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GAMP 5

A Risk-Based Approach to Compliant GxP Computerized Systems

Second Edition



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Preface

The COVID-19 global pandemic underlined the essential role of innovation and technical advance in the protection of public health. This Second Edition of the *ISPE GAMP® 5 Guide* is intended to support such innovation and technical advance while safeguarding product quality and patient safety.

Such innovation is essential for life sciences industries in providing value to society while also controlling costs and reducing time to market.

Operating in a highly regulated industry may lead practitioners to apply prescriptive and rigid compliance-based approaches that are not commensurate with and not effective in managing any actual risk to the product and the patient.

This Guide facilitates the effective and efficient use of valuable resources by the application of appropriate and proportionate practices, encouraging innovative approaches to managing risk to patient safety, product quality, and data integrity, while supporting benefit to public health.

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1 Introduction

GAMP guidance aims to safeguard patient safety, product quality, and data integrity in the use of GxP computerized systems. It 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.

GAMP provides practical guidance that:

- Facilitates the interpretation of regulatory requirements
- Establishes a common language and terminology
- Promotes a system life cycle approach based on good practice
- Clarifies roles and responsibilities

It is not a prescriptive method or a standard, but rather provides pragmatic guidance, approaches, and tools for the practitioner.

When applied with expertise and good judgment, this Guide offers a robust, cost-effective approach.

The approach described in this document is designed to be compatible with a wide range of other models, methods, and schemes including:

- Quality systems standards and certification schemes, such as the ISO 9000 Series [1]
- ISO 14971 [2]: Medical devices – Application of risk management to medical devices
- Schemes for assessing and improving organization capability and maturity, such as Capability Maturity Model Integration® (CMMI) [3]
- Software process models such as ISO 12207 [4]
- Iterative, and incremental (Agile) software development methods and models
- Approaches to IT service management, such as ITIL [5]

Where possible, terminology is harmonized with standard international sources such as ICH [6] and ISO [7].

This Guide aims to be fully compatible with the approach described in the ASTM E2500 Standard Guide for Specification, Design, and Verification of Pharmaceutical and Biopharmaceutical Manufacturing Systems and Equipment [8].

GAMP is an ISPE Community of Practice. For further information see www.ispe.org.

1.1 Rationale for GAMP 5 Second Edition

This Second Edition Guide aims to protect patient safety, product quality, and data integrity by facilitating and encouraging the achievement of computerized systems that are effective, reliable, and of high quality.

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While the overall approach, framework, and key concepts remain unchanged, technical content of the Guide has been updated to reflect the increased importance of IT service providers including cloud service providers, evolving approaches to software development including incremental and iterative models and methods, and increased use of software tools and automation to achieve greater control, higher quality, and lower risks throughout the life cycle.

Associated with this is the reinforcement of the message that the GAMP specification and verification approach is not inherently linear but also fully supports iterative and incremental (Agile) methods.

Guidance on the application of new and developing technological areas such as Artificial Intelligence and Machine Learning (AI/ML), blockchain, cloud computing, and Open-Source Software (OSS) has been included or updated.

The importance of critical thinking and the application of patient-centric, risk-based approaches (aimed at quality and safety) versus primarily compliance-driven approaches is further underlined. Concepts of computerized systems assurance as discussed as part of the US FDA Center for Devices and Radiological Health (CDRH) Case for Quality program [9] are also explored and applied.

Links and references to GAMP guidance on the topic area of record and data integrity have been added.

The following ISPE initiatives and topic areas are supported and links and synergies with them have been considered:

Knowledge Management – focusing on how organizations create, manage, and use knowledge throughout the life cycle of a product, enabling organizations to better manage their knowledge as a key asset, in turn improving the effectiveness of the pharmaceutical quality system, and providing operational benefits. [10]

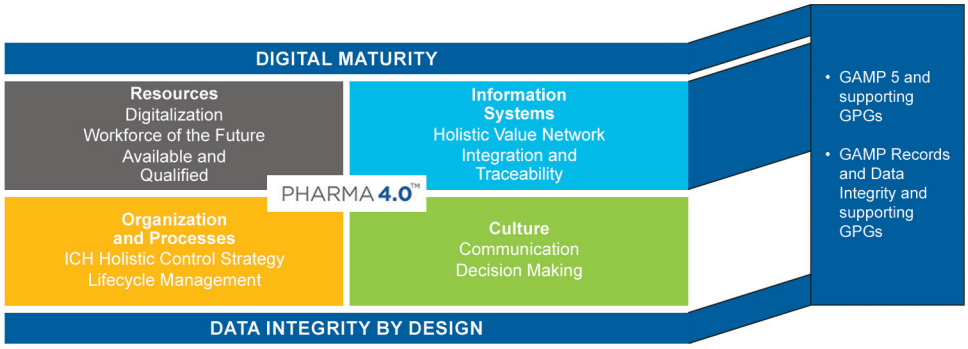
APQ (Advancing Pharmaceutical Quality) – building industry-for-industry tools and programs to help companies assess and improve their quality operations. [11]

Pharma 4.0™ – providing guidance, aligned with the regulatory requirements specific to the pharmaceutical industry, to accelerate Pharma 4.0 transformations. Also known as the Smart Factory, the objective of Pharma 4.0 is to enable organizations involved in the product life cycle to leverage the full potential of digitalization to provide faster innovations for the benefit of patients. [12]

Digital maturity and data integrity by design are enablers to an effective digitalization strategy and are underpinned by well-managed automation and information systems. GAMP guidance aims to ensure that GxP computerized systems are fit for intended use, and that GxP electronic records and data are managed throughout the data life cycle in order to ensure data integrity. See Figure 1.1.

GAMP guidance adopts a patient-centric risk-based approach that enables innovation while demonstrating compliance with regulatory requirements. Pharma 4.0 builds on best practices based on ISPE Guidelines that are enhanced by the digital transformational approach to real time data driven processes.

Figure 1.1: Pharma 4.0 [13]



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1.2 New and Revised Material

New guidance has been included on the following topics:

- Appendix D8 – Agile
- Appendix D9 – Software Tools
- Appendix D10 – Distributed Ledger Systems (Blockchain)
- Appendix D11 – Artificial Intelligence and Machine Learning (AI/ML)
- Appendix M11 – IT Infrastructure
- Appendix M12 – Critical Thinking

Significantly updated guidance has been included on the following topics:

- Appendix D1 – Specifying Requirements
- Appendix S2 – Electronic Production Records

As a result of the above additions and revisions, the following guidance included in the previous version of this Guide have been removed:

- Appendix D2 – Functional Specifications
- Appendix O7 – Repair Activity
- Appendix S5 – Managing Quality within an Outsourced IS/IT Environment

The overall GAMP 5 framework, key concepts, system life cycle, specification and verification approach, and Quality Risk Management (QRM) process (aligned with ICH Q9 [14]) remains unchanged.

1.3 Purpose

The purpose of this Guide is to provide a cost-effective framework of good practice to ensure that computerized systems are effective and of high quality, fit for intended use, and compliant with applicable regulations. The framework aims to safeguard patient safety, product quality, and data integrity while also delivering business benefit. This Guide also provides suppliers to the life-science industry with guidance on the development and maintenance of systems by following good practice.

Patient safety is affected by the integrity of critical records, data, and decisions, as well as those aspects affecting physical attributes of the product. The phrase “patient safety, product quality, and data integrity” is used throughout this Guide to underline this point.

This Guide is intended for use by **regulated companies, suppliers, and regulators.** Suppliers include providers of software, hardware, equipment, system integration services, IT service providers, and IT support services, both internal and external to the regulated company.

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The Guide has been designed for use by a wide range of disciplines and responsibilities, including:

- Management
- Quality Unit
- Research
- Development
- Manufacture
- Laboratory
- Engineering
- IT
- Support Staff
- All associated suppliers

GAMP documents are guides and not standards. It is the responsibility of regulated companies to establish policies and procedures to meet applicable regulatory requirements. Consequently, it is inappropriate for regulated companies, suppliers, or products to claim that they are GAMP certified, approved, or compliant.

1.4 Scope

This Guide applies to computerized systems used in regulated activities covered by:

- 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 Pharmacovigilance Practices (GVP)
- Medical Device Regulations (where applicable and appropriate, e.g., for systems used as part of production or the quality system, and for some examples of Software as a Medical Device (SaMD[1]))

These are collectively known as GxP regulations (see Chapter 2 for full definition).

This Guide provides an approach that is suitable for all types of computerized systems, focusing on those based on standard and configurable products, but equally applicable to custom (bespoke) applications.

[1] Medical devices have their own regulatory framework and standards (e.g., ISO 13485 [16], ISO 14971 [17], and IEC 62304 [18]), typically require individual approval, and are often subject to clinical trial evaluation after software verification. GxP computerized systems as discussed in this Guide usually support internal regulated company GxP business processes, whereas SaMD is typically a product in the hands of patients or health care providers.

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The principles described can be applied to a wide range of computerized systems. Detailed application of these principles to specific system types (e.g., IT, infrastructure, process control systems, and analytical laboratory systems) is described in supporting *ISPE GAMP Good Practice Guides* [15].

Not all the activities defined in this Guide will apply to every system. The scalable approach, with application of critical thinking, enables regulated companies to select the appropriate system life cycle activities.

This Guide is also consistent with other regulatory demands such as Sarbanes-Oxley (SOX)[2] and those associated with data privacy. The use of this Guide, however, does not guarantee compliance with, or replace, these regulatory demands, which will define additional requirements where they are applicable.

It is recognized that there are acceptable methods other than those described in this Guide. This Guide is not intended to place any constraints on innovation and development of new concepts and technologies.

1.4.1 Supplier Aspects

The computerized system life cycle described in this Guide for a regulated company should not be confused with the need for a defined approach or method for software development, which is the responsibility of the supplier.

This Guide defines activities and responsibilities expected of the supplier in the provision of products and services. These activities perform an important role in supporting regulated company activities. The supplier may be a third party or an internal group of the regulated company. Such internal groups should follow processes consistent with the regulated company Quality Management System (QMS).

This Guide uses various diagrams to represent the system life cycle. These diagrams often present relationships in a linear representation. This is not intended to constrain the choice of development methods and models. Suppliers should use the most appropriate methods and models, which may include iterative and incremental (Agile), evolutionary, exploratory, and prototyping techniques, or the use of DevOps approaches (see also Appendix D8).

Modern systems may have a complex supply chain involving multiple suppliers. This Guide aims to meet the needs of each group.

1.5 Business Benefits

Effective, reliable, and high-quality computerized systems assist in achieving the primary objectives of patient safety, product quality, and data integrity, but there are major business benefits in having a defined process that delivers systems fit for intended use, on time, and within budget. Systems that are well defined and specified are easier to support and maintain, resulting in less downtime and lower maintenance costs. Adoption of the approaches described in this Guide will assist regulated companies in managing business risk as well as quality risks.

Specific benefits to both regulated companies and suppliers include:

- Reduction of cost and time taken to achieve and maintain compliance
- Early defect identification and resolution leading to reduced impact on cost and schedule
- Cost-effective operation and maintenance
- Effective change management and continual improvement

[2] The US Sarbanes-Oxley law [19], specifically Section 404, mandates control of computer systems that generate financial records. Many of the good practice principles and electronic records management controls are relevant to compliance with this law.

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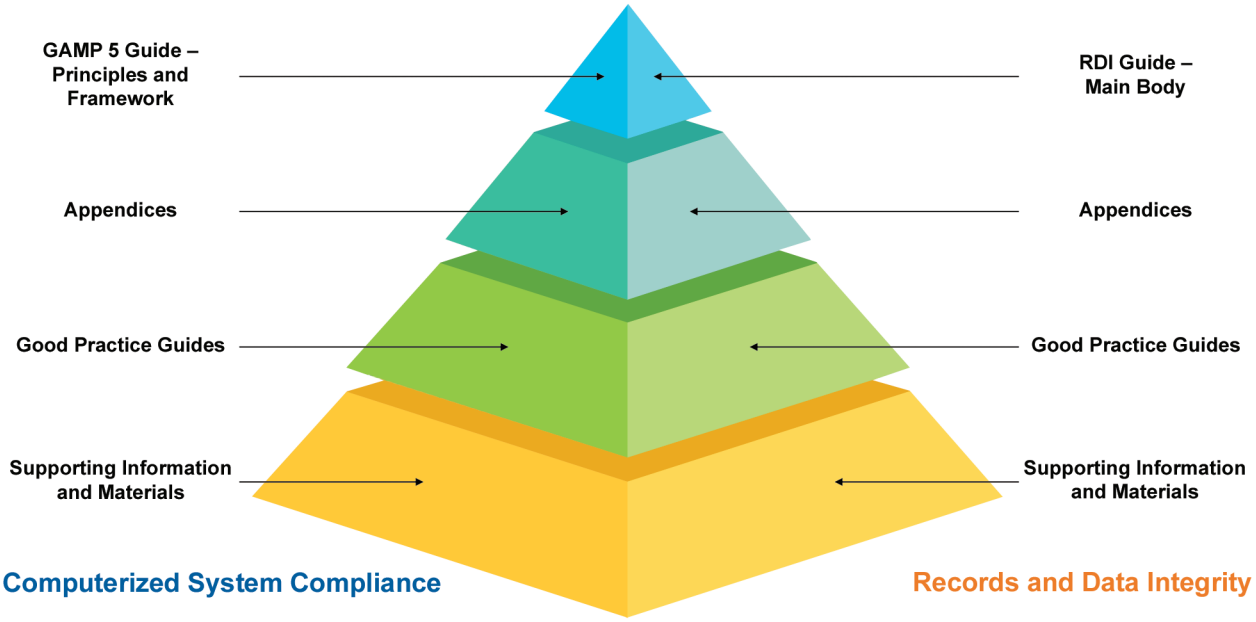
- Enabling of innovation and adoption of new technology
- Providing frameworks for user/supplier cooperation
- Assisting suppliers to produce required documentation
- Promotion of common system life cycle, language, and terminology
- Providing practical guidelines and examples
- Promoting pragmatic interpretation of regulations

1.6 Structure

1.6.1 Overview of GAMP Documentation Structure

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, as shown in Figure 1.2.

Figure 1.2: GAMP Documentation Structure [20]



This Guide comprises a main body and a set of supporting appendices.

The main body provides principles and a life cycle framework applicable to GxP regulated computerized systems.

Practical guidance on a wide range of topics is provided in the supporting appendices.

Separate *ISPE GAMP Good Practice Guides* [15] cover the application of these general principles and framework to specific types of systems and platforms. Other GAMP GPGs provide detailed approaches to specific activities and topics. For information about available *ISPE GAMP Good Practice Guides,* see www.ispe.org.

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