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Review

Strengthening Pharmaceutical Quality Control Laboratories: Inspection-Ready Implementation of the World Health Organization Good Practices for Pharmaceutical Quality Control Laboratories and Pathways to Prequalification

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Abstract

Pharmaceutical quality control laboratories are essential to ensuring the safety and quality of medicines. The World Health Organization (WHO) Good Practices for Pharmaceutical Quality Control Laboratories (GPPQCL) provide a framework for establishing reliable and inspection-ready laboratory systems. This review critically evaluates the implementation of GPPQCL, examining practical challenges, policy gaps, and variability in adoption across different settings. A structured narrative approach was used to analyze World Health Organization (WHO) guidance, international standards, and relevant literature (2010–2026), with an emphasis on inspection expectations and real-world practices. Effective implementation depends on robust quality management systems, validated methods, competent personnel, and strong data integrity practices. However, challenges such as infrastructure limitations, method standardization, and uneven data governance persist, particularly in resource-limited environments. Evidence from WHO-prequalified laboratories shows that risk-based implementation and capacity-building initiatives can support compliance and international recognition. Overall, GPPQCL provides a practical framework for strengthening laboratory systems, enhancing regulatory confidence, and supporting global efforts to ensure the quality of medicines.

Keywords: good laboratory practices; pharmaceutical quality control; implementation; inspection

1. Introduction

Ensuring the quality, safety, and efficacy of medicines depends fundamentally on the integrity of analytical testing performed by pharmaceutical quality control laboratories. These laboratories serve as critical pillars within national medicines regulatory systems, generating scientific evidence used for product registration, post-marketing surveillance, market authorization decisions, and public procurement. Inaccurate or unreliable laboratory results can lead to regulatory failures, distribution of substandard or falsified medicines, and significant public health risks.

To harmonize global laboratory practices and promote consistent quality standards, the World Health Organization developed the Good Practices for Pharmaceutical Quality Control Laboratories (GPPQCL) [1]. These guidelines establish comprehensive requirements covering governance, quality management systems (QMS), personnel competence, equipment qualification, analytical method validation, documentation control, data integrity, and continuous improvement. GPPQCL principles are closely aligned with internationally recognized standards such as ISO/IEC 17025 [2], while remaining specifically tailored to the regulatory and public health functions of medicines control laboratories.

In many low- and middle-income countries, quality control laboratories operate under significant constraints, including limited resources, outdated infrastructure, and high testing workloads [3]. Nevertheless, increasing global emphasis on regulatory convergence, reliance mechanisms, and procurement transparency has intensified the need for internationally recognized laboratory performance. World Health Organization (WHO) prequalification of quality control laboratories has emerged as a benchmark of technical competence and system maturity, signaling compliance with GPPQCL-aligned requirements and enhancing global confidence in laboratory-generated data [4,5,6].

Despite the availability of the guidelines, practical implementation of GPPQCL presents organizational, technical, and cultural challenges. Laboratories must establish structured QMS frameworks, ensure traceability of analytical results, maintain validated methods, manage equipment lifecycle processes, and embed risk-based continuous improvement mechanisms. Furthermore, inspection expectations increasingly emphasize data integrity, impartiality, and documented evidence of effective quality oversight.

This review critically evaluates the implementation of GPPQCL as defined by the World Health Organization. Beyond summarizing regulatory requirements, the paper examines gaps between guideline expectations and real-

world laboratory practices, analyzes implementation challenges across different resource settings, and proposes an inspection-oriented framework to support sustainable compliance and international recognition.

2. Methodology

This review was conducted using a structured narrative approach with elements of systematic literature review methodology to ensure transparency and reproducibility. Relevant literature was identified through electronic database searches and institutional sources.

2.1 Data Sources and Search Strategy

A comprehensive search was performed in databases including PubMed + Scopus + Web of Science + Google Scholar, as well as official publications from the World Health Organization and the United States Pharmacopeia Promoting the Quality of Medicines (PQM) program. Search terms included combinations of: "GPPQCL", "pharmaceutical quality control laboratory", "WHO prequalification", "ISO/IEC 17025", "data integrity", and "laboratory quality systems".

2.2 Inclusion Criteria

Publications between 2010 and 2026 were included, focusing on WHO guidelines, regulatory documents, peer-reviewed articles, and technical reports addressing pharmaceutical quality control laboratories, GPPQCL implementation, laboratory strengthening programs, and data integrity practices.

2.3 Exclusion Criteria

sources focusing exclusively on GMP manufacturing processes without relevance to quality control laboratories, non-English publications, and articles lacking methodological or regulatory relevance were excluded.

2.4 Study Selection and Synthesis

Relevant documents were screened based on title, abstract, and full-text review. Key themes were identified and synthesized into structured sections, including regulatory frameworks, implementation strategies, challenges, and case studies. Emphasis was placed on aligning findings with inspection expectations and real-world laboratory practices.

2.5 Literature Retrieval and Review Methodology

This review adopted a structured narrative approach incorporating selected elements of systematic literature retrieval to ensure transparency, reproducibility, and breadth of evidence synthesis. Literature relevant to GPPQCL, pharmaceutical laboratory quality systems, laboratory accreditation, and regulatory inspection practices was identified through electronic database searches and targeted retrieval of regulatory guidance documents.

Electronic searches were conducted using databases including PubMed, Scopus, Web of Science, and Google Scholar, alongside official publications from the World Health Organization, the United States Pharmacopeia PQM/PQM+ program, the International Organization for Standardization, and major medicines regulatory authorities. Search terms included combinations of "pharmaceutical quality control laboratory", "GPPQCL", "WHO quality control laboratory", "ISO/IEC 17025", "pharmaceutical laboratory accreditation", "data integrity", "quality management system", and "WHO prequalification laboratory".

The literature search focused primarily on publications issued between 2010 and 2026, corresponding to the period following publication of WHO Good Practices for Pharmaceutical Quality Control Laboratories. Earlier foundational references were included where necessary to contextualize the historical evolution of laboratory quality systems. Articles, technical reports, WHO Technical Report Series documents, regulatory guidance papers, and peer-reviewed publications were included if they addressed laboratory quality systems, inspection readiness, analytical quality assurance, data integrity, or pharmaceutical laboratory strengthening.

In addition to evidence retrieval, particular attention was given to identifying research gaps and underexplored areas within the existing literature. A critical review of the available evidence revealed that most publications focus predominantly on descriptive compliance requirements, accreditation achievements, and guideline interpretation, whereas comparatively fewer sources critically assess the effectiveness, sustainability, and operational impact of GPPQCL implementation in real laboratory settings. Furthermore, evidence remains limited regarding the long-term effects of GPPQCL adoption on analytical reliability, inspection outcomes, turnaround time, and public health indicators.

Important contextual gaps were also identified in relation to low- and middle-income countries (LMICs), where implementation barriers such as limited infrastructure, workforce shortages, and restricted digital capacity remain insufficiently characterized in published sources. Similarly, despite increasing regulatory emphasis on data integrity and laboratory digitalization, relatively few sources evaluate the practical maturity of electronic systems, audit trail governance, or cost-effective pathways toward digital transformation in pharmaceutical quality control laboratories.

Rather than conducting a formal systematic review or meta-analysis, the objective of this review was to provide a critical synthesis of operational, regulatory, and implementation-related issues affecting GPPQCL adoption across diverse laboratory settings. Particular emphasis was placed on identifying implementation barriers, policy gaps, inspection expectations, and opportunities for strengthening laboratory systems, especially in resource-constrained

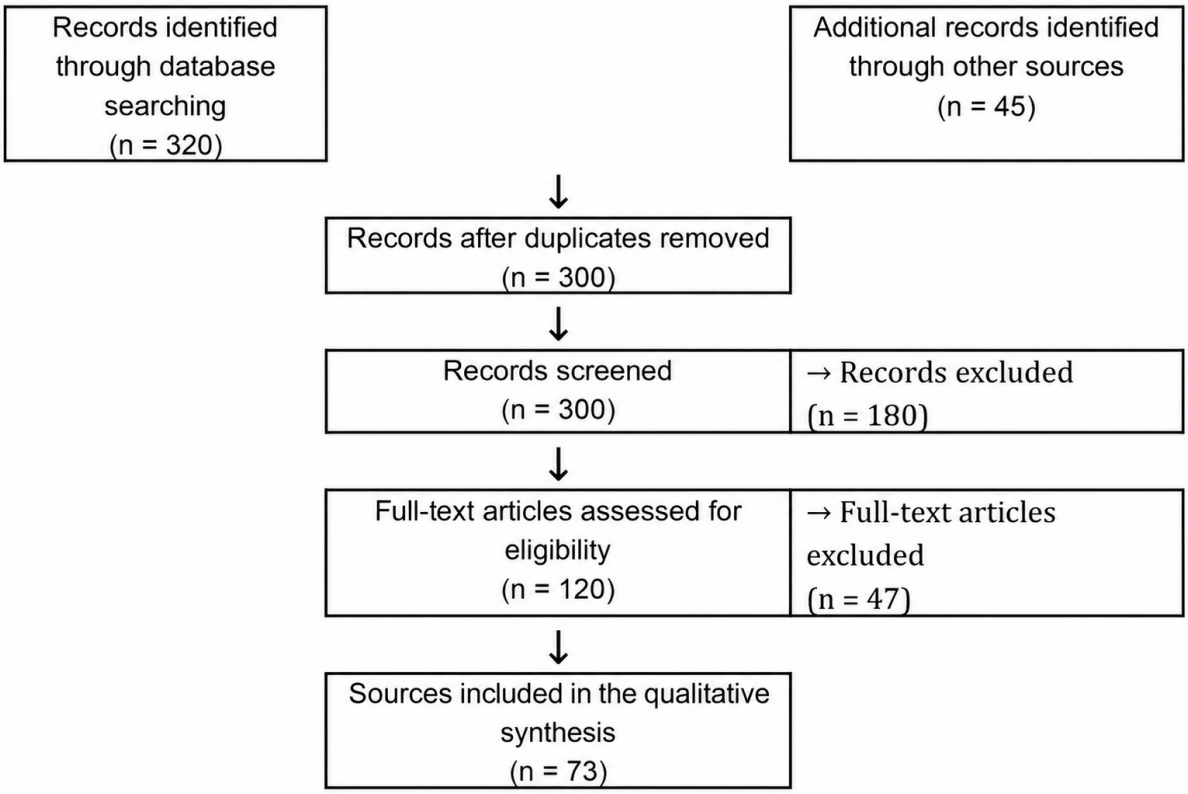

Fig. 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram. All figures included in the manuscript were created using ChatGPT.

settings. By integrating both evidence synthesis and critical appraisal, this review aims to move beyond guideline description toward a more analytical understanding of how GPPQCL can be implemented effectively and sustainably.

2.6 PRISMA Consideration

Although this study is primarily a narrative review, elements of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) approach [7] were applied to guide literature identification, screening, and reporting processes.

The study selection process is summarized in Fig. 1, following a structured PRISMA-based approach.

3. Background/Regulatory Context

Pharmaceutical quality control laboratories operate within a complex regulatory environment that demands adherence to both national and international standards. Historically, laboratory practices varied widely, leading to inconsistent results, limited reproducibility, and challenges in global regulatory acceptance of data. To address this, the WHO developed GPPQCL, providing a harmonized framework that complements existing regulatory standards such as ISO/IEC 17025:2017 (General requirements for the competence of testing and calibration laboratories) and WHO Good Manufacturing Practices (GMP) for medicines [1,2].

While ISO/IEC 17025 focuses on laboratory competence, validation, and impartiality, GPPQCL incorporates additional considerations specific to pharmaceutical quality control, including:

1. Compliance with regulatory reporting requirements for pharmaceutical testing.

2. Guidance on laboratory safety and environmental controls.

3. Management of reference standards and test samples.

4. Structured procedures for handling out-of-specification (OOS) results [8,9,10,11].

This integration ensures that laboratories can meet both technical competence expectations and the specific regulatory demands of pharmaceutical quality control [1].

GPPQCL has global relevance because regulatory agencies increasingly recognize WHO guidelines as the benchmark for prequalification and inspection of quality control (QC) laboratories. Laboratories implementing GPPQCL gain international credibility, facilitating the acceptance of analytical data across borders and supporting the WHO Prequalification of Medicines Programme. For example, the Bangladesh National Control Laboratory gained international recognition by aligning its operations with GPPQCL, thereby enhancing confidence in its test results and enabling participation in international regulatory frameworks [12].

Table 1. Comparison of GPPQCL versus ISO/IEC 17025.

Feature	GPPQCL	ISO/IEC 17025
Focus	Pharmaceutical QC Laboratories	General Testing Laboratories
Regulatory alignment	WHO Prequalification	Global Accreditation
Guidance detail	Detailed pharmaceutical-specific guidance	Broad laboratory standards
Implementation purpose	Regulatory compliance, medicines quality assurance	General laboratory competence and accreditation

GPPQCL, Good Practices for Pharmaceutical Quality Control Laboratories; QC, quality control; WHO, World Health Organization.

In summary, GPPQCL addresses both the technical and regulatory gaps in laboratory operations, bridging the requirements of ISO/IEC 17025 and GMP with practical guidance tailored to pharmaceutical QC. This dual focus ensures that laboratories not only produce reliable data but also comply with global quality expectations, forming the foundation for harmonized testing practices and international recognition [13,14]. Table 1. compares GPPQCL to ISO/IEC 17025.

4. Principles of GPPQCL

The World Health Organization's GPPQCL is built upon several fundamental principles designed to ensure that laboratory results are accurate, reliable, and reproducible, while maintaining compliance with regulatory expectations. These principles form the foundation for laboratory operations and are applicable across all types of pharmaceutical quality control laboratories, whether public, private, or manufacturer-based.

4.1 Quality Management System (QMS)

A robust QMS lies at the heart of GPPQCL implementation. It establishes a structured approach to laboratory operations, defining policies, responsibilities, and objectives to consistently achieve high-quality outputs. Key components include a quality manual, documented procedures for all activities, and a system for corrective and preventive actions (CAPA) to address deviations or non-conformities. The QMS also ensures continuous monitoring of laboratory performance and supports internal audits and management reviews, which are essential for sustaining compliance and promoting continuous improvement.

4.2 Documentation and Record Control

GPPQCL emphasizes the critical role of proper documentation in maintaining data integrity. Laboratories must implement controlled systems for document approval, distribution, revision, and archival. This includes standard operating procedures (SOPs), test protocols, calibration records, and certificates of analysis (CoA). Accurate and complete records provide traceability of test results, facilitate regulatory inspections, and enable reproducibility of analytical methods.

4.3 Personnel Competence and Training

Qualified and well-trained personnel are essential for reliable laboratory operations. GPPQCL requires laboratories to define roles and responsibilities, establish competency criteria, and implement structured training programs. Ongoing professional development ensures that staff remain proficient in analytical techniques, safety practices, and regulatory requirements.

4.4 Equipment and Facility Management

Laboratories must ensure that facilities and equipment are suitable for their intended use. This includes proper laboratory layout, controlled environmental conditions, and appropriate safety measures. Equipment should undergo installation qualification (IQ), operational qualification (OQ), and performance qualification (PQ), with regular calibration and maintenance to guarantee consistent analytical performance.

4.5 Analytical Methods and Test Procedures

GPPQCL emphasizes the use of validated and standardized analytical methods. Laboratories must ensure that reference standards are traceable and that all test procedures are documented in SOPs. Data generated must be accurate, complete, and securely recorded, supporting the integrity of test results and ensuring regulatory compliance.

4.6 Risk Management and Safety

Laboratory operations under GPPQCL incorporate a risk-based approach to safety and quality. Laboratories are expected to identify potential risks to analytical accuracy, personnel, and environmental safety, and implement preventive measures. This includes chemical, biological, and operational hazards, with emergency preparedness plans to maintain continuity of operations.

The principles of GPPQCL collectively ensure that pharmaceutical quality control laboratories operate with high standards of reliability, compliance, and safety. By integrating a strong QMS, competent personnel, validated methods, and risk-based controls, laboratories can generate credible data, support regulatory assessments, and achieve international recognition.

5. Stepwise Implementation Guide

Implementing GPPQCL requires a structured, detailed approach, ensuring that laboratories translate principles into daily practices. The following expanded guide provides a comprehensive roadmap for laboratories seeking compliance, reliability, and international recognition.

5.1 Establishing a Quality Management System (QMS)

The establishment of a robust QMS is the cornerstone of GPPQCL implementation. It serves as the primary mechanism through which a pharmaceutical quality control laboratory demonstrates scientific integrity, operational control, and regulatory compliance. Within the WHO Good Practices for Pharmaceutical Quality Control Laboratories framework, the QMS is not merely a documentation structure. It is an integrated governance system designed to ensure that analytical results are reliable, reproducible, traceable, and legally defensible.

At the highest level, the QMS must be anchored in a formally approved quality policy issued by laboratory management. This policy should explicitly affirm the laboratory's commitment to impartiality, independence, compliance with pharmacopeial standards, and adherence to national and international regulatory requirements. Regulatory authorities expect this commitment to be measurable. Therefore, the policy must be operationalized through defined quality objectives supported by key performance indicators. These may include predefined thresholds for analytical error rates, turnaround time compliance, audit findings, deviation closure timelines, and calibration adherence. Periodic evaluation of these metrics during management review ensures that quality performance is continuously monitored. It also ensures alignment with strategic regulatory objectives.

Organizational governance is another critical regulatory expectation. The QMS must clearly define reporting lines, authorities, and responsibilities. This ensures independence between testing operations and quality oversight. The quality manager must possess sufficient authority and autonomy. This includes overseeing audits, managing deviations, verifying corrective and preventive actions, and, when necessary, suspending analytical activities if compliance is jeopardized. Regulatory inspections frequently examine whether quality oversight is structurally independent from routine testing functions. This separation safeguards objectivity and mitigates conflicts of interest.

Document and record control represent foundational regulatory controls within the QMS. All laboratory processes must be governed by approved SOPs. These include sample receipt, chain-of-custody documentation, analytical testing, equipment calibration, and final reporting. Documents require formal version control, documented review and approval, defined distribution, and controlled archival. Obsolete procedures must be promptly withdrawn to prevent unintended use. Record management systems must ensure full traceability of analytical data. This includes raw data, chromatograms, calculations, and electronic audit trails where applicable. Increasingly, regulators emphasize compliance with data integrity principles. Data must be attributable, legible, contemporaneous, original, accurate, complete, consistent, enduring, and available throughout the retention period.

Personnel competency management must demonstrate that analytical results are generated by adequately qualified staff. Continuous training is essential. Job descriptions, qualification requirements, training curricula, and competency assessments must be documented. Regulatory inspections frequently assess whether analysts performing critical tests have documented evidence of training and periodic requalification. Ongoing evaluation of technical proficiency is particularly important. This applies to complex analytical techniques such as chromatographic and dissolution testing.

Equipment lifecycle management is also closely scrutinized during regulatory review. The QMS must incorporate formal procedures for equipment selection, installation qualification, operational qualification, and performance qualification. It must also include calibration scheduling, preventive maintenance, and breakdown management. Instruments should be uniquely identified. They must be accompanied by calibration status indicators and maintenance logs. When calibration deviations occur, the laboratory must conduct impact assessments. These assessments determine whether previously reported results are affected. This step is essential for maintaining the regulatory defensibility of analytical data.

Analytical method validation [15,16] is a scientifically critical component of the QMS. Methods must be demonstrated to be suitable for their intended purpose before routine use. Validation parameters include specificity, accuracy, precision, linearity, range, robustness, and sensitivity. These should be evaluated according to internationally recognized guidelines. Validation documentation must be complete, reviewed, and approved prior to implementation. Continued monitoring of method performance is advisable. This ensures long-term reliability, particularly for high-risk or stability-indicating assays.

A structured deviation management and CAPA system is indispensable for regulatory compliance. All deviations must be formally recorded and investigated. This includes OOS results. Investigations should use systematic root cause analysis methodologies. Corrective actions must address the immediate issue. Preventive actions should eliminate underlying systemic causes. Regulators expect CAPA effectiveness to be verified and documented. This demonstrates that implemented measures have successfully mitigated the identified risks.

Internal audits and management reviews provide the feedback loop necessary for sustained compliance and continuous improvement. Internal audits should be conducted at defined intervals using structured checklists aligned with

GPPQCL requirements. Audit findings must be categorized by criticality and linked to corrective action plans. Management review meetings should evaluate audit outcomes, quality metrics, resource adequacy, complaint trends, and emerging regulatory expectations. These reviews ensure executive accountability and strategic oversight of the QMS.

Finally, the integration of risk-based thinking throughout the QMS strengthens regulatory resilience. High-risk processes should be systematically identified. These may include complex analytical methods, stability testing, or high-volume sample handling. Resources can then be allocated proportionally. Enhanced controls should be implemented where needed. Embedding risk management into daily operations ensures that quality oversight remains proactive rather than reactive.

In regulatory terms, a fully implemented QMS under GPPQCL provides demonstrable evidence that the laboratory operates under controlled conditions. It confirms that scientifically sound data are generated. It also ensures a continuous state of inspection readiness. The QMS transforms quality from a procedural requirement into a governance framework. Ultimately, it safeguards public health by ensuring the integrity and reliability of pharmaceutical testing.

Critical Perspective: While a robust QMS is widely recognized as essential for compliance, implementation quality varies considerably between laboratories. In resource-constrained settings, excessive documentation requirements may strain operational efficiency and divert attention from analytical performance. Consequently, laboratories should adopt risk-based prioritization approaches to ensure that quality systems remain practical, proportionate, and sustainable.

Tip: Maintain a QMS dashboard summarizing audit findings, CAPA status, and training compliance. This supports efficient and informed management review.

5.2 Organizational Structure and Personnel

Effective implementation of GPPQCL requires a clearly defined organizational structure supported by competent and adequately trained personnel. A well-structured governance framework ensures accountability, preserves technical integrity, and enables the consistent enforcement of quality decisions across all laboratory functions.

A formal organizational chart should be established and maintained as part of the QMS. This chart must clearly define reporting relationships, lines of authority, and functional independence where necessary. At minimum, the structure should include laboratory management, a designated quality manager, technical supervisors or section heads, analysts, and appropriate support staff. Clearly documented job descriptions must specify qualifications, responsibilities, decision-making authority, and reporting obligations for each role. Transparent reporting lines are particularly critical to ensure that quality-related decisions can be made independently of operational or commercial pressures.

Central to this structure is the role of the quality manager. The quality manager holds primary responsibility for overseeing QMS implementation and ensuring compliance with GPPQCL requirements. This includes management of document control systems, coordination of internal audits, oversight of deviation and OOS investigations, and supervision of CAPA programs. The quality manager should have sufficient authority and direct access to top management to enforce quality decisions without undue influence. Functional independence between quality oversight and routine testing operations is essential to maintain impartiality and regulatory credibility.

Technical supervisors or section heads are responsible for the scientific integrity of assigned analytical areas, such as chromatography, microbiology, or physicochemical testing. Their duties typically include method oversight, technical review of analytical data, mentoring of junior analysts, and ensuring compliance with approved procedures. Analysts, in turn, are responsible for performing tests according to validated methods and approved SOPs, documenting results accurately, and promptly reporting deviations or atypical findings.

Personnel competency represents one of the most critical determinants of laboratory reliability under the GPPQCL framework. Even the most advanced infrastructure and validated analytical methods cannot ensure data integrity if laboratory personnel lack adequate technical expertise, regulatory awareness, or procedural discipline. Therefore, GPPQCL requires that pharmaceutical quality control laboratories establish a structured and documented system for personnel qualification, training, competency assessment, and continuous professional development.

At the organizational level, the laboratory must define clear job descriptions outlining educational qualifications, technical experience, and functional responsibilities for each position. These requirements should align with the complexity of assigned analytical tasks. For example, analysts performing chromatographic assays, dissolution testing, or impurity profiling should possess formal academic training in pharmaceutical sciences, chemistry, or related disciplines, in addition to demonstrated hands-on experience.

Initial qualification of personnel must include documented onboarding training that covers laboratory safety, good documentation practices, data integrity principles, sample handling procedures, and relevant standard operating procedures. Regulatory inspections frequently assess whether newly recruited staff are permitted to perform independent testing only after completing documented training and supervised competency evaluation. This evaluation should include both theoretical assessment and practical demonstration of analytical proficiency.

Beyond initial qualification, GPPQCL emphasizes ongoing competency assurance. Laboratories must implement periodic requalification programs to verify sustained proficiency, particularly for critical analytical techniques. Competency reassessment may include direct observation, proficiency testing, blind sample analysis, or performance trend monitoring. In high-risk testing environments, such as stability-indicating assays or pharmacopoeial compliance testing, regular technical reassessment is essential to maintain regulatory confidence.

Training programs should extend beyond technical skills to include regulatory and quality system awareness [17]. Personnel must understand deviation management procedures, OOS investigation protocols, CAPA processes, and audit expectations. Increasingly, regulators place significant emphasis on data integrity training, requiring personnel to understand principles such as attributable, legible, contemporaneous, original, and accurate documentation practices. Laboratories must maintain documented evidence that such training has been delivered and periodically reinforced.

The QMS should include a structured training management system that tracks training needs, schedules refresher sessions, and documents training effectiveness. Individual training files must be maintained for each employee, containing records of qualifications, completed training sessions, competency assessments, and authorization to perform specific tests. These records are frequently reviewed during inspections to confirm that only qualified personnel conduct regulated testing activities.

Professional development should be encouraged as part of long-term capacity building. Participation in external workshops, regulatory training programs, proficiency testing schemes, and collaborative networks enhances analytical capability and strengthens the laboratory's readiness for WHO prequalification or other regulatory recognition. In resource-limited settings, strategic partnerships and international technical support programs may play an essential role in sustaining competency development.

From a regulatory perspective, personnel competency management under GPPQCL serves two primary purposes: first, to ensure the scientific validity of analytical results, and second, to demonstrate inspection readiness through documented evidence of qualification and oversight. A laboratory that systematically manages training, verifies competency, and maintains comprehensive records establishes a defensible foundation for reliable pharmaceutical quality control testing.

Collectively, a well-defined organizational structure combined with systematic competency management strengthens laboratory governance, enhances data reliability, and demonstrates regulatory compliance. By ensuring that roles are clearly assigned, authority is appropriately distributed, and personnel are adequately trained and documented, pharmaceutical quality control laboratories establish a robust foundation for sustained GPPQCL implementation and continuous quality improvement.

Example: A QC laboratory might implement monthly proficiency testing for analysts to verify accuracy and consistency across routine methods [1].

5.3 Facilities and Equipment Management

Facilities and equipment constitute the operational backbone of a pharmaceutical quality control laboratory. Regulatory inspectors consider infrastructure control a high-risk area because deficiencies in environmental management, equipment qualification, calibration, or maintenance directly compromise analytical accuracy, reproducibility, and data integrity [18]. Therefore, GPPQCL implementation requires that facilities and equipment systems be scientifically justified, systematically documented, and inspection-ready at all times.

5.3.1 Laboratory Design and Environmental Control

Laboratory design must support logical workflow and minimize risks of mix-ups, cross-contamination, and environmental interference. Inspectors typically evaluate whether testing areas are appropriately segregated according to activity, such as raw material testing, in-process control, finished product analysis, reference standard storage, and microbiological examination where applicable.

The physical layout should promote unidirectional workflow from sample receipt to testing and reporting, thereby reducing the possibility of sample confusion. Dedicated areas for sample preparation, instrument operation, and documentation are considered good practice. Where hazardous solvents or volatile reagents are used, appropriate ventilation systems and fume hoods must be installed and qualified.

Environmental conditions are subject to particular scrutiny. Temperature, humidity, and lighting must be controlled and monitored where they can affect analytical performance or sample stability. For example, excessive humidity may affect weighing accuracy or hygroscopic materials, while temperature fluctuations can influence chromatographic retention times or reference standard stability. Inspectors expect to see:

1. Defined environmental specifications.
2. Continuous or periodic monitoring records.
3. Alarm systems for excursions where necessary.
4. Documented assessment and corrective action when environmental limits are exceeded.

Failure to investigate environmental excursions that could impact analytical results is a common inspection observation.

5.3.2 Equipment Qualification (IQ, OQ, PQ)

All major analytical instruments must undergo documented qualification prior to routine use. Inspectors routinely request qualification files for high-risk instru-

ments such as high-performance liquid chromatography (HPLC) systems, gas chromatography (GC) systems, UV-Visible (UV–Vis) spectrophotometers, dissolution testers, balances, and stability chambers [19,20,21].

Qualification should include:

○ **IQ**: Verification that equipment is installed according to manufacturer specifications and environmental requirements.

○ **OQ**: Demonstration that the instrument operates within predefined operational parameters.

○ **PQ**: Confirmation that the instrument consistently performs according to intended analytical application under routine conditions.

Qualification protocols must be approved prior to execution, and reports should include raw data, deviations (if any), and final approval signatures. Inspectors assess whether qualification acceptance criteria are scientifically justified and whether requalification is performed after major repairs, relocation, or software upgrades.

Use of unqualified or partially qualified equipment is considered a critical compliance deficiency.

5.3.3 Calibration and Preventive Maintenance

Calibration ensures measurement traceability and analytical reliability. A formal calibration program must define:

1. Calibration frequency.
2. Acceptance criteria.
3. Reference standards traceable to national or international standards.
4. Documentation requirements.

For example, analytical balances may require daily verification checks and periodic full calibration, while HPLC pumps, detectors, and autosamplers may require scheduled calibration according to manufacturer guidance or internal risk assessment. Inspectors frequently compare calibration schedules against instrument logs to verify compliance.

Preventive maintenance programs must also be established and documented. These should be risk-based and aligned with manufacturer recommendations. Maintenance activities may include replacement of pump seals, lamp checks in spectrophotometers, detector validation, or mechanical inspection of dissolution apparatus.

A common inspection finding involves overdue calibration or maintenance without documented risk assessment. Laboratories must ensure that no instrument is used beyond its calibration due date unless justified and formally assessed.

5.3.4 Equipment Logs and Data Integrity

Each instrument should have an individual logbook documenting:

1. Date of use.
2. Analyst name.
3. Type of analysis performed.
4. Calibration status.
5. Maintenance interventions.
6. Observed malfunctions.

Inspectors often cross-verify analytical reports against instrument logs to ensure traceability. Gaps, overwritten entries, or incomplete logs raise data integrity concerns.

Where computerized systems are used, user access control, audit trails, and backup systems must be validated and periodically reviewed.

5.3.5 Backup and Contingency Planning

Operational continuity is another inspection focus. Laboratories must demonstrate preparedness for equipment failure through documented contingency measures. These may include:

1. Availability of backup instruments.
2. Service contracts with defined response times.
3. Agreements with qualified external laboratories.
4. Business continuity procedures for critical testing.

Inspectors may evaluate whether contingency arrangements are realistic and previously tested. Extended downtime of critical instruments without alternative arrangements can compromise regulatory commitments, particularly for stability studies or batch release testing.

5.3.6 Inspection Red Flags in Facilities and Equipment Management

Regulatory observations frequently arise from:

1. Inadequate segregation of laboratory areas.
2. Lack of environmental monitoring or uninvestigated excursions.
3. Incomplete or outdated qualification documentation.
4. Overdue calibration or maintenance.
5. Use of equipment after failed calibration.
6. Missing instrument log entries.
7. Absence of backup arrangements.

Addressing these proactively strengthens compliance posture and reduces regulatory risk.

In conclusion, robust facilities and equipment management under GPPQCL requires scientifically justified laboratory design, comprehensive qualification of instruments, systematic calibration and maintenance programs, controlled environmental monitoring, and effective contingency planning. Laboratories that integrate these elements into their QMS demonstrate technical reliability, inspection readiness, and sustained analytical integrity.

Tip: A digital logbook for equipment calibration and maintenance can improve traceability and reduce manual errors.

5.4 Analytical Methods and Testing Practices

The scientific credibility of a pharmaceutical quality control laboratory ultimately depends on the reliability of

its analytical methods and the integrity of its testing practices. Regulatory inspectors consider this section one of the most technically critical components of GPPQCL implementation because analytical deficiencies directly compromise batch release decisions, stability conclusions, and public health protection. Therefore, analytical methods must be validated, standardized, controlled, and consistently executed under a documented and auditable framework.

5.4.1 Method Validation and Revalidation

All analytical procedures used for regulatory decision-making must be validated to demonstrate their suitability for intended use. Inspectors routinely review method validation protocols and reports to confirm that essential performance characteristics are established and scientifically justified. These characteristics typically include:

1. Accuracy.
2. Precision (repeatability and intermediate precision).
3. Specificity.
4. Linearity and range.
5. Limit of Detection (LOD).
6. Limit of Quantification (LOQ).
7. Robustness.

Validation documentation must define acceptance criteria before execution and include complete raw data, statistical analysis, and approved conclusions. Inspectors assess whether validation studies were performed under conditions representative of routine use.

Revalidation is required when significant changes occur that could affect method performance. Such changes may include introduction of new analytical equipment, software upgrades, changes in reagents or columns, modification of method parameters, or transfer of the method between laboratories. Inspectors expect documented change control procedures [22,23,24] linking method modifications to risk assessment and revalidation decisions. Failure to reassess validated status after major changes is a common regulatory observation.

For pharmacopoeial methods, laboratories must still verify suitability under local conditions, particularly when instrumentation differs from that described in the monograph.

5.4.2 Reference Standards Management

Reference standards are central to analytical traceability and result accuracy. Inspectors examine whether the laboratory maintains a controlled inventory system for primary and secondary reference materials [25].

The laboratory must demonstrate:

1. Traceability of primary standards to recognized pharmacopoeial or certified sources.
2. Proper qualification of in-house secondary standards against primary standards.
3. Documentation of lot numbers, receipt dates, certificates of analysis, and assigned expiry or retest dates.
4. Defined storage conditions consistent with manufacturer recommendations.
5. Monitoring of storage environments where required.

Reference standard preparation records must include weighing data, preparation calculations, and analyst verification. Inspectors frequently verify whether expired standards were used in testing and whether potency corrections were properly applied. Inadequate control of reference materials represents a significant compliance risk.

5.4.3 Sample Handling and Chain of Custody

Proper sample management prevents mix-ups, contamination, and degradation. Inspectors commonly trace a selected sample from receipt to final report to evaluate control systems [26,27,28].

The laboratory must maintain documented procedures covering:

1. Sample receipt and registration.
2. Unique sample identification and labeling.
3. Storage conditions before testing.
4. Segregation of samples to prevent cross-contamination.
5. Retention and disposal procedures.

Chain-of-custody documentation should ensure traceability at every stage. Environmental conditions for sample storage must be controlled and monitored where relevant. Inspectors may review whether stability samples were stored under specified conditions and whether any temperature excursions were investigated.

Unlabeled samples, incomplete receipt records, or inadequate storage segregation are considered serious procedural weaknesses.

5.4.4 Data Integrity and ALCOA+ Compliance

Data integrity requirements have evolved significantly, with the World Health Organization issuing updated guidance in WHO Technical Report Series No. 1033, Annex 4 (2021), which strengthens expectations for governance of electronic and paper-based data. This guidance emphasizes ALCOA+ (attributable, legible, contemporaneous, original, Accurate, complete, consistent, enduring, and available) principles, audit trail review, access control, and risk-based data management approaches, reflecting current inspection practices [29,30,31,32].

1. Attributable: Data must clearly identify who performed the action and when.
2. (Example: Analytical results must be linked to a specific analyst, date, and instrument.)
3. Legible: Records must be readable, permanent, and understandable throughout their retention period.
4. Contemporaneous: Data must be recorded at the time the activity is performed, not retrospectively.

5. Original: The record must be the first capture of the data or a verified true copy (e.g., raw chromatograms, original instrument printouts, validated electronic files).

6. Accurate: Data must be correct, free from errors, and supported by proper calculations and verification.

7. Complete: All data—including repeat analyses, OOS results, and audit trails—must be retained.

8. Consistent: Data must follow chronological order and standardized procedures.

9. Enduring: Records must be durable and securely stored (paper or validated electronic systems).

10. Available: Data must be accessible for review, audit, or inspection throughout the retention period.

Inspectors assess whether raw data entries are traceable to the individual performing the work, recorded at the time of activity, and protected from unauthorized alteration. Electronic systems must have controlled user access, password protection, audit trails, and validated backup procedures.

Audit trail reviews are increasingly expected for computerized chromatographic systems. Inspectors may examine deleted injections, reintegration events, or repeated analyses to verify that retesting practices are scientifically justified and documented. Unexplained data deletion or selective reporting represents a critical violation.

Laboratories must establish procedures for data review, including second-person verification of calculations, chromatographic integration, and transcription accuracy. Data review must be documented and attributable.

Critical Perspective: Although electronic systems improve traceability and facilitate audit readiness, digitalization alone does not guarantee data integrity. Weak governance, inadequate access controls, poor audit trail oversight, and insufficient staff competency may perpetuate compliance risks despite technological investments. Therefore, digital transformation should be accompanied by strong procedural controls, training, and quality oversight mechanisms.

5.4.5 Reporting and Certificates of Analysis (CoA)

The final analytical report and CoA serve as official regulatory documents. Inspectors evaluate whether reports are clear, complete, and scientifically defensible.

A compliant CoA should include:

1. Product identification and batch number.

2. Reference to applicable specifications or monographs.

3. Individual test results with units.

4. Acceptance criteria.

5. Statement of compliance or non-compliance.

6. Date of analysis.

7. Authorized signatory approval.

Reports must reflect actual tested results without selective omission. Where out-of-specification results occurred, the investigation outcome must be documented prior to batch disposition. Inspectors often compare raw data with reported results to confirm consistency and completeness.

Authorization of CoAs should be restricted to designated qualified personnel. Signature control—electronic or manual—must prevent unauthorized release.

5.4.6 Inspection Red Flags in Analytical Control

Common deficiencies cited during inspections include:

1. Incomplete or poorly justified validation studies.

2. Lack of revalidation following equipment or procedural changes.

3. Expired or inadequately qualified reference standards.

4. Missing raw data or undocumented reintegration.

5. Weak audit trail review practices.

6. Inconsistent or unclear CoA reporting.

7. Analysts conducting tests without documented method authorization.

Proactive control of these areas significantly reduces regulatory risk.

In summary, analytical method control and testing practices form the scientific core of GPPQCL compliance. Laboratories must ensure validated methods, traceable reference standards, secure data systems, controlled sample handling, and transparent reporting mechanisms. When these systems operate cohesively within the QMS framework, the laboratory demonstrates technical competence, data integrity, and regulatory reliability during inspection and external audit.

Example: A lab testing a finished product could include batch number, sample condition, method references, and analyst initials on the CoA for complete traceability.

5.5 Safety and Risk Management

A proactive and systematic approach to safety and quality risk management is integral to effective implementation of GPPQCL. Regulatory authorities increasingly expect laboratories not only to comply with prescriptive safety requirements but also to demonstrate structured risk-based thinking in both occupational safety and analytical quality assurance. Inspectors assess whether hazards are formally identified, risks are evaluated scientifically, and mitigation measures are documented, implemented, and periodically reviewed.

5.5.1 Hazard Identification and Risk Evaluation

The first step in safety management is comprehensive hazard identification. Laboratories must evaluate chemical, biological, physical, and operational risks associated with their activities. This includes routine analytical procedures, storage of reagents and reference standards, sample handling, waste disposal, and equipment operation.

Chemical hazards are particularly significant in pharmaceutical laboratories. For example, volatile organic solvents such as methanol or acetonitrile require adequate ventilation systems, proper storage in flammable cabinets, clearly defined spill management procedures, and appropriate personal protective equipment (PPE). Inspectors often verify the availability of Safety Data Sheets (SDS), chemical labeling compliance, and compatibility-based storage segregation.

Biological risks may arise in microbiological testing environments and require containment controls, sterilization procedures, and biosafety training. Operational risks include electrical hazards, compressed gases, pressurized systems, and rotating mechanical components in analytical instruments.

Inspectors expect documented risk assessments identifying hazards, estimating severity and likelihood, and defining mitigation controls. Informal or undocumented hazard recognition is generally considered insufficient.

5.5.2 Preventive Controls and Safety Infrastructure

Preventive measures must be implemented proportionate to identified risks [33]. These typically include:

1. Engineering controls such as fume hoods, ventilation systems, fire suppression equipment, and spill containment kits.
2. Administrative controls including SOPs for safe handling, waste disposal procedures, and restricted access policies.
3. PPE such as laboratory coats, gloves, eye protection, and respiratory protection where required.

Waste management procedures must address segregation of chemical, biological, and general laboratory waste. Inspectors frequently review contracts with licensed waste disposal providers and records of hazardous waste disposal.

Evidence of preventive maintenance of safety equipment—such as periodic inspection of fire extinguishers, eye wash stations, safety showers, and ventilation systems—is also assessed during inspections. Inadequate maintenance of safety systems may result in regulatory observations.

5.5.3 Emergency Preparedness and Response

Emergency preparedness is a critical component of laboratory risk management [34]. Laboratories must establish documented procedures covering foreseeable emergencies, including:

1. Fire incidents.
2. Chemical spills.
3. Major solvent leaks.
4. Electrical failures.
5. Equipment malfunction affecting safety or sample integrity.

Emergency response plans should define roles and responsibilities, evacuation routes, communication procedures, and reporting requirements. Inspectors may verify the visibility of emergency instructions, availability of spill kits, and accessibility of emergency exits.

Periodic drills should be conducted to ensure personnel familiarity with response procedures. Documentation of drill execution, observations, and corrective actions demonstrates active safety oversight. Absence of drill records or lack of staff awareness during interviews may indicate superficial implementation.

5.5.4 Quality Risk Assessment and Analytical Impact

Beyond occupational safety, inspectors increasingly evaluate how laboratories apply quality risk management principles to analytical processes. A structured, risk-based approach ensures that potential failures affecting data reliability are systematically identified and mitigated [35,36,37].

Laboratories should conduct formal quality risk assessments for critical processes such as:

1. Method transfer.
2. Equipment qualification.
3. Data management systems.
4. Environmental monitoring.
5. Change control implementation.

Common tools include risk matrices and Failure Mode and Effects Analysis (FMEA), which allow prioritization of risks based on severity, occurrence, and detectability. Risk assessment outcomes should guide decisions regarding validation scope, control measures, monitoring frequency, and contingency planning.

Inspectors expect risk assessments to be documented, periodically reviewed, and integrated into management review processes. Risk assessments performed solely for inspection purposes, without evidence of operational use, are easily identified during audits.

5.5.5 Inspection Red Flags in Safety and Risk Management

Regulatory observations frequently arise from:

1. Absence of documented hazard assessments.
2. Incomplete or outdated Safety Data Sheets.
3. Inadequate chemical storage segregation.
4. Expired fire extinguishers or non-functional safety equipment.
5. Lack of documented emergency drills.
6. Risk assessments not linked to corrective actions.
7. Failure to evaluate analytical impact following incidents (e.g., temperature excursions, equipment failure).

Common inspection deficiencies observed in pharmaceutical quality control laboratories are summarized in Table 2 (Ref. [1,4]). These inspection red flags highlight recurring compliance gaps and provide a practical reference for laboratories to prioritize high-risk areas during GP-PQCL implementation and inspection preparation.

Table 2. Expanded common inspection red flags in pharmaceutical quality control laboratories aligned with GPPQCL.

Area	Inspection red flag	Underlying cause	Regulatory impact	Typical 2026 findings (inspection trend)	Inspection classification	Mitigation/Best practice
Documentation & records	Incomplete, illegible, or backdated records	Poor documentation culture; lack of SOP clarity	Loss of traceability; unreliable data	Hybrid paper-electronic inconsistencies; metadata/time-stamp discrepancies; retrospective data entry	Critical/Major	Enforce ALCOA+ principles; implement document control SOPs; real-time recording
Data integrity	Absence of audit trail review; unauthorized data changes	Weak IT controls; lack of awareness	Data falsification risk; regulatory rejection	Disabled audit trails; uncontrolled administrator privileges; unreviewed electronic audit trails	Critical	Implement audit trail review SOP; restrict access; periodic DI audits
Data integrity	Missing raw data (e.g., chromatograms)	Poor archiving systems	Inability to reconstruct the analysis	Missing electronic metadata; deleted sequences; inaccessible cloud/server archives	Critical	Maintain secure raw data storage; validated electronic systems
Equipment management	Expired calibration or missing calibration records	Inadequate maintenance planning	Invalid analytical results	Electronic calibration alerts ignored; incomplete digital maintenance logs	Critical	Automated calibration tracking; preventive maintenance program
Equipment qualification	Lack of IQ/OQ/PQ documentation	Weak qualification procedures	Equipment not fit for purpose	Missing electronic lifecycle documentation; incomplete qualification traceability	Major	Perform full qualification; maintain lifecycle documentation
Analytical methods	Use of unvalidated or partially validated methods	Limited expertise; poor SOPs	Non-reproducible results; regulatory non-compliance	Spreadsheet-based calculations lacking validation; unverified software workflows	Critical	Conduct full validation per ICH; document validation reports
Analytical methods	No system suitability testing	Weak method control practices	Reduced method reliability	Automated SST bypassed or not electronically documented	Major	Include SST criteria in SOPs; enforce before analysis
Sample management	Sample mix-ups or lack of traceability	Poor labeling and logging systems	Incorrect test results	Weak barcode/LIMS integration; incomplete electronic chain-of-custody	Critical	Implement sample tracking system (LIMS/logbooks)
Reference standards	Use of expired or non-traceable standards	Poor inventory control	Inaccurate quantification	Inventory software not synchronized with expiry tracking	Major	Maintain inventory system; track lot numbers and expiry
Training & competency	Lack of documented training records	Informal training processes	Analyst errors; inconsistent results	Missing electronic training logs; incomplete competency dashboards	Major	Competency-based training matrix; periodic reassessment

Table 2. Continued.

Area	Inspection red flag	Underlying cause	Regulatory impact	Typical 2026 findings (inspection trend)	Inspection classification	Mitigation/Best practice
Training & competency	Analysts performing tests without qualification	Poor supervision	Increased analytical errors	Electronic authorization controls not linked to analyst permissions	Critical	Authorization system for analysts; training certification
CAPA system	Repeated deviations without root cause analysis	Weak CAPA framework	Recurring non-compliance	CAPA systems lacking effectiveness checks or overdue closure tracking	Major	Implement structured RCA (e.g., FMEA, 5-Why); verify effectiveness
Deviation handling	Deviations not documented or investigated	Poor quality culture	Hidden errors; audit failure	Deviations omitted from electronic QMS workflows	Critical	Mandatory deviation reporting SOP; investigation workflow
QMS governance	Absence of management review	Weak leadership oversight	Lack of continuous improvement	KPI dashboards not reviewed; incomplete digital quality metrics	Major	Conduct periodic management reviews; track KPIs
Internal audits	No internal audit program or ineffective audits	Lack of trained auditors	Undetected compliance gaps	Electronic audit findings not trended or risk-ranked	Major	Risk-based audit schedule; trained internal auditors
Data systems (Digital)	Shared user accounts in computerized systems	Poor access control	Loss of accountability	Generic logins; inadequate role-based permissions; cybersecurity vulnerabilities	Critical	Unique user IDs; role-based access control
Data systems (Digital)	No data backup or recovery system	Weak IT infrastructure	Data loss risk	Inadequate cloud backup validation; failed recovery testing	Major	Automated backup systems; disaster recovery plans
Environmental controls	Uncontrolled temperature/humidity	Inadequate monitoring systems	Sample degradation; invalid results	Non-integrated environmental monitoring systems; missing electronic alarms	Major	Environmental monitoring and alarm systems
Safety & risk management	Inadequate handling of hazardous chemicals	Lack of safety protocols	Safety incidents; regulatory concern	Electronic incident reporting systems not utilized	Major	PPE enforcement; safety SOPs; regular training
Change control	Changes implemented without formal approval	Lack of change management system	Uncontrolled variability	Untracked software configuration changes; undocumented instrument software updates	Major	Formal change control SOP; risk-based evaluation

Source: Adapted from WHO GPPQCL (2024) [1] and WHO Prequalification of quality control laboratories [4]. CAPA, corrective and preventive actions; QMS, quality management systems; IQ, installation qualification; OQ, operational qualification; PQ, performance qualification; SOP, standard operating procedure; IT, information technology; SST, system suitability; LIMS, laboratory information management system; KPI, key performance indicator; ALCOA+, attributable, legible, contemporaneous, original, accurate, complete, consistent, enduring, and available; DI, data integrity; RCA, root cause analysis; FMEA, Failure Mode and Effects Analysis; PPE, personal protective equipment.

Proactive identification and mitigation of such vulnerabilities significantly enhance inspection readiness.

In conclusion, safety and risk management within GPPQCL extends beyond compliance with basic occupational safety rules. It requires systematic hazard identification, documented preventive controls, structured emergency preparedness, and integration of quality risk management into analytical operations. Laboratories that adopt a risk-based culture demonstrate not only regulatory compliance but also operational resilience, protection of personnel, and sustained analytical reliability.

Tip: Integrate safety risk logs with QMS CAPA systems for continuous improvement.

5.6 Internal Audits and Management Review

Sustained adherence to GPPQCL requires systematic monitoring of compliance, effectiveness, and performance. Regulatory inspectors view internal audits and management review as key indicators of quality system maturity. A laboratory that actively evaluates its own performance and implements corrective measures demonstrates proactive governance and regulatory reliability.

5.6.1 Internal Audits

Internal audits serve as structured, independent assessments of whether laboratory operations conform to GPPQCL requirements, approved SOPs, and regulatory expectations. Inspectors typically review the internal audit program to determine whether it is comprehensive, risk-based, and effectively implemented [38,39,40,41].

An effective internal audit system should include:

1. A documented annual audit schedule covering all quality system elements.

2. Audit checklists aligned with GPPQCL clauses and laboratory SOPs.

3. Defined auditor qualifications ensuring objectivity and competence.

4. Formal audit reports documenting observations, risk classification, and required corrective actions.

Audits should evaluate critical domains such as document control, equipment qualification, calibration records, environmental monitoring, training documentation, analytical method validation, data integrity practices, and reporting procedures. Inspectors often compare internal audit findings with regulatory inspection outcomes; failure to detect obvious deficiencies internally may indicate superficial audit practices.

Auditor independence is a critical inspection expectation. Personnel should not audit their own work. In smaller laboratories where full independence is difficult, documented justification and compensatory controls are expected.

Audit reports must clearly distinguish between observations, root cause analysis, corrective actions, preventive actions, responsible persons, and completion timelines. Evidence of follow-up verification is essential. Inspectors frequently examine whether previously identified findings were effectively closed and whether recurrence has been prevented.

5.6.2 Management Review

Management review represents the highest level of quality oversight within the laboratory governance structure. Regulatory authorities expect laboratory leadership to periodically evaluate the overall effectiveness of the QMS, rather than relying solely on operational staff.

Management review meetings should be conducted at defined intervals—commonly annually or semi-annually—and formally documented. Agendas typically include:

1. Internal and external audit outcomes.

2. Status and effectiveness of CAPA.

3. Trend analysis of deviations, OOS results, and complaints.

4. Equipment performance and downtime trends.

5. Environmental monitoring results.

6. Training effectiveness and competency status.

7. Resource adequacy (staffing, infrastructure, budget).

8. Risk assessment updates.

Inspectors assess whether management review minutes reflect meaningful evaluation and decision-making rather than routine administrative approval. Evidence of strategic actions—such as allocation of additional resources, procedural revisions, or targeted retraining—demonstrates active leadership engagement.

Absence of documented management review or superficial review without measurable outcomes is frequently cited as a quality system weakness.

5.6.3 Continuous Improvement and CAPA Effectiveness

Continuous improvement is a core principle of GPPQCL implementation. Audit findings, deviation investigations, risk assessments, and inspection observations should serve as drivers for system enhancement.

5.6.3.1 The Following Actions Must Be Taken by Laboratory After the Audit. 1. Conduct root cause analysis using structured methodologies.

2. Develop CAPA plans.

3. Define measurable implementation timelines.

4. Verify CAPA effectiveness after implementation.

Inspectors evaluate whether CAPA addresses systemic causes rather than superficial symptoms. Repeated recurrence of similar findings suggests ineffective root cause analysis or weak preventive controls.

5.6.3.2 Continuous Improvement May Include. 1. Revision of SOPs.

2. Enhancement of training programs.

3. Upgrade of analytical equipment.

4. Strengthening of data integrity safeguards.

5. Process redesign to reduce variability.

Trend analysis is particularly valued by regulators. Laboratories that monitor recurring deviations, equipment failures, or analyst errors demonstrate maturity in quality risk management.

5.6.3.3 Inspection Red Flags in Audit and Review Systems. Common regulatory observations include:

1. Irregular or undocumented internal audits.

2. Checklists not aligned with current GPPQCL requirements.

3. Lack of auditor independence.

4. CAPA implemented without effectiveness verification.

5. Management review minutes lacking substantive evaluation.

6. Repeated deficiencies across audit cycles.

Proactively addressing these weaknesses strengthens inspection readiness and organizational resilience.

In summary, internal audits and management review function as the feedback and governance mechanisms of the GPPQCL framework. When properly implemented, they ensure sustained compliance, promote accountability, and drive continuous improvement. Laboratories that maintain structured audit programs, engaged leadership oversight, and effective CAPA management demonstrate a mature quality culture and strong preparedness for regulatory inspection.

Example: A laboratory may track audit findings in a digital dashboard showing trends over time, highlighting recurring issues for priority action.

5.7 External Recognition and Prequalification

WHO prequalification represents a critical milestone for laboratories, demonstrating compliance with international standards and enabling participation in global procurement systems. Achieving GPPQCL compliance prepares laboratories for WHO prequalification and international recognition [42]:

- **Prequalification**: Demonstrate adherence to GPPQCL principles through documentation and inspection by WHO or regulatory authorities.
- **Global Acceptance**: Facilitates acceptance of laboratory results by other regulatory agencies, reducing duplicative testing and supporting international trade in medicines [43].

Example: Bangladesh National Control Laboratory gained international recognition after aligning its processes with GPPQCL, enabling broader acceptance of its test results by WHO and regional regulators.

This expanded stepwise guide provides practical, actionable steps for laboratories to implement GPPQCL comprehensively. By integrating a strong QMS, qualified personnel, validated analytical methods, risk-based safety practices, and continuous improvement, laboratories ensure regulatory compliance, enhance reliability of results, and achieve international credibility. GPPQCL implementation workflow is pictorially shown in Fig. 2.

6. Challenges and Mitigation Strategies

While GPPQCL provides a comprehensive framework for quality control laboratories, its effective implementation often encounters technical, operational, and organizational challenges. Regulatory inspectors frequently observe that even well-intentioned laboratories face obstacles in maintaining consistent compliance due to limitations in infrastructure, personnel, equipment, or procedural maturity. Recognizing these challenges and applying proactive mitigation strategies is essential for successful adoption of GPPQCL and for sustaining a state of inspection readiness.

Challenges in GPPQCL implementation can manifest across multiple domains: laboratory infrastructure, analytical capabilities, personnel competency, regulatory awareness, and organizational governance. Left unaddressed, these limitations may compromise the reliability of analytical results, reduce operational efficiency, and increase the risk of regulatory non-conformities. Therefore, laboratories must adopt a structured, risk-based approach to identify vulnerabilities and implement appropriate corrective and preventive measures.

6.1 Resource and Infrastructure Limitations

A primary challenge faced by many laboratories, particularly in resource-constrained or developing regions, relates to physical infrastructure, equipment availability, and financial constraints. Limited laboratory space, inadequate environmental control, and insufficient access to high-quality analytical instruments can impede full compliance with GPPQCL requirements. In addition, shortages of certified reference standards or controlled storage facilities may compromise analytical accuracy and traceability.

From a regulatory perspective, inspectors are particularly sensitive to infrastructure deficiencies that could affect sample integrity, method performance, or data reliability. For example, insufficient separation of sample handling zones can increase the risk of cross-contamination, while lack of environmental monitoring may impact temperature- or humidity-sensitive tests. Similarly, failure to implement validated instruments or to maintain proper calibration can be cited as critical deviations.

6.1.1 Mitigation Strategies

6.1.1.1 Prioritization of Critical Investments. Laboratories should identify high-risk analytical tests and allocate resources to validate and maintain instruments essential for regulatory compliance. For instance, HPLC systems, analytical balances, and dissolution testers may take precedence over lower-risk equipment. Capital investments

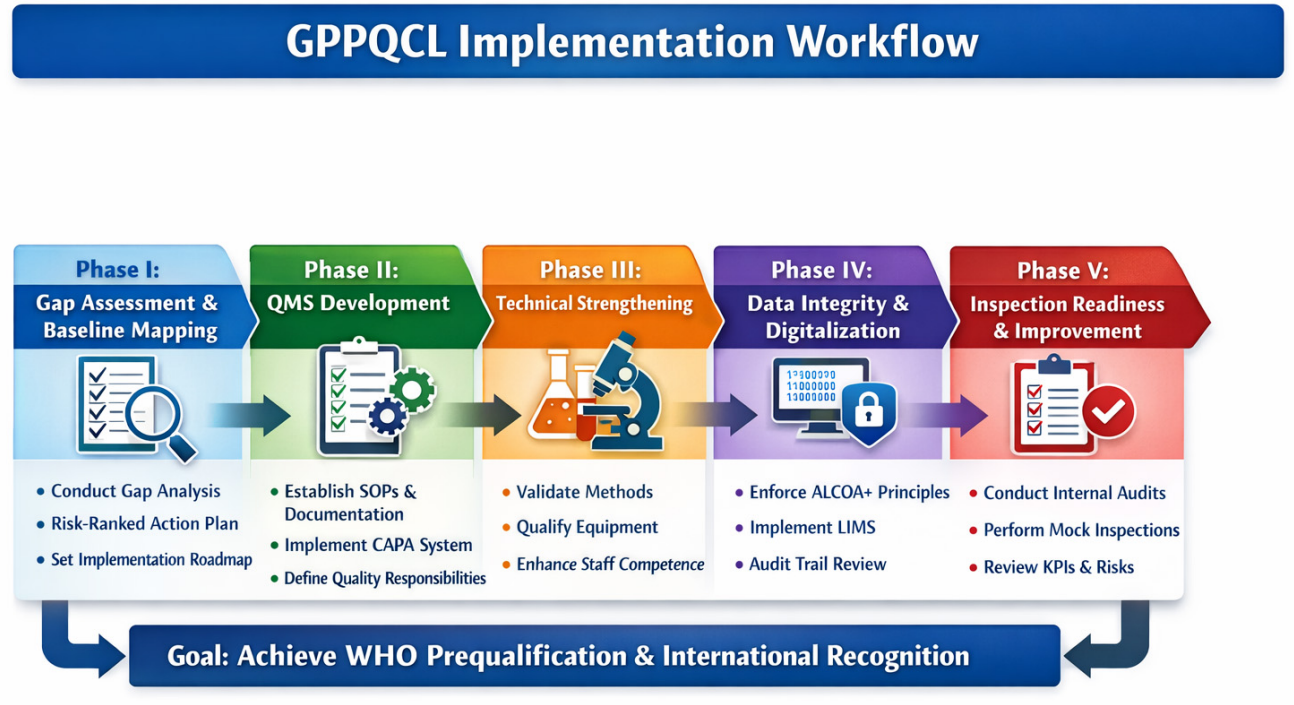

Fig. 2. Five-phase workflow for inspection-oriented GPPQCL implementation.

should be guided by a risk-based assessment aligned with the laboratory's scope of testing.

6.1.1.2 Shared Services and Regional Networks. Where individual laboratories cannot justify acquisition of specialized equipment, participation in shared-service models or regional laboratory networks may provide access to advanced analytical capabilities. Collaborative agreements can enable laboratories to perform complex assays, stability studies, or pharmacopoeial testing without duplicating high-cost infrastructure.

6.1.1.3 Optimization of Existing Infrastructure. Laboratories can maximize the utility of existing facilities through strategic workflow organization, effective segregation of testing areas, and controlled environmental monitoring within available resources. Even modest improvements in sample handling pathways, storage conditions, or environmental monitoring frequency can significantly reduce the risk of analytical errors and demonstrate proactive quality management to inspectors.

By addressing resource and infrastructure challenges through targeted prioritization, collaboration, and optimization, laboratories can maintain compliance with GPPQCL requirements despite operational constraints. Such proactive strategies also enhance inspection readiness, as regulators increasingly evaluate how laboratories identify, mitigate, and document risks associated with resource limitations.

6.1.2 Example

A small QC laboratory may implement rotational access to expensive HPLC systems, combined with stringent scheduling and SOP-driven method validation, to maximize the utility of limited equipment.

6.2 Personnel Competency and Training Gaps

Successful implementation of GPPQCL hinges on the presence of adequately trained and competent personnel. Laboratories frequently encounter challenges when staff lack sufficient experience, technical expertise, or regulatory awareness. Inadequately trained analysts may inadvertently introduce errors during sample preparation, testing, or data recording, compromising the reliability of test results and increasing the likelihood of regulatory non-compliance. Inspectors often focus on personnel competency as a key determinant of analytical credibility, and gaps in training can result in observations related to data integrity, procedural deviations, or method misapplication.

Personnel-related challenges may arise from several sources, including high staff turnover, limited access to formal training programs, evolving analytical methodologies, or insufficient understanding of regulatory expectations under GPPQCL. Inexperienced analysts are particularly vulnerable to errors in complex assays such as chromatographic impurity profiling, dissolution testing, or stability-indicating procedures. Without structured oversight and continuous development, these gaps can perpetuate recurring deviations and undermine quality system effectiveness.

6.2.1 Mitigation Strategies

6.2.1.1 Structured Onboarding and Competency-Based Training. Laboratories should implement comprehensive induction programs for new hires, covering laboratory safety, analytical techniques, documentation practices, regulatory requirements, and data integrity principles. Competency assessments should follow training to ensure analysts are authorized to perform specific tests only after demonstrated proficiency.

6.2.1.2 Regular Proficiency Testing. To verify and reinforce analytical skills, laboratories should conduct periodic proficiency assessments, including blind sample testing, spiked sample analysis, or inter-laboratory comparisons. Such evaluations help identify gaps in technique or interpretation, enabling targeted retraining and supporting regulatory inspection readiness.

6.2.1.3 Continuing Education and Workshops. Continuing professional development is essential for maintaining up-to-date analytical competency and awareness of evolving GPPQCL requirements. Participation in workshops, e-learning modules, and professional seminars fosters skill enhancement and promotes adoption of best practices.

6.2.1.4 Training Documentation and Evaluation. Comprehensive training records must be maintained for each staff member, including onboarding completion, refresher courses, competency assessments, and authorization status. Periodic evaluation of training effectiveness through performance reviews, audit findings, or skill assessments ensures the laboratory maintains a competent workforce aligned with regulatory expectations.

6.2.2 Example

Laboratories often utilize blind sample testing or inter-laboratory comparisons to objectively assess analyst proficiency. These exercises not only reinforce analytical skills but also provide verifiable documentation for inspections demonstrating that personnel competency is actively monitored and maintained.

By systematically addressing training and competency gaps, laboratories can minimize analytical errors, enhance staff confidence, and strengthen overall QMS effectiveness. Moreover, proactive personnel development fosters a culture of quality and prepares the laboratory for successful regulatory inspections.

6.3 Data Integrity and Documentation Challenges

Data integrity represents the cornerstone of GPPQCL, underpinning the scientific credibility of all analytical results and regulatory submissions. Laboratories often face challenges in maintaining complete, accurate, and traceable data due to manual transcription errors, inconsistent documentation practices, or inadequate oversight of electronic systems. Regulatory inspectors increasingly focus on data integrity as a high-risk area; deficiencies can result in critical observations or non-compliance findings that jeopardize laboratory certification and batch release authorization.

Common data integrity challenges include incomplete or missing laboratory records, inconsistent reporting formats, unverified calculations, and unauthorized alterations of data. Manual data transcription from instruments to logbooks or spreadsheets is particularly error-prone, increasing the risk of inaccurate reporting. In addition, inadequate oversight of electronic systems or poorly defined access controls can compromise audit trails and traceability, which are essential during inspections.

6.3.1 Mitigation Strategies

6.3.1.1 Electronic Laboratory Notebooks (ELNs) and LIMS Implementation. Adoption of electronic systems reduces transcription errors, enforces standardized documentation practices, and provides automated, tamper-evident audit trails. Properly configured ELNs and Laboratory Information Management Systems (LIMS) enable real-time data capture, facilitate review and approval workflows, and ensure secure storage and retrieval of analytical records.

6.3.1.2 Application of ALCOA+ Principles. Laboratories must apply ALCOA+ principles to all data management practices. Data should be Attributable to the individual performing the activity, Legible and readable, contemporaneously recorded at the time of the experiment, Original or a verified true copy, and Accurate with respect to measurements and calculations. Additionally, data should be Complete, Consistent, Enduring over its retention period, and readily Available for review during inspections.

6.3.1.3 Periodic Data Integrity Audits. Regular internal audits should evaluate compliance with data integrity requirements, both for manual and electronic systems. Audits verify the completeness of records, confirm proper access control, assess the robustness of audit trails, and identify potential vulnerabilities or recurring errors. Audit findings should feed into CAPA plans to continually improve documentation practices.

6.3.2 Example

Laboratories may perform retrospective review of ELN audit trails to confirm that all chromatographic integrations, sample calculations, and deviations have been appropriately recorded and approved. Such proactive monitoring not only reinforces compliance but also provides documented evidence of data governance for regulatory inspections.

By addressing data integrity challenges through electronic systems, adherence to ALCOA+ principles, and systematic auditing, laboratories strengthen analytical reliability, minimize errors, and demonstrate robust documentation

practices. These measures are critical for regulatory confidence and form a foundational element of inspection readiness under GPPQCL.

6.4 Equipment Calibration and Maintenance Issues

Proper calibration and maintenance of laboratory instruments are fundamental to generating accurate, reliable, and reproducible analytical results. Regulatory inspections frequently focus on instrument qualification, calibration, and maintenance records because deficiencies in these areas can directly compromise method performance, data integrity, and overall laboratory compliance. Instruments that are improperly maintained, operated beyond calibration limits, or inadequately verified can lead to analytical errors, out-of-specification results, method deviations, and negative audit findings.

Common challenges include overdue calibration, incomplete maintenance logs, unverified repairs, or lack of performance verification following instrument servicing. These gaps can result in unreliable measurements, inconsistent test results, or delayed batch release. Inspectors often cross-reference analytical results with calibration and maintenance records; inconsistencies or missing documentation are considered serious non-conformities.

6.4.1 Mitigation Strategies

6.4.1.1 Preventive Maintenance Schedule. Laboratories should establish and rigorously follow preventive maintenance schedules aligned with manufacturer recommendations and GPPQCL requirements. Critical instruments such as HPLC systems, balances, dissolution testers, and spectrophotometers should undergo routine checks, servicing, and performance verification to ensure consistent operation. Preventive maintenance helps preempt unexpected equipment failures and minimizes operational downtime.

6.4.1.2 Comprehensive Calibration and Service Documentation. Detailed records of all calibration activities, service interventions, and performance verification tests must be maintained. These records should include instrument identification, dates of calibration, reference standards used, acceptance criteria, observed results, corrective actions taken, and signatures of authorized personnel. Inspectors use these logs to verify traceability, confirm adherence to schedules, and assess the integrity of analytical results.

6.4.1.3 Staff Training in Instrument Handling and Troubleshooting. Proper operation and routine troubleshooting by laboratory personnel reduce the risk of equipment damage, measurement errors, and prolonged downtime. Training programs should emphasize manufacturer-recommended handling procedures, recognition of abnormal instrument behavior, and immediate escalation protocols for faults or failures. Competent staff ensure that instruments remain within validated performance limits and that minor operational issues are promptly resolved before they affect analytical outcomes.

6.4.2 Example

A laboratory may implement monthly performance verification of HPLC pumps and detectors using standard solutions, documenting flow rates, retention times, and detector response. Any deviation triggers immediate recalibration or servicing, ensuring reliable analytical results and audit-ready records for inspectors.

By proactively managing instrument calibration and maintenance, laboratories can prevent analytical errors, maintain compliance with GPPQCL, and demonstrate operational reliability to regulators. Systematic scheduling, meticulous documentation, and well-trained personnel collectively contribute to inspection readiness and long-term sustainability of quality laboratory operations.

6.5 Method Validation and Standardization Challenges

Analytical method validation and standardization are central pillars of GPPQCL, ensuring that laboratory results are scientifically robust, reproducible, and compliant with regulatory expectations. Laboratories frequently encounter challenges in validating methods or applying standardized procedures, particularly when analyzing complex formulations such as multi-component fixed-dose combinations, stability-indicating assays, or novel drug products. Inadequate validation can result in inaccurate measurements, cross-interference, inconsistent results, and potential non-compliance during audits or inspections.

Challenges typically arise from limited access to fully validated methods, insufficient technical expertise, variations in instrumentation, or local adaptation of published procedures. Inspectors often review validation reports to confirm that key parameters—accuracy, precision, specificity, linearity, LOD/LOQ, and robustness—have been appropriately demonstrated. Partial or undocumented validation, unclear acceptance criteria, or lack of method standardization can lead to regulatory observations.

6.5.1 Mitigation Strategies

6.5.1.1 Use of Established Methods. Wherever feasible, laboratories should adopt documented, validated methods from pharmacopeias, WHO-approved reference sources, or recognized regulatory guidelines. Utilizing these methods minimizes the need for extensive internal development while ensuring compliance with recognized quality standards.

6.5.1.2 Full or Partial Method Validation. When existing methods are adapted to local instruments, reagents, or sample matrices, laboratories must conduct full or partial validation to confirm suitability under specific operational conditions. This includes verifying critical parameters such as selectivity, linearity, accuracy, precision, and robustness.

Proper documentation of the validation process, including raw data, statistical analysis, and approval signatures, is essential for inspection readiness.

6.5.1.3 Clear SOPs and Cross-Referencing. Standard operating procedures should clearly define the analytical method, sample preparation steps, acceptance criteria, and calculation procedures. Cross-referencing SOPs to the original pharmacopeial or regulatory sources provides traceability and transparency, reinforcing confidence during inspections.

6.5.2 Example

For a multi-drug fixed-dose combination, laboratories may perform selectivity testing to confirm that all active ingredients are correctly quantified without interference from excipients or co-formulated components. This ensures reliable measurement of each analyte and minimizes the risk of erroneous batch release decisions.

By systematically addressing method validation and standardization challenges, laboratories enhance analytical reliability, maintain compliance with GPPQCL, and demonstrate scientific rigor to regulators. Structured adoption of validated methods, rigorous internal verification, and transparent documentation collectively contribute to robust laboratory performance and inspection readiness.

6.6 Managing Change and Continuous Improvement

The successful adoption of GPPQCL often necessitates significant changes in laboratory workflows, organizational culture, documentation practices, and quality oversight. Resistance to change, lack of leadership engagement, or insufficient monitoring can compromise implementation and slow progress toward full compliance. Regulatory inspectors increasingly evaluate whether laboratories not only implement quality systems but also demonstrate a culture of continuous improvement and proactive change management.

Change management challenges may manifest as staff reluctance to adopt new SOPs, inconsistent adherence to updated procedures, or gaps in training for modified workflows. Without systematic oversight, these changes may introduce operational inconsistencies, procedural deviations, or data integrity risks. Inspectors may probe whether modifications are properly documented, communicated, and evaluated for effectiveness.

6.6.1 Mitigation Strategies

6.6.1.1 Clear Communication of GPPQCL Benefits. Effective change begins with transparent communication. Laboratory leadership should explain the rationale, benefits, and regulatory requirements associated with GPPQCL adoption. Understanding how changes improve data reliability, operational efficiency, and regulatory readiness encourages staff engagement and reduces resistance.

6.6.1.2 Structured Change Management Approach. Laboratories should apply formal change management processes that define milestones, responsibilities, timelines, and verification checkpoints. This includes documenting changes to SOPs, workflows, instruments, or analytical methods, and ensuring proper training and authorization before implementation. Risk-based assessment of changes should guide prioritization and resource allocation.

6.6.1.3 Monitoring and Continuous Improvement. Internal audits, CAPA systems, and management reviews provide feedback mechanisms to evaluate the effectiveness of implemented changes. Observations from audits and inspections should be systematically addressed, with lessons learned integrated into SOP revisions, training updates, and process optimization. Trend analysis of deviations, audit findings, and CAPA outcomes supports continuous refinement of laboratory operations.

6.6.2 Example

When introducing a new validated HPLC method for multi-component analysis, the laboratory may update SOPs, provide competency-based training for analysts, and monitor method performance during initial implementation. Internal audits can confirm adherence to the new procedure, while management reviews evaluate whether the method meets analytical and regulatory expectations.

By actively managing change and fostering a culture of continuous improvement, laboratories strengthen organizational resilience, enhance quality performance, and maintain sustained compliance with GPPQCL. Effective change management ensures that quality systems evolve in a controlled, transparent, and scientifically justified manner, assuring both staff and regulators.

Although implementing GPPQCL presents challenges, laboratories can overcome them through careful planning, resource prioritization, structured training, robust documentation, and a strong culture of quality and continuous improvement. Addressing these challenges proactively ensures compliance, reliability of results, and readiness for international recognition. The key challenges encountered during GPPQCL implementation, along with their root causes, regulatory implications, and mitigation strategies, are summarized in Table 3 (Ref. [1]).

6.6.3 Critical Perspective

Although GPPQCL provides a comprehensive implementation framework, compliance success is often influenced by contextual realities such as funding, workforce stability, regulatory maturity, and technological readiness. A uniform implementation model may therefore be unrealistic, particularly in low-resource environments. Future implementation strategies may benefit from adaptive, risk-based models that balance regulatory expectations with operational feasibility.

Table 3. Challenges and mitigation strategies in GPPQCL implementation.

Challenge	Root causes	Regulatory/Quality risk	Inspection perspective	Mitigation strategies
Resource and infrastructure limitations	Limited funding; inadequate laboratory space; lack of advanced instrumentation; poor environmental controls	Compromised analytical accuracy; inability to perform required tests; delays in testing	Inspectors may issue major/critical findings for inadequate facilities or unsuitable testing environment	Prioritize high-risk equipment; implement phased upgrades; optimize workflow and zoning; use regional/shared laboratories; seek donor or program support
Personnel competency and training gaps	Insufficient training programs; high staff turnover; lack of competency assessments	Analytical errors; inconsistent results; non-compliance with SOPs	Review of training records often reveals gaps; lack of competency evidence is a frequent observation	Develop structured training matrix; conduct regular competency assessments; implement proficiency testing; maintain training records and effectiveness evaluation
Data integrity and documentation challenges	Manual systems; lack of audit trails; poor documentation practices; weak supervision	Data manipulation risk; loss of traceability; unreliable results	Critical inspection findings related to ALCOA+ violations; missing or incomplete records	Implement LIMS/ELN where feasible; enforce ALCOA+ principles; conduct data integrity audits; strengthen supervisory review
Equipment calibration and maintenance issues	Lack of maintenance planning; budget constraints; inadequate vendor support	Inaccurate measurements; invalid results; method failure	Expired calibration or missing records often lead to major findings	Establish preventive maintenance schedules; maintain calibration logs; use service contracts; train staff in basic troubleshooting
Method validation and standardization challenges	Limited access to validated methods; lack of expertise; variability in instruments and reagents	Non-reproducible results; cross-interference; regulatory non-compliance	Inspectors review validation reports; incomplete validation is a common deficiency	Use pharmacopeial/WHO methods; perform full/partial validation; standardize SOPs; document validation thoroughly
Change management and resistance to implementation	Organizational resistance; lack of leadership engagement; inadequate communication	Inconsistent application of procedures; implementation delays	Inspectors assess change control and effectiveness of implementation	Apply structured change management; define responsibilities and timelines; communicate benefits; monitor implementation through audits
Weak QMS integration	Fragmented documentation; lack of CAPA system; poor management oversight	Repeated deviations; lack of continuous improvement; systemic failures	Absence of CAPA effectiveness and management review is frequently cited	Strengthen QMS architecture; implement CAPA tracking; conduct management reviews; integrate quality policy across operations
Limited digitalization and technology adoption	Dependence on paper-based systems; limited IT infrastructure; cost constraints	Increased transcription errors; reduced traceability; inefficiency	Inspectors assess audit trails and data security; lack of digital controls raises concerns	Gradual implementation of LIMS; hybrid systems (paper + electronic); ensure data backup and controlled access
Supply chain and reference standards issues	Delays in procurement; limited availability of certified reference materials; storage issues	Use of expired or non-traceable standards; inaccurate quantification	Inspectors verify traceability and storage conditions of standards	Maintain inventory control system; ensure proper storage; establish reliable suppliers; track lot numbers and expiry dates
Regulatory and policy gaps	Lack of national guidelines; weak regulatory enforcement; inconsistent standards	Variability in laboratory performance; reduced confidence in results	Inspectors may identify gaps between national and WHO expectations	Align national policies with GPPQCL; strengthen regulatory oversight; adopt international best practices

Source: Adapted from WHO GPPQCL (2024) [1]. ELN, electronic laboratory notebooks.

7. Critical Appraisal and Policy Gaps in GPPQCL Implementation

While GPPQCL provides a comprehensive and structured framework for ensuring the reliability and integrity of medicines testing, their implementation in real-world settings reveals several practical and policy-related limitations. A critical evaluation of available literature and regulatory experience indicates that, despite clear guidance from the World Health Organization, significant variability exists in the extent and effectiveness of adoption across laboratories.

One of the primary challenges is the lack of harmonized implementation across different regulatory environments, particularly in LMICs. Laboratories often operate under resource constraints that limit their ability to fully comply with infrastructure, equipment qualification, and data integrity requirements. As a result, implementation tends to be selective rather than comprehensive, focusing on high-priority elements while deferring others.

Another key gap relates to the limited availability of published empirical studies evaluating GPPQCL implementation outcomes. Much of the existing literature is descriptive or programmatic, with few peer-reviewed studies assessing performance improvements, cost implications, or long-term sustainability. This limits evidence-based policy development and benchmarking across laboratories.

The relationship between GPPQCL and ISO/IEC 17025 also presents an area of ongoing discussion. While both frameworks share common principles such as competence, traceability, and quality management, GPPQCL incorporates regulatory and public health-specific requirements that are not fully addressed by ISO standards. However, the absence of a fully integrated or harmonized model can lead to duplication of effort or uncertainty in implementation strategies, particularly for laboratories pursuing dual compliance.

Data integrity remains another critical concern. Although recent WHO guidance has strengthened expectations around ALCOA+ principles and computerized systems, implementation maturity varies significantly, especially in laboratories transitioning from paper-based to electronic systems. Weaknesses in audit trail review, access control, and data governance continue to be observed during inspections.

Finally, GPPQCL implementation is inherently resource-dependent, requiring sustained investment in infrastructure, training, and quality systems. This creates disparities between well-funded laboratories and those operating in constrained environments, potentially limiting equitable access to internationally recognized testing capabilities.

Addressing these gaps requires a shift from guideline adoption to context-adapted implementation strategies, supported by capacity-building programs, regional collaboration, and increased documentation of implementation outcomes. Strengthening the evidence base and promoting integration with complementary standards such as ISO/IEC 17025 will further enhance the global applicability and impact of GPPQCL.

8. Implementation Strategy for GPPQCL Adoption: An Inspection-Oriented Framework

Effective implementation of the GPPQCL requires more than procedural compliance; it demands a structured, risk-based transformation aligned with inspection expectations and a sustainable quality culture. The World Health Organization framework emphasizes governance, technical competence, data integrity, and continuous improvement—elements that must be embedded systematically rather than introduced in isolation.

An inspection-oriented implementation strategy can be conceptualized as a five-phase progression model, ensuring both regulatory compliance and operational maturity.

8.1 Phase I: Gap Assessment and Baseline Mapping

Implementation begins with a comprehensive gap analysis against WHO GPPQCL requirements and, where relevant, ISO/IEC 17025 clauses. This baseline assessment should evaluate governance structures, documentation systems, equipment status, method validation practices, personnel competence, and data integrity controls.

From an inspection perspective, documented evidence of a structured gap analysis demonstrates leadership oversight and risk awareness. Laboratories should categorize deficiencies based on criticality (e.g., data integrity risks, expired calibrations, unvalidated methods) and develop a prioritized corrective action plan with defined timelines and responsibilities.

Deliverables at this stage typically include:

1. Gap assessment report.
2. Risk-ranked remediation plan.
3. Implementation roadmap approved by management.

This phase ensures that implementation is strategic rather than reactive.

8.2 Phase II: Quality Management System (QMS) Architecture Development

Following baseline mapping, laboratories should establish or restructure their QMS architecture. This involves defining the quality policy, clarifying organizational responsibilities, and implementing a hierarchical documentation system (quality manual, SOPs, work instructions, forms, and records).

Inspection expectations focus heavily on document control, traceability, deviation management, and CAPA systems. Therefore, laboratories must ensure:

1. Controlled issuance and revision of SOPs.
2. Formal deviation handling procedures.

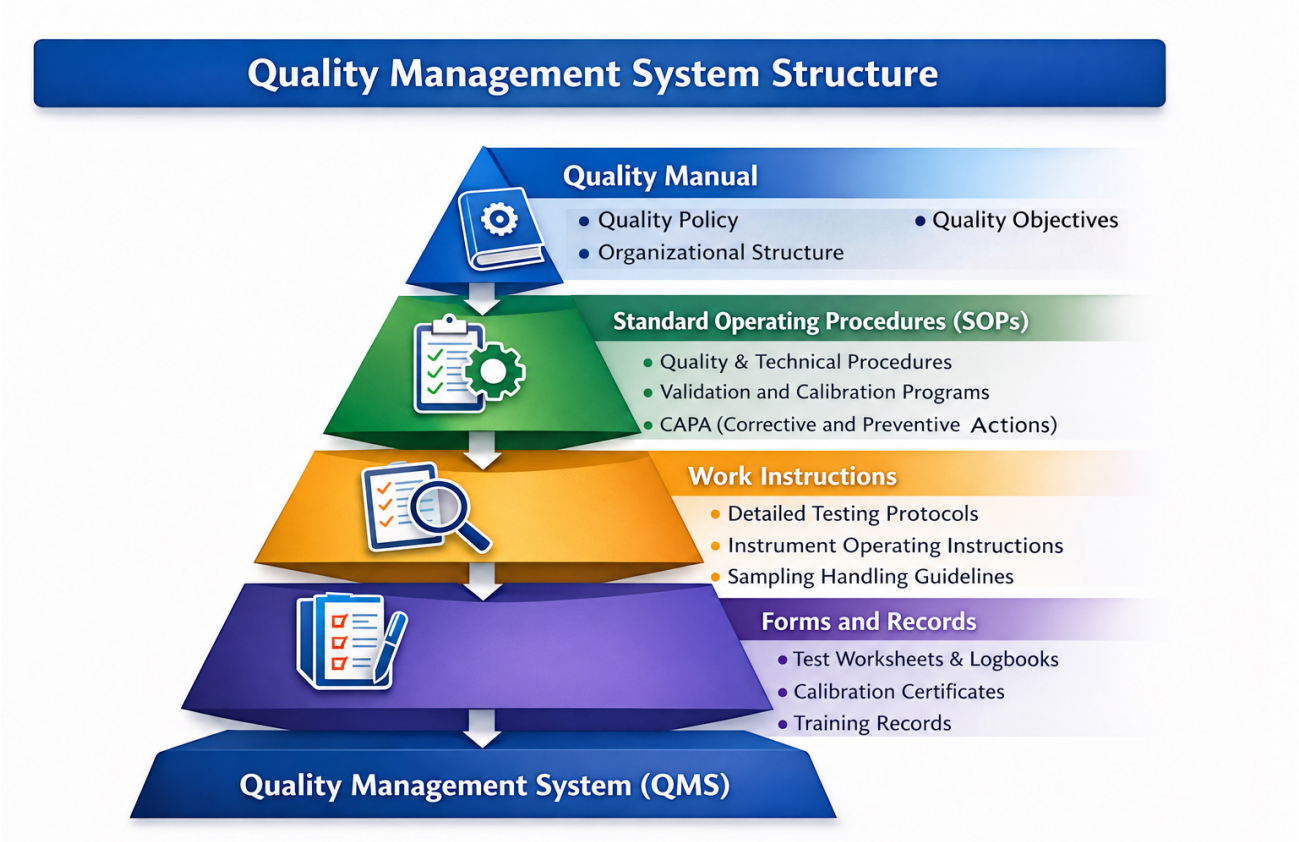

Fig. 3. The hierarchical structure of the laboratory quality management system.

3. Root cause analysis methodologies.
4. CAPA tracking with effectiveness verification.

A functioning QMS demonstrates that compliance is systematic and not dependent on individual performance alone.

The hierarchical structure of the laboratory quality management system is illustrated in Fig. 3, demonstrating the relationship between the quality manual, SOPs, work instructions, and operational records.

8.3 Phase III: Technical Strengthening and Competence Development

Technical reliability is central to GPPQCL implementation. This phase addresses equipment lifecycle management, analytical method validation, and personnel competency.

Equipment must undergo IQ, OQ, and PQ, with preventive maintenance and calibration schedules aligned with manufacturer guidance and risk classification. Inspectors typically verify calibration traceability, service documentation, and instrument performance verification records.

Method validation and verification activities must be documented, particularly when adapting pharmacopeial procedures to local matrices or multi-component formulations. Validation parameters such as accuracy, precision, specificity, linearity, and robustness should be supported by statistically sound data.

Simultaneously, competency frameworks should define qualification requirements, ongoing training, proficiency testing participation, and periodic reassessment. Inspection findings frequently highlight gaps in competency documentation; thus, structured training matrices are essential.

8.4 Phase IV: Data Integrity and Digital Integration

Modern inspection trends place significant emphasis on data integrity principles, particularly adherence to ALCOA+ attributes (Attributable, Legible, Contemporaneous, Original, Accurate, Complete, Consistent, Enduring, and Available).

Laboratories should implement measures such as:

1. Controlled access to computerized systems.
2. Audit trail review procedures.
3. Secure data backup systems.
4. Periodic data integrity risk assessments.

Where feasible, LIMS enhance traceability and reduce manual transcription errors. Even in resource-limited settings, procedural safeguards and supervisory review mechanisms must ensure that analytical data are reliable and tamper-resistant.

Inspection readiness increasingly depends on demonstrable data governance controls.

8.5 Phase V: Inspection Readiness and Continuous Improvement

The final phase focuses on sustainability and performance monitoring. Internal audits, conducted according to a defined schedule and risk-based methodology, provide objective evidence of compliance. Management reviews should evaluate audit outcomes, key performance indicators (KPIs, e.g., turnaround time, OOS rates, CAPA closure timelines), customer feedback, and resource adequacy.

Mock inspections and peer reviews are valuable tools for identifying latent weaknesses before formal WHO assessments. Corrective actions should not merely address isolated deficiencies but strengthen systemic resilience.

Continuous improvement ensures that GPPQCL implementation remains dynamic rather than static, supporting long-term eligibility for WHO prequalification and international recognition.

8.6 Strategic Integration and Sustainability

Successful GPPQCL adoption depends on leadership commitment, clear accountability structures, and cultural acceptance of quality principles. Laboratories that integrate governance oversight, technical rigor, risk management, and digital traceability into a unified system demonstrate higher inspection maturity and operational stability.

Ultimately, a phased, inspection-aligned implementation strategy transforms GPPQCL from a compliance checklist into a sustainable institutional framework. By embedding structured quality systems, competent personnel, validated methodologies, and robust documentation practices, pharmaceutical quality control laboratories can strengthen regulatory confidence, achieve international recognition, and contribute meaningfully to global medicines quality assurance.

9. Critical Analysis of Research Gaps and Future Directions

Despite the increasing adoption of GPPQCL, important research and implementation gaps remain insufficiently addressed. Existing literature predominantly focuses on guideline descriptions, accreditation status, and compliance outcomes, whereas comparatively little attention has been paid to operational effectiveness, sustainability, and long-term quality performance under real-world laboratory conditions.

9.1 Limited Evidence on Implementation Effectiveness

Although WHO-prequalified laboratories are often cited as successful examples of GPPQCL adoption, published studies rarely quantify the direct impact of implementation on analytical accuracy, deviation reduction, turnaround times, or public health outcomes. Most available evidence is descriptive and lacks longitudinal performance assessment. Future studies should incorporate measurable quality indicators and performance benchmarking across laboratories.

9.2 Underrepresentation of Low- and Middle-Income Countries (LMICs)

The practical realities of GPPQCL implementation in resource-limited settings remain insufficiently characterized. Laboratories in low-income countries frequently face infrastructure limitations, reagent shortages, unstable supply chains, and workforce turnover. However, few studies critically evaluate adaptive implementation strategies suitable for these environments. Context-specific implementation frameworks are therefore needed to improve feasibility and sustainability.

9.3 Limited Research on Data Integrity Maturity

Although data integrity has become a central regulatory expectation, published evidence evaluating digital maturity, electronic systems adoption, and audit trail governance in pharmaceutical quality control laboratories remains sparse. Future investigations should explore cost-effective digital transformation strategies for laboratories transitioning from paper-based systems.

9.4 GPPQCL–ISO Integration Challenges

The relationship between GPPQCL implementation and ISO/IEC 17025 accreditation remains insufficiently explored. While both frameworks are frequently implemented simultaneously, little evidence exists regarding the operational burden, overlap, or complementary benefits of dual implementation. Comparative studies are needed to define best integration practices.

9.5 Need for Risk-Based and Predictive Quality Systems

Current implementation models remain largely compliance-driven and reactive. Emerging quality paradigms increasingly emphasize risk-based oversight, predictive maintenance, digital monitoring, and real-time quality analytics. Future GPPQCL frameworks may benefit from incorporating artificial intelligence–assisted deviation detection, remote auditing capabilities, and integrated laboratory informatics.

Critical Perspective

Importantly, GPPQCL implementation should not be viewed solely as a compliance exercise. Excessive focus on documentation may unintentionally encourage “inspection readiness” over genuine quality culture. Sustainable laboratory strengthening requires organizational commitment, continuous competency development, and investment in scientific capability rather than procedural conformity alone.

10. Case Studies and Examples of GPPQCL Implementation

The practical adoption of GPPQCL is best illustrated through real-world laboratory experiences. Documented case studies demonstrate how laboratories have implemented structured quality systems, strengthened analytical capabilities, and achieved international recognition through WHO prequalification. These examples highlight the feasibility of GPPQCL implementation across diverse operational contexts and provide practical lessons for laboratories seeking compliance.

10.1 Bangladesh National Control Laboratory (NCL)

The National Control Laboratory of Bangladesh exemplifies a successful GPPQCL adoption in a resource-constrained environment. Confronted with a high testing workload and limited infrastructure, the laboratory undertook a structured approach to align all operations with GPPQCL principles. Key initiatives included establishing a robust QMS, implementing competency-based training for analysts, upgrading critical analytical equipment, and deploying electronic data management systems to ensure traceability and data integrity. These coordinated efforts culminated in WHO prequalification in 2020, confirming compliance with international standards for medicines quality testing [12]. The recognition enhanced the credibility of the laboratory's results at both national and international levels and provided a benchmark for other laboratories in similar contexts.

10.2 Drug Physicochemical Laboratory—Ghana

In West Africa, the Drug Physicochemical Laboratory under the Ghana Food and Drugs Authority achieved WHO prequalification for chemical testing in 2022, becoming the first national medicines quality control laboratory in the region to do so. The laboratory's success was underpinned by the implementation of a structured QMS, strengthening of analytical competencies, and strict adherence to data integrity practices aligned with GPPQCL requirements [44,45]. Today, the laboratory functions as a regional center of excellence, delivering internationally recognized testing services and supporting regulatory oversight, procurement decisions, and capacity-building initiatives across neighboring countries.

10.3 Karaganda Medicines Quality Control Laboratory—Kazakhstan

The Karaganda Medicines Quality Control Laboratory in Kazakhstan represents the first WHO-prequalified medicines quality control laboratory in Central Asia, achieving compliance with GPPQCL standards in 2020. Through technical support and capacity building provided by the USP-PQM program, the laboratory enhanced its QMS, method validation procedures, and analytical capabilities [46]. WHO prequalification facilitated international recognition, positioning the laboratory as a regional reference center for essential medicines testing, including anti-tuberculosis medicines. The case illustrates how structured technical assistance combined with internal quality initiatives can accelerate GPPQCL adoption in emerging regulatory contexts.

10.4 Other WHO Prequalified Laboratories

While detailed operational narratives are not available for all laboratories, WHO's global list of prequalified quality control laboratories confirms adherence to GPPQCL-aligned standards [45]. A summary of some WHO Prequalified QC Laboratories is shown in Table 4 (Ref. [12,45]).

These laboratories have demonstrated compliance with core GPPQCL principles, including validated analytical methods, robust documentation practices, staff competency assurance, and fully functional quality management systems. Collectively, they provide evidence that GPPQCL implementation is achievable across diverse geographic, technical, and organizational settings.

The reviewed case studies confirm that successful GPPQCL implementation requires the integration of robust quality management systems, skilled and competent personnel, validated analytical methods, and strong documentation practices. Achieving compliance ensures reliable and reproducible results, strengthens regulatory confidence, and provides laboratories with international recognition through WHO prequalification. These examples collectively demonstrate that GPPQCL adoption is both feasible and beneficial, contributing to global pharmaceutical quality assurance and improved public health outcomes.

In addition to individual laboratory case studies, global laboratory strengthening initiatives such as the United States Pharmacopeia PQM program and WHO capacity-building efforts have played a critical role in supporting GPPQCL implementation in low- and middle-income countries [47,48,49,50,51,52,53,54,55,56,57]. These programs provide technical assistance, training, and infrastructure support, enabling laboratories to progressively align with international standards and achieve WHO prequalification.

11. Discussion

The implementation of GPPQCL represents a significant step forward in standardizing pharmaceutical quality control laboratory practices, particularly in low- and middle-income countries. Unlike ISO/IEC 17025, which primarily focuses on general laboratory competence and accreditation, GPPQCL provides a regulatory-oriented framework specifically tailored for pharmaceutical laboratories, integrating aspects of safety, data integrity, method validation, and regulatory reporting.

Table 4. Summary of some WHO prequalified QC laboratories.

Laboratory	Country	Scope/Recognition	Reference
National Control Laboratory (NCL)	Bangladesh	Chemical testing, WHO prequalified	[12]
Drug Physicochemical Laboratory	Ghana	Chemical testing, WHO prequalified	[45]
Mission for Essential Drugs & Supplies (MEDS)	Kenya	Prequalified QC testing	[45]
National Quality Control Laboratory (NQCL)	Kenya	Prequalified QC testing	[45]
Beijing Institute for Drug Control	China	Prequalified QC testing	[45]
Auriga Research Pvt Ltd	India	Prequalified QC testing	[45]

11.1 Comparison With ISO/IEC 17025

While both GPPQCL and ISO/IEC 17025 share core principles such as quality management, personnel competence, and equipment validation, there are key distinctions:

1. Scope and Focus: ISO/IEC 17025 emphasizes technical competence and accreditation for any testing laboratory, whereas GPPQCL is specifically designed for pharmaceutical QC labs and emphasizes regulatory compliance, method validation for medicinal products, and safety considerations.

2. Regulatory Recognition: GPPQCL aligns closely with WHO prequalification requirements, enabling international recognition without necessarily seeking formal accreditation, whereas ISO/IEC 17025 accreditation is globally recognized but may not address regulatory reporting or pharmaceutical-specific safety protocols.

3. Operational Detail: GPPQCL provides explicit guidance on sample handling, data integrity, reporting, and CAPA for pharmaceutical testing, whereas ISO/IEC 17025 provides a more generalized framework applicable across scientific disciplines.

This comparison highlights that while ISO/IEC 17025 provides a baseline for laboratory competence, GPPQCL is a specialized, regulatory-focused standard that complements or can be implemented alongside ISO/IEC 17025 in pharmaceutical settings.

While ISO/IEC 17025 provides a robust and internationally recognized framework for demonstrating laboratory competence, its scope is intentionally generic and not specific to the pharmaceutical sector. In operational settings, GPPQCL, as defined by the World Health Organization, complements ISO/IEC 17025 by incorporating regulatory and public health–oriented requirements that are critical for medicines evaluation. These include structured approaches to method suitability for complex pharmaceutical formulations, integration with national regulatory decision-making processes, and alignment with post-marketing surveillance activities. Consequently, GPPQCL does not replace ISO/IEC 17025 accreditation but extends it, ensuring that technically competent laboratories also meet the specific expectations of pharmaceutical regulation. Laboratories implementing both frameworks benefit from dual assurance: international technical credibility through ISO/IEC 17025 and regulatory relevance through GPPQCL, resulting in a more comprehensive and inspection-ready quality system.

11.2 Implications of GPPQCL Implementation

The practical adoption of GPPQCL has several implications:

1. Enhanced Reliability of Test Results: Laboratories implementing GPPQCL demonstrate reproducible and accurate analytical outcomes, crucial for medicines quality assurance.

2. Global Recognition and Regulatory Acceptance: Compliance enables laboratories to achieve WHO prequalification, facilitating international trust in test results and reducing duplication of testing for medicines procurement.

3. Capacity Building: Implementation fosters a culture of continuous improvement, strengthening personnel skills, laboratory management systems, and safety practices.

4. Risk Management: GPPQCL integrates quality risk management at all levels, from sample handling to data reporting, ensuring that potential errors or deviations are proactively addressed.

These benefits collectively enhance public health protection by ensuring that medicines meet required quality standards.

11.3 Challenges and Lessons Learned

Despite clear advantages, real-world implementation of GPPQCL is not without challenges:

1. Resource Constraints: Laboratories in resource-limited settings may struggle with the financial and technical requirements of full implementation, particularly in acquiring equipment and digital data management systems.

2. Training and Competency Gaps: Ensuring staff are competent in advanced analytical techniques and quality systems requires ongoing investment in training and assessment.

3. Data Management: Maintaining integrity and traceability of analytical results, especially during transitions from paper-based to electronic systems, remains a critical challenge.

Lessons from prequalified laboratories, such as Bangladesh NCL, Ghana FDA, and Karaganda QCL, indicate that phased implementation, targeted investment in

Fig. 4. Future trends in pharmaceutical quality assurance.

critical systems, and structured capacity building are effective strategies to overcome these challenges.

Despite the robustness of the GPPQCL framework, its effectiveness ultimately depends on laboratories' capacity to operationalize its requirements within local constraints. This highlights the need for adaptable implementation models rather than rigid compliance approaches.

11.4 Future Directions

The evolution of GPPQCL is expected to focus on:

1. Digital transformations: Increased adoption of electronic laboratory management systems (ELNs, LIMS) for real-time monitoring, audit readiness, and data integrity [58,59,60,61].

2. Harmonization with international standards: Integration with ISO/IEC 17025, ISO 9001, and pharmacopeial standards to facilitate broader recognition and efficiency [62,63,64].

3. Advanced analytical techniques: Incorporation of high-resolution methods, automation, and risk-based analytical strategies for complex formulations [65,66,67].

4. Regional and global networks: Expansion of collaborative networks among laboratories to share best practices, harmonize quality systems, and support regulatory oversight [68,69,70,71,72].

These trends underscore the growing importance of GPPQCL in strengthening pharmaceutical quality systems globally and ensuring consistent public health protection. These future trends are described in Fig. 4.

The discussion highlights that GPPQCL offers a specialized, regulatory-focused framework for pharmaceutical quality control laboratories, complementing general laboratory standards like ISO/IEC 17025. Real-world adoption demonstrates significant benefits in test reliability, regulatory acceptance, and capacity building, while lessons from challenges provide a roadmap for effective implementation. Moving forward, digitalization, harmonization, and regional collaboration will be central to the evolution and wider adoption of GPPQCL standards.

12. Conclusion

Good Practices for Pharmaceutical Quality Control Laboratories provide a robust operational and regulatory framework for strengthening pharmaceutical testing systems. However, successful implementation extends beyond procedural compliance and depends on the effective integration of quality management systems, technical competency, data integrity, and risk-based governance. Persistent implementation barriers—including infrastructure limitations, workforce gaps, and uneven digital maturity—highlight the need for context-sensitive approaches, particularly in low- and middle-income settings.

Critically, the long-term value of GPPQCL lies not only in achieving inspection readiness or accreditation but in strengthening confidence in medicine quality across healthcare systems. Reliable pharmaceutical testing supports regulatory decision-making, improves post-marketing surveillance, reduces circulation of substandard

and falsified medicines, and ultimately protects patient safety. Future efforts should prioritize sustainable laboratory strengthening, digital transformation, and evidence-based implementation models that maximize public health impact.

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The single author was responsible for the conception of ideas presented, writing, and the entire preparation of this manuscript.

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Declaration of AI and AI-Assisted Technologies in the Writing Process

During the preparation of this work, the author used ChatGPT in order to create figures. After using this tool, the author reviewed and edited the content as needed and takes full responsibility for the content of the publication.

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