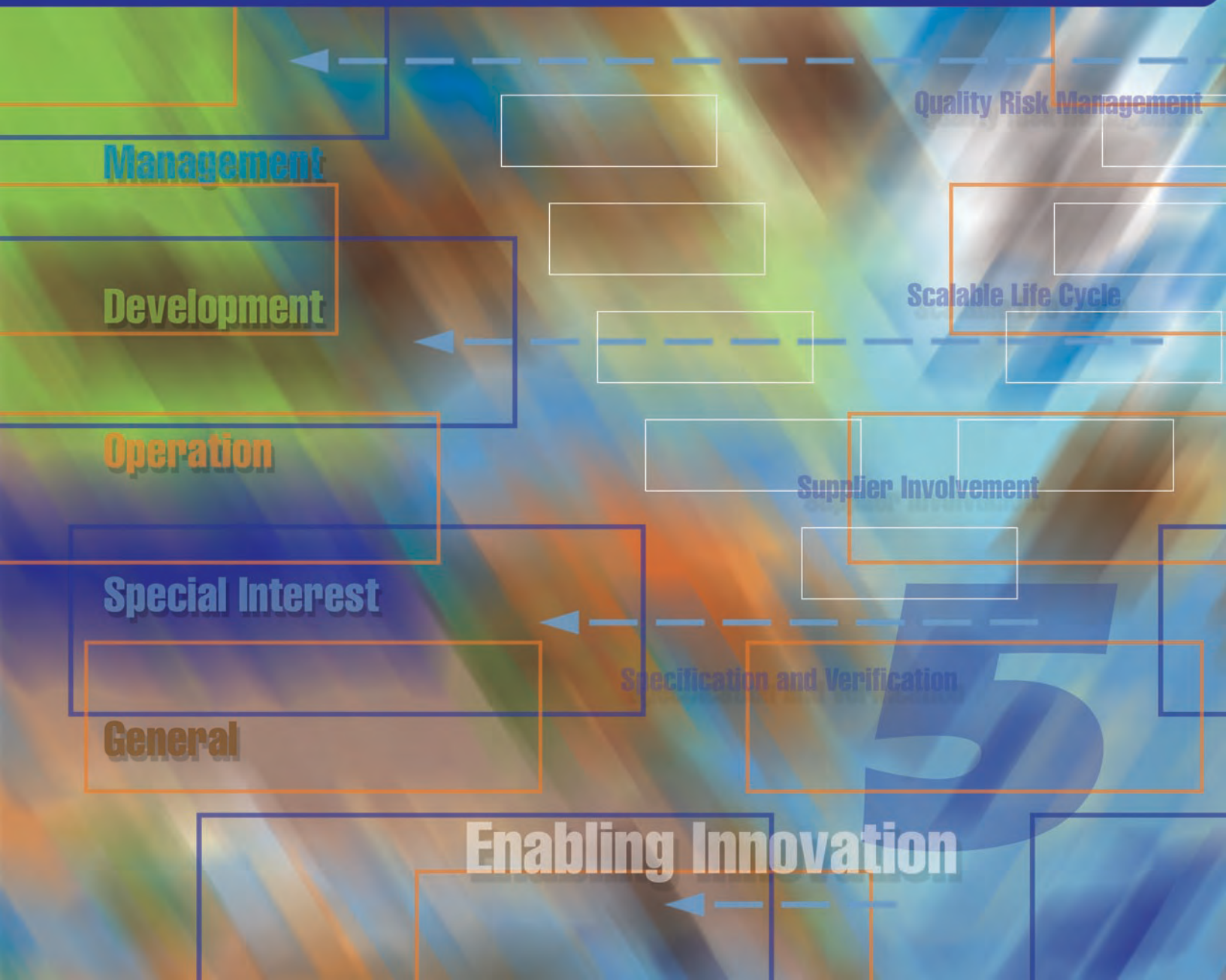
GAMP 5

A Risk-Based Approach to Compliant GxP Computerized Systems



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A Risk-Based Approach to Compliant GxP Computerized Systems

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This Guide is meant to assist pharmaceutical manufacturing companies in managing GxP Regulated systems. ISPE cannot ensure and does not warrant that a system managed in accordance with this Guide will be acceptable to regulatory authorities. Further, this Guide does not replace the need for hiring professional engineers or technicians.

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Foreword

Changing Environment – Regulatory and Industry Initiatives

The pharmaceutical industry is responding to the challenge of significantly improving the way drug development and manufacturing is managed.

New concepts are being developed and applied, including science based risk management approaches, a focus on product and process understanding, and the application of Quality by Design concepts.

Many of these ideas are defined and described in the FDA 21st Century Initiative, new ICH documents such as Q8 Pharmaceutical Development, Q9 Quality Risk Management, and Q10 Pharmaceutical Quality System, ISPE's Product Quality Lifecycle Implementation (PQLI) initiative, and various supporting industry consensus standards, such as the *ASTM E2500 Standard Guide for Specification, Design, and Verification of Pharmaceutical and Biopharmaceutical Manufacturing Systems and Equipment*.

As these new ideas and ways of working are being established, the industry will for some time be in a period of transition.

GAMP® guidance must evolve to meet the needs of the changing environment, and integrate fully with ISPE initiatives such as PQLI, and the revision of the ISPE Baseline® Guide on Commissioning and Qualification. There is both a need and an opportunity to make activities related to all types of computerized systems efficient, effective, and focused on patient safety.

New and Innovative Approaches

Where a computer system is regarded as one component of a wider manufacturing process or system, particularly in an integrated Quality by Design environment, specific and separate computerized system validation may not be necessary. This environment requires both complete product and process understanding and that the critical process parameters can be accurately and reliably predicted and controlled over the design space. In such a case, the fitness for intended use of the computer system within the process may be adequately demonstrated by documented engineering or project activities together with subsequent Process Validation or continuous quality verification of the overall process or system. The same principle applies to the adoption of Process Analytical Technology (PAT).

These innovative approaches are available and useable now if the appropriate pre-requisites are met. While acknowledging that not all regulated companies will be in a position to, or will choose to, fully embrace the new approaches immediately, this Guide is intended to encourage the adoption of such approaches and in no way to be a barrier.

Improving Quality Practice

During the period of transition, the industry continues to need practical guidance based on current good practice – giving practitioners the tools to do the job today, while building a bridge to new approaches. This Guide aims to describe current good practice in order to satisfy the needs of the majority of practitioners involved with computerized systems, while also enabling new and innovative approaches, e.g., for process systems in a Quality by Design environment. These innovative approaches and the application of principles to specific system types will be explored in detail in subsequent documents.

In the meantime, key aspects supportive of ISPE PQLI and ASTM E2500 are addressed immediately to make current activities as effective and efficient as possible. These include:

- focusing on aspects critical to the patient
- avoiding duplication of activities (e.g., by fully integrating engineering and computer system activities so that they are performed only once)
- leveraging supplier activities to the maximum possible extent, while still ensuring fitness for intended use
- clarifying the roles of Subject Matter Experts and Quality Assurance
- scaling all life cycle activities and associated documentation according to risk, complexity, and novelty
- acknowledging that traditional linear or waterfall development models are not the most appropriate in all cases

These are reflected in the Key Concepts upon which this Guide is based, and in the detailed content of this Guide.

This Guide is deliberately flexible with regard to terminology – focusing on value-added activities and avoiding unnecessary activities is the main intent, and different regulated companies and suppliers may choose to use a wide range of different terms. In line with the principles of ASTM 2500, this Guide adopts specification and verification as overall terms describing specific life cycle activities, but does not discard the general life cycle validation framework to reflect current industry practice for companies that decide to maintain these practices rather than applying the new concepts.

Further details may be found in Appendix S1 Alignment with ASTM E2500.

Extended Scope and Application

Coupled with these initiatives in development and manufacturing, a wide and ever-increasing range of local and global networked computerized systems are being used throughout the product life cycle. Many of these are fundamental to GxP activities.

Accuracy and integrity of records and data is essential throughout the product life cycle, from research and development through pre-clinical studies, clinical trials, production and quality control to marketing. The *GAMP Good Practice Guide: A Risk-Based Approach to Compliant Electronic Records and Signatures* provides further guidance on this topic, and should be read in conjunction with this Guide.

Achieving compliance and fitness for intended use for all GxP regulated systems in a pragmatic and efficient manner is essential.

This Guide aims to address the need to safeguard public health, product quality, and data integrity while at the same time enabling innovation and technological advance.

Dr. Guy Wingate, Chair GAMP COP Council
Dr. Arthur (Randy) Perez, Chair GAMP Americas Steering Committee
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Editorial

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General Appendices

1 Introduction

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.

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 responsibility

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, such as those of the Institute of Electrical and Electronics Engineers (IEEE), and certification schemes, such as the International Organization for Standardization (ISO) 9000 Series
- schemes for assessing and improving organization capability and maturity, such as Capability Maturity Model Integration® (CMMI)
- software process models, such as the various spiral models, or ISO 12207
- software development methods, such as Rapid Application Development (RAD), Agile, Rational Unified Process® (RUP), or Extreme Programming (XP)
- approaches to IT service management, such as the IT Infrastructure Library® (ITIL)

Where possible, terminology is harmonized with standard international sources such as International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) and ISO.

This Guide aims to be fully compatible with the approach described in the *American Society for Testing and Materials (ASTM) E2500 Standard Guide for Specification, Design, and Verification of Pharmaceutical and Biopharmaceutical Manufacturing Systems and Equipment.*

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

1.1 Rationale for GAMP 5

This revision of GAMP has been significantly updated to align with the concepts and terminology of recent regulatory and industry developments including:

- ICH Guidance Q8, Q9, and the forthcoming Q10: setting out expectations for the application of science- and risk-based approaches to drug development and manufacture supported by pharmaceutical quality systems

- Product Quality Lifecycle Implementation (PQLI): an initiative launched by ISPE to help industry to implement ICH guidance
- US Food and Drug Administration (FDA) current Good Manufacturing Practices (cGMPs) for the 21st Century Initiative and associated guidance: promoting science based risk management
- Pharmaceutical Inspection Cooperation Scheme (PIC/S) Guidance on Good Practices for Computerised Systems in Regulated GxP Environments: clarifying regulatory expectations
- Emerging industry standards such as those produced by the ASTM E55 Committee[1] promoting process understanding, control, and capability for drug development and manufacture

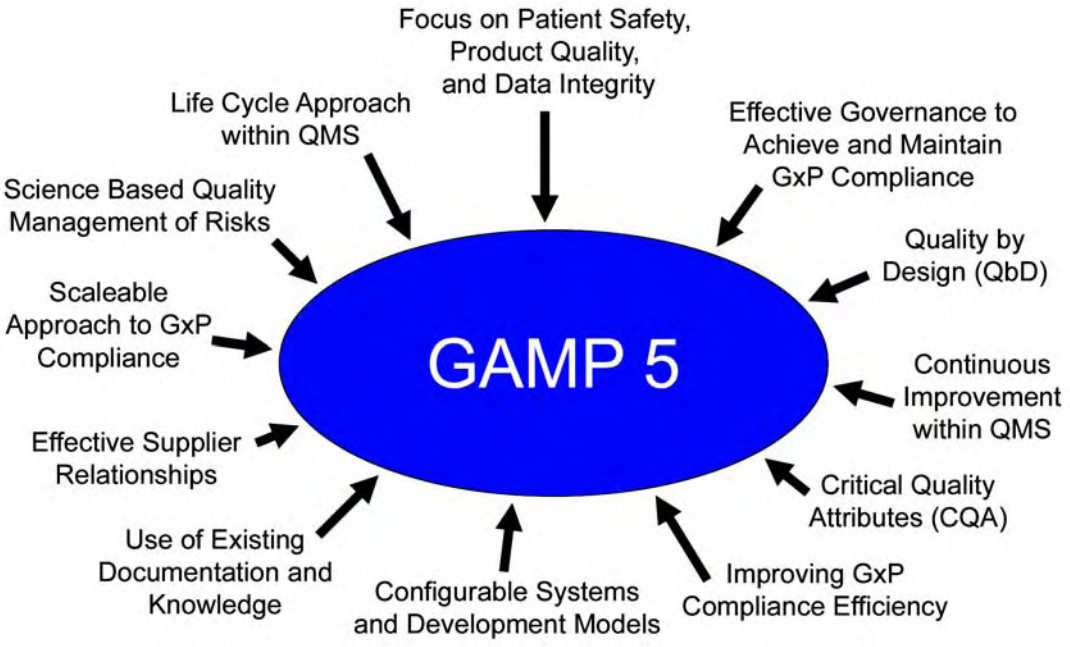
These regulatory and industry developments focus attention on patient safety, product quality, and data integrity. This is a key driver for this Guide.

In addition to this, there is the need to:

- avoid duplication of activities (e.g., by fully integrating engineering and computer system activities so that they are only performed once)
- leverage supplier activities to the maximum possible extent, while still ensuring fitness for intended use
- scale all life cycle activities and associated documentation according to risk, complexity, and novelty
- recognize that most computerized systems are now based on configurable packages, many of them networked
- acknowledge that traditional linear or waterfall development models are not the most appropriate in all cases

These regulatory and industry developments and expectations lead to the drivers shown in Figure 1.1.

Figure 1.1: Drivers for GAMP 5



[1] Including, but not limited to, *ASTM E2500 Standard Guide for Specification, Design, and Verification of Pharmaceutical and Biopharmaceutical Manufacturing Systems and Equipment.*

1.2 New and Revised Material

Particular emphasis is given in this Guide on providing a cost effective approach to compliance and demonstrating fitness for intended use. To support this, new and updated guidance is given on:

- a complete system life cycle approach as part of a Quality Management System (QMS), from concept to retirement
- a scaleable approach to achieve and maintain GxP compliance driven by novelty, complexity, risk to patient safety, product quality, and data integrity
- clarifying the role of the Quality Unit, and introducing the roles of process owner, system owner, and Subject Matter Experts (SMEs)
- in the GMP environment, stressing the importance of clear requirements based on a thorough understanding of the science and of the Critical Quality Attributes (CQAs) of the development and manufacturing process and drug products, to facilitate the adoption of a Quality by Design (QbD) approach
- the leveraging of supplier documentation and knowledge, wherever possible, to avoid unnecessary duplication
- improving efficiency by promoting practical and effective interpretation of GAMP guidance
- maximizing use of documentation from activities, such as development and commissioning, as verification evidence
- the importance of effective governance to achieve and maintain compliance
- identifying opportunities for process and system improvements based on periodic review, root-cause analysis, and Corrective and Preventive Action (CAPA)

New information is provided in specific appendices on the following topics of special interest to industry:

- alignment with ASTM E2500
- organizational change
- outsourcing
- electronic batch recording
- end user applications, such as spreadsheets and small databases
- patch management

In summary, this Guide has been updated to address the changing environment, while still satisfying international GxP regulatory expectations, current at time of publication. This Guide represents industry good practice at time of publication and remains compatible with the principles presented in GAMP 4. The scope has been widened to include related industries and their suppliers, including biotechnology and systems used in medical device manufacturing (excluding software embedded within the medical devices).

1.3 Purpose

The purpose of this Guide is to provide a cost effective framework of good practice to ensure that computerized systems are 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 document 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, and IT support services, both internal and external to the regulated company.

This 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 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)
- Medical Device Regulations (with the exception of software embedded within medical devices)

These are collectively known as GxP regulations (see Section 2 of this Guide 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.

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 GAMP Good Practice Guides (see Appendix G1).

Not all the activities defined in this Guide will apply to every system. The scaleable approach 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] However, the use of this Guide does **not** guarantee compliance with, or replace, these regulatory demands.

It is recognized that there are acceptable methods other than those described in this Guide. The 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 typically 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.

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 RAD or prototyping techniques.

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

There are major business benefits in having a defined process that delivers systems that are 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.

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

[2] The US Sarbanes-Oxley law, 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.

ISPE GAMP 5: A RISK-BASED APPROACH TO COMPLIANT GXP COMPUTERIZED SYSTEMS