CODEN (USA): IJPB07 ISSN: 2320-9267

Indian Journal of Pharmaceutical and Biological Research (IJPBR)
Journal homepage: www.ijpbr.in

Research Article DOI: https://doi.org/10.30750/ijpbr.6.4.11

Advances in Clinical Biochemistry Laboratory Quality Assurance: Analytical Accuracy, Error Prevention, and Diagnostic Reliability

Nnamdi Eneh[1*], Kazeem Abdulrazaq[2], Habeeb Damilola Yusuf[3], Olatunde Adesoji Aladegba[4]

[1]Independent National Electoral Commission (INEC) Staff Clinics, Abuja, Nigeria
[2]General Hospital Doma, Nasarawa, Nigeria
[3]Healthwise Social Enterprise, Nigeria
[4]Department of Chemistry, University of Lagos, Lagos, Nigeria

ARTICLE INFO:

Article history:
Received: 17 September 2018
Received in revised form:
22 November 2018
Accepted: 24 November 2018
Available online: 31 December 2018

Keywords:
Quality assurance, internal quality control, external quality assessment, total testing process, laboratory error, Six Sigma, metrological traceability, analytical performance specifications, ISO 15189, patient safety

Abstract

Clinical biochemistry results inform a large share of medical decisions, from screening and diagnosis to therapeutic monitoring and prognosis. The reliability of these results depends on a quality assurance system that spans the entire testing process, not only the analytical phase. Over the past two decades, laboratory medicine has moved from a narrow focus on internal quality control of instruments toward a patient-centred view of quality that includes test selection, specimen collection, analysis, reporting, and interpretation. This review summarises the advances in clinical biochemistry quality assurance up to 2018 and situates them within related work on laboratory infrastructure, disease surveillance, safety and risk management, maintenance engineering, and data governance. It examines the epidemiology of laboratory errors across the total testing process, the evolution of internal quality control from Levey-Jennings charts and Westgard multirules to risk-based and Six Sigma designs, the role of external quality assessment and metrological traceability in achieving harmonised and accurate results, and the 2015 Milan consensus on analytical performance specifications. It also considers pre-analytical and post-analytical error prevention, quality indicators, accreditation to ISO 15189:2012, the impact of total laboratory automation and middleware, and quality management of point-of-care testing. The evidence shows that while analytical error rates have fallen dramatically, extra-analytical phases now account for most errors, and that genuine diagnostic reliability requires integrating analytical excellence with process control, standardisation, and clinical communication.

1. Introduction

Laboratory test results are frequently cited as influencing between 60% and 70% of clinical decisions, and clinical biochemistry accounts for the majority of tests performed in most hospital laboratories (Bonini et al., 2002; Plebani, 2006). Because these results are used to diagnose disease, adjust drug doses, and trigger urgent interventions, an inaccurate or misreported value can propagate directly into patient harm. Quality assurance (QA) in this setting refers to the planned and systematic activities that provide confidence that a laboratory result is fit for its intended clinical purpose.

Historically, laboratory quality was equated with analytical quality, and quality control programmes concentrated on the precision and accuracy of analysers. The publication of the Institute of Medicine report "To Err Is Human" in 1999 shifted attention toward systems thinking and patient safety (Kohn et al., 2000), and subsequent studies demonstrated that most laboratory errors originate outside the analytical phase (Carraro et al., 2007; Plebani, 2006; Plebani et al., 1997). Concurrently, advances in automation, informatics, metrology, and statistics have transformed the tools available to the laboratory. By 2018, the field had converged on a broad definition of laboratory quality that encompasses the "brain-to-brain loop" described by Lundberg, extending from the clinician's decision to order a test to the action taken on its result (Lundberg, 1981).

The aims of this review are to (i) describe the current understanding of error across the total testing process; (ii) summarise developments in analytical quality management, including internal quality control (IQC), external quality assessment (EQA), traceability, and performance specifications; (iii) review strategies for preventing extra-analytical errors; (iv) consider the organisational frameworks, technologies, and infrastructure that support diagnostic reliability; and (v) integrate these strands into a conceptual model. The paper is organised as follows: Section 2 describes

***Corresponding Author: Nnamdi Eneh,** Independent National Electoral Commission (INEC) Staff Clinics, Abuja, Nigeria. **E-Mail:** namdyeneh@gmail.com

the research method; Section 3 presents and discusses the results, including the conceptual model, implications, limitations, and directions for future research; and Section 4 concludes.

2. Research Method

2.1 Review Design

This paper is a comprehensive narrative review with an integrative synthesis. A narrative design was chosen because laboratory quality assurance draws on heterogeneous evidence, including observational error studies, statistical and metrological theory, consensus statements, international standards, and professional guidelines, which are not suited to quantitative pooling. The integrative element consisted of mapping findings from these sources onto the phases of the total testing process and onto the organisational conditions that support them, which provided the basis for the conceptual model in Section 3.12.

2.2 Sources and Selection

The review drew on three groups of sources published up to December 2018. The first comprised landmark empirical and methodological publications in clinical chemistry and laboratory medicine on laboratory error, internal quality control, external quality assessment, traceability, measurement uncertainty, performance specifications, and pre- and post-analytical quality (Carraro et al., 2007; Levey et al., 1950; Miller et al., 2011; Plebani, 2006; Plebani et al., 1997; Sandberg et al., 2015; Westgard et al., 1981). The second comprised international standards and guidelines from the International Organization for Standardization, the Clinical and Laboratory Standards Institute, the IFCC, and the EFLM (Clinical and Laboratory Standards Institute, 2011; Clinical and Laboratory Standards Institute, 2016; International Organization for Standardization, 2012; International Organization for Standardization, 2016). The third was a curated seed set of related publications from neighbouring fields, including diagnostic laboratory infrastructure, disease surveillance, safety and risk management, maintenance engineering, procurement, and data governance, selected because they address mechanisms that also govern laboratory quality (Adaramola et al., 2018; Aminu-Ibrahim et al., 2018; Mbonu et al., 2018; Obriki et al., 2018; Yusuf et al., 2018).

Sources were included if they were published in or before 2018, addressed a component of the testing process or of the quality system that supports it, and offered either empirical evidence, a recognised standard or consensus position, or a transferable conceptual framework. Publications after 2018 were excluded so that the review reflects the state of knowledge at that time. Grey literature was limited to regulatory and standards documents.

2.3 Analysis and Synthesis

Each source was read for its main contribution and classified by testing phase (pre-pre-analytical, pre-analytical, analytical, post-analytical, post-post-analytical) and by quality system element (analytical foundations, process control, organisational and infrastructure enablers). Themes were then compared across sources to identify points of consensus, unresolved debates, and gaps. The resulting themes are reported in Sections 3.1 to 3.11, and the relationships between them were abstracted into the layered model presented in Section 3.12.

3. Results and Discussion

This section reports the results of the synthesis in eleven themes (Sections 3.1 to 3.11), moving from the epidemiology of error through analytical quality management to the extra-analytical phases, organisational systems, and supporting technology. These results are then integrated into a conceptual model (Section 3.12) and discussed together with their implications, limitations, and directions for future research (Sections 3.13 to 3.16).

3.1 The Total Testing Process and the Epidemiology of Laboratory Error

The total testing process (TTP) is conventionally divided into pre-pre-analytical, pre-analytical, analytical, post-analytical, and post-post-analytical phases (Plebani, 2006). The outer phases, test request and interpretation of results, occur largely outside the laboratory and under the control of clinicians, which makes them difficult to monitor but critical to outcomes.

Landmark studies by Plebani and Carraro in 1997 and their follow-up in 2007 showed that the overall frequency of laboratory errors fell substantially over a decade, yet the distribution remained skewed toward extra-analytical phases (Carraro et al., 2007; Plebani et al., 1997). In the 2007 study, pre-analytical errors accounted for approximately 62% of identified errors, post-analytical errors for about 23%, and analytical errors for roughly 15%. Similar patterns have been reported internationally, with pre-analytical errors consistently comprising between 46% and 68% of all errors (Bonini et al., 2002; Lippi et al., 2011). Most errors caused no patient harm, but a meaningful minority led to inappropriate investigation or treatment, and a proportion were judged to be preventable.

These data have reshaped the QA agenda. Analytical quality remains essential, since an analytical error that goes undetected affects every patient sample in a run, but improvement of diagnostic reliability increasingly depends on controlling the steps that surround the analyser. Conceptual frameworks for strengthening diagnostic quality systems in resource-limited clinical laboratories reach the same conclusion (Yusuf et al., 2018).

3.2 Internal Quality Control: From Statistical Rules to Risk-based Design

3.2.1 Foundations

Statistical quality control in clinical chemistry dates to Levey and Jennings, who in 1950 adapted Shewhart control charts for laboratory use (Levey et al., 1950). Control materials of known expected value are analysed alongside patient samples, and results are plotted against the established mean and standard deviation. In 1981, Westgard and colleagues introduced a multirule procedure that combines several control rules (for example 1-3s, 2-2s, R-4s, 4-1s, and 10-x) to improve error detection while keeping false rejections low (Westgard et al., 1981). The Westgard rules became the de facto standard for IQC worldwide.

3.2.2 Quality Control Design and Six Sigma

A major advance has been the recognition that QC rules and frequencies should be selected according to the quality required for a test and the observed performance of the method, rather than applied uniformly (Westgard et al., 2016). Power function graphs and operational specifications charts allow laboratories to estimate the probability of detecting a critical systematic error for a given rule and number of control measurements.

Table 1: Distribution and common sources of error across the total testing process

Phase	Approximate share of errors	Typical sources
Pre-pre-analytical	Often included with pre-analytical	Inappropriate test selection, wrong test ordered, incorrect patient identification on request, missing clinical information
Pre-analytical	46% to 68%	Haemolysis, clotted or insufficient samples, wrong container or anticoagulant, labelling errors, delayed transport, improper storage, IV fluid contamination
Analytical	7% to 15%	Calibration error, reagent deterioration, instrument malfunction, interferences (lipaemia, icterus, heterophile antibodies, biotin), undetected QC failure
Post-analytical	13% to 23%	Transcription error, delayed or failed reporting of critical results, inappropriate reference intervals, incorrect units
Post-post-analytical	Poorly quantified	Misinterpretation of results, failure to act on results, failure to follow up pending tests

The Six Sigma metric, calculated as (TEa minus |bias|) divided by CV, where TEa is the allowable total error and all terms are expressed as percentages at a medical decision concentration, provides a single number describing how many standard deviations of method variation fit within the quality requirement. Methods performing at 6 sigma or above can be controlled with simple rules and few control measurements, whereas methods below 4 sigma require multirule procedures, more frequent QC, and often method improvement (Westgard et al., 2016). Sigma metrics have been widely adopted in clinical biochemistry since about 2010 to benchmark analysers, choose QC strategies, and prioritise improvement efforts. A recognised limitation is that sigma values depend strongly on the TEa source chosen, which can vary several-fold between regulatory, biological variation, and state-of-the-art criteria.

Lean and Six Sigma methods form part of a wider movement toward automation, analytics, and digital transformation in operations management, which offers transferable lessons for laboratory managers (Agboada et al., 2018).

Table 2: Illustrative relationship between sigma metric and QC strategy

Sigma metric	Method performance	Suggested QC approach
6 or more	World class	Single rule (for example 1-3.5s) with 2 control measurements; low run frequency acceptable
5 to 6	Excellent	Simple rules (1-3s) with 2 controls per run
4 to 5	Good	Multirule (1-3s/2-2s/R-4s) with 2 to 4 controls per run
3 to 4	Marginal	Full multirule with 4 or more controls, increased run frequency, consider method improvement
Below 3	Poor	QC cannot assure quality reliably; method replacement or improvement needed

3.2.3 Risk Management and Frequency of Qc

The Clinical and Laboratory Standards Institute (CLSI) guideline EP23-A (2011) introduced risk management principles to QC planning, encouraging laboratories to identify failure modes, estimate their likelihood and severity, and design an individualised quality control plan (Clinical and Laboratory Standards Institute, 2011). In the United States, this approach underpinned the Individualized Quality Control Plan (IQCP) option under CLIA, implemented from 2016. CLSI C24 (fourth edition, 2016) further emphasised that QC frequency should be determined by the number of patient results that could be affected between QC events (Clinical and Laboratory Standards Institute, 2016). Parvin and colleagues formalised this concept with the metric of expected number of unreliable final patient results, MaxE(NUF), which links QC design directly to patient risk (Parvin, 2008).

3.2.4 Patient-based Quality Control

Patient-based real-time quality control (PBRTQC) uses the patient data stream itself to detect analytical shifts. Techniques include the average of normals (Hoffmann et al., 1965), moving averages and exponentially weighted moving averages, moving medians, and delta checks. These methods can detect errors between scheduled QC events and are not affected by the commutability problems of control materials. Advances in middleware and computing power had, by 2018, made these approaches practical in high-throughput laboratories, although optimal parameter selection and validation remained active areas of research.

3.2.5 Control Materials and Commutability

A persistent challenge is that many commercial control materials are not commutable with patient samples, meaning they do not react in the same way across measurement procedures (Miller et al., 2006). Non-commutable materials can mask or exaggerate reagent lot changes and calibration shifts. Laboratories are therefore encouraged to use third-party controls independent of the manufacturer's calibrators, to verify new reagent lots with patient samples, and to set control limits from their own data rather than relying on package insert ranges.

3.3 External Quality Assessment and Proficiency Testing

External quality assessment (EQA), also called proficiency testing, involves the analysis of samples distributed by an independent provider and comparison of results with those of other laboratories or with a reference value. EQA is mandatory for accreditation in most jurisdictions and serves educational, regulatory, and surveillance functions (International Organization for Standardization, 2012).

The value of EQA depends heavily on the design of the scheme. Miller and colleagues described a classification in which the most informative schemes use commutable samples with values assigned by reference measurement procedures, allowing assessment of true accuracy rather than agreement with a peer group (Miller et al., 2011). Peer-group evaluation with non-commutable samples can confirm that a laboratory performs like others using the same method, but cannot reveal method-specific bias. Schemes with commutable, reference-assigned samples, such as those operated for creatinine, glucose, cholesterol, and HbA1c in several countries, have exposed clinically significant between-method biases and driven manufacturer recalibration (Miller et al., 2011; Myers et al., 2006).

Modern EQA has also expanded beyond the analytical phase. Programmes now assess interpretation of results, reporting of critical values, pre-analytical handling, and the detection of interferences, reflecting the TTP perspective.

3.4 Metrological Traceability, Standardisation, and Harmonisation

Accurate and comparable results across laboratories and over time require that measurement results be traceable, through an unbroken chain of calibrations, to higher-order reference materials and reference measurement procedures, ideally to SI units (Panteghini, 2009; Vesper et al., 2009). The European Union In Vitro Diagnostic Medical Devices Directive (98/79/EC) required manufacturers to ensure traceability of calibrator values, and the Joint Committee for Traceability in Laboratory Medicine (JCTLM), established in 2002, maintains a database of reference materials, methods, and services.

Standardisation has been achieved for a number of well-defined analytes. The IFCC reference system for HbA1c, combined with national glycohaemoglobin standardisation programmes, made HbA1c sufficiently reliable to be adopted as a diagnostic criterion for diabetes (Hoelzel et al., 2004). Standardisation of creatinine to isotope dilution mass spectrometry (IDMS) enabled widespread reporting of estimated glomerular filtration rate (Myers et al., 2006). Similar efforts have improved total cholesterol, vitamin D (through the Vitamin D Standardization Program), and enzyme activity measurements using IFCC primary reference procedures at 37 degrees Celsius.

For many analytes, especially complex proteins, hormones, and tumour markers, higher-order references are lacking. In these cases, harmonisation aims to achieve equivalent results using consensus approaches (Plebani, 2013). The International Consortium for Harmonization of Clinical Laboratory Results, founded in 2013, coordinates prioritisation and harmonisation activities. Harmonisation also extends to terminology, units, reference intervals, and reporting formats, all of which influence diagnostic reliability.

3.4.1 Measurement Uncertainty

ISO 15189:2012 requires laboratories to estimate the measurement uncertainty (MU) of quantitative results and make it available on request (International Organization for Standardization, 2012). Two broad approaches exist: the "bottom-up" approach of the Guide to the Expression of Uncertainty in Measurement (GUM), which combines individual uncertainty components, and the more practical "top-down" approach, which uses long-term IQC imprecision and the uncertainty of calibrator values. Debate continues on whether bias should be corrected or included in MU and on the relationship between MU and the total error model favoured by many clinical laboratories (Oosterhuis et al., 2016; Theodorsson, 2017). Both frameworks agree, however, that quantifying variability is essential to interpreting results near decision limits and to evaluating serial changes.

3.5 Analytical Performance Specifications

Quality control and EQA require a definition of how good a method needs to be. The 1999 Stockholm consensus proposed a hierarchy of models for setting quality specifications, ranking clinical outcome studies highest, followed by biological variation, professional recommendations, regulatory requirements, and state-of-the-art performance (Kenny et al., 1999).

The 2014 EFLM Strategic Conference in Milan simplified this into three models, published as a consensus statement in 2015: (1) the effect of analytical performance on clinical outcomes, (2) components of biological variation of the measurand, and (3) the state of the art (Sandberg et al., 2015). The choice of model depends on the measurand and its clinical use. Outcome-based specifications are preferred when the test has a central role in diagnosis or management and suitable studies exist, as for HbA1c, cholesterol, or cardiac troponin. Biological variation models apply to measurands under homeostatic control, with desirable imprecision commonly set at less than half the within-subject biological variation and desirable bias at less than a quarter of the combined within- and between-subject variation.

The Milan conference also recognised that much published biological variation data were of uncertain quality. The EFLM Biological Variation Working Group developed the Biological Variation Data Critical Appraisal Checklist (BIVAC) and the European Biological Variation Study (EuBIVAS) to produce robust estimates (Aarsand et al., 2018). These efforts, ongoing in 2018, are expected to refine performance specifications and reference change values used for interpreting serial results.

Table 3: Milan 2015 models for analytical performance specifications

Model	Basis	Example applications
Model 1: Clinical outcome	Direct or indirect (simulation) studies of the effect of analytical performance on clinical decisions or outcomes	HbA1c, glucose, total cholesterol, cardiac troponin
Model 2: Biological variation	Within-subject and between-subject biological variation of the measurand	Electrolytes, creatinine, enzymes, many routine chemistry analytes
Model 3: State of the art	Highest level of performance achievable technically, or achieved by a defined proportion of laboratories	Analytes where models 1 and 2 cannot be applied, such as some urine and rare analytes

3.6 Prevention of Pre-analytical Errors

Because the pre-analytical phase is the largest source of laboratory error, its control has become a principal focus of QA (Lippi et al., 2011; Plebani et al., 2015). The EFLM Working Group on Preanalytical Phase (WG-PRE) has been especially active in producing recommendations and harmonisation initiatives (Lippi et al., 2015).

3.6.1 Patient Identification and Labelling

Misidentification errors are relatively uncommon but potentially catastrophic, particularly in transfusion and when results are filed in the wrong record. Measures include two-identifier verification, positive patient identification with barcoded wristbands, labelling at the bedside, and electronic order entry linked to label printing. Delta checks, which flag implausible changes from a patient's previous result, can detect some misidentified samples after the fact.

3.6.2 Sample Quality: Haemolysis, Lipaemia, and Icterus

Haemolysis is the most frequent cause of unsuitable samples, especially in emergency departments, and can falsely increase potassium, lactate dehydrogenase, aspartate aminotransferase, and other analytes (Lippi et al., 2018). Modern chemistry analysers measure serum indices spectrophotometrically, providing objective and semi-quantitative estimates of haemolysis (H), icterus (I), and lipaemia (L). This has replaced subjective visual inspection and allows automated rules for result suppression or commenting based on analyte-specific interference thresholds. Standardisation of how indices are reported and of interference thresholds remained a work in progress in 2018.

3.6.3 Phlebotomy, Transport, Storage, and Supply

Standardised venous blood collection practice, as described in CLSI GP41 and the 2018 joint EFLM-COLABIOCLI recommendation for venous blood sampling, reduces variability arising from tourniquet time, order of draw, tube filling, and mixing (Simundic et al., 2018). Pneumatic tube systems, temperature during transport, time to centrifugation, and storage conditions all affect analyte stability. Evidence-based stability data and clear rejection criteria are important components of the laboratory's quality system.

Reliable testing also requires an uninterrupted supply of reagents, calibrators, and consumables. Frameworks for strategic procurement optimisation and for linking inventory availability to equipment uptime, although developed for energy operations, translate directly to laboratory procurement and stock control (Okonkwo et al., 2018a; Okonkwo et al., 2018b).

3.6.4 Appropriateness of Test Requests

Inappropriate test ordering, both over-use and under-use, represents a pre-pre-analytical error with consequences for cost, false positive findings, and missed diagnoses. Interventions include computerised decision support, demand management rules (for example minimum retesting intervals), reflex and reflective testing, and education (Badrick, 2013). Reflective testing, in which the laboratory specialist adds tests or comments based on the results and clinical context, illustrates the expanding consultative role of the clinical biochemist.

3.7 Post-analytical Quality and Result Interpretation

Post-analytical processes determine whether an accurate result reaches the right clinician in time and is correctly understood. Key elements include:

- **Critical result communication:** laboratories must define critical (alert) limits in agreement with clinicians, establish timely notification procedures, and document read-back confirmation. Surveys have shown wide variation in critical limits and notification times between laboratories, prompting harmonisation efforts.
- **Autoverification:** rule-based release of results through middleware, using QC status, instrument flags, serum indices, delta checks, and limit checks, reduces transcription errors and turnaround times while allowing staff to focus on exceptions. CLSI AUTO10 provides guidance on designing and validating these rules.
- **Reference intervals and decision limits:** the IFCC Committee on Reference Intervals and Decision Limits has promoted multicentre studies and the use of common reference intervals where methods are standardised (Ceriotti et al., 2010). Inappropriate intervals can lead to misclassification even when analytical performance is excellent.
- **Interpretative commenting:** expert comments add diagnostic value but vary in quality; EQA schemes for interpretative comments have been established in several countries to assess and improve this activity.
- **Report design:** clear presentation of units, reference intervals, flags, and cumulative results reduces misinterpretation in the post-post-analytical phase.

3.8 Quality Indicators

Quality indicators (QIs) are objective measures that allow a laboratory to monitor performance across the TTP and compare itself with others. ISO 15189:2012 requires laboratories to establish QIs (International Organization for Standardization, 2012). The IFCC Working Group on Laboratory Errors and Patient Safety (WG-LEPS) developed a Model of Quality Indicators that covers key processes across all phases, together with harmonised definitions and a reporting system (Sciacovelli et al., 2017). Data from participating laboratories have been used to establish performance specifications for QIs, graded as optimal, desirable, or minimum, often expressed on a sigma scale (Plebani et al., 2015). A 2016 consensus conference in Padua further refined the list and prioritised indicators.

Table 4: Examples of quality indicators across the total testing process

Phase	Example quality indicators
Pre-analytical	Percentage of misidentified requests; samples haemolysed, clotted, or of insufficient volume; samples in wrong container; inappropriate test requests; samples damaged in transport
Analytical	Number of unacceptable EQA results; tests without IQC or with IQC failures; percentage of results with inadequate inter-laboratory agreement
Post-analytical	Reports delivered outside agreed turnaround time; critical values notified late; incorrect reports issued and corrected
Outcome related	Clinician and patient satisfaction; number of complaints; adverse events attributable to laboratory error

3.9 Accreditation and Quality Management Systems

ISO 15189, "Medical laboratories: Requirements for quality and competence", first published in 2003 and revised in 2007 and 2012, has become the international standard for medical laboratory accreditation (International Organization for Standardization, 2012). Unlike general ISO 9001 certification, ISO 15189 assesses both management system requirements and technical competence, including method validation and verification, measurement uncertainty, IQC, EQA, and pre- and post-analytical processes. The 2012 edition placed greater emphasis on risk, the extra-analytical phases, and continual improvement.

Accreditation has been associated with improved documentation, staff training, traceability of actions, and a culture of continual improvement. Countries in all regions, including a growing number in Africa through initiatives such as the WHO Stepwise Laboratory Quality Improvement Process Towards Accreditation (SLIPTA) and the Strengthening Laboratory Management Toward Accreditation (SLMTA) programme, have used accreditation frameworks to strengthen laboratory systems (Yao et al., 2014). Lean and Six Sigma management approaches, root cause analysis, failure mode and effects analysis (FMEA), and incident reporting systems complement accreditation by providing practical tools for process improvement.

3.9.1 Standard Procedures and Staff Competence

Procedural standardisation and workflow optimisation in other high-volume service settings show how standard procedures reduce variation and error (Uchechi et al., 2018), and competency frameworks with structured onboarding support the documented staff competence that accreditation requires (Ukadike, 2018). Offline-first digital learning designs make continuing training feasible for laboratory staff in low-connectivity environments (Unamma et al., 2018), and pedagogical strategies developed for resource-constrained educational settings can inform how practical laboratory skills are taught (Bobga et al., 2018).

3.9.2 Safety Science, Risk Management, and Audit

Laboratory quality management shares its foundations with occupational safety and risk management. Data-driven occupational safety risk control, integrated heat stress risk models for industrial operations, and operational integrity frameworks that balance productivity with safety compliance in high-risk work all illustrate the shift from reactive to proactive risk control (Arumosoye & Obriki, 2018; Nwangwu et al., 2018; Obriki et al., 2018). Predictive compliance monitoring that mines consumer complaint data for systemic safety risks offers a model for treating laboratory complaints and incident reports as quality signals (Adeyelu, 2018).

Technology-enabled risk assessment frameworks for internal audit quality support the internal audits that ISO 15189 requires (Akomolafe et al., 2018).

3.10 Technology, Automation, Infrastructure, and Informatics

Total laboratory automation (TLA) integrates pre-analytical processing (sorting, centrifugation, decapping, aliquoting), analysis, and post-analytical storage and retrieval. TLA reduces manual handling errors, improves turnaround time, and standardises sample processing. However, automation introduces new failure modes, such as software errors, carry-over, and dependence on correct barcode reading, which must be included in risk assessments.

Analyser uptime depends on maintenance strategy. Predictive and condition-based maintenance and risk-based inspection of ageing equipment, developed for power and offshore assets, offer models for managing automated laboratory platforms (Adaramola et al., 2018; Obetta & Ninduwezuor-Ehiobu, 2018; Obetta, 2018). Many laboratory instruments, including centrifuges, mixers, and pumps, are driven by single-phase induction motors, and multi-objective optimisation of motor losses, weight, and performance is relevant to equipment efficiency and reliability (Amayo & Popoola, 2017a; Amayo, 2017; Amayo et al., 2015). Stable electrical power is equally important for analyser performance and specimen storage, and

work on voltage control in networks with distributed generation and on solar power integration for small facilities addresses a constraint common to many laboratories in sub-Saharan Africa (Oshevire et al., 2017; Sunday & Omoegun, 2018). Statistical estimation of daily solar radiation supports the planning of such solar installations (Odejobi & Ahmed, 2018a), and UAV-based inspection of transmission lines improves the reliability of the grid supply on which laboratories depend (Dagodzo, 2018a; Dagodzo, 2018b).

3.10.1 Laboratory Infrastructure and Facility Design

The physical laboratory is part of the quality system. Sustainable diagnostic laboratory infrastructure models for emerging and resource-constrained health systems, and spatial planning strategies that improve diagnostic accuracy, safety, and throughput, show that facility design directly influences result quality (Aminu-Ibrahim et al., 2018; Ogbete et al., 2018). In humid regions, building envelope design that responds to climatic variables helps maintain the temperature and humidity conditions that reagents, analysers, and specimens require (Nwafor et al., 2018). Humidity also accelerates corrosion of metal fittings and equipment, and plant-derived green corrosion inhibitors illustrate low-cost protective approaches (Atta et al., 2018).

3.10.2 Information Systems and Surveillance

Laboratory information systems and middleware support autoverification, real-time QC monitoring, Westgard rule evaluation, patient-based QC, and the collection of quality indicators. Electronic order communication reduces transcription and identification errors. Automated image analysis, such as template matching to detect architectural distortion in mammograms, shows how algorithmic detection is extending across diagnostic services (Ejofodomi et al., 2014). Electronic order and result exchange also depends on reliable connectivity and IT platforms, including telecommunication network quality, scalable and secure cloud messaging architectures, energy-efficient data centre resource allocation, and the performance of shared enterprise systems under high concurrency (Ahmed & Odejobi, 2018a; Ahmed & Odejobi, 2018b; Amayo & Popoola, 2017b; Odejobi & Ahmed, 2018b). Structured continuous integration and deployment practices offer a model for validating changes to laboratory software before release (Badmus et al., 2018).

At population level, laboratory data feed integrated disease surveillance systems whose value depends on the quality of the underlying data, as an evaluation of IDSR implementation and DHIS2 data quality in Benue State, Nigeria, has shown (Ekemezie et al., 2018). Data analytics and early applications of machine learning were, by 2018, being explored for detecting sample mix-ups, predicting erroneous results, and optimising QC.

3.10.3 Data Integrity, Privacy, and Cybersecurity

As laboratories become digital, data protection becomes part of result reliability. Legal and ethical risk modelling for enterprise data protection, classification of insider threats, and offline assessment of security-critical systems address risks to the integrity and confidentiality of results (Akeju et al., 2018; Ladapo et al., 2018; Mbonu et al., 2018).

3.10.4 New Analytical Technologies and Interferences

Advances in analytical technology also raise new quality issues. Liquid chromatography tandem mass spectrometry (LC-MS/MS) offers improved specificity for steroids, vitamin D, and therapeutic drugs but requires robust laboratory-developed test validation. Immunoassay interferences, including heterophile antibodies, macro-analytes, and high-dose biotin supplementation, received renewed attention after reports of misdiagnosis of thyroid disease and false-negative troponin results in patients taking biotin, leading to a US FDA safety communication in 2017 (U.S. Food and Drug Administration, 2017).

3.11 Quality Assurance in Point-of-care Testing

Point-of-care testing (POCT) brings measurements of glucose, blood gases, electrolytes, cardiac markers, coagulation parameters, and HbA1c closer to the patient, shortening time to decision (Nichols, 2007). POCT devices are often operated by non-laboratory staff with variable training, which increases the risk of pre-analytical and operator errors. Effective POCT governance includes a multidisciplinary committee, laboratory oversight, operator training and certification, device connectivity for automatic data capture and lockout of uncertified users, regular IQC and EQA, and comparison with central laboratory methods. ISO 22870 specifies requirements for POCT quality and competence in conjunction with ISO 15189 (International Organization for Standardization, 2016).

3.12 Conceptual Model

Synthesising the literature, this review proposes an Integrated Laboratory Quality Assurance Model (Figure 1). The model treats diagnostic reliability, defined as results that are accurate, timely, appropriate to the clinical question, and correctly used, as the outcome of three interacting layers rather than of analytical performance alone (Lundberg, 1981; Plebani, 2006).

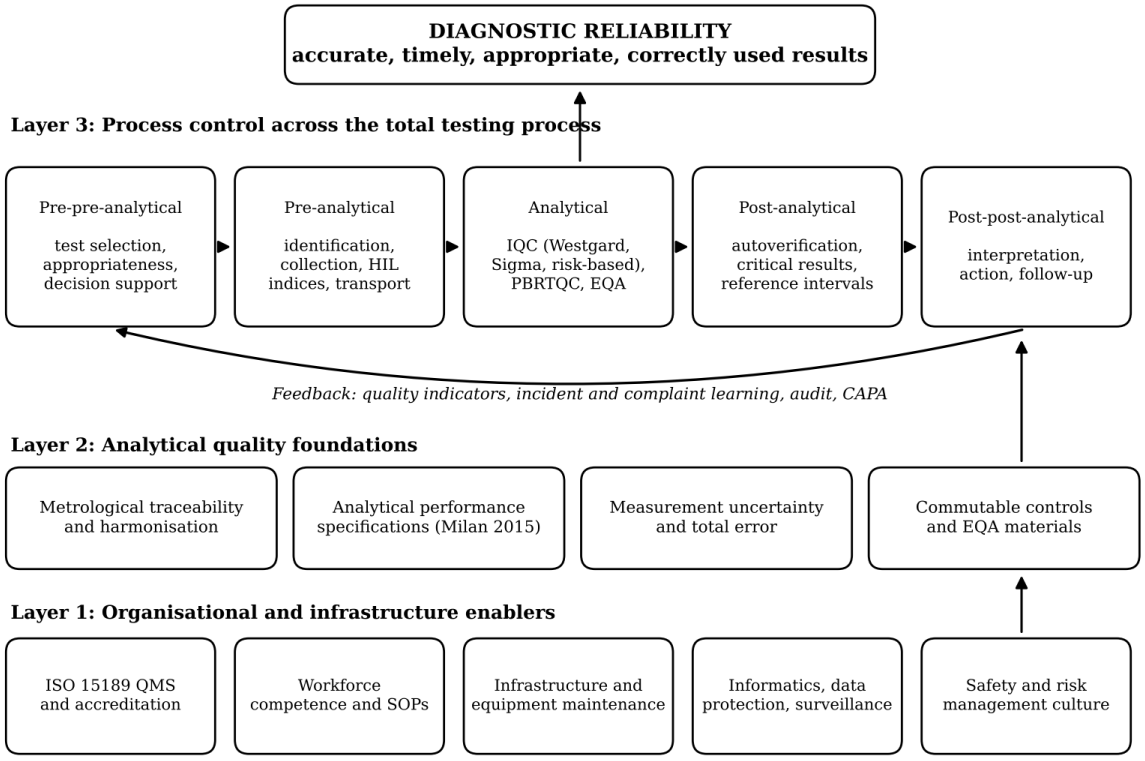


Figure 1: Integrated Laboratory Quality Assurance Model for diagnostic reliability (developed from the reviewed literature)

Layer 1, organisational and infrastructure enablers, comprises the quality management system and accreditation (International Organization for Standardization, 2012; Yao et al., 2014), workforce competence and standard procedures (Uchechi et al., 2018; Ukadike, 2018), laboratory infrastructure and equipment maintenance (Adaramola et al., 2018; Aminu-Ibrahim et al., 2018; Ogbete et al., 2018), informatics, data protection, and surveillance (Ekemezie et al., 2018; Mbonu et al., 2018), and a safety and risk management culture (Akomolafe et al., 2018; Obriki et al., 2018). These conditions determine whether the higher layers can function.

Layer 2, analytical quality foundations, comprises metrological traceability and harmonisation (Panteghini, 2009; Plebani, 2013), evidence-based analytical performance specifications (Sandberg et al., 2015), quantification of measurement uncertainty and total error (Oosterhuis et al., 2016; Theodorsson, 2017), and commutable control and EQA materials (Miller et al., 2006; Miller et al., 2011). These define what an accurate result is and how much error is acceptable.

Layer 3, process control across the total testing process, applies these foundations to each phase, from test selection and specimen collection through IQC, PBRTQC, and EQA to autoverification, critical result communication, and clinical interpretation (Lippi et al., 2015; Parvin, 2008; Sciacovelli et al., 2017; Westgard et al., 2016). A feedback loop of quality indicators, incident and complaint learning, internal audit, and corrective action connects the phases and returns information from later to earlier steps (Adeyelu, 2018; Plebani et al., 2015; Sciacovelli et al., 2017).

The model yields three propositions. First, weaknesses in a lower layer limit what upper layers can achieve, so excellent IQC cannot compensate for poor traceability or inadequate infrastructure. Second, because most errors arise outside the analytical phase, the marginal return on improving extra-analytical controls generally exceeds that of further tightening analytical QC once methods reach high sigma performance (Carraro et al., 2007; Westgard et al., 2016). Third, the feedback loop is the mechanism through which a laboratory learns, so the maturity of its indicator, incident, and audit systems predicts its capacity for sustained improvement.

3.13 Discussion

The literature shows a clear trajectory. Analytical error rates fell substantially between the 1990s and 2018 as instruments, statistical QC, traceability, and standardisation matured (Carraro et al., 2007; Hoelzel et al., 2004; Myers et al., 2006; Plebani et al., 1997). The Milan framework gave laboratories a defensible basis for quality goals (Sandberg et al., 2015), and sigma metrics and risk-based QC planning allowed QC effort to be matched to method performance and patient risk (Clinical and Laboratory Standards Institute, 2011; Parvin, 2008; Westgard et al., 2016). At the same time, the share of errors arising in pre- and post-analytical phases remained high, which explains the shift of attention toward specimen quality, identification, critical result communication, and test

appropriateness (Lippi et al., 2011; Lippi et al., 2018; Plebani et al., 2015).

Several tensions remain unresolved. The total error and measurement uncertainty frameworks coexist uneasily, and laboratories receive inconsistent guidance on whether to correct or incorporate bias (Oosterhuis et al., 2016; Theodorsson, 2017). Performance specifications depend heavily on the model and data source chosen, and biological variation estimates were being re-evaluated through BIVAC at the time of this review (Aarsand et al., 2018). EQA can only reveal true accuracy where commutable, reference-assigned materials exist, which is not yet the case for many measurands (Miller et al., 2006; Miller et al., 2011).

Table 5: Components of the Integrated Laboratory Quality Assurance Model

Layer	Components	Example evidence base
Layer 1: Enablers	ISO 15189 QMS; workforce competence and SOPs; infrastructure and maintenance; informatics and data protection; safety and risk culture	ISO 15189:2012; SLMTA; facility design and maintenance frameworks
Layer 2: Analytical foundations	Traceability and harmonisation; performance specifications; measurement uncertainty and total error; commutable materials	JCTLM; Milan 2015 consensus; GUM and total error debate
Layer 3: Process control	Controls in each TTP phase plus a feedback loop of QIs, incident learning, audit, and CAPA	IFCC WG-LEPS indicators; EFLM WG-PRE; CLSI EP23-A and C24
Outcome	Diagnostic reliability: accurate, timely, appropriate, correctly used results	Brain-to-brain loop; patient safety literature

Evidence from neighbouring fields reinforces the model's emphasis on enablers. Frameworks from safety and risk management show how proactive, data-driven risk control and learning from complaints and incidents sustain improvement (Adeyelu, 2018; Arumosoye & Obriki, 2018; Nwangwu et al., 2018; Obriki et al., 2018), maintenance engineering shows how predictive and condition-based maintenance protects equipment availability (Adaramola et al., 2018; Obetta & Ninduwezuor-Ehiobu, 2018; Obetta, 2018), and procurement and inventory frameworks address the supply continuity that testing depends on (Okonkwo et al., 2018a; Okonkwo et al., 2018b). These sources are conceptual rather than laboratory-specific, so their transferability should be tested empirically, but they point to the same conclusion as the laboratory literature: reliability is a property of the whole system.

The same analytical reliability underpins neighbouring applications of biochemical analysis, such as characterising the chemical constituents and antimicrobial activity of traditional botanicals (Gbadamosi & Obogo, 2013) and predicting subsurface contamination pathways and contaminant migration at remediation sites (Azeez & Badmus, 2018; Lamidi & Olamide, 2018), and assessing the acceptability of feed formulations and the physiological responses of livestock to them in veterinary and animal science (Aye & Tawose, 2015; Aye & Tawose, 2016).

3.14 Implications

3.14.1 Implications for Laboratory Practice

Laboratories should base QC rules and frequencies on sigma performance and patient risk rather than applying uniform rules (Clinical and Laboratory Standards Institute, 2016; Westgard et al., 2016); adopt objective serum indices, autoverification, and delta checks to control specimen quality and reporting (Lippi et al., 2018); implement harmonised quality indicators across all phases (Sciacovelli et al., 2017); and treat equipment maintenance, supply continuity, and data security as part of the quality system rather than as separate administrative functions (Adaramola et al., 2018; Mbonu et al., 2018; Okonkwo et al., 2018a).

3.14.2 Implications for Policy and Regulation

Regulators and accreditation bodies can strengthen reliability by supporting EQA schemes with commutable, reference-assigned materials, encouraging national harmonisation of reference intervals and critical limits, and extending stepwise accreditation programmes such as SLIPTA and SLMTA in resource-limited settings (Ceriotti et al., 2010; Miller et al., 2011; Yao et al., 2014). Investment in laboratory infrastructure and surveillance data quality should be planned as part of national quality strategies (Aminu-Ibrahim et al., 2018; Ekemezie et al., 2018). Reviews of statutory reporting and compliance frameworks in sub-Saharan Africa show that regulatory reporting systems, on which laboratory oversight also relies, need clear frameworks and reform to close compliance gaps (Dogbatsey & Ebhojie, 2018).

3.14.3 Implications for Education and Management

Training for laboratory professionals should extend beyond analytical technique to quality planning, risk management, incident analysis, and communication with clinicians. Laboratory managers can draw on safety leadership and audit frameworks to build a culture in which errors are reported and learned from (Akomolafe et al., 2018; Obriki et al., 2018; Ukadike, 2018). Financial analytics for value creation and compliance analytics frameworks can help managers justify investment in quality and monitor regulatory obligations (Lawal & Oduleye, 2018a; Lawal & Oduleye, 2018b).

3.15 Limitations

This review has several limitations. It is a narrative rather than a systematic review, so it did not use a registered protocol, exhaustive database searching, or formal quality appraisal, and the selection of sources may reflect the author's judgement. Restricting the evidence to publications up to 2018 excludes later developments. Much of the error epidemiology comes from single-centre or European studies, which may not

generalise to all settings. Several seed publications from neighbouring fields are conceptual frameworks without laboratory-specific empirical testing. Finally, the conceptual model has not been validated and should be regarded as a framework for further study rather than an established theory.

3.16 Future Research

The synthesis points to the following research priorities:

- **Linking quality to outcomes:** few studies directly demonstrate the impact of analytical or process quality on patient outcomes, limiting the use of outcome-based performance specifications.
- **Commutability and traceability gaps:** many measurands still lack reference systems, and non-commutable control and EQA materials limit assessment of true accuracy.
- **Reconciling error models:** integrating the total error and measurement uncertainty frameworks into coherent, practical guidance for routine laboratories.
- **Extra-analytical phases:** improving test appropriateness and result follow-up requires collaboration with clinicians and health information systems beyond the laboratory walls.
- **Resource-limited settings:** ensuring affordable, sustainable QA, including access to quality controls, EQA, and trained personnel, remains a priority in low- and middle-income countries.
- **Data-driven quality:** patient-based QC, big data analytics, and artificial intelligence offer opportunities for continuous, real-time quality monitoring, but need rigorous validation.

In addition, the conceptual model proposed here should be tested empirically, for example by assessing whether laboratories with stronger Layer 1 enablers and more mature feedback systems achieve better quality indicator performance and fewer patient-affecting errors.

4. Conclusion

Quality assurance in clinical biochemistry has evolved from a narrow focus on analyser performance to a comprehensive, patient-centred system covering the entire testing process. Analytical accuracy has improved through better instruments, metrological traceability, standardisation programmes, evidence-based performance specifications, and statistically designed QC. At the same time, recognition that most errors arise in the pre- and post-analytical phases has driven the adoption of quality indicators, automation, autoverification, standardised phlebotomy, and structured communication of critical results. Accreditation to ISO 15189 provides an overarching framework that ties these elements together, and related fields, from safety science and maintenance engineering to surveillance and data governance, supply tools the laboratory can adopt. Diagnostic reliability ultimately depends on integrating analytical excellence with robust process control and close collaboration between laboratory professionals and clinicians, so that every result is not only accurate, but also appropriate, timely, and correctly used for patient care.

References

Aarsand, A. K., Røraas, T., Fernandez-Calle, P., Ricos, C., Díaz-Garzón, J., Jonker, N., Perich, C., González-Lao, E., Carobene, A., Minchinela, J., Coşkun, A., Simón, M., Álvarez, V., Bartlett, W. A., Fernández-Fernández, P., Boned, B., Braga, F., Corte, Z., Aslan, B., & Sandberg, S. (2018). The biological variation data critical appraisal checklist: A standard for evaluating studies on biological variation. *Clinical Chemistry, 64*(3), 501-514.

Adaramola, T. S., Fadero, S., & Gideon, E. N. (2018). Predictive maintenance and condition monitoring in critical power and energy infrastructure. *Iconic Research and Engineering Journals, 2*(5), 454-477. https://doi.org/10.64388/IREV2I5-1722489

Adeyelu, O. O. (2018). A predictive compliance monitoring framework for detecting systemic safety risks through aviation consumer complaint data. *Iconic Research and Engineering Journals, 1*(8), 250-276. https://doi.org/10.64388/IREV1I8-1718478

Agboada, P., Ezeako, R., Okoli, I. E., & Uzondu, C. S. (2018). Digital transformation in operations management: A review of advances in automation, analytics, and process redesign. *International Journal of Engineering Technology Research & Management, 2*(11), 109-134.

Ahmed, K. S., & Odejobi, O. D. (2018a). Conceptual framework for scalable and secure cloud architectures for enterprise messaging. *IRE Journals, 2*(1), 1-15.

Ahmed, K. S., & Odejobi, O. D. (2018b). Resource allocation model for energy-efficient virtual machine placement in data centers. *IRE Journals, 2*(3), 1-10.

Akeju, B., Edivri, J., Ogbole, J. I., Okoruwa, P. O., Fadayomi, O., & Abolaji, T. O. (2018). Conceptual model for insider threat classification and risk modeling in complex digital systems. *Iconic Research and Engineering Journals, 1*(9), 476-492. https://doi.org/10.64388/IREV1I9-1713778

Akomolafe, O., & Agu, M. U. (2018). A conceptual model for enhancing internal audit quality through technology-enabled risk assessment frameworks. *Iconic Research and Engineering Journals, 1*(9), 458-475.

Amayo, E. B. (2017). Multi algorithm of loss objective function of a single phase induction motor. *International Journal of Development Research, 7*(5), 12805-12810.

Amayo, E. B., & Popoola, T. T. (2017a). Multi algorithm of weight objective function of a single phase induction motor. *International Journal of Trend in Research and Development, 4*(2), 184-188.

Amayo, E. B., & Popoola, T. T. (2017b). Scientific study of telecommunication deployment in achieving quality network. *International Journal of Trend in Research and Development, 4*(5), 311-314.

Amayo, E. B., Ubeku, E., & Oshevire, P. (2015). Multi algorithm of a single objective function of a single phase induction motor. *Journal of Multidisciplinary Engineering Science and Technology, 2*(12), 3400-3403.

Aminu-Ibrahim, A. Y., Ogbete, J. C., & Ambali, K. B. (2018). Developing sustainable diagnostic laboratory infrastructure models for emerging and resource

constrained health systems. *Iconic Research and Engineering Journals, 1*(8), 118-132. https://doi.org/10.64388/IREV1I8-1713586

Arumosoye, O. M., & Obriki, O. D. (2018). Development of an integrated heat stress risk conceptual model for industrial operations in extreme environments. *Iconic Research and Engineering Journals, 1*(12), 141-160. https://doi.org/10.64388/IREV1I12-1714415

Atta, S., Asomani, E., & Adenuga, O. M. (2018). A systematic review of green corrosion inhibitors from agricultural extracts for mild steel protection in acidic and alkaline media. *International Journal of Engineering and Modern Technology, 4*(1), 64-97. https://doi.org/10.56201/ijemt.vol.4.no1.2018.pg64.97

Aye, P. A., & Tawose, O. M. (2015). Acceptability and utilization of graded levels of Gmelina arborea leaves and cassava peels concentrate by West African dwarf sheep. *International Journal of Advances in Agriculture, 4*(2), 415-422. https://doi.org/10.24297/jaa.v4i2.4272

Aye, P. A., & Tawose, O. M. (2016). Physiological responses of West African dwarf sheep fed graded levels of Gmelina arborea leaf and cassava peel concentrates under different management systems. *Agriculture and Biology Journal of North America, 7*(4), 185-195. https://doi.org/10.5251/abjna.2016.7.4.185.195

Azeez, L. O., & Badmus, O. B. (2018). Data-driven framework for predicting subsurface contamination pathways in complex remediation projects. *Iconic Research and Engineering Journals, 2*(5), 312-335.

Badmus, O., Dosunmu, A. A., & Ozowara, D. E. (2018). A systematic review of CI/CD pipeline strategies in Salesforce DevOps: Tools, practices, and deployment outcomes. *Iconic Research and Engineering Journals, 2*(6).

Badrick, T. (2013). Evidence-based laboratory medicine. *Clinical Biochemist Reviews, 34*(2), 43-46.

Bobga, M. A., Boakye, K., Ogbona, C. S., & Yeboah, T. J. (2018). Pedagogical strategies for teaching students with learning difficulties in resource-constrained schools. *Iconic Research and Engineering Journals, 2*(4), 173-194. https://doi.org/10.64388/IREV2I4-1714176

Bonini, P., Plebani, M., Ceriotti, F., & Rubboli, F. (2002). Errors in laboratory medicine. *Clinical Chemistry, 48*(5), 691-698.

Carraro, P., & Plebani, M. (2007). Errors in a stat laboratory: Types and frequencies 10 years later. *Clinical Chemistry, 53*(7), 1338-1342.

Ceriotti, F., Henny, J., Queraltó, J., Ziyu, S., Özarda, Y., Chen, B., Boyd, J. C., & Panteghini, M. (2010). Common reference intervals for aspartate aminotransferase (AST), alanine aminotransferase (ALT) and gamma-glutamyl transferase (GGT) in serum: Results from an IFCC multicenter study. *Clinical Chemistry and Laboratory Medicine, 48*(11), 1593-1601.

Clinical and Laboratory Standards Institute. (2011). Laboratory quality control based on risk management; Approved guideline (CLSI document EP23-A). CLSI.

Clinical and Laboratory Standards Institute. (2016). Statistical quality control for quantitative measurement procedures: Principles and definitions (4th ed., CLSI guideline C24). CLSI.

Dagodzo, D. (2018a). A conceptual framework for UAV integration into national power grid inspection programs. *Iconic Research and Engineering Journals, 2*(5), 391-412. https://doi.org/10.64388/IREV2I5-1716082

Dagodzo, D. (2018b). A review of UAV applications in electrical transmission line inspection: Methods, technologies, and challenges. *Iconic Research and Engineering Journals, 2*(6), 234-254. https://doi.org/10.64388/IREV2I6-1716083

Dogbatsey, E. A., & Ebhojie, O. (2018). Budget compliance and statutory reporting in Sub-Saharan Africa: A systematic review of frameworks, gaps, and reform pathways. Zenodo. https://doi.org/10.5281/zenodo.20446859

Ejofodomi, O. A., Gideon, E. N., Oladipo, G. O., & Oshomah, E. R. (2014). Automated detection of architectural detection in mammograms using template matching. *International Journal of Biomedical Science and Engineering, 2*(1), 1-6. https://doi.org/10.11648/j.ijbse.20140201.11

Ekemezie, U. C., Ohunyon, G., & Sydney, E. (2018). Evaluating IDSR implementation in Benue State, Nigeria: DHIS2 data quality and surveillance capacity. *Iconic Research and Engineering Journals, 2*(6).

Gbadamosi, I. T., & Obogo, S. F. (2013). Chemical constituents and in vitro antimicrobial activities of five botanicals used traditionally for the treatment of neonatal jaundice in Ibadan, Nigeria. *Nature and Science, 11*(10), 130-135.

Hoelzel, W., Weykamp, C., Jeppsson, J. O., Miedema, K., Barr, J. R., Goodall, I., Hoshino, T., John, W. G., Kobold, U., Little, R., Mosca, A., Mauri, P., Paroni, R., Susanto, F., Takei, I., Thienpont, L., Umemoto, M., & Wiedmeyer, H. M. (2004). IFCC reference system for measurement of hemoglobin A1c in human blood and the national standardization schemes in the United States, Japan, and Sweden: A method-comparison study. *Clinical Chemistry, 50*(1), 166-174.

Hoffmann, R. G., & Waid, M. E. (1965). The "average of normals" method of quality control. *American Journal of Clinical Pathology, 43*, 134-141.

International Organization for Standardization. (2012). ISO 15189:2012 Medical laboratories: Requirements for quality and competence. ISO.

International Organization for Standardization. (2016). ISO 22870:2016 Point-of-care testing (POCT): Requirements for quality and competence. ISO.

Kenny, D., Fraser, C. G., Hyltoft Petersen, P., & Kallner, A. (1999). Consensus agreement: Strategies to set global analytical quality specifications in laboratory medicine. *Scandinavian Journal of Clinical and Laboratory Investigation, 59*(7), 585.

Kohn, L. T., Corrigan, J. M., & Donaldson, M. S. (Eds.). (2000). To err is human: Building a safer health system. National Academy Press.

Ladapo, O. O., Dosunmu, A. A., Jooda, D., & Abolaji, T. O. (2018). Lessons learned from offline assessment of security-critical systems: The case of Microsoft Active Directory. *Iconic Research and Engineering Journals, 2*(6), 277-299. https://doi.org/10.64388/IREV2I6-1717205

Lamidi, O. B. A., & Olamide, A. (2018). Spatially explicit risk modeling framework for tracking subsurface contaminant migration in data-limited remediation sites. *Iconic Research and Engineering Journals, 2*(6), 178-198.

Lawal, O. A., & Oduleye, T. E. (2018a). A conceptual model for financial analytics driven enterprise value creation in technology firms. *Iconic Research and Engineering Journals, 2*(2).

Lawal, O. A., & Oduleye, T. E. (2018b). A review and conceptual framework for tax governance and cross-border compliance analytics. *Iconic Research and Engineering Journals, 2*(5).

Levey, S., & Jennings, E. R. (1950). The use of control charts in the clinical laboratory. *American Journal of Clinical Pathology, 20*(11), 1059-1066.

Lippi, G., Banfi, G., Church, S., Cornes, M., De Carli, G., Grankvist, K., Kristensen, G. B., Ibarz, M., Panteghini, M., Plebani, M., Nybo, M., Smellie, S., Zaninotto, M., & Simundic, A. M. (2015). Preanalytical quality improvement: In pursuit of harmony, on behalf of European Federation for Clinical Chemistry and Laboratory Medicine (EFLM) Working Group for Preanalytical Phase (WG-PRE). *Clinical Chemistry and Laboratory Medicine, 53*(3), 357-370.

Lippi, G., Cadamuro, J., von Meyer, A., & Simundic, A. M. (2018). Practical recommendations for managing hemolyzed samples in clinical chemistry testing. *Clinical Chemistry and Laboratory Medicine, 56*(5), 718-727.

Lippi, G., Chance, J. J., Church, S., Dazzi, P., Fontana, R., Giavarina, D., Grankvist, K., Huisman, W., Kouri, T., Palicka, V., Plebani, M., Puro, V., Salvagno, G. L., Sandberg, S., Sikaris, K., Watson, I., Stankovic, A. K., & Simundic, A. M. (2011). Preanalytical quality improvement: From dream to reality. *Clinical Chemistry and Laboratory Medicine, 49*(7), 1113-1126.

Lundberg, G. D. (1981). Acting on significant laboratory results. *JAMA, 245*(17), 1762-1763.

Mbonu, I. S., Aliliele, C., Iwuanyanwu, U., & Oluoha, O. M. (2018). A conceptual framework for legal and ethical risk modeling in enterprise data protection governance systems. *Iconic Research and Engineering Journals, 2*(2), 207-226. https://doi.org/10.64388/IREV2I2-1714911

Miller, W. G., Jones, G. R. D., Horowitz, G. L., & Weykamp, C. (2011). Proficiency testing/external quality assessment: Current challenges and future directions. *Clinical Chemistry, 57*(12), 1670-1680.

Miller, W. G., Myers, G. L., & Rej, R. (2006). Why commutability matters. *Clinical Chemistry, 52*(4), 553-554.

Myers, G. L., Miller, W. G., Coresh, J., Fleming, J., Greenberg, N., Greene, T., Hostetter, T., Levey, A. S., Panteghini, M., Welch, M., & Eckfeldt, J. H. (2006). Recommendations for improving serum creatinine measurement: A report from the Laboratory Working Group of the National Kidney Disease Education Program. *Clinical Chemistry, 52*(1), 5-18.

Nichols, J. H. (2007). Point of care testing. *Clinics in Laboratory Medicine, 27*(4), 893-908.

Nwafor, M. I., Uduokhai, D. O., Ifechukwu, G. O., Stephen, D., & Aransi, A. N. (2018). Impact of climatic variables on the optimization of building envelope design in humid regions. *Iconic Research and Engineering Journals, 1*(10), 322-335.

Nwangwu, C. V., Duvbiama-Owasanoye, O. A., & Onwumere, A. (2018). A framework for operational integrity in high-risk drilling: Balancing productivity and safety compliance. *Iconic Research and Engineering Journals, 2*(5), 436-453.

Obetta, P. C. (2018). A risk-based inspection concept for fitness-for-service assessment of ageing pressure vessels on offshore joint venture facilities. *Iconic Research and Engineering Journals, 2*(5), 497-520. https://doi.org/10.64388/IREV2I5-1722578

Obetta, P. C., & Ninduwezuor-Ehiobu, N. (2018). A condition-based maintenance concept for CALM buoy bearings and swivels to improve offshore crude export availability. *Iconic Research and Engineering Journals, 2*(6), 385-410. https://doi.org/10.64388/IREV2I6-1722579

Obriki, O. D., & Arumosoye, O. M. (2018). Conceptual modeling of data-driven occupational safety risk control in large-scale energy infrastructure projects. *Iconic Research and Engineering Journals, 1*(7), 169-189. https://doi.org/10.64388/IREV1I7-1714414

Odejobi, O. D., & Ahmed, K. S. (2018a). Statistical model for estimating daily solar radiation for renewable energy planning. *IRE Journals, 2*(5), 1-12.

Odejobi, O. D., & Ahmed, K. S. (2018b). Performance evaluation model for multi-tenant Microsoft 365 deployments under high concurrency. *IRE Journals, 1*(11), 92-107.

Ogbete, J. C., Aminu-Ibrahim, A. Y., & Ambali, K. B. (2018). Optimizing laboratory spatial planning strategies to improve diagnostic accuracy, safety, and clinical throughput. *Iconic Research and Engineering Journals, 2*(1), 87-113. https://doi.org/10.64388/IREV1I7-1713587

Okonkwo, C. S., Ogunwole, O., & Okeke, O. T. (2018a). Framework for strategic procurement optimization in oil and gas operations. *Iconic Research and Engineering Journals, 1*(7), 153-168. https://doi.org/10.64388/IREV1I7-1713119

Okonkwo, C. S., Ogunwole, O., & Okeke, O. T. (2018b). Model for inventory availability and plant uptime

improvement in energy facilities. *Iconic Research and Engineering Journals, 2*(4), 160-172. https://doi.org/10.64388/IREV2I4-1713120

Oosterhuis, W. P., & Theodorsson, E. (2016). Total error vs. *measurement uncertainty: Revolution or evolution? Clinical Chemistry and Laboratory Medicine, 54*(2), 235-239.

Oshevire, P., Eyenubo, O. J., & Amayo, B. (2017). Voltage control in the presence of distributed generation. *ATBU Journal of Science, Technology and Education, 5*(2), 165-173.

Panteghini, M. (2009). Traceability as a unique tool to improve standardization in laboratory medicine. *Clinical Biochemistry, 42*(4-5), 236-240.

Parvin, C. A. (2008). Assessing the impact of the frequency of quality control testing on the quality of reported patient results. *Clinical Chemistry, 54*(12), 2049-2054.

Plebani, M. (2006). Errors in clinical laboratories or errors in laboratory medicine? *Clinical Chemistry and Laboratory Medicine, 44*(6), 750-759.

Plebani, M. (2013). Harmonization in laboratory medicine: The complete picture. *Clinical Chemistry and Laboratory Medicine, 51*(4), 741-751.

Plebani, M., & Carraro, P. (1997). Mistakes in a stat laboratory: Types and frequency. *Clinical Chemistry, 43*(8), 1348-1351.

Plebani, M., Sciacovelli, L., Aita, A., Pelloso, M., & Chiozza, M. L. (2015). Performance criteria and quality indicators for the pre-analytical phase. *Clinical Chemistry and Laboratory Medicine, 53*(6), 943-948.

Sandberg, S., Fraser, C. G., Horvath, A. R., Jansen, R., Jones, G., Oosterhuis, W., Petersen, P. H., Schimmel, H., Sikaris, K., & Panteghini, M. (2015). Defining analytical performance specifications: Consensus statement from the 1st Strategic Conference of the European Federation of Clinical Chemistry and Laboratory Medicine. *Clinical Chemistry and Laboratory Medicine, 53*(6), 833-835.

Sciacovelli, L., Lippi, G., Sumarac, Z., West, J., Garcia del Pino Castro, I., Furtado Vieira, K., Ivanov, A., & Plebani, M. (2017). Quality indicators in laboratory medicine: The status of the progress of IFCC Working Group "Laboratory Errors and Patient Safety" project. *Clinical Chemistry and Laboratory Medicine, 55*(3), 348-357.

Simundic, A. M., Bölenius, K., Cadamuro, J., Church, S., Cornes, M. P., van Dongen-Lases, E. C., Eker, P., Erdeljanovic, T., Grankvist, K., Guimaraes, J. T., Hoke, R., Ibarz, M., Ivanov, H., Kovalevskaya, S., Kristensen, G. B. B., Lima-Oliveira, G., Lippi, G., von Meyer, A., Nybo, M., ... Vermeersch, P. (2018). Joint EFLM-COLABIOCLI recommendation for venous blood sampling. *Clinical Chemistry and Laboratory Medicine, 56*(12), 2015-2038.

Sunday, E. A., & Omoegun, G. O. (2018). Integrating solar power solutions in small-scale manufacturing industries in Nigeria. *International Journal of Scientific Research in Science, Engineering and Technology, 4*(8), 832-853.

Theodorsson, E. (2017). Uncertainty in measurement and total error: Tools for coping with diagnostic uncertainty. *Clinics in Laboratory Medicine, 37*(1), 15-34.

U.S. Food and Drug Administration. (2017, November 28). The FDA warns that biotin may interfere with lab tests: FDA safety communication. FDA.

Uchechi, N., Ominyi, M., & Jones, B. C. (2018). Procedural standardization and workflow optimization in high-volume dispute resolution clinics: A systematic review. *Iconic Research and Engineering Journals, 2*(6), 420-452. https://doi.org/10.64388/IREV2I6-1722789

Ukadike, C. A. (2018). Competency frameworks and onboarding redesign in professional services: A conceptual model for return on investment. *International Journal of Social Sciences and Management Research, 4*(9), 42-62. https://doi.org/10.56201/ijssmr.v4.no9.2018.pg.42.62

Unamma, U. M.-L., Okwesa, I. J., Iwuanyanwu, U., & Ajiga, D. (2018). An offline-first design framework for digital learning in low-connectivity environments. *Iconic Research and Engineering Journals, 2*(3), 192-211. https://doi.org/10.64388/IREV2I3-1722627

Vesper, H. W., & Thienpont, L. M. (2009). Traceability in laboratory medicine. *Clinical Chemistry, 55*(6), 1067-1075.

Westgard, J. O., & Westgard, S. A. (2016). Quality control review: Implementing a scientifically based quality control system. *Annals of Clinical Biochemistry, 53*(1), 32-50.

Westgard, J. O., Barry, P. L., Hunt, M. R., & Groth, T. (1981). A multi-rule Shewhart chart for quality control in clinical chemistry. *Clinical Chemistry, 27*(3), 493-501.

Yao, K., Maruta, T., Luman, E. T., & Nkengasong, J. N. (2014). The SLMTA programme: Transforming the laboratory landscape in developing countries. *African Journal of Laboratory Medicine, 3*(2), 194.

Yusuf, H. D., & Abdulrazaq, K. (2018). A conceptual framework for strengthening diagnostic quality systems in resource-limited clinical laboratories. *Iconic Research and Engineering Journals, 1*(11), 145-179. https://doi.org/10.64388/IREV1I11-1723090

Cite this article: **Nnamdi Eneh, Kazeem Abdulrazaq, Habeeb Damilola Yusuf, Olatunde Adesoji Aladegba.** Advances in Clinical Biochemistry Laboratory Quality Assurance: Analytical Accuracy, Error Prevention, and Diagnostic Reliability. **Indian J. Pharm. Biol. Res.2018; 6(4):55-67.**

All © 2018 are reserved by Indian Journal of Pharmaceutical and Biological Research
This Journal is licensed under a **Creative Commons Attribution-Non Commercial -Share Alike 3.0 Unported License.** This article can be downloaded to **ANDROID OS** based mobile.