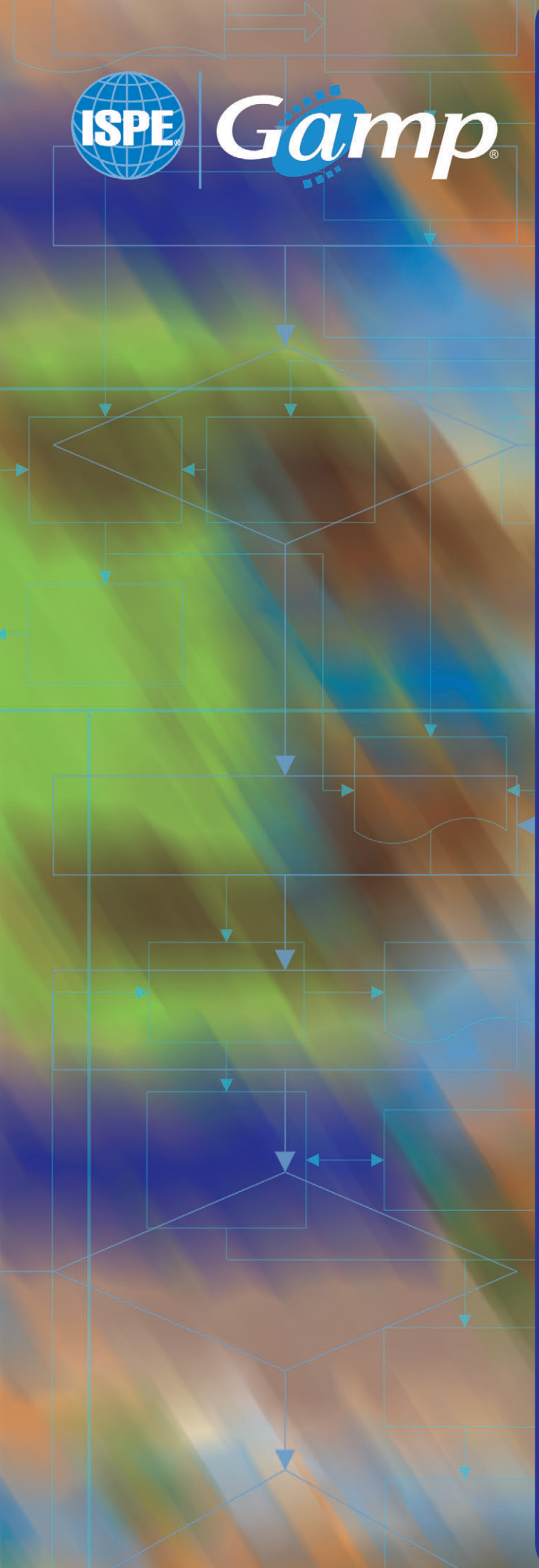

GAMP Good Practice Guide

# A Risk-Based Approach to Calibration Management

Second Edition

# Weiler Engineering...IT'S SAFER INSIDE

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GAMP Good Practice Guide

# A Risk-Based Approach to Calibration Management

## Second Edition

**Disclaimer:**
This Guide is meant to assist pharmaceutical companies in managing calibration. The GAMP COP Calibration Special Interest Group 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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ISBN 978-1-936379-00-2

# Preface

Calibration is an essential element in ensuring compliance in the pharmaceutical and associated regulated life science industries. To ensure success, calibration should be managed effectively, by appropriately qualified and competent personnel. If neglected, calibration is capable of compromising product and process quality, facility, safety, environmental and patient safety, and dramatically increasing costs.

The GAMP® Good Practice Guide: A Risk-Based Approach to Calibration Management provides guidance in setting up a calibration management system, which will give a structured approach to instrument risk assessment, calibration program management, documentation, and corrective actions, essential to regulatory compliance.

It is intended to cover both process and laboratory instrumentation.

There has been a change in regulatory expectations and in associated industry guidance documents. The FDA has been actively promoting a risk-based approach to GMP as part of the 21st Century Initiative. The change in approach to validation and compliance now puts more focus on the integrity, security, and reliability of process control systems and the instrumentation supporting them. The benefit will be a focused calibration effort that concentrates on risks to product quality and public safety. Such a focus also should be cost-effective.

The process of establishing clear procedures and performing risk assessments will allow calibration activities to be managed to concentrate the most resource where it is most needed. This Guide offers a pragmatic approach, based on risk assessment, to provide effectiveness and regulatory compliance as cost effectively as possible.

# Acknowledgements

The following members of the GAMP COP Calibration Special Interest Group (SIG) worked on one or more of the sections of this document and volunteered countless hours to attend meetings and review the many drafts, which were produced over an 18 month period.

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The GAMP COP Calibration SIG would like to acknowledge the support of their direct management and companies in this endeavor. The GAMP COP Calibration SIG would like to thank all those involved in reviewing this Guide for providing valuable comment, including regulatory authorities within Europe and several organizations in the Americas, Australia, Europe, Japan, and New Zealand.

Members of the GAMP COP Council and Steering Committees, along with the ISPE Technical Documents Executive Committee are thanked for their participation in the review of this Guide.


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# Table of Contents

# 1 Introduction

The ISPE GAMP® Good Practice Guide: A Risk-Based Approach to Calibration Management discusses controlling risk to product quality and patient safety.

It discusses issues in calibration management along with existing industry good practice to address those issues. It also considers enhancing business benefits by managing and documenting calibration.

This Guide describes a risk-based approach to calibration management, and seeks to be in clear alignment with other related ISPE Guides and initiatives.

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

Application of this Guide should help to ensure a consistent approach to calibration management in line with regulatory expectations; therefore, the overall risk of compliance failures may be reduced. When applied with expertise and good judgment, this Guide offers a robust, cost effective approach to calibration management.

The approach described considers the full life cycle of instrument management, covering requirements to satisfy regulators and giving guidance on good practice in the pharmaceutical industry. It is a building block for use in qualification, verification, and validation.

The approach described 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), (Reference 14, Appendix 16)
- Certification schemes, such as the International Organization for Standardization (ISO) 9001 Series (Reference 11, Appendix 16)
- ANSI/ISA standard approaches to labeling and tagging (Reference 9, Appendix 16)

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.

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

## 1.1 Rationale

Making the correct decisions depends largely on whether the correct information is acquired. This information is often gathered through measurement; therefore, it is critical that the information is reliable, accurate, and traceable.

The calibration of process control instruments may drift, due to the complexity of their construction and the environmental conditions in which they operate. This drift may be significant within a short period of time and accounts for the requirement for periodic recalibration.

Concentrating resources in the most important areas will maximize their effectiveness. The process of risk assessment will help in achieving this and in reducing costs.

This Guide discusses the importance of calibration and the need/benefits of focusing on critical instruments. If a parameter is not measured, control cannot be assured. Effective calibration management is essential in assuring control and compliance.

The performance of an instrument should be such that there is high confidence that the process has remained within the desired range, i.e., indicated value and associated measurement uncertainty will remain within desired limits.

Instruments should be assessed for potential impact on product quality and patient safety, as well as their accuracy and their stability. Effective calibration is essential in achieving a high degree of confidence that a manufacturing process remains within the defined operating limits.

## 1.2 New and Revised Material

The GAMP Good Practice Guide: A Risk Based Approach to Calibration Management Second Edition has been updated to address the changing environment, while still satisfying international GxP regulatory expectations, current at time of publication. The scope has been widened to include related industries, laboratory, and analytical instrumentation.

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

- ICH Guidance Q8 (R2), Q9, and Q10: setting out expectations for the application of science and risk-based approaches to drug development and manufacture supported by pharmaceutical quality systems (References 1, 2, and 3, Appendix 16)

- US Food and Drug Administration (FDA) current Good Manufacturing Practices (cGMPs) for the 21st Century Initiative and associated guidance (Reference 5, Appendix 16): promoting science based risk management

- Product Quality Lifecycle Implementation (PQLI): an initiative launched by ISPE to help industry to implement ICH guidance (Reference 15, Appendix 16)

This Guide aims to be fully compatible with the approach described in the American Society for Testing and Materials (ASTM) E2500 (Reference 19, Appendix 16).

This Guide represents industry good practice at time of publication and remains compatible with the principles presented in the first edition of this Guide, ISPE GAMP Good Practice Guide: Calibration Management (2002).

**The Following Areas Have Been Addressed as Part of this Revision:**

1. Alignment with current thinking on the risk-based approach, including the concepts of design and control space.

2. Software systems for supporting calibration both as scheduling and data recording tools. Software system should include the provision of historical data to assist in calibration optimization, e.g., Historical Analysis Graphs, Failure Alarms via email or text, Drift Analysis to predict failures.

3. internal and external auditing of systems and the use of supplier systems and documentation

4. changes in the cGMP, including:

    - SOP requirements

    - contractor competency assessment

- documentation sign off (paper or electronic)
- verification versus qualification

5. guidance on the application of measurement uncertainty estimates and assumptions
6. physical labeling and tagging schemes (including tagging structure)
7. integration of instrumentation into process control systems
8. use of programmable/configurable intelligent instruments
9. use of electronic calibration devices
10. inclusion of laboratory and analytical instrumentation as part of the scope of the Guide
11. update of example documents in line with current industry thinking, including:
    - multi function calibration certificate
    - unique calibration certificate numbering
    - loop commissioning
    - non-routine verification
    - audit check lists
    - activity reference standards

## 1.3 Purpose

The purpose of this Guide is to provide a cost effective framework of good calibration management practice to ensure that activities that affect product quality and patient safety are supported by a robust calibration management system which is fit for purpose and compliant with applicable regulations. The framework aims to safeguard patient safety, product quality, Environment, Health, and Safety (EHS), and data integrity while also delivering business benefit.

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 ‘product quality and patient safety’ 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 calibration activities, recording systems, and support services, both internal and external to the regulated company.

The GAMP Good Practice Guide: A Risk-Based Approach to Calibration Management is intended for use by engineers, Quality Assurance (QA), and personnel involved in the management of calibration in a regulated environment for use by a wide range of disciplines and responsibilities, including:

- management
- quality unit
- research

- development
- manufacture
- distribution
- laboratory
- engineering
- support staff
- all associated suppliers

The objective of this Guide is to provide a practical approach to calibration management within the pharmaceutical and associated regulated life science industries, to satisfy relevant regulatory bodies, and improve operational effectiveness.

## 1.4 Scope

The scope of the Guide includes quality, safety, and environmental issues as well as the regulatory requirements of the pharmaceutical and associated regulated life science industries.

This Guide focuses on the regulatory implications of designing guidelines following the principles established by GAMP Council in 2005. Technical processes of calibration management are outside the scope of this Guide, which focuses on the management of activities required to achieve regulatory compliance.

This Guide describes a system of calibration management, which defines what needs to be done, when, by whom, and why. This Guide also describes the principles and suggests a prioritized, effective method for meeting the calibration needs of the pharmaceutical industry and satisfying the requirements of regulatory authorities.

This Guide applies to calibration used in regulated activities covered by:

- Good Manufacturing Practice (GMP) (pharmaceutical, including Active Pharmaceutical Ingredient (API), veterinary, and blood processing)
- 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.

GAMP documents are guides and not standards. It is the responsibility of regulated companies to establish policies and procedures to meet applicable regulatory requirements.

Not all the activities defined in this Guide will apply to every system. 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 and adoption of new concepts and technologies.