premier consulting

GUIDE

GxP Quality Guidelines and Regulations: Frequently Asked Questions

GxP refers collectively to several types of "good practice" quality guidelines and regulations, each serving a specific purpose. In pharmaceutical product development, these include, but are not limited to:

- GCP – good clinical practice
- GLP – good laboratory practice
- GMP – good manufacturing practice

GxP standards broadly cover what are commonly referred to as the "5 Ps":

- Procedures
- Processes
- People
- Premises
- Products

Rigorously following GxP guidelines safeguards consumer health by preventing poor quality and ineffective or adulterated products.

What are the consequences of GxP noncompliance?

Sponsors and their partners may face serious consequences, including financial penalties and litigation, if they do not follow GxP regulations. Sponsors may receive a **warning letter** if regulators determine they have significantly disregarded federal regulations and potentially endangered public safety. The sponsor must submit a corrective plan and complete the agreed-upon action steps and confirm with the Food and Drug Administration (FDA) before continuing development.

In more serious instances, a sponsor may have a product **recalled** if it poses a risk due to adulteration or misbranding – incorrect labeling – or receive a **consent decree** if it does not correct regulatory violations and the product presents a definite risk to the public. Companies that receive consent decrees must cease operations, remedy the issues, and pass verification audits before resuming operations.

Why is it important to have a quality management system (QMS) to ensure GxP compliance?

A robust QMS supports the underlying principles of GxP – data integrity, traceability, and accountability – and allows you to share files and reports among groups, all in a secure environment. A well-designed quality system provides the tools to:

- Define, publish, and revise standard operating procedures for each process or functional area
- Mitigate risk at every phase by identifying and managing corrective and preventive actions to reduce errors
- Control processes to achieve requisite standards in end products and foster continuous improvement
- Update procedures in response to regulatory changes or new market opportunities
- Provide documentation promptly during inspection or regulatory audits
- Record and archive data to verify that tasks have been completed; data should be attributable, legible, contemporaneous, original, and accurate

Good clinical practice

What is GCP?

GCP is an international ethical and scientific quality standard for clinical trials intended to ensure the safety of human subjects involved in research. It was developed by the International Council for Harmonisation, which defines global standards for clinical trials involving humans that governments can adapt into regulations.

Applicable U.S. GCP specifications are FDA 21 CFR 50 (protection of human subjects), 21 CFR 54 (financial disclosure), 21 CFR 56 (institutional review boards), and 21 CFR 312 (trial administration for an investigational new drug application). The European Medicines Agency provides direction through its Clinical Trial Directive (2001/20/EC) and GCP Directive (2005/28/EC).

What are the core principles of GCP?

- The anticipated benefits of a clinical trial should always outweigh the risks
- Trials should be based on sound scientific evidence, observe ethical standards, and comply with detailed protocols
- The rights, consent, safety, and well-being of human trial participants are of utmost importance
- All personnel must have the required education, training, and experience
- All data are recorded, managed, and stored to enable accurate reporting, verification, and interpretation
- The investigational drug should be manufactured in compliance with GMP and used according to protocol

Good laboratory practice

What is GLP?

GLP is a set of rules and criteria for conducting nonclinical toxicology and other safety studies in support of clinical trials and subsequent marketing applications. Toxicology data form the basis for determining a safe first-in-human dose of an investigational drug. GLP ensures that the research performed meets a minimum standard to protect the safety of human subjects.

In the United States, GLP specifications are defined under FDA 21 CFR 58. Comparable European Medical Association (EMA) directives and Organisation for Economic Co-operation and Development principles apply in the European Union.

What are the core principles of GLP?

- **Resources:** The R&D organizational structure and responsibilities should be clearly defined with adequate qualified and trained staff; facilities and equipment must be sufficient for the purpose
- **Characterization:** For studies designed to evaluate the properties of pharmaceutical compounds, staff must have details about the investigational drug and system used in testing
- **Rules:** The study protocol must be documented, and written standard operating systems (SOPs) are required to provide the technical detail for testing
- **Results:** The final report should define how the study was performed, explain scientific data interpretation, and present conclusions
- **Quality assurance:** Quality assurance staff monitoring compliance must be independent of personnel conducting the study

Good manufacturing practice

What is GMP?

GMP spells out requirements for the production of investigational drugs and biologics to assure proper identification, quality, purity, and strength for patient safety and efficacy. The governing U.S. regulations for GMP are FDA 21 CFR 210-211 (drugs) and 21 CFR 600 (biologics). The EMA has promulgated similar directives for the European Union.

What are the core principles of GMP?

- SOPs for processes and design specifications for equipment and premises are described and documented
- Employees have appropriate qualifications and training
- Manufacturing processes are clearly defined and managed. Process changes are reviewed and validated
- Manufacturing facilities must maintain a clean, controlled environment
- Manufacturing data is recorded to confirm that specified procedures have been followed, and drug products are of the prescribed quality and quantity; deviations are documented and investigated
- Quality defects are examined, and actions are taken to prevent a recurrence
- Historical records for tracing each batch of the product are retained
- Products are packaged and labeled correctly

Best practices for GxP compliance

You can ensure compliance with GxP provisions and maintain quality assurance by establishing a robust QMS that adheres to FDA regulations. Tips for charting a smooth course include:

- **Hire** employees qualified to maintain the QMS
- **Allocate** sufficient staff to manage and meet QMS requirements
- **Develop** SOPs that detail control of facilities, equipment, laboratory operations, and data recording
- **Conduct** annual employee training on GxP standards and SOPs
- **Challenge** the QMS with periodic internal audits:
  - For GCP, audit potential clinical sites before starting trials to certify their readiness and prevent delays
  - During GLP studies, perform phase audits
  - For GMP, a preapproval inspection (PAI) helps assure the FDA that a named production facility is capable of manufacturing a drug and that submitted data are accurate and complete. Before scheduling a formal PAI, it is highly recommended to have a qualified party challenge your QMS from the regulators' perspective and perform PAI readiness training for all employees

With deep expertise across all relevant GxPs, Premier Consulting can help clients implement a comprehensive quality management system, providing quality oversight, ensuring regulatory compliance, and preparing for audits in all phases of drug development. Learn more about our quality assurance capabilities.

premier consulting

GUIDE

About Premier Consulting

Premier Consulting is a strategic product development and global regulatory consulting company dedicated to helping biotech innovators transform their life-changing ideas and breakthrough science into new medical treatments.

Our end-to-end solutions in strategy, regulatory, nonclinical, clinical, CMC, quality, and commercial help sponsors build and execute development plans that meet regulatory requirements and deliver results for sponsors and the patients they serve.

Premier Consulting
3800 Paramount Parkway
Suite 400
Morrisville, NC 27560