peripherals.

Any custom software required as part of MES, such as new interfaces, should be considered Category 5, for which more rigorous testing is required. For further information on test strategy, execution, and reporting, as well as supplier and automated testing, see GAMP 5, Appendix D5.

3.7.4 Specific Aspects to Consider

For MES, aspects that require particular consideration to ensure adequate testing include:

- power failure testing, especially brownout (low voltage situations without complete power loss)

Brownouts can result in some, but not all systems reset with possible data and sequence synchronization issues.

- prevention against loss of critical data or loss of control action

- ease of controlled restart

- system access and security features

- audit trails and logging of critical actions including manual interactions

- manual data entry features and testing methods

- electronic signature integrity

- alarms and error messages

- critical calculations

- critical transactions

- transfer of critical data into other packages or systems for further processing

- interfaces and data transfers

- backup and restore

- data archival and retrieval

- ability to deal with high volume loads especially if the system is accessed by many users as part of a network application

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- test data
- normalization of data

In addition, MES may involve substantial integration and interface activities.

3.7.5 Integration and Interface Testing

Planning should identify clearly how systems and components in the MES Domain need to be integrated. For an integrated testing approach to be feasible, it is important that the implementation program is under change management to ensure there is no adverse impact on previously tested components. This includes having a unified process if different Project Change Control approaches are being used for various components of the MES Domain. This is particularly important for MES and equipment that are verified in a modular fashion by system, function, room, area, or site.

The test strategy should define the approach to testing of interfaces.

Interfaces may be documented and managed as independent systems, or as a component of one of the source data systems. The approach should consider:

- whether a particular system is dominant in generating or storing data
- whether data transmission flow is one-way or duplex
- whether one system previously exists or is installed first and the interface can be assigned to it
- whether the interface is comprised of middleware (non-configured, configured, or custom) or the interface is a constituent part of one system or database

Interface testing should include tests for data integrity, performance under load, and error reporting at a minimum.

Tests should cover each data flow transfer (e.g., daily download, batched data transfer, or real-time data). Once installed in a production environment, the interface should be verified to have the correct connectivity to applications and databases. See Appendix 3 and Appendix 6.

3.8 Data Migration

3.8.1 Data Migration Planning

Migration or the transfer of data from one system to another is a key issue when planning and executing MES projects. Data migration plans should be based on risk and developed to describe execution and verification activities for transferring permanent, historical, or live real time data from existing systems to test or production systems. For further information, see GAMP 5, Appendix D7 (Reference 5, Appendix 14).

Migrating system data from existing corporate or site systems involves planning for:

- availability of data migration tools
- development of scripts
- current state of site based systems (active, retired, archived, under revision, or upgrade)
- cutover strategy from test to production systems

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- access times to operational systems and applications
- electronic data conversion or move
- verification
- backup and archiving of data sets

Existing systems may be staged to become obsolete or may become part of an MES Domain. For systems that will become part of an MES Domain, the data should be examined for compatibility of format and structure. Migration plans should address any internal reformatting or schema changes required for access by other systems.

3.8.2 Data Migration Execution and Verification

Migration may involve changing data to a different format during the process to fit new system constructs or standards. In some cases, this entails transferring data from paper to electronic format. Migration from one electronic system to another may involve script or code development. Development of these should consider the requirements for ensuring data and referential integrity.

Verification of migrated data includes:

- confirmation the correct number of data records were transferred
- verification of data values and format
- verification of scripts or code used to translate data
- appropriate data sampling and comparison of migrated data to original data whether the original data is paper or electronic format
- review and approval of migration results by appropriate Quality Unit representatives for test or production systems

The verification of data should be performed by reviewing the data directly in the database using software utilities (e.g., SQL) or indirectly through the use of the applications involved in the migration. Data review may be performed manually or via a controlled software utility or tool.

The verification of data using a sampling approach should be performed based on an approved procedure or established standards (e.g., ANSI/ASQC).

Depending on test and implementation methods, historical data may have to be migrated to test systems to ensure a realistic and appropriate test environment.

A data migration report should be generated and may be part of associated system documentation.

3.8.3 Migration Data Types

Specific data may be loaded in advance (static data), but other data cannot as it may be subject to continuous change (dynamic data).

Migration and its verification should be carefully planned during the start-up and cut-over period. Procedural and technical controls to prevent modification by users, administrators, or other electronic systems should be established prior to migration. Data types to support the migration and verification procedures may be described by some broad categories, such as:

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- Static System Specification nomenclature, abbreviations, symbols, and dimensional conversions
- Static Specification Tables, which contain the parameter data that will not change from process to process
- Dynamic Specification tables are typically business process and product specific that are updated at the beginning of execution to define materials, processes, process equipment, and assets like scales, instruments, and storage containers for use in the process to be run.
- Dynamic status tables are updated as a result of executing the business process rules or recording information about non-automated operations.
- Dynamic application specific data is created from business operations, consumption of materials, and production creation.
- Dynamic history (logs or tables) data are the data that becomes the audit trails and internal transaction logs.

3.9 Reporting and Release

Projects often require different stages of hardware and infrastructure availability (e.g., development, testing, and production environment) in preparation for system release.

Providing effective environments may be very difficult or costly due to the number of systems and technologies involved. As a result, projects may need to consider the use of simulation (test) environments.

Well managed system handover from the project team to the process owner, system owner, and operational users is a pre-requisite for effectively maintaining the compliance of a system.

Therefore, reports should be produced summarizing:

- activities performed
- deviations from the plan
- outstanding or corrective actions
- statement of fitness for intended use of the system
- systems and resources to support ongoing maintenance are in place and tested
- disaster recovery and Business Continuity measures are in place and tested

For further information, see GAMP 5, Appendix M7 (Reference 5, Appendix 14).

Organizations should ensure a controlled and documented cutover process from development and testing to production with documentation demonstrating that release criteria have been met. Planning should allow for any phased cutover steps and the time and resources to perform them. Cutover criteria should include the following, as appropriate:

- confirmation of completion of verification activities
- Outstanding actions or deviations have been addressed. This may include risk-based decisions for:
  - Corrective and Preventive Action (CAPA) or other closeout requirements and criteria

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- planned, on-going verification in the production environment

- Data archiving for obsolete legacy systems has been executed. Future data retrieval methods have been developed.

- Existing test data has been removed from production systems.

- Data migration to production systems has been successful.

3.10 Supporting Processes

The key supporting activities for MES project development are:

1. Risk Management

2. Configuration Management, including Project Change Control

3. Release Management

3.10.1 Risk Management

Quality Risk Management is a systematic process for the assessment, control, communication, and review of risks to patient safety, product quality, and data integrity, based on a framework consistent with ICH Q9 (Reference 1, Appendix 14). It is used:

- to identify risks and to remove or reduce them to an acceptable level

- as part of a scaleable approach that enables regulated organizations to select the appropriate life cycle activities for a specific system

For MES, an initial risk assessment is required to understand the overall system impact as described in Section 3.2.1. This should be followed by one or more functional risk assessments as the system specification and design are developed, as described in Section 3.3.1.

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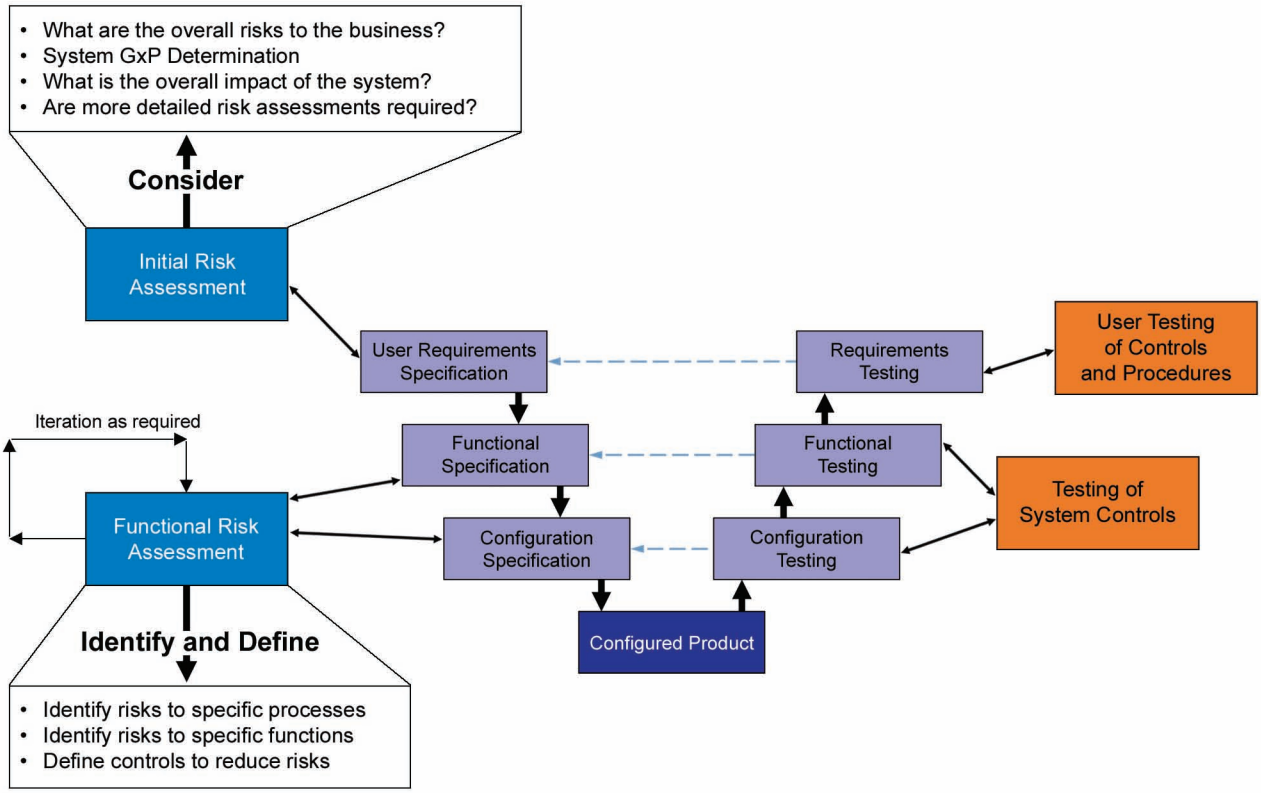
Figure 3.2: Risk-Based Approach for Configured Product (Category 4)



MES functionality poses particular challenges during the project life cycle, in that they may be complex and found on multiple systems with extensive interfaces. The MES Domain approach provides a practical framework for assessing and managing risks associated with these challenges.

3.10.1.1 MES and Functional Domain Approach and Risk Management

There is a distinction between an MES Domain and a Functional Domain. An **MES Domain** may be viewed as **all** the functionality related to Manufacturing Operations and management, and a **Functional Domain** may be viewed as a list of related functions that perform a particular set of tasks within the overall MES Domain. Individual functions may reside in more than one Functional Domain.

The MES and Functional Domain approach facilitates identification and grouping of related functions and data, including across system boundaries, which can be assessed together for risk. This helps ensure a consistent assignment of risk attributes to functionality that may be physically or logically separated in the systems architecture. MES implementations typically have a relatively high level of risk because of the likely impact on product quality and the difficulty of adequately documenting processes, requirements, and design because of complex data pathways through a number of related functions and common tasks.

Using an MES and Functional Domain approach, a matrix can be developed from requirements and specifications to show which functionality across systems is linked to a common task or data. Each matrix can become a Functional Domain, or related functions within the matrix may be grouped into one or more Functional Domains. Risk assessments may be made for each of these Functional Domains. Testing methods and criteria may then be developed and applied to items in the Functional Domain as described in this Guide. See Appendix 3.

3.10.1.2 Considerations when Assessing Risks

Important points to consider when assessing the risks associated with a Functional Domain include:

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- understanding customization verses configuration
- Working with suppliers or system integrators to create matrices of components, such as scripts or linked code (e.g., Visual Basic for Applications (VBA)), that is not in the standard system or application. This item list requires additional attention in testing because of increased risk. High-risk components may not be concentrated in any one Functional Domain. An additional use of a Functional Domain approach can be to group all functionality with a common set of risk attributes into a Functional Domain for which a consistent approach for specification and verification is established.
- Understanding how code types differ. For example, ladder logic functionality is simpler and more controlled than custom programming using programming languages such as VBA and C++.
- Understanding how the intended use of a system or component may affect the product or process. For example, a simple device with large potential impact to product may warrant more rigorous supplier assessment and verification.
- Understanding critical steps in the manufacturing of products. such as weighing components, order of addition, manual instructions, in-process product sampling and testing, and verification of actual results to process limits. Issues encountered with these operations may impact the quality, efficacy, and safety of the product, as well as the safety of Operations personnel near processing equipment.
- understanding the levels of complexity and integration of interfaces
- Understanding functionality used for execution of Quality Assurance and Quality Control activities, e.g., product disposition, RBE (see Appendix 8).

3.10.1.3 Example Risk Controls

Example controls for identified risks associated with MES include:

- design of redundancies in systems and infrastructure to assure high overall reliability and availability of systems and data
- storage area networks
- making more than one workstation available in a work area
- operational recovery from backup systems through technical and procedural methods across multiple systems
- SOPs for pausing and restarting production operations to minimize impact on processes and data
- automatic recovery from fail-safe conditions, where possible
- automatic or manual (procedural) update and resynchronization of data after a system or communications interruption, including data and transaction buffering

3.10.2 Configuration Management

Configuration Management provides the necessary policies, guidelines, and procedures to document and control the components of the MES Domain systems and supporting networks (hardware, software, and related documentation) throughout their life cycles. During project implementation, the Configuration Management activities typically consist of:

- identification and documentation of system elements

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- status accounting of system configuration items
- reconciliation of system configuration versus required characteristics
- controlling change via Project Change Control

Any involvement of the supplier in these processes should be defined and contractually agreed. For further information, see GAMP 5, Appendix M8 (Reference 5, Appendix 14).

Establishing a configuration baseline for each rollout of the MES program should provide a baseline reference point for operational Change Control, ongoing evaluations, maintenance, and future system assessments or Periodic Reviews.

Periodic system quality audits should continue to verify current MES configurations and conformance with specifications to ensure ongoing regulatory compliance.

The following should be considered for components being integrated within a phased MES implementation:

- definitions of status nomenclature, such as “installed, configured, commissioned, operationally tested, released to Operations”
- criteria to be met for each status to be achieved
- a status management process whereby each milestone is defined, status achievement is recorded and updated as appropriate, and communicated to all concerned

Configuration Management becomes particularly difficult when multiple suppliers and integrators are working on different parts of an MES or an integrated set of systems. Procedures should be developed to ensure accurate and timely communications and scheduling that prevent completed work from being affected by ongoing implementation and testing. For further information, see Appendix 12.

3.10.3 Release Management

Release Management provides methods for defining criteria and responsibilities for releasing equipment, applications, system modules, and systems at each stage of implementation. Processes should include consideration of system boundaries and interfaces to determine impact of new or altered components on the MES Domain implementation.

For further information, see Appendix 12.

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