World Academy of Science, Engineering and Technology
International Journal of Pharmacological and Pharmaceutical Sciences
Vol:15, No:12, 2021

Disparities versus Similarities: WHO GPPQCL and ISO/IEC 17025:2017 International Standards for Quality Management Systems in Pharmaceutical Laboratories

M. A. Okezue, K. L. Clase, S. R. Byrn, P. Shivanand

***Abstract*—**Medicines regulatory authorities expect pharmaceutical companies and contract research organizations to seek ways to certify that their laboratory control measurements are reliable. Establishing and maintaining laboratory quality standards are essential in ensuring the accuracy of test results. 'ISO/IEC 17025:2017' and 'WHO Good Practices for Pharmaceutical Quality Control Laboratories (GPPQCL)' are two quality standards commonly employed in developing laboratory quality systems. A review was conducted on the two standards to elaborate on areas on convergence and divergence. The goal was to understand how differences in each standard's requirements may influence laboratories' choices as to which document is easier to adopt for quality systems. A qualitative review method compared similar items in the two standards while mapping out areas where there were specific differences in the requirements of the two documents. The review also provided a detailed description of the clauses and parts covering management and technical requirements in these laboratory standards. The review showed that both documents share requirements for over ten critical areas covering objectives, infrastructure, management systems, and laboratory processes. There were, however, differences in standard expectations where GPPQCL emphasizes system procedures for planning and future budgets that will ensure continuity. Conversely, ISO 17025 was more focused on the risk management approach to establish laboratory quality systems. Elements in the two documents form common standard requirements to assure the validity of laboratory test results that promote mutual recognition. The ISO standard currently has more global patronage than GPPQCL.

***Keywords*—**ISO/IEC 17025:2017, laboratory standards, quality control, WHO GPPQCL.

I. Introduction

ESTABLISHING and maintaining international standards are essential components for laboratories that conduct tests to verify the quality of medicines that maintain public health. One of the purposes of establishing these standards is to ensure the accuracy of reports produced from these test facilities [1]. To maintain the desired quality for pharmaceutical products, a feedback mechanism, quality control (QC), is implemented, and remedial actions are enacted when deviations from standards are observed [2]. The management systems operated by these medicines' QC laboratories are based on international pharmaceutical standards (see Table I). From this list of laboratory standards, the two most common for medicine testing labs in many low- and middle-income economies are 'ISO/IEC 17025' and 'World Health Organization (WHO) Good Practices for Pharmaceutical Quality Control Laboratories (GPPQCL)' [1]-[5]. This study shows one of these quality standards seems more widely adopted than the other.

TABLE I
International Standards Applicable to Laboratories

Standard	Focus
ISO/IEC 17025*	General requirements for the competence of testing and calibration laboratories
ISO 15189	Medical laboratories – particular requirements for quality and competence
ISO/IEC 17043	Conformity assessment – General requirements for proficiency testing
ISO 13528	Statistical methods for use in proficiency testing by interlaboratory comparison
OECD GLP	Organization for Economic Co-operation and Development (OECD) principles on good laboratory practice
ISO Guide 34	The general requirement for the competence of reference material producers
ISO 8402	Quality management and quality assurance – vocabulary
ISO 19011	Guidelines for quality and/or environmental management system auditing
ISO 9001	Quality management systems – requirements
WHO GPPQCL*	WHO Good Practices for Pharmaceutical Quality Control Laboratories
21 CFR Ch. I (4–1–11 Edition) PART 210 & 211	Current Good Manufacturing Practice in Manufacturing, Processing, Packing, or Holding of Drugs

Table adapted from Valdivieso-Gómez, V., & Aguilar-Quesada, R. (2018) [1], [40].

*ISO/IEC 17025 and WHO GPPQCL are commonly used for medical testing laboratories in low- and mid- resource settings. Adapted from lab-quality standards and their implementation [5].

A. Origin of The WHO GPPQCL and ISO 17025

Through the WHO, the United Nations (UN) supplies essential medicines for national programs in high disease burdened countries. The UN has senior pharmaceutical advisers who seek to coordinate member countries' medicine policies without duplicating roles. Therefore, this 'Inter-agency Pharmaceutical Coordination' (IPC) group recommended the WHO PQ program to streamline quality procedures for medicine procurement [6]. As part of an effort to provide quality, safe and efficient medicines to low- and medium-income countries, the WHO, through its prequalification (PQ) program, certifies laboratories that meet the GPPQCL standards. The WHO PQ program was initiated in 2001. It provides an opportunity for laboratories to be assessed with strict regulatory standards that ensure their test results are

acceptable to international global funding agencies like the UNICEF and World Bank [6]. WHO pre-qualified laboratories serve the role of testing medicines distributed under the donor programs of these international agencies and therefore need to maintain a high-level quality management system (QMS).

In line with this expectation, the WHO GPPQCL guidelines provide information on the QMS. The analysis of active pharmaceutical ingredients (APIs), excipients, and finished products should be performed to demonstrate that reliable results are obtained. The goal is that compliance with this standard helps promote international harmonization in testing activities and hence mutual recognition of laboratory results [1]. The WHO standard can be implemented by pharmaceutical quality control laboratories such as national, commercial, or nongovernmental facilities [1]. WHO uses the PQ mechanism in high disease burden regions to ensure that medical products supplied by procurement agencies meet global standards of quality, safety, and efficacy [7].

For the other standard, from a historical account, ISO was formed from two organizations, ISA (International Federation of the National Standardizing Associations) and the UNSCC (United Nations Standards Coordinating Committee), in 1946. The group later allied with the International Electrotechnical Commission (IEC), and together their technical committees develop standards for various fields [8]. Currently, the organization is funded through contributions from national standard bodies of 164 countries and the sale of ISO Standards [9].

ISO had developed over 23,224 standards by 2020 [10]. One of the organization's quality-related standards, the ISO/IEC 17025 document, was developed to promote confidence in the operation of laboratories (Testing, Calibrating, or Sampling labs). Therefore, many laboratories that conduct tests on other items besides medicines can be accredited with ISO/IEC 17025. The ISO standard stipulates documents and procedures a QC laboratory should implement, to show they can generate valid results. The standard can be used by organizations performing laboratory activities, irrespective of their personnel size or number of processes [4]. In general, laboratories determine their competence areas and apply to attain ISO/IEC 17025 accreditation in those specific testing areas. After that, such testing facilities are recognized for competence in those identified test areas. Laboratories that conform to standards in this document will also generally operate by following the principles of ISO 9001 [4]. The current 2017 version of 17025 standard, which has risk-management orientation, supersedes an earlier 2005 edition, which contained more details of "how" each standard requirement could be achieved [11]-[13]. The acceptance of results between countries is facilitated if laboratories conform to the ISO/IEC 17025 document since adopting the standards enhances mutual recognition of results [4].

B. Current Status for Implementing GPPQCL and ISO/IEC 17025 Standards in Testing Laboratories

Though these two standards guide improvement procedures in quality control laboratories, there is a wide gap in the number of organizations currently using them. In 2019, data from the International Laboratory Accreditation body (ILAC) website, see Fig. 1, indicated that over 60,000 testing laboratories worldwide had been accredited against ISO/IEC 17025 [14]. This number includes laboratories accredited against the old ISO/IEC 17025 (1990 and 2005) and the new 2017 version of the standard. Similarly, Grochau et al., in their studies on the American landscape, cited several laboratories accredited against the ISO standard [15].

Conversely, reports from the WHO website acknowledged that by 16th March 2020, worldwide, out of several hundreds of laboratories that expressed their interest to participate in the prequalification procedure, only 55, see Fig. 2, had been assessed and found to comply with GPPQCL standards' requirements [16]. There are obvious gains associated with WHO PQ for laboratories, including being assigned a medicines test center for international donor agencies. The question may then be, why are so many laboratories finding it difficult to attain the WHO PQ status?

Several studies have been conducted outlining experiences of laboratories that are accredited against the ISO standard. Some enumerated the challenges faced in implementing the standards' requirement [17]-[22], others elaborated on merits derived from accreditation [23]-[25], even laboratories affiliated with some educational institutions have achieved ISO 17025 accreditation [19], [26], [27]. However, some studies expressed skepticism on the perceived value that ISO accreditation adds to the quality systems in organizations, compared to the costs associated with attaining the status [28], [29].

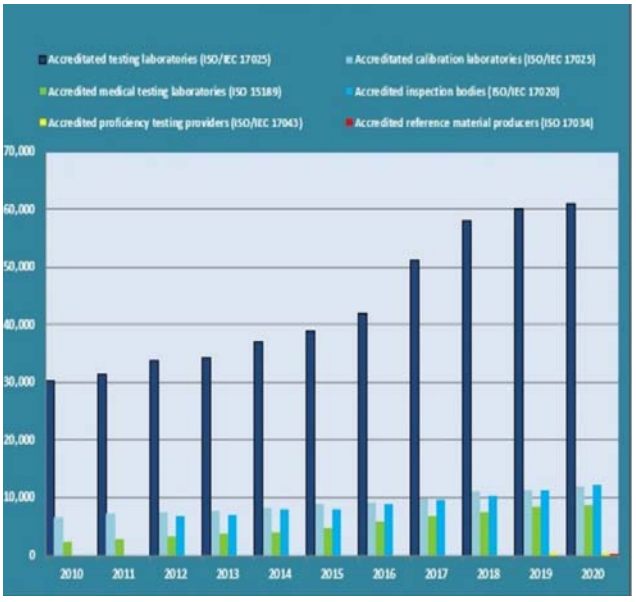

Fig. 1 Worldwide, there are over 60,000 testing laboratories accredited against ISO/IEC 17025. Source, ILAC – facts and figures [14]

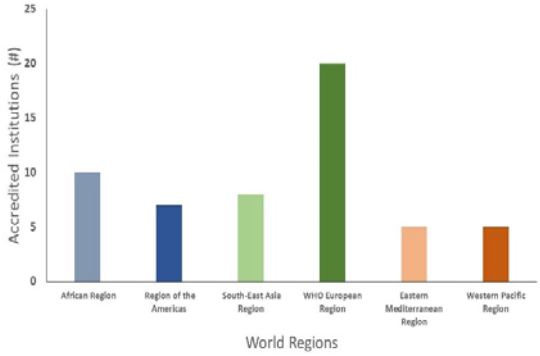

Fig. 2 Distribution of laboratories that have attained WHO prequalification status using GPPQCL standard. Data from WHO List of Prequalified Quality Control Laboratories [16]

Current literature does not show that any research has compared the laboratory standards from these two entities. More so, contrary to several available works on the implementation of ISO 17025, there is a paucity of literature on facilities operating with the WHO GPPQCL standards. This may be related to the smaller number of manufacturers or laboratories that have obtained satisfactory prequalification assessments [30]. Though Mao and Yang (2017) conducted gap analysis in China to access the difficulties faced in achieving WHO GPPQCL, their findings were similar to other studies that highlighted similar challenges with attaining ISO 17025 accreditation [26], [27], [31]. A question then arises, why are there fewer laboratories operating their quality systems under WHO standards? This study conducted an in-depth analysis, examined various components in both standards to unearth plausible factors that may account for the seemingly higher level of preference for implementing ISO 17025.

II. Method

The two standards were reviewed to understand the different elements contained in both documents as well as the areas of overlap and outright divergence. Using literature sources, our team identified how laboratories have attained these standards. And finally, explored possible reasons for the observed differences in the number of laboratories that are currently operating with either standard.

The study conducted an in-depth review of the World Health Organization Good practices for pharmaceutical quality control laboratories (WHO GPPQCL) and ISO/IEC 17025:2017 standards. The literature for the WHO GPPQCL standard was assessed via the web as annex 1 of the guidance document [1]; similarly, an electronic copy of the ISO standard was used to obtain the relevant data.

The different elements of both standards were examined and categorized under the following general themes or elements, self-identified from the two documents. The list outlines the management and technical requirements.

1. Standard objectives and applicability
2. Matters relating to conflicts of interests
3. Infrastructural and management systems
4. Equipment and traceability components
5. Laboratory processes, including analytical methods, handling samples, and measurements of uncertainties
6. Quality management systems
7. Computerization
8. Laboratory Safety

Direct quotes were compared verbatim in the 'objectives' and 'applicability' sections of both standards to reflect the accurate translation of the expectations. After assessing the elements of both standards, similar and divergent emerging items were also linked within both documents.

The areas of convergence were determined by interpretation of the activities necessary to fulfill each standard's requirement. If these were found to overlap sufficiently, then that part was identified as an area of convergence. However, if there were significant differences in the activities required to fulfill either standard's requirement, that was recorded as an area of divergence. After that, the study mapped the differences and similarities in the standards' requirements by numerical lists that reflected areas of significant similarities and differences.

Finally, through a review of previous works and available literature, this study further attempted to provide suggested models for attaining the standards. For this inquiry, the two laboratory standards' requirements were assessed by experienced reviewers who had used both documents for more than 15 years.

III. Results

A total of 15 elements were reviewed for both standards and are available as Tables IV and V in the appendix section. Table II summarized four elements: objectives, infrastructure and management systems, equipment, and safety. The GPPQCL differed in financial and safety requirements; however, it had overlaps in equipment and infrastructural components.

The list of elements reviewed for both standards is shown in Table III under the following subsections: objectives, applicability, impartiality, confidentiality, infrastructure and management systems, equipment, traceability, laboratory processes, handling samples, document and records controls, measurements uncertainties, quality management systems, computerized systems, and safety. Overall, the study found several similarities and a few differences in activities required to meet both the WHO GPPQCL and ISO/IEC 17025 standards.

TABLE II
REPRESENTATIVE ITEMS FROM ELEMENTS REVIEWED FOR WHO GPPQCL AND ISO/IEC 17025:2017

Element	WHO GPPQCL	ISO/IEC 17025	Convergence	Divergence
Objectives	provide advice on the QMS within which tests on API and FPP should be performed to demonstrate that reliable results are obtained.	Provide requirements that enable labs to demonstrate competency, and the ability to generate valid results	Reliability and validity of laboratory results; lead to local and international mutual recognition	GPPQCL emphasizes future budgets that will ensure continuity
Infrastructure and management systems	Part One Organization and management	Structural Requirements (5) Resources requirements (6)	1. legal authorization 2. Authorized personnel 3. Organizational charts 4. Chain of custody & competence requirements 5. Environmental monitoring	GPPQCL requires 1. substitutes/deputies for key management personnel 2. designate QAM
Equipment	Equipment, instruments and other devices Part 1 (8)	Equipment 6.4	1. Maintenance Plan 2. Calibration & metrological traceability 3. Intermediate checks 4. Equipment labeling	No major differences observed
Safety	1. General and specific rules, and regular training 2. Requires SOPS for safety-related issues:	Not applicable	None	There are no requirements for laboratory workers safety in the ISO document,

TABLE III
LIST OF ELEMENTS FROM WHO GPPQCL AND ISO/IEC 17025:2017 STANDARDS

Element (Requirement)	No. of convergent overall Items	No. of divergent overall Items
Objectives	1	1
Applicability	2	1
Impartiality	1	1
Confidentiality	1	1
Infrastructure and management systems	7	2
Equipment	6	0
Traceability	2	1
Laboratory processes	5	1
Analytical methods	6	0
Handling samples	4	1
Documents and Records - controls	11	4
Measurement Uncertainty	1	1
Quality Management Systems (QMS)	6	3
Computerized systems	5	1
Safety	0	4*
Total	58	22

Depicts the number of areas of convergence and divergence in overall elements self-identified in both documents.
* ISO 17025: 2017 does not address laboratory safety components.

A. Subdivisions in the Standards

The two documents are subdivided into sections that stipulate recommended procedures for handling laboratory activities at various stages, from sample receipt to generating reports. The WHO GPPQCL document consists of four (4) main parts: 'management and infrastructure', 'materials and devices', 'working procedures', and lastly, 'safety'. Similarly, the ISO/IEC 17025:2017 contains requirements for general, structural, process, and Management Systems components (see Appendix, Table IV).

1. Standards' Objectives, Applicability and Ethics

The general aim for both standards is to achieve quality management systems performances that can assure high levels of accuracy and reliable laboratory results. Both documents have similar requirements for ethical conduct in generating reports for products. Laboratories that implement these standards will demonstrate confidentiality in conducting quality control tests.

2. Infrastructure and Management Systems

Laboratories are required to be legally authorized to conduct testing of medicinal products. The laboratory management should be well defined, e.g. in charts that display organizational structure or hierarchy of personnel reporting system. Additionally, laboratory management should provide funds to cover costs for facilities, an adequate number of qualified personnel, and equipment. Also, environmental conditions where testing activities are conducted should be fit for purpose, so that they do not negatively impact the validity of test results.

3. Equipment, Traceability, and Measurement Uncertainties

Laboratories conduct tests using measuring equipment, tools,

and devices. To ensure reliable data are generated, it is expected that these are calibrated or verified at regular intervals stipulated in a laboratory maintenance/calibration schedule. In reviewing the chain of custody for all test results conducted, the items must be traceable to NIST (national institutes of standards and technology) primary standards used in calibrating laboratory equipment and other testing tools [32]. The standards also require laboratories to stipulate the measurement uncertainties associated with the tests conducted for some categories of reports or when required by the customer.

4. Handling Samples, Laboratory Processes and Analytical Methods

Various categories of customers submit samples for laboratory tests. These items should be appropriately labeled to ensure traceability and avoid mix-ups between different samples received for testing. The laboratories handle medicinal products submitted in line with an agreement signed with their clients. Furthermore, the laboratories are expected to conduct tests using appropriately validated analytical methods and require customer approval before any major changes to their contracts.

5. Maintaining Documents and Records

Laboratory QMS should ensure that all documents and records used to generate test reports are maintained in line with principles that ensure data integrity. These records are also expected to be archived properly for periods stipulated by regulatory requirements of countries where these laboratories conduct business.

6. Computerized Systems

Where laboratories choose to computerize their activities, the standards require steps to validate their systems to assure data integrity. The need for validation also applies to all computers linked to equipment used in generating data for all laboratory processes and tests reports.

7. Quality Management Systems (QMS)

The standards require laboratories to establish a QMS that is sufficient to ensure the reliability of results. QMS covers documents and records, improvements, corrective actions, internal audits, and management review activities.

8. Laboratory Safety

Significantly, safety requirements are not documented in ISO/IEC 17025:2017 but are a main component in the WHO laboratory standard. Institutions are required to ensure the safety of the workforce and visitors to the laboratory, against chemical, mechanical, electrical, and other forms of hazards. The WHO GPPQCL has an extensive list of measures a laboratory should employ to mitigate safety risks. Some of the items in this extensive list include the provision of personal protective equipment (PPEs), fire extinguishers, safety and hazard signs, and regular fire drills.

IV. Summary of General Requirements for GPPQCL and ISO/IEC 17025 Laboratory Standards

To ascertain the quality of medicinal products, a testing laboratory analyzes samples submitted by customers. The integrity of these samples must be maintained from the point of receipt to when the laboratory releases a final report. There are standard requirements for equipment, tools, and other consumables, employed in maintaining a chain of custody for laboratory samples.

From this review, there was more convergence than divergence in the requirements for Equipment, Document/records, QMS, Computerized Systems, Infrastructure, and Management Systems. Overall, there are 58 similar and 22 dissimilar items of activities required to satisfy both standards.

A detailed review of similarities and differences in the two standards with regards to the different elements or requirements are shown in Table V. Finally, from the number of elements self-identified in both standards, a higher percentage, 58 out of 80 items (72%) of both documents, depicted areas of convergence. On the other hand, a smaller proportion, 22 out of 80 items (28%), were requirements that had a divergent focus to implement both standards (Figs. 3 and 4).

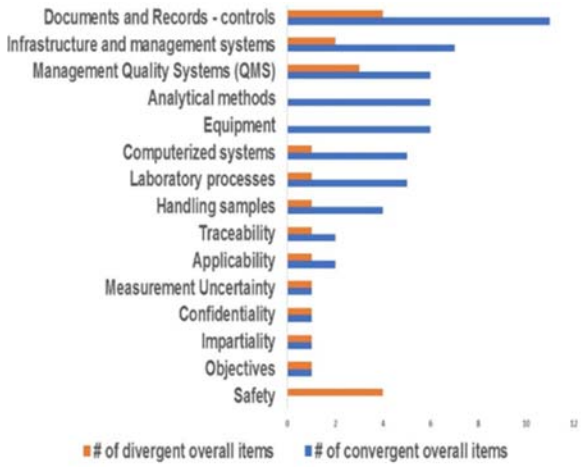

Fig. 3 Summary of elements/requirements from WHO GPPQCL and ISO 17025:2017 standards, depicted larger areas of convergence than divergence in overall items assessed

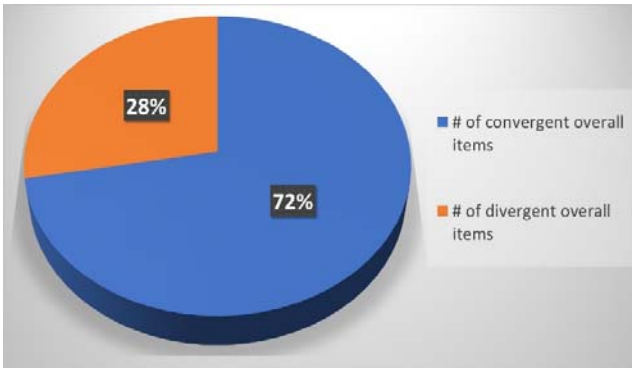

Fig. 4 Percentage of convergent versus divergent requirements from WHO GPPQCL and ISO/IEC 17025:2017 standards

V. DISCUSSIONS

The overall objectives of the two standards were set to enable pharmaceutical laboratories to operate within a quality system that demonstrates they will consistently produce reliable results. We believe that compliance with these standards promotes mutual recognition of laboratory results and facilitates international commerce; this view was shared by other authors [23], [33]. Though both standards can be applied in various quality control settings, WHO GPPQCL was not suitable for laboratories set up to offer calibration services. Furthermore, pharmaceutical microbiology laboratories operate with a different WHO standard, more suited for testing in that field [34]. Conversely, the ISO 17025: 2017 standard can be applied in all testing, calibration, and sampling laboratories, increasing the scope of facilities that can adopt it to maintain a quality system.

A. Financial Considerations

In further considerations to objectives of both standards, though it is evident that there are financial costs associated with accreditation [35], WHO has a public health mandate [36], therefore GPPQCL has specific requirements to ensure business continuity. As a result, laboratories must provide adequate budgets for systems' procedures; these budgets are critical in WHO prequalification audits [1]. However, ISO does not have similar global health responsibility [8]; therefore, ISO 17025 audits do not implicitly access a laboratory's financial capacity to maintain its quality systems. This factor will favor organizations with fewer funds and those situated in lower-resource settings [20]. This assumption aligns with a quote from an interview conducted by an author who interviewed the founding members of ISO. A respondent [8, p. 18] offered the following statement "We went to London, we Swiss, hoping to create a new organization which would do the work of standardization in a democratic way, and not cost too much money" [8]. An indication that ISO accreditation should be an affordable venture.

B. Requirements for Number of Key Personnel

Equally important is that both documents require ethical standards to maintain impartiality and confidentiality while conducting laboratory tests. The ISO 17025:2017 stipulates the need to assess processes to identify potential risks and provide mitigation strategies to be employed. Both the ISO and WHO standards specify legal requirements for laboratories as a business enterprise. Also, both standards require that labs have an adequate number of trained personnel that work in a purpose-built facility. Also, WHO requirements are bounded by principles of Good Manufacturing Practices (GMP) [37]; as a result, the requirement necessitates designating a quality manager who ensures overall compliance to the standard. Additionally, GPPQCL specified having an assistant to every key position. This may present a barrier for small-scale laboratories which may not have assistants for key roles. This will also translate to additional costs when more personnel are to be employed. However, ISO does not have this requirement, which makes compliance easier for smaller laboratories.

C. Mode of Conducting Audits

Though the equipment requirements for both standards are the same, the WHO prequalification audit is all-encompassing, it trails test items from entry, to exit from the laboratory. Therefore, the WHO scheme audits all equipment required for every test related to the item, as per the approved analytical procedure used. Consequently, GPPQCL requires the laboratory to be furnished with all the equipment, tools, and devices necessary to conduct all tests stipulated in the official compendia used to test the items. However, ISO standards require the laboratory to show competence only in scopes of interest. Therefore, a laboratory may decide to acquire accreditation for only the test scopes it can maintain. With this flexibility, laboratories can plan to add more test scopes as their quality system matures. Therefore, considering the high financial costs associated with accreditation [35], equipment needs may contribute significantly to why more facilities are accredited to the ISO standard than WHO GPPQCL. In our opinion, this may be a significant contributory factor to the higher numbers of accreditations against ISO 17025 [14], as the process allows the laboratories to demonstrate competence only in the areas they choose.

D. Keeping Records and Document Needs

Although both standards have similar specifications regarding the chain of custody to ensure sample traceability, the GPPQCL documentation requirements for handling samples are more elaborate. The more rigorous documentation demands in the WHO standard may form a barrier to a small-scale laboratory, which may not have fully developed its quality system. Whereas the risk-based approach required for the ISO standard encourages compliance, as these facilities only need to implement a level of documentation relevant to their identified process needs. This assumption was somewhat congruent with other authors who discussed the lean approach of ISO/IEC 7025:2017 standard [11], [38].

Similarly, because WHO guidelines are closely related to GMP requirements, the retention periods for documents and records in GPPQCL stipulate a minimum of five and 15 years for regular and investigation samples, respectively. This may also present a difficult onus for compliance. The ISO requirement is less stringent so that the laboratory can provide a risk-based justification for lower retention periods.

E. Ease of Implementation

To further strengthen the case for why more laboratories are accredited against ISO 17025, the standard's QMS requirement is more flexible; It offers two options, 'A' and 'B'. Organizations already accredited to ISO 9001 standards [39], can therefore easily migrate to ISO/IEC 17025:2017, which is the 'B' option in the document. With the ISO/IEC 17025 standard, many laboratories leverage the flexibility of accrediting a few test scopes and then adding more, as their QMS matures over time.

Besides, although the requirements for computerized systems are similar for both standards, from the undocumented experience of one of the authors of this study, the GPPQCL audit is more in-depth for computer systems validation. This

may relate to the fact that ISO 17025 aims to demonstrate competence in test scopes, whereas GPPQCL audits all linkages within the laboratory systems. Therefore, the auditing style for both standards may slightly vary for in-depth documentation requirements. Moreover, ISO audit expectation is a more risk-based approach; therefore, mitigation strategies play a vital role in successful compliance assessments [31].

F. Safety Requirement

Finally, while the ISO standard has no requirements for safety, the GPPQCL lists general rules for laboratory safety. Part 4 of the standard is dedicated to this all-important item to protect personnel exposed to potential hazards in the laboratory environment. We consider this further aspect proof that the WHO standard is more encompassing and takes a holistic approach to laboratory audit to ensure process continuity. Though this safety component adds extra costs to implementing this standard, the laboratory environment, if not properly monitored, is prone to various forms of hazards. Therefore, the WHO document aims to reduce these hazards to minimal risks for employees and customers entering the laboratory environment [5]. This study suggests safety assessment should be an important determinant for the level of maturity and robustness of a laboratory's QMS.

VI. Conclusions

Quality control laboratory standards provide the requirements that ensure accuracy in assessing pharmaceutical products. Compliance with recommendations in WHO GPPQCL or ISO/IEC 17025:2017 standards promotes international harmonization of laboratory practices and facilitates mutual recognition of results. Pharmaceutical laboratories can operate their quality systems based on either of the two standards. Though there are several areas of overlap (similarities) between the two documents, this review identified several factors, including costs, and ease of implementation, as plausible reasons why a greater number of testing laboratories prefer to adopt the ISO/IEC 17025 over the WHO GPPQCL standard. Currently, the ISO standard has more global patronage than the WHO document. The safety element in the WHO GPPQCL standard forms a component that highly distinguishes it from the ISO/IEC 17025 standard requirements.

VII. Recommendation for Future Studies

To overcome the challenges laboratories face in adopting WHO GPPQCL standards, a future inquiry will proffer suggestions of mitigation strategies that can be employed. The models will be targeted towards laboratories operating within low-income economies, a guide to achieving WHO prequalification status using limited funds. The models will present practical procedures that can meet the critical requirements of the WHO GPPQCL standards.

Acknowledgments

Sr. Zita Ekeocha and Joanne Lax are appreciated for their support and guidance in writing this manuscript.

References

[1] World Health Organization. Annex 1 WHO good practices for pharmaceutical quality control laboratories 2010.
[2] Mitra A. Fundamentals of quality control and improvement: John Wiley & Sons; 2016.
[3] Valdivieso-Gómez V., Aguilar-Quesada R. Quality Management Systems for Laboratories and External Quality Assurance Programs. InTech; 2018.
[4] International Standard Organisation. ISO/IEC 17025:2017 General Requirements for the Competence of Testing and Calibration Laboratories. ISO/IEC 17025:2017(E) ed: International Standards Organization; 2017.
[5] WHO. Laboratory Quality Standards and their Implementation. New-Delhi, India: World Health Organization, Regional Office for South-East Asia; 2011 (cited 2020 15 June). Available from: https://apps.who.int/iris/bitstream/handle/10665/205405/B4741.pdf?sequence=1.
[6] Fm't Hoen E, Hogerzeil HV, Quick JD, Sillo HB. A quiet revolution in global public health: The World Health Organization's Prequalification of Medicines Programme. Journal of public health policy. 2014;35(2):137-61.
[7] WHO PQP. Prequalification of medicines by WHO. World Health Organization; 2013.
[8] ISO Central Secretariat. Friendship Among Equals: Recollections from ISO's first fifty years. Geneva. Switzerland: ISO Central Secretariat; 1996 (cited 2020 June 9). Available from: https://www.iso.org/files/live/sites/isoorg/files/about%20ISO/docs/en/Friendship_among_equals.pdf.
[9] ISO. ISO About us: Structure and Governance 2020 (Available from: https://www.iso.org/structure.html.
[10] ISO Standard Catalogue: ICS: ISO; 2020 (cited 2020 June 9). Available from: https://www.iso.org/standards-catalogue/browse-by-ics.html.
[11] McInturff T., editor Changes to ISO/IEC 17025: 2017 A High-Level Overview. 2018 IEEE Symposium on Electromagnetic Compatibility, Signal Integrity and Power Integrity (EMC, SI & PI); 2018; Long Beach, CA, USA: IEEE.
[12] Anastasopoulos G. The new ISO/IEC 17025:2017. CAL LAB the International Journal of Metrology. 2017:pp. 30–5.
[13] Ghernaout D., Aichouni M., Alghamdi A. Overlapping ISO/IEC 17025: 2017 into Big Data: A Review and Perspectives. International Journal of Science and Qualitative Analysis. 2018;4(3):83.
[14] ILAC. International Laboratory Accreditation Cooperation: Facts and figures 2020 (Available from: https://ilac.org/about-ilac/facts-and-figures/.
[15] Grochau I. H., Caten C. S. T., De Camargo Forte M. M. Current American landscape in laboratory accreditation according to ISO/IEC 17025. Accreditation and Quality Assurance. 2017;22(2):57-62.
[16] WHO PQ Team. WHO List of Prequalified Quality Control Laboratories March 2020 (31). Available from: https://extranet.who.int/prequal/sites/default/files/documents/PQ_QCLabsList_29.pdf.
[17] Abrahamsen R. K. Experience of accreditation of an analytical laboratory and certification of the quality system in dairies. Meieriposten. 1998;87(9):274-80.
[18] Anastasopoulos G. I., Ramakrishnan P. S., Anastasopoulos I. G., editors. Improving Performance of Testing Laboratories – A Statistical Review and Evaluation. Sustainable Issues in Transportation Engineering GeoMEast 2019 Sustainable Civil Infrastructures; 2019: Springer.
[19] Oliver E. L. Implementation of ISO/IEC 17025 Practices in Small and Academic Laboratories. Ann Arbor, MI: The University of Nebraska-Lincoln; 2018.
[20] Tene C. V. T., Yuriev A., Boiral O. Adopting ISO management standards in Africa: barriers and cultural challenges. ISO 9001, ISO 14001, and New Management Standards: Springer, Cham; 2018. p. 59-82.
[21] Tsimillis K. C. Data integrity: requirements set in the accreditation standards. Accreditation and Quality Assurance. 2019;24(3):165-71.
[22] Masanza M. M., Nqobile N., Mukanga D., Gitta S. N. Laboratory capacity building for the International Health Regulations (IHR 2005) in resource-poor countries: the experience of the African Field Epidemiology Network (AFENET). BMC Public Health. 2010;10(Suppl. 1): S8.
[23] Zima T. Accreditation of Medical Laboratories–System, Process, Benefits for Labs. Journal of medical biochemistry. 2017;36(3):231-7.
[24] Nicklin W., Fortune T., van Ostenberg P., O'Connor E, McCauley N. Leveraging the full value and impact of accreditation. International Journal for Quality in Health Care. 2017;29(2):310-2.

[25] Lebedynets V., Tkachenko O. Formation of the Quality Management Systems at state laboratories for a medicines control. Technology transfer: innovative solutions in medicine. 2017:64-6.
[26] Putri Z. T., Fahma F., Sutopo W., Zakaria R. A. Framework to Measure Readiness Level of Laboratory for Implementing ISO/IEC 17025: A Case Study. IOP Conference Series: Materials Science and Engineering. 2019; 495:012011.
[27] Cebekhulu B. M. B., Mugova C., editors. Quality Control in a University Laboratory: Evaluating the Gap between ISO/IEC-17025 Requirements and the Thin Section Laboratory's Processes. 7 International Conference on Industrial Engineering and Operations Management (IEOM); 2017; Bristol, UK.
[28] Wilson I. G., Smye M., Wallace I. J. C. Meta-audit of laboratory ISO accreditation inspections: measuring the old emperor's clothes. MicrobiologyOpen. 2016;5(1):95-105.
[29] Wilson I. G. Accreditation—a verification ritual lacking verification. BMJ: British Medical Journal (Online). 2018;363.
[30] WHO PQ Team. WHO List of Prequalified Quality Control Laboratories. July 2019. p. 31.
[31] Habibie M. H., Basuki B., editors. Risk-based thinking on calibration and testing laboratory: Current challenge in transition period. IOP Conf Series: Materials Science and Engineering; 2019: IOP Publishing.
[32] The quality calibration handbook; developing and managing a calibration program Portland: Ringgold Inc; 2007 (Scitech Book News, 31:(n/a). Available from: Retrieved from https://search-proquest-com.ezproxy.lib.purdue.edu/docview/200132833?accountid=13360.
[33] Sevgi L. Accreditation: Crucial in World Trade, Public Safety, and Human Rights. IEEE Antennas and Propagation Magazine. 2014;56(4):265-75.
[34] World Health Organisation. WHO good practices for pharmaceutical microbiology laboratories. In: WHO Technical Report Series. No.961, editor. 2011. p. 25.
[35] Association of Public Health Laboratories. Laboratory Costs of ISO/IEC 17025 Accreditation: A 2017 Survey Report. Silver Spring, MD: Association of Public Health Laboratories; 2018.
[36] WHO. Essential medicines and health products 2020 (Available from: https://www.who.int/medicines/areas/quality_safety/quality_assurance/guidelines/en/.
[37] WHO. Essential medicines and health products: GMP questions and answers 2020 (Available from: https://www.who.int/medicines/areas/quality_safety/quality_assurance/gmp/en/.
[38] Elapanda S., Rao U. V. A., Choudary K. S. A. Integration of lean six sigma framework in testing laboratories Quality Management System with specific reference to ISO 17025. Journal of Management (JOM). 2019;6(3):pp. 1-13,.
[39] Tricker R. ISO 9001: 2015 for small businesses. London and New York: Routledge; 2016.
[40] Valdivieso-Gómez, V., & Aguilar-Quesada, R. (2018). Quality management systems for laboratories and external quality assurance programs: InTech.

APPENDIX

TABLE IV
OVERVIEW OF ELEMENTS CONTAINED IN WHO GPPQCL AND ISO/IEC 17025:2017 STANDARDS

WHO good practices for pharmaceutical quality control laboratories (GPPQCL)	ISO/IEC 17025:2017 General requirements for the competence of testing and calibration laboratories
Part one. Management and infrastructure	**4 General requirements**
1. Organization and management	4.1 Impartiality
2. Quality management system	4.2 Confidentiality
3. Control of documentation	**5 Structural requirements**
4. Records	Resource requirements
5. Data-processing equipment	6.1 General
6. Personnel	6.2 Personnel
7. Premises	6.3 Facilities and environmental conditions
8. Equipment, instruments, and other devices	6.4 Equipment
9. Contracts	6.5 Metrological traceability
Part two. Materials, equipment, instruments, and other devices	6.6 Externally provided products and services
10. Reagents	**7 Process requirements**
11. Reference substances and reference materials	7.1 Review of requests, tenders, and contracts
12. Calibration, verification of performance, and qualification of equipment, instruments, and other devices	7.2 Selection, verification, and validation of methods
13. Traceability	7.2.1 Selection and verification of methods
Part three. Working procedures	7.2.2 Validation of methods
14. Incoming samples	7.3 Sampling
15. Analytical worksheet	7.4 Handling of test or calibration items
16. Validation of analytical procedures	7.5 Technical records
17. Testing	7.6 Evaluation of measurement uncertainty
18. Evaluation of test results	7.7 Ensuring the validity of results
19. Certificate of analysis	7.8 Reporting of results
20. Retained samples	7.8.1 General
Part four. Safety	7.8.2 Common requirements for reports (test, calibration, or sampling)
21. General rules	7.8.3 Specific requirements for test reports
(1)	7.8.4 Specific requirements for calibration certificates
	7.8.5 Reporting sampling – specific requirements
	7.8.6 Reporting statements of conformity
	7.8.7 Reporting opinions and interpretations
	7.8.8 Amendments to reports

	7.9 Complaints
	7.10 Nonconforming work
	7.11 Control of data and information management
	8 Management system requirements
	8.1 Options
	8.1.1 General
	8.1.2 Option A
	8.1.3 Option B
	8.2 Management system documentation (Option A)
	8.3 Control of management system documents (Option A)
	8.4 Control of records (Option A)
	8.5 Actions to address risks and opportunities (Option A)
	8.6 Improvement (Option A)
	8.7 Corrective actions (Option A)
	8.8 Internal audits (Option A)
	8.9 Management reviews (Option A)
	Annex A (informative) Metrological traceability
	Annex B (informative) Management system options
	(4)

TABLE V
COMPARISON DEPICTING VARIOUS AREAS OF CONVERGENCE AND DIVERGENCE OF REQUIREMENTS FOR ISO AND WHO STANDARDS

Element (Requirement)	WHO GPPQCL	ISO/IEC 17025	Convergence	Divergence
Objectives	"These guidelines provide advice on the quality management system within which the analysis of active pharmaceutical ingredients (APIs), excipients and pharmaceutical products should be performed to demonstrate that reliable results are obtained. Compliance with the recommendations provided in these guidelines will help promote international harmonization of laboratory practices and will facilitate cooperation among laboratories and mutual recognition of results" "Special attention should be given to ensure the correct and efficient functioning of the laboratory. Planning and future budgets should ensure that the necessary resources are available……. Means and procedures should be in place (in case of possible supply problems) to ensure that the laboratory can continue its activities" (1)	"This document has been developed to promote confidence in the operation of laboratories. This document contains requirements for laboratories to enable them to demonstrate they operate competently and can generate valid results. Laboratories that conform to this document will generally comply with the principles of ISO 9001" "The use of this document will facilitate cooperation between laboratories and other bodies, and assist in the exchange of information and experience, and in the harmonization of standards and procedures. The acceptance of results between countries is facilitated if laboratories conform to this document." (4)	Reliability and validity of laboratory results; lead to local and international mutual recognition	GPPQCL emphasizes system procedures for planning and future budgets that will ensure continuity
Element (Requirement)	**WHO GPPQCL**	**ISO/IEC 17025**	**Convergence**	**Divergence**
Applicability	"These guidelines apply to any pharmaceutical quality control laboratory, be it national, commercial, or nongovernmental. However, they do not include guidance for those laboratories involved in the testing of biological products, e.g. vaccines and blood products. Separate guidance for such laboratories is available" "These guidelines are consistent with the requirements of the WHO guidelines for good manufacturing practices (1) and with the requirements of the International	Used by laboratories that perform one or more of the following activities: (1) testing; (2) calibration; (3) sampling, associated with subsequent testing or calibration	1. QC laboratories in pharmaceutical companies and NMRA. 2. Both cannot be applied to laboratories handling blood samples	1. WHO GPPQCL cannot be used in calibration labs, Microbiology labs

	Standard ISO/IEC 17025:2005 (2), and provide detailed guidance for laboratories performing quality control of medicines"			
Impartiality	1.3(b) Certify management and staff do not have conflicts of interest (COI) that will adversely impact their work.	4.1 (4.1.1- 4.1.5) Management commitment to impartiality in carrying out laboratory activities. Identify risks to impartiality, and have plans for elimination or mitigation	1. The laboratory should manage COI to avoid negative impacts on activities.	1. 17025 require a risk assessment to identify potential risks and mitigation plan.
Confidentiality	1.3(c) Should have procedures that ensure confidentiality of the information supplied by laboratory customers, including protection of archived data	4.2 (4.2.1 – 4.2.4) A laboratory shall be committed to managing the confidentiality of all activities with its customers etc. Lab to inform the customer of what constitutes private and public information	1. Confidentiality of all laboratory activities and customer information	1. ISO 17025 standard is more detailed as per confidentiality legal requirements

Element (Requirement)	**WHO GPPQCL**	**ISO/IEC 17025**	**Convergence**	**Divergence**
Infrastructure and management systems	Part One. Management and infrastructure 1. Organization and management.	Structural Requirements (5) Resources requirements (6**)**	2. 1. The laboratory should be legally authorized to carry out activities. 2. Managerial and technical personnel with authority and resources to carry out activities. 3. Organizational charts showing inter-relationships 4. Effective communication 5. Chain of custody for samples (traceability) 6. Document competence requirements for functions influencing laboratory activities. 7. Environmental monitoring to prevent adverse events that negatively impact the validity of reports	2. 1. GPPQCL requires 1. laboratory nominate trained substitutes/deputies for key management and specialized scientific personnel (part 1.3 (g)) 2. designate a member of staff as ***a quality manager*** who will ensure compliance with the QMS (part 1.3 (j)) 3. ISO 17025 does not stipulate title for the person with that responsibility (see clause 5.6.a)
Equipment	Equipment, instruments and other	Equipment 6.4	1. Maintenance	No major differences observed

	devices Part 1 (8)		Plan 2. Verification before use and after maintenance or repair activities 3. Calibration to ensure metrological traceability of reported results 4. Intermediate checks to maintain confidence in equipment performance (ISO 6.4.10) 5. Maintain equipment records 6. Equipment status labeling	
Element (Requirement)	**WHO GPPQCL**	**ISO/IEC 17025**	**Convergence**	**Divergence**
Traceability	Traceability Part 2 (13)	Metrological traceability (6.5)	1. Results of the analysis are traceable to a primary reference standard 2. measurement results are traceable to the International System of Units (SI)	1. ISO 17025 gives more details for metrological traceability
Laboratory Processes	Part 1 Contracts (9)	Process requirements (7) Review of requests, tenders, and contracts	1. Laboratories provide a procedure for the acquisition of supplies and services that impact the quality of tests conducted. 2. Subcontracting of activities to laboratories having comparable QMS 3. Customer approval is required if testing is to be outsourced 4. The laboratory takes final responsibility for all test reports 5. Requires laboratory shall inform a customer if a method requested is out of date or inappropriate; resolve any issues before tests start.	1. ISO 17025 has additional information on reviewing contracts when deviations occur.
Analytical Methods	Testing part 3 (17) Validation of analytical procedure	Selection, verification, and validation of methods (7.2)	1. A laboratory shall use appropriate up to date	No major differences observed

	part 3 (16)		methods for all activities 2. Availability to personnel 3. The method to be used is communicated to the customer	
Element (Requirement)	**WHO GPPQCL**	**ISO/IEC 17025**	**Convergence**	**Divergence**
Analytical Methods			4. A laboratory shall use appropriate up to date methods for all activities 5. Availability to personnel 6. The method to be used is communicated to the customer 7. Laboratory-developed or modified methods can be used (ISO 7.1.2.4), (WHO pg. 82, line 7) 8. Verification and system suitability tests (16.3-16.4, WHO), 9. Major change requires revalidation	No major differences observed
Handling samples	Working Procedure Part 3	Handling of test or calibration items (7.4)	1. Registration and labeling of samples for traceability 2. Appropriate storage for sample 3. Sampling plan requirement (GPPQCL: part3, 14.4) (ISO:7.3) 4. Ensures adequate size to conduct required tests	1. GPPQCL requires test request forms and analytical worksheets for documenting technical records
Documents and Records	Part 1: Document (3), Records (4)	Provides 2 options: A and B In option 'A', the QMS system ensures control of documents and records. 8.3 & 8.4 Option 'B', document and records are controlled using ISO 9001 principles	Documents are: 1. Authorized before use 2. Uniquely identified 3. Periodically reviewed 4. Track changes 5. Current versions in circulations 6. Available at points of use Records are: 1. Controlled in line with principles ALCOA Plus for data integrity. 2. Both documents similar in 4 major areas	GPPQCL specified: 1. Need for a 'Master list' of document 2. Minimum retention period of 5 years for a document. GPPQCL specified: 1. Product shelf-life plus 1 year as retention period for records. 2. 15 years for investigation products, unless national regulations are more stringent.
Element (Requirement)	**WHO GPPQCL**	**ISO/IEC 17025**	**Convergence**	**Divergence**

Measurement uncertainty	Analytical test report part 3 (18.9-18.10)	Evaluation of measurement uncertainty (7.6)	1. Pharmacopoeia limits are set considering MU and process capability indices.	1. GPPQCL requires reporting MU for investigative samples where concentration is requested.
Management quality Systems (QMS)	Quality management system part1 (2)	Management system requirements (8**)**	A laboratory shall establish, document, implement and maintain a QMS that is sufficient to ensure the reliability of results. The QS should include 1. Documentation 2. Control of records and QS documents 3. Improvements 4. Corrective actions 5. Internal audits 6. Management reviews N: B GPPQCL combines 3 & 4 as CAPA.	1. ISO 17025 has two options A and B (based on ISO9001) for implementing QMS. 2. ISO 17025 (8.5) requires actions to address risks and opportunities under option A. 3. GPPQCL requires a quality manual to document QMS, but a laboratory for manufacturers may have the information in another document
Computerized systems	Data processing equipment part 1(5)	Control of data and information management (7.11)	1. Protected from unauthorized access 2. Computer system validated 3. Data integrity 4. The system should enable audit trail 5. Electronic data backed up regularly	1. No major differences observed

Element (Requirement)	**WHO GPPQCL**	**ISO/IEC 17025**	**Convergence**	**Divergence**
Safety	1. General and specific rules for all laboratory workers. Including safety signs and regular training 2. Requires SOPS for safety-related issues: Material safety data sheets, eating ethics, fire-fighting gadgets, Personal Protective Equipment, handling toxic samples, facility electrical fittings, laboratory gases, and first-aid measures.	N/A	No area of similarity, ISO 17025: 2017 does not address safety	1. There are no considerations for laboratory workers' safety in the ISO document, whereas WHOGPPQCL dedicated 'part 4' of the standards to address various aspects of laboratory safety.