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EQA programmes for AMR testing: the African and Asian approaches



LAB CULTURE

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ADVANCING THE LABORATORY PROFESSION AND NETWORKS IN AFRICA

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External Quality Assessment is not an option, it is a necessity

The laboratory plays a critical role in the healthcare system by ensuring correct diagnosis of diseases, effective treatment and follow up of patients. Over 70% of clinical decisions rely on laboratory diagnosis and it is of utmost importance that test result can be trusted. During pandemics, such as the COVID-19, testing capacity needs to be quickly scaled up and decentralized in less specialized settings to address diagnostics in the context of community transmission. Ensuring the reliability and effectiveness of laboratory testing for decision making is critical for clinical and public health and in situations of routine and emergency.

Quality assurance (QA) is defined simply as the right test result at the right time, on the right specimen, from the right patient, with result/interpretation based on correct reference date, and at the right place. An important component of QA is external quality assessment (EQA), which allows a laboratory's testing performance to be compared to the performance of a peer group of laboratories, national reference or World Health Organization (WHO) reference laboratories. There are three EQA methods that can be applied: 1) proficiency testing (PT), 2) rechecking/retesting and 3) on-site evaluation.

Regardless of the method used, the ultimate goal of EQA programmes is to provide unbiased assessments of testing performance, detect non-conformities and correct them

as part of continuous quality improvement of laboratory facilities and networks. The coverage and effectiveness of international and national EQA programmes in medical laboratories of Africa is uneven, illustrating a critical gap in the implementation of quality management systems, and a missed opportunity to support progress toward ISO 15189 accreditation.

During the COVID-19 pandemic, ASLM and Africa CDC organized the emergency provision of rounds of EQA proficiency testing (PT) panels for SARS-CoV-2 (funded by RESOLVE to Save Lives and Unitaids). This collaboration complemented the already established efforts of WHO External Quality Assessment Programme, reaching out to more than 250 newly activated COVID-19 testing sites across 15 countries. The coordinated distribution of EQA PT distribution in COVID-19 testing laboratories highlighted the magnitude of the unmet need for EQA PT testing in emergency situations and the insufficient capacity to distribute, supervise, report performance results and conduct corrective actions at national and sub-national levels.

In line with the various calls to improve access to diagnostics, countries, manufacturers and various laboratory stakeholders have worked together to implement diagnostics and various technology innovations supporting testing, all the way down to the community. With the number of

tests increasing across various disease programmes, the question arises: have we been paying enough attention to assure the continuous quality of these tests? As we fill the gaps in access to diagnostic towards achieving Universal Health Coverage and the requirements of the International Health Regulations, let us reflect on the price we pay for poorly quality-assured diagnostics. Each time we place a new instrument or a new test kit in a laboratory or a clinic at the point of care, we need to close the loop and think about the systems, resources and responsibilities ensuring that test errors are reported, corrected and prevented.

Participating in international or national EQA programmes and working towards improved testing performance should be the rule and not a fancy exception only reserved to well-funded disease programmes, public health emergencies or private laboratories. In fact, every laboratory conducting clinical testing and concerned about reliable results, should be demanding to partake in EQA.

In this issue, we cover some key principles of EQA and highlight the bottlenecks and misconceptions

preventing the implementation of quality-assured tests across essential diseases and throughout diagnostic networks.

The articles shared here will provide some reflections, best practices and recommendations for advancing EQA programmes as part as robust and sustainable quality management systems.



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World Health Organization programme to support external quality assessment for antimicrobial resistance testing in Africa

In Africa, communicable diseases and associated outbreaks constitute the most important public health problems, with the potential to pose prominent health security threats in communities. The economic and social impact of these diseases is enormous. In this context, national public health laboratories (NPHLs) are mandated to generate data to guide disease prevention, control and surveillance activities. The Integrated Disease Surveillance and Response strategy adopted by the Regional Committee for Africa in 1998,¹ and World Health Organization (WHO) Resolution AFR/RC58/R2 adopted by the 58th session of the Regional Committee,² recommended strengthening the ability of NPHLs to provide accurate, reliable and prompt confirmation of epidemics for appropriate public health response, thus enhancing national and global health security. In addition, this strategy promotes laboratory-based surveillance for antimicrobial resistance.

The Integrated Disease Surveillance and Response technical guidelines recommend the use of standard laboratory diagnostic methods for priority diseases. In many African countries, lack of standardised methods and shortage of funds for qualified staff and regular supplies, affects laboratories' ability to reliably detect and confirm suspected infectious diseases, despite this being a critically important component of functional disease surveillance. Developing and maintaining high quality NPHL services requires political will, financial and managerial commitment to provide qualified staff, training, equipment, consumables, reagents and physical facilities. Regular assessment of performance of NPHLs is essential in ensuring the reliability of results.

Antibiotic resistance is a worldwide health threat aggravating the impact of bacterial infections. At least 700 000 people die annually due to antibiotic-resistant pathogens, and this figure is projected to reach 10 million by 2050.³ It is a severe and growing global health security risk, which needs to be prioritised at the country, regional and international levels. The development and implementation of national antimicrobial resistance (AMR) action plan that complement international efforts are a major step towards containment. Global partnerships need to be strengthened, because the responsibility for reducing AMR calls for collaborative action in all sectors (human health, animal health, agriculture and environment), in line with the 'One Health' approach.

AMR is a progressively increasing global problem, and drug-resistant pathogens kill at least 25 000 people annually in the European Union alone¹. In the last decade the number of antimicrobial agents that can be used for treatment of multidrug resistant organisms has become very limited². In some clinical conditions the empirical prescription of antibiotics is necessary and de-escalation policy implementation is critical for all healthcare facilities. The European Centre for Disease Prevention and Control has estimated that to date 30-50% of all antimicrobials prescribed to human patients are unnecessary, and over-prescription of antimicrobials further promotes the development and spread of resistance.^{1, 2}

The detection and monitoring of the AMR spread rests on laboratory testing for phenotypic and genetic markers of resistance. Laboratory-based surveillance relies on accurate antimicrobial susceptibility testing (AST) data. Additionally, specimen



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submission practices and collection of demographic, clinical and other data using adequate protocols contribute to the establishment of epidemiologically-driven surveillance programmes. For credible and reliable AMR surveillance, it is essential that countries support laboratory systems capable of providing good quality data in a standardised format. Quality assurance for bacteriology testing is lacking in several national reference laboratories in the WHO African Region, which are on the front line for confirmation of priority outbreak-prone diseases.⁴

AST aims to ensure that suitable antibiotics are prescribed and to monitor the selection and emergence of resistant pathogens in infected individuals. Information on local patterns of antimicrobial susceptibility can be collected using AST, so that policies guiding the empiric choice of therapy can be based on current data on local resistance trends (also known as the local or institutional antibiogram). AST can also help to identify isolates with defined resistance mechanisms of major interest to infection prevention and control (for example, extended-spectrum β -lactamase producers, carbapenemase-producing Enterobacteriaceae, methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant enterococci). Furthermore, AST is key for the assessment of resistance incidence and prevalence in epidemiological studies that examine the origin and spread of resistance, including studies on the effectiveness of measures taken to counteract spread⁴. Critically important

aspects of AST are reliable, accurate and repeatable test results. For that purpose, external quality assessment programs should be implemented in all laboratories that perform bacterial identification and antibiotic susceptibility testing.

The term 'external quality assessment' (EQA) is used to describe a method/process that allows testing conducted by a laboratory, testing site or individual user to be compared to that of a source outside the laboratory – namely, a peer group of laboratories or a reference laboratory or testing site.⁵ Importantly, participation in EQA programme provides documented evidence of the testing capacity for routine and reference laboratories. EQA participants should be encouraged to improve the quality and delivery of the service if

which program to select, based on their scope of activities. National EQA programs are very useful in support of relevant testing range in the country and even can address some specialised tests; on other hand, regional and international programs are robust, provide statistical analysis, and provide required expertise. Other factors to consider with regional and international programs are language barriers, the stability of test items, and shipment costing.

There are a number of EQA providers available to support bacteriology programs worldwide but there are not many in developing countries. In that respect WHO and other non-governmental organisations are focusing on development of a national and regional EQA programs by providing various supports. WHO

has supported participation of the Public Health Microbiology Laboratories in Africa; in the WHO African Region External Quality Control System programme for *Salmonella* and *Shigella* species and the Ethiopian Public Health Institute indicated 89.9% agreement with expected results for antimicrobial susceptibility testing.⁶

One of the long standing programmes supported by WHO was a joint EQA programme with the South African National Institute for Communicable Diseases (NICD). In July 2002, WHO launched an external quality assessment programme to test the proficiency of microbiological testing for epidemic-prone diseases by laboratories in the African Region.⁷ The NICD, a division of the National Health Laboratory

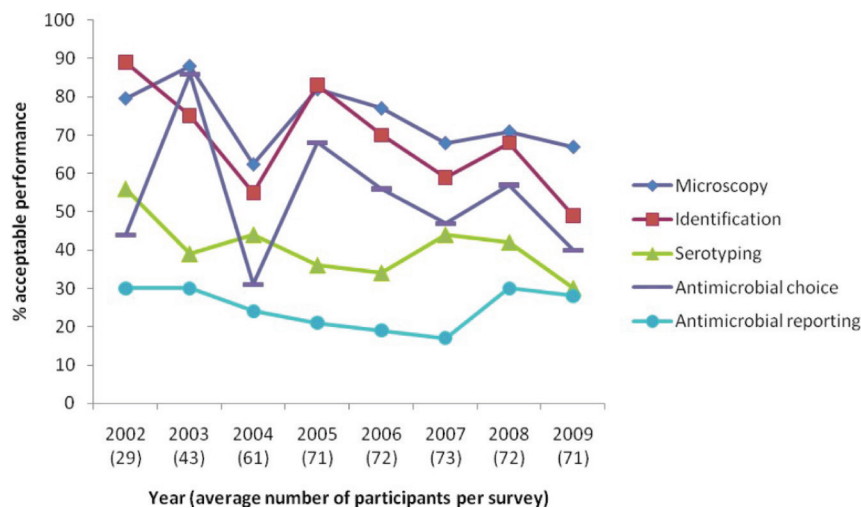
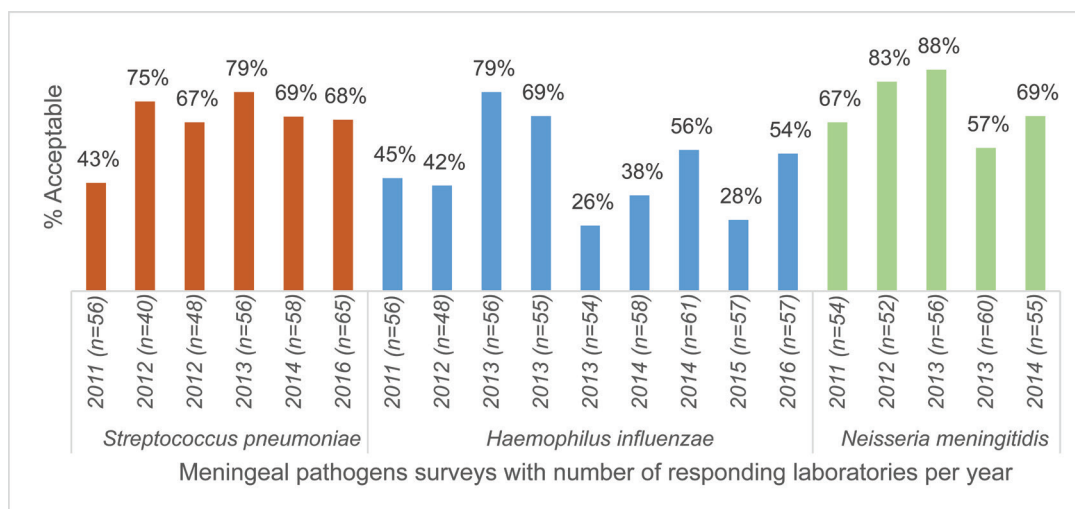


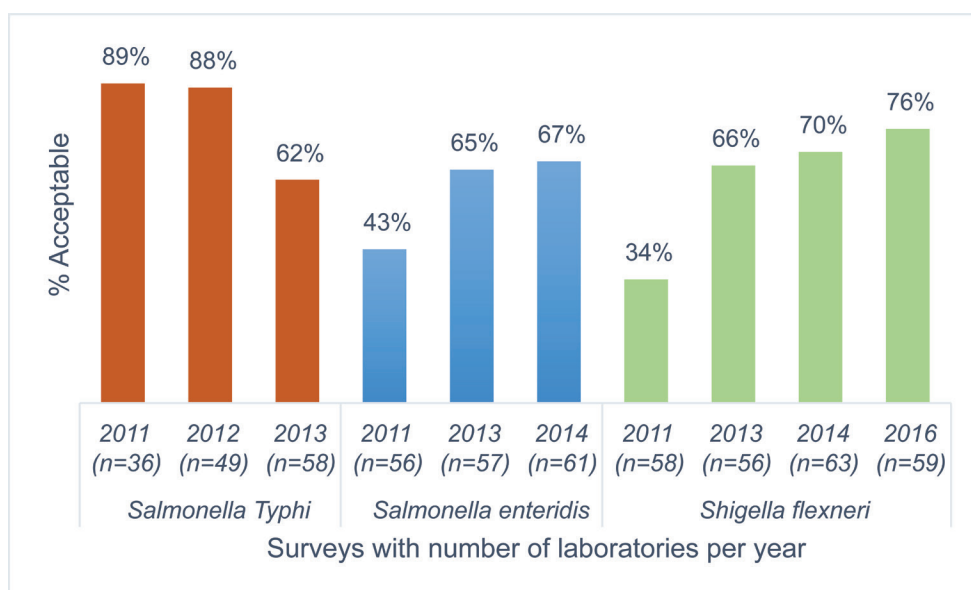
Figure 1. Performance of African laboratories that participated in the meningitis pathogens component of an external quality assessment programme, 2002–2009.⁷

needed. For EQA providers it might be challenging to provide concrete support to laboratories to improve their performance but they certainly should provide advice and help to address their quality procedures.

EQA programs are organized at national, regional and international levels. All of these programs play specific roles in assessing laboratory quality.⁵ Each participating laboratory should make a decision about



are national reference laboratories for the Global Antimicrobial Resistance Surveillance Scheme. Published data⁷ showed that the seven-year performance of AST by public health laboratories in the African Region was poorly done, particularly for reporting (Figure 1). These data illustrated the strengths



and weaknesses of participating laboratories and constitute an evidence-based tool for improving laboratory quality in the region. In the next phase the more detailed programme addressing AST was introduced and acceptable results for the period 2011-2016 showed slight improvement (61%), on average (for antimicrobial testing) (Figure 2).⁸

These few publications provide strong evidence to support the statement that AST is the most challenging part of EQA programmes in bacteriology in the African Region. Therefore, we should emphasise the detailed requirements for specific EQA materials that need to be prepared for AMR.

One of the most important aspects of the quality of AST reporting is that they follow the latest versions of recommended standards for antimicrobial susceptibility testing (from the Clinical Laboratory Standards Institute or European Committee on Antimicrobial Susceptibility Testing), with an emphasis on adequate use of quality control strains. Also, each laboratory needs to update its standard operating procedures, based on annual changes in recommendations, as those will be the focus of

Figure 2. Antimicrobial susceptibility testing results.

Results from the World Health Organization and South Africa's National Institute for Communicable Diseases external quality assessment programme for national public health laboratories conducted 2011–2016 are shown for *S. pneumoniae*, *H. influenzae*, *N. meningitidis*, *Salmonella Typhi*, *Salmonella Enteritidis*, and *Shigella flexneri* isolates (n = number of responding laboratories).⁸

Service of South Africa, provided technical coordination following an agreement with the co-funders, the WHO Regional Office for Africa and the WHO office in Lyon, France⁷. The NICD commenced sending specimens for laboratory identification of selected agents of bacterial enteric diseases, bacterial meningitis and general bacterial pathogens with emphasize on antimicrobial susceptibility testing over the next eighteen years. In addition, they were tasked to advise WHO about the needs of participating laboratories, to correct

deficiencies and maintain proficiency and to further extend the external quality assessment programme to include antimicrobial resistance testing in more detail.⁸ This programme was revised in 2018 to include organisms and AST reporting for antibiotics from the WHO Global Antimicrobial Resistance Surveillance Scheme.

WHO EQA programmes were initially focused on the NPHLs, and in the recent programme ministries of health from each country were invited to nominate laboratories that

assessments. Clearly, this excludes assessment of testing for antibiotics still under development.

From the latest WHO EQA programme for AMR, results for both AST testing and those released to clinicians were suboptimal, namely below the acceptable target of 80%. As indicated by Gerald Forae in an editorial, most African institutional laboratories lack consistency and accuracy which resulted in compromised sensitivity and specificity⁹.

In conclusion, until the responsible authority of each country prioritises implementation of a laboratory quality system, particularly in bacteriology, as their mandate, there will be suboptimal performance of laboratory testing for detection of AMR.

As Jim O'Neill in a Wellcome Trust report³ mentioned, without the policies to control spread of AMR, the future will become disturbing and will cost human lives.

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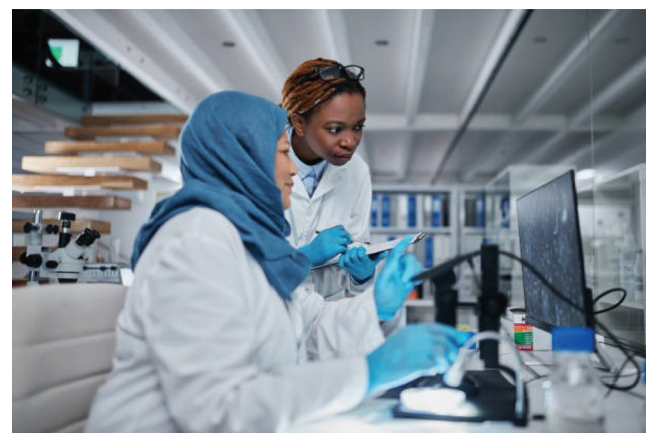
External quality assessment programmes to improve testing for infectious diseases in Africa

Despite the increasing burden of non-communicable diseases in Africa¹, infectious diseases remain responsible for more than 40% of deaths in the African region with nearly 4 million deaths in 2016². Of recently emerged and re-emerging infections, some are associated with newly discovered microorganisms such as *Rickettsia felis*, considered a common cause of fever in Africa³; others are known historical diseases such as plague and cholera; and some are diseases related to previously known microorganisms that have recently caused massive outbreaks with worldwide impact, such as Ebola virus, Zika virus and Chikungunya virus⁴. The COVID-19 pandemic caused by the most recently discovered coronavirus, severe

diseases present one of the greatest potential barriers to achievement of the United Nations' third Sustainable Development Goal⁷. Infectious disease surveillance is becoming increasingly important in African countries because of ongoing disease emergence, and because strains of pathogens, such as those causing tuberculosis, malaria, cholera, dysentery and pneumonia, are developing resistance to common and inexpensive antimicrobial drugs⁸. There is growing awareness among many African countries that more needs to be done to combat antimicrobial resistance, and several antimicrobial resistance surveillance schemes have been initiated on the continent⁹.

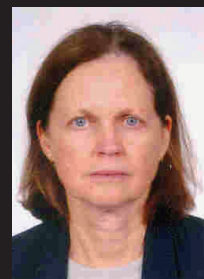
Laboratory services are vital for infectious diseases detection, including emerging public health threats in the context of the Global Health Security Agenda, and monitoring antimicrobial drug resistance¹⁰. Systems to manage laboratory quality are therefore essential to support the increasing need for rapid, accurate diagnosis of infectious diseases. The consequences of poor laboratory quality are well known and include delayed

diagnosis, unnecessary or incorrect treatment, waste of resources, increased costs and poor patient outcomes. International standards and guidelines for laboratory quality management systems have been established^{11,12} that describe a systematic approach to a set of essential activities covering all aspects of laboratory operations, including work processes, management of resources, ongoing monitoring to ensure quality-assured results, and continuous improvement processes¹³. Laboratory quality assurance,



acute respiratory coronavirus 2 or 'SARS-CoV-2', is a defining global health crisis that is also impacting routine healthcare services and patients' access to care. Although emerging infectious diseases and those with immediate impact often dominate the global health agenda, HIV/AIDS, tuberculosis, and malaria remain major health priorities⁵.

Infectious diseases place a high burden on public health and also impact local and global economics and political stability⁶. In African countries, infectious



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a critical aspect of laboratory quality management, includes measures to promote quality through internal (internal quality control) and external (external quality assessment) processes¹⁴. The World Health Organization defines external quality assessment (EQA) as a system for objectively checking a laboratory's performance using an external agency or facility¹⁵. EQA can be applied in three main ways: 1) Proficiency testing (PT), where an external provider sends samples of undisclosed results to laboratories or individual testers and provides feedback on results; 2) Rechecking or retesting samples in higher level or peer laboratories (inter-laboratory comparison); and 3) On-site assessment by an approved evaluator. The exchange of samples among selected laboratories (inter-laboratory comparisons) is more appropriate for highly specialised tests for which proficiency testing schemes may not be available. EQA provides an objective measure of an individual laboratory's performance and points to areas that require corrective action; they allow comparisons between different testing facilities within a country or across regions (benchmarking); they can provide early warning of potential problems with kits or equipment (post-market surveillance); and they identify training needs and impact of training programmes. Participation in EQA assures a laboratory's customers, including clinicians and patients, as well as health authorities, that the laboratory is producing reliable results. Currently, in most countries participation in EQA schemes is voluntary, although laboratories are increasingly seeking enrollment to meet accreditation requirements, which requires EQA participation for tests included in the scope of accreditation.

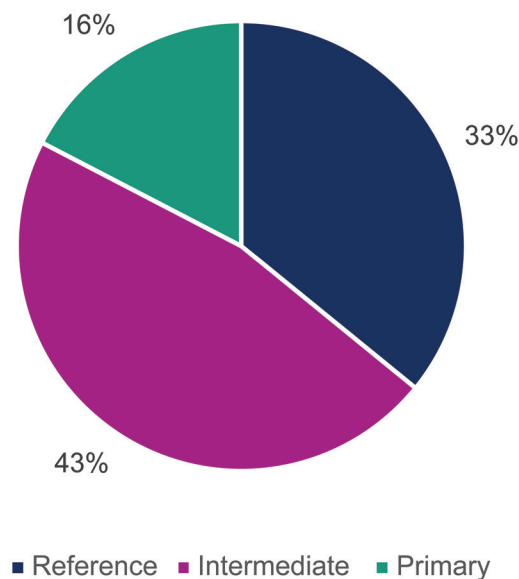


Figure 1. Types of laboratories participating in EQA in Africa, 2016-2018. Primary laboratories included district, sub-county or community level laboratories. (Source: ASLM)

Each EQA approach has advantages and disadvantages. PT schemes cannot adequately assess the pre-analytical phase of laboratory testing, although some may incorporate an element of sample preparation, such as staining of fixed slides. PT schemes can target a single test or a range of tests, can be organised at regional, national and international levels, and should be certified to meet the international ISO 17043 standard for proficiency testing, which affirms the quality of the PT scheme¹⁶. Retesting samples is a time-consuming exercise and requires recognised expertise at testing points. Samples need to be selected randomly and the number of samples must be sufficient to provide statistically significant data on laboratory error. On-site evaluation is ideal but has limited practical application; its value also depends on the expertise of the assessor. However, on-site assessments give a true picture of a laboratory's overall performance and offer real-time guidance for improvements. Of all approaches, PT is the most cost-effective, and on-site assessments the most costly. All EQA schemes should be supportive and educational, never

punitive, and therefore time to delivery of reports is critical, since delays are unhelpful and demotivating to staff.

Two recent surveys were conducted under the Fleming Fund programme, coordinated by the African Society for Laboratory Medicine, to explore participation in EQA for antimicrobial susceptibility testing (AST) by laboratories in sub-Saharan African countries. In one survey, a questionnaire was submitted to laboratories performing AST testing during 2016–2018 in 12 countries in West, East,

Central and Southern Africa (Edwin Shumba, *personal communication*). Of 344 responding laboratories, 182 (53%) reported participation in inter-laboratory comparison or EQA schemes for pathogen identification and AST. Of these, 33% were reference laboratories, 43% intermediate level laboratories, and 16% primary (district, sub-county or community) level laboratories (**Figure 1**). A quarter of reference laboratories did not participate in EQA schemes for AST.

The second study explored the scope, coverage, uptake and business models of regional EQA programmes in 11 sub-Saharan African countries through a literature review, and key informant interviews with representatives of national public health laboratories and seven regional and international EQA providers (Tjeerd Datema, *personal communication*) (**Box 1**). A range of EQA programmes offered proficiency testing panels for AST in Africa, including programmes supported by the World Health Organization Regional Office for Africa, governmental, private-not-for-profit, and private-for-profit organisations; the majority were provided at no cost to participants. International EQA providers included the United Kingdom National External Quality Assessment

Scheme, College of American Pathologists, Centers for Disease Control and Prevention and One World Accuracy. Examples of EQA providers offering PT panels for AST at regional level were the National Institute for Communicable Diseases, South Africa^{17, 18}; the Zimbabwe National Quality Assurance Programme; and Human Quality Assessment Services, Kenya. In Kenya,

The presentation containing details on the literature review and interviews are available upon request from author Tjeerd Datema, t.datema@datos-advice.nl.

BOX 1.

Nigeria, Uganda and Tanzania, national EQA programmes operated by the countries' national public health laboratories include samples for AST. A major challenge for many regional and national EQA providers was achieving financial sustainability: most regional and national programmes were not breaking even. Other challenges were related to logistics (panel production; transportation – especially across borders – and assuring sample integrity during shipment); communication with participating laboratories, and data management.

The study highlighted the relatively low response rates by enrolled laboratories in Africa. Reasons included reagent stock-outs, inadequate laboratory staffing, non-functional equipment, inability to reconstitute EQA samples, poor appreciation of the value of EQA, lack of confidence in scheme quality, absence of policies and regulatory frameworks that mandate participation in EQA, and fears of repercussions based on outcomes.

Although these studies focused on provision and participation in EQA for AST, these findings can be generalised to EQA provision and participation in general. The diversity of challenges identified for both

providing and participating in EQA programmes show that diverse interventions are required at all levels of national laboratory systems. To ensure financial sustainability, whether donor funded, supported through national budgets, private-not-for-profit (run on a cost-recovery basis), or private-for-profit, mapping of costs of EQA programme operations is essential. Major costs

include fixed costs, such as personnel, equipment and infrastructure, and variable costs, such as reagents and consumables, panel distribution, and communications. Identifying all direct and indirect costs is essential to designing viable business models that can assure sustainable, quality EQA programmes across the continent.

To reduce barriers to EQA participation and uptake, countries need to establish national laboratory (quality) policies and regulatory frameworks that facilitate development of home-grown EQA schemes, importation of EQA panels, rapid distribution of EQA panels across countries, effective communication and information management systems with rapid return of results, and mandatory participation. One pivotal measure is the introduction of a laboratory licensing system requiring laboratories to implement a quality management system in compliance with international standards (such as International Standards Organization 15189, the international standard for quality and competence of medical laboratories) or tiered national laboratory standards. The impact of EQA programmes is maximised when quality management system processes are in place to address non-conformities, and areas of improvement are identified for continuous laboratory quality improvement. The interventions needed are complex and cannot

be implemented by laboratories and EQA providers alone. Continued advocacy and sustained action is required from organisations at international and regional levels, including the Africa Centres for Disease Control and Prevention and partners, national governments, and national and international laboratory associations alike.

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What is the difference between quality control, quality assurance, external quality assessment and quality management system?

Many people still struggle with or get confused by these terms: quality control (QC), quality assurance (QA), quality management system (QMS) and external quality assessment (EQA). Although these terms are different, some activities under these topics are interrelated. In order to clarify the difference, I will define each of these terms as they relate to the field of laboratory medicine. It is also important to highlight upfront that medical laboratory quality has evolved over several decades, with the initial focus on QC of examination methods expanding to QA of process performance, and more recently, implementation of a QMS for an integrated systematic approach to quality throughout the entire laboratory.

Quality Control

QC is defined as a set of procedures designed to monitor the test method and the results to ensure appropriate test system performance. Complete performance of QC must include testing QC materials (controls), charting the results on control charts, analyzing the results, then

performing root cause analysis and taking corrective action when the results are out of control. QC is not performed primarily to fulfill a requirement, but to ensure that reportable results are authentic and free from performance errors arising from methods, machines, materials, man or environment.

Quality Assurance

QA is defined as a part of quality management focused on providing confidence that quality requirements will be fulfilled. QA is the day-to-day practice that encompasses all procedures and activities directed toward ensuring that a specified quality of product or service is achieved and maintained. In the testing environment, this process includes monitoring of raw materials, supplies, instruments and procedures; specimen collection, transport, storage and processing; recordkeeping; calibration and maintenance of equipment; quality control procedures; proficiency testing; training of personnel; and all else involved in the production of the data reported.



Patrick Mateta

**Vice-President,
Global Health
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Clinical and Laboratory
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United States of America

Mr. Patrick Mateta is a medical scientist by profession who has mentored and conducted laboratory audits in more than 22 countries spread across four continents. He has also facilitated workshops that have trained 1000+ laboratory professionals. Mr. Mateta oversees laboratory strengthening activities at CLSI, which is active in more than 12 countries on four continents.



Elements	QC	QA	QMS
Focus	Method control	Process management	Laboratory-wide system
Scope	Verified examination method controlled to ensure production of correct results by: <ul style="list-style-type: none"> • Instrument's internal controls • Manufacturer's control materials • Purchased external control materials 	Accuracy and efficiency of: <ul style="list-style-type: none"> • Pre-examination processes • Examination processes • Post-examination processes 	Effectiveness and sustainability of the management and technical processes that support and move work through the laboratory
Limitations	Does not prevent pre-examination or post-examination errors	Does not prevent errors that occur outside the path of workflow processes listed above	No limitations, by including all aspects of laboratory management and technical operations
Evolution of levels	QC was the beginning of quality measures in the medical laboratory.	QA's process focus is broader than QC's method focus.	A QMS's system-wide focus is broader than QC's method focus and QA's process focus.

Adapted from CLSI's QMS01: A Quality Management System Model for Laboratory Services, 5th Edition (2019).

Quality Management System

A QMS is a systematic approach that describes, documents, implements, measures, and monitors the effectiveness of laboratory work operations in meeting regulatory and accreditation requirements and that promotes the efficient use of resources. The ultimate goal of this activity is to meet the expectations of laboratory customers. It ensures that the organizational structure, responsibilities, policies, processes, procedures and resources to direct, control and improve an organization with regard to quality are clearly defined and documented. The table below compares these three different aspects of quality:

It must be noted that although some laboratories have successfully implemented a QMS, in much of the world, many laboratories are operating at or below the QA level. The need to upgrade to a QMS approach has become evident from worldwide reports describing medical errors in present-day healthcare systems and from reports of the cost of both good and poor quality on laboratory operations. Therefore, maintaining QA requires an integrated QMS approach that provides an opportunity to deliver consistent, high-quality and cost-effective laboratory services.

External Quality Assessment

Finally, there is EQA, a system for objectively checking the

laboratory's performance using an external agency or facility. EQA allows for comparison of a laboratory's testing to a source outside of the laboratory, such as peer group or reference laboratory. In many settings, EQA is used interchangeably with proficiency testing (PT). However, PT is just one of the methods for conducting EQA. Rechecking or retesting, e.g. slides that have been read are rechecked by a reference laboratory, is another EQA method. When it is difficult to conduct traditional PT or rechecking, for example, in instances of very contagious pathogens or during emerging infections, EQA can be conducted by on-site evaluation.

Meet Patience Dabula

Patience Dabula has been a National Quality Assurance Manager at the South African National Health Laboratory Service (NHLS) since 2011. She has a Master's degree in Biomedical Technology with 18 years' experience in implementing Total Quality Management for different ISO standards in public health and clinical trial laboratories, Proficiency Testing Schemes (PTS) and Support Service departments. She is a Strengthening Laboratory Medicine Toward Accreditation (SLMTA) Hero and 'Patron of SLMTA' who leads the implementation of SLMTA in South Africa. She is the South African Stepwise Laboratory Improvement Process Towards Accreditation (SLIPTA) Focal Point, South African National Accreditation System (SANAS) Lead Assessor and a member of three ISO committees of the South African Bureau of Standards (SABS). Under her leadership, the NHLS accredited over 60 laboratories. Mrs Dabula heads one of the Southern African Development Community (SADC) Regional Centres of Excellence (RCE) for Quality, is in charge of the Health Technology Assessment Unit (HTA) and the NHLS's PTS providing over 30 schemes to more than 25 Countries, the latest being SARS-CoV-2 PTS. She is a member of, and has served on, several committees, including the WHO Technical Working Group that developed guidelines on post market surveillance (PMS), the Quality Control for Molecular Diagnostics (QCMD) PTS International Advisory Board, the South African Point of Care Testing (POCT) Policy development committee and the Pan African Harmonization Working Party (PAHWP). Her work experience includes Branch Manager in Quality Assurance, part-time Lecturer in a University of Technology, Analytical Project Manager, Project Manager and Training and QA Officer supporting laboratories in several African countries and in India.



Patience Dabula

What key experiences from your childhood, schooling or professional training led you to a career in laboratory medicine?

I am a Medical Technologist who specialized in Microbiology and later found a home in quality assurance. It was during my high school years when a University of Technology sent their marketing department to talk to students about possible careers to follow when I first heard of Medical Technology. I knew then that this was a career for me. Following that I chose the subjects that would allow me to qualify for it and the rest is history.

As the National Manager for Quality Assurance at South Africa's National Health Laboratory Service, what is your day-to-day role? How did you become the National

Quality Assurance Manager for the NHLS (what was required, what previous experience helped you get where you are)?

Days are different but there are few common activities that

are always taken care of daily. I advise both NHLS's internal and external customers on quality related matters, and I develop and review documents related to policies, processes or procedures. There are many activities related to accreditation of laboratories or ISO Certification of support services with various stakeholders. This might include audits, training, representing NHLS at meetings, implementing new systems, or dealing with finance. I oversee provision, development, improvement and analysis of proficiency testing schemes and human resource management.

The position required a medical laboratory professional with the following experience: 10 years of laboratory work, laboratory accreditation, management and a proven track record in quality management. When I started the



Patience Dabula with ASLM 2018 Co-Chair, NHLS AARQA Executive, South African CDC Laboratory Advisor, NHLS Project Manager after receiving 27 awards for laboratory accreditation at the ASLM 2018 conference in Abuja, Nigeria, in December 2018. [Photo: ASLM]

job in 2011, I had worked as a Technologist in a laboratory for over 10 years, had implemented Quality Management Systems in laboratories and had four of them accredited. I had spent time training and acting as a QA Officer supporting laboratories in several African countries and India, and I had experience as a Quality Manager, Analytical Manager and Project Manager in clinical trial laboratories. In addition, I had served as a part-time Lecturer at a University of Technology and had over five years' experience as a South African National Accreditation System (SANAS) Lead Assessor.

What is the relationship of the National Health Laboratory Service to ASLM?

The NHLS is one of the organizations that was actively involved in the formation of ASLM in 2011. It played a fundamental role in ASLM conferences and chaired the first round table for the Ministerial Call for Action in 2012. Managers of the NHLS Co-Chaired the ASLM 2014 and 2016 conferences in South Africa.



Patience Dabula with three PTS staff members and two students from local schools during South Africa's Cells C Annual Take a Girl Child to Work Day in May 2018. [Photo credit: Guy Hall, NHLS]

The NHLS takes part in many ASLM activities and in addition provides ASLM with leadership support in several of its initiatives including response to the COVID-19 pandemic and previous epidemics, providing proficiency testing and availing Master Trainers and Auditors for SLIPTA in many countries.

What do you see as the most important emerging challenges related to quality assurance in Africa over the next 5 years?

With the COVID-19 pandemic consuming a lot of resources in both developed and developing countries, funding for Quality Assurance activities may be compromised as countries focus on other priorities and recover from the financial drain. Additionally, the focus to get more laboratories accredited has shifted. Laboratories are losing staff members due to infections, and accreditation bodies both in and out of the continent are not conducting an initial assessment during travel restrictions.

Separate from the impact of the pandemic, participation in External Quality assessment and Proficiency Testing Schemes is decreasing. This is partly due to donor funding diminishing over several years in many countries. Countries are also still not prioritizing quality in their budgets as economies continue to be further challenged, especially now in 2020. Chances are this also affects setting up of internal quality controls during testing.

How can ASLM work with your organization and others in



Patience Dabula with Proficiency Testing Scheme staff in during shipment when the NHLS was shipping the first SARS-CoV-2 PTS in June 2020. [Photo credit: Mahlatse Maleka, NHLS]



your position to meet those challenges?

ASLM has quality of laboratory services as one of its strategic pillars and this has been seen in several of its initiatives including accreditation. ASLM can continue using organisations like the NHLS in various countries to advocate for funding quality-related activities, as these will improve lives and reduce mortality rates on the continent. We can guide decision makers to understand

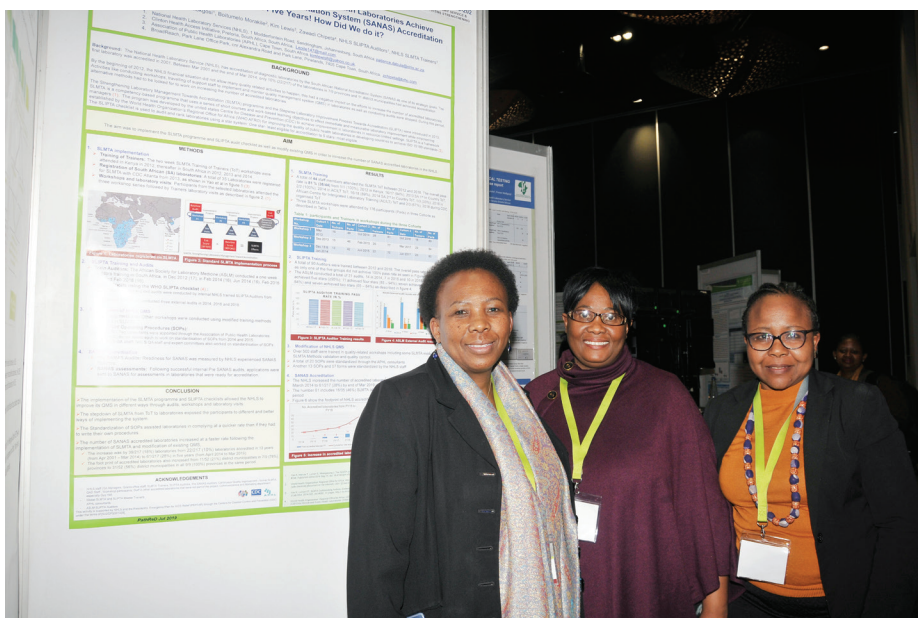
that it is cheaper to have reliable, good quality results to guide policy and control the spread of diseases. It is also important to continue sharing experiences and resources to further implement activities that have been successful through available platforms.

What is your best advice for the next generation of African laboratory scientists? How can they best equip themselves

and their communities for the challenges to come?

A career in laboratory science is diverse, it allows you to branch out to many different fields that are interesting. It is important to identify areas of interest early in your career, so that you can further your studies and concentrate on strengthening your skills in those areas.

There are many training platforms, use them to equip yourself. Countries on the continent need leaders that are dedicated to making a difference in their working area then share their experience with others. The same way our borders are porous when it comes to infections and diseases, you should also be that way when it comes to productive information sharing. The continent needs all of us to put our heads together, share the available resources and close gaps to the benefit of Africans. Prepare yourself to be versatile and flexible, so that you can easily adapt and respond to areas where laboratories are needed in addressing different communicable and non-communicable diseases facing us now and in the future.



Patience Dabula near her poster with NHLS SLIPTA Trainers, Internal and Pre SANAS Auditors who are also ASLM and NHLS SLIPTA Auditors during the NHLS Pathology and Research Development Congress in July 2019. [Photo credit: Guy Hall, NHLS]

Improve EQA sustainability in Africa: Think like an economist

In our experience, it is easy to start a national external quality assessment (EQA) program, but very difficult to keep it going. While this is probably a general principle for all activity (dieting and exercise come to mind), we have reflected on the underlying reasons why this is so for EQA and, more importantly, whether there are ways to systematically improve sustainability. This paper explores how thinking like an economist could improve EQA sustainability in Africa, and globally. It proposes development of an online open source dashboard integrating disparate sources of data to allow EQA providers to focus their efforts in the most effective manner possible. The fundamental question we ask is:

How might an economist allocate a scarce resource – money – to maximize public health improvement in selecting EQA programs and prioritizing participation and remedial follow-up?

Our group is an accredited EQA provider with a social enterprise commitment to make EQA globally sustainable. We have almost 20 years' experience training national EQA providers around the world. In Africa, we have worked with more than 30 current and aspiring national EQA providers. These groups are typically laboratory oversight bodies, public health agencies and national reference laboratories, which operate under their respective ministries of health.

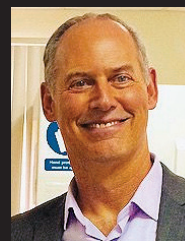
In practical terms, an EQA provider generally has fixed funds. At issue is *which programs and remedial follow-up should it provide and to which participants?* Those deceptively simple questions were posed to us when we were invited several years ago to join an African national EQA advisory

board. Those questions yielded a straightforward, three-part conceptual answer.

First, EQA providers should select EQA programs that correspond to the burden of disease in their countries. The definitive resource here is the Global Burden of Disease dataset compiled by the Institute for Health Metrics and Evaluation (IHME) of the University of Washington <http://www.healthdata.org/>. EQA providers can use this dataset to identify ranked causes of death in their countries with metrics of premature deaths (yearly lives lost [YLL]), disability (years lived with disability [YLD]) and the sum of both (disability-adjusted life years [DALY]). EQA providers can then select programs that correspond to diseases with the greatest DALY in their countries. Linking national EQA strategy to specific diseases with quantified DALY to specific tests provides a rational, economic basis to select and prioritize EQA programs.

In our experience, most EQA providers select EQA programs that correspond to diseases of major burden in their countries. While they clearly understand DALY, YLL and YLD, these concepts do not explicitly inform their selection of EQA programs, nor do they figure in calculating efficacy of their programs. The root problem is that EQA, as currently conceived, simply does not provide convenient access to this information to guide their selection of EQA programs. A good start would be to link EQA to curated datasets on local disease burden from IHME to provide objective selection criteria.

Second, EQA providers should prioritize participants for a given programme ranked by their volume of patient testing. A subscription in an EQA programme has the same cost independent of patient



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Global Burden of Disease (GBD)

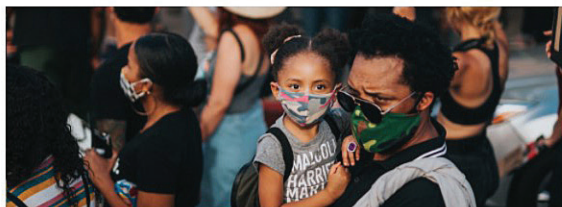
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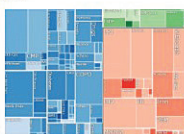


The Lancet: Latest global disease estimates reveal perfect storm of rising chronic diseases and public health failures fuelling COVID-19 pandemic

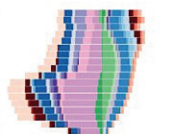
Most comprehensive global study—analysing 286 causes of death, 369 diseases and injuries, and 87 risk factors in 204 countries and territories—reveals how well the world's population were prepared in terms of underlying health for the impact of the COVID-19 pandemic.



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test volume. However, the value of an EQA programme scales directly with patient test volume. Here's a simple example. Laboratory A performs 100 HIV viral load tests per month. Laboratory B performs 1000 HIV viral load tests per month. If an EQA provider can fund only one EQA subscription, should it go to laboratory A or B? An economist would select laboratory B as its test volume, and accompanying opportunity for improvement, is ten times that of laboratory A. Selecting laboratory A over B would be a clear misallocation of scarce EQA funding. Our observation is that testing typically conforms to a Pareto distribution, in which 80% of testing is done by 20% of laboratories. To an economist, prioritizing EQA to those 20% of laboratories would be economically efficient and maximize potential public health improvement.

In our experience, EQA providers clearly understand the concept of allocating scarce EQA subscriptions based on test volumes. But

they lack information on their participants' test menus and test volumes that would enable them to do so. Again, the root problem is that EQA, as currently conceived, simply does not capture this information so that it can be used by EQA providers to allocate EQA subscriptions. The obvious fix is to re-engineer EQA to capture test menus and test volumes. Third, EQA providers should prioritize remedial follow-up to participants based on patient impact. This essentially re-uses the logic of patient test volumes. Here's another example. Let's assume that there is a defined, efficacious, remedial follow-up that costs \$2000 United States dollars (USD) per laboratory. Laboratory C performs 10 HIV viral load tests per month and fails 80% of its EQA. Laboratory D performs 10 000 HIV viral load tests per month and fails 20% of its EQA. If an EQA provider can only fund one remedial follow-up, should it go to laboratory C or D? In other words, *should remedial follow up be*

prioritized based on failure rates or patient impact? To the economist, the answer would be crystal clear. Providing a \$2000 USD remedial follow-up to laboratory D would improve 24 000 patient test results per year, at a cost of \$0.83 USD per result. The same remedial follow-up to laboratory C would only improve 96 patient test results per year, at a cost of \$20.83 USD per result.

Again, in our experience, EQA providers understand the concept of prioritizing remedial follow-up based on patient impact. But since they lack patient test volumes, they typically prioritize remedial follow-up based on failure rates. Moreover, creating effective remedial follow-up is very difficult given the inherent complexity of testing, and the number of variables affecting aberrant performance. Once again, EQA as currently conceived, simply does not capture sufficient information to enable EQA providers to properly diagnose aberrant performance and provide informed remedial follow-up. A good start, however, would be to extend EQA to include standardized troubleshooting checklists by discipline, and to use data from other quality processes such as internal quality controls and the Stepwise Laboratory Quality Improvement Process Towards Accreditation to inform remedial follow-up.

An economist would observe that EQA providers do not make explicit economic cases for EQA investment by governments, international groups, participants and in vitro diagnostics manufacturers (in countries with reagent tenders). It is taken as an article of faith at laboratory conferences that EQA is an investment, not a cost. Fair enough, but the economist would naturally ask for the return on investment (ROI) for a given EQA investment. The inability to present a credible, detailed ROI

for EQA puts EQA providers at a competitive disadvantage. EQA funders themselves have their own scarce resources which they need to allocate among multiple, competing uses. Receiving a cogent ROI for EQA would enable them to make an informed business case for investing in EQA versus other opportunities.

EQA providers are generally passive recipients of EQA funding. Providing ROI for EQA would enable them to more actively propose funding scenarios to EQA funders. To be sure, creating a cogent ROI for EQA investments is complicated and would definitely require clear guidance and expertise from healthcare economists. But economists in general, and healthcare economists specifically, routinely tackle complicated problems and create workable, extensible models.

Presenting EQA with a cogent ROI would significantly change the conversation with EQA funders. For example, a funder could seek to invest \$X for each of three years with a national EQA provider. The provider would create a projected ROI for programmes selected on burden of disease (DALY, YLLs, YLDs) and allocated to participants whose collective test volumes represent the Pareto 80 / 20 distribution. The EQA provider would measure performance at baseline and at each successive test event. These data, shared with the funder, would track changes over time with associated clinical impact and support a calculation of actual versus projected ROI.

These concepts have been well received by EQA providers. They

readily appreciate how integrating economic principles into EQA could improve sustainability. But, these concepts have not been made operational by any EQA provider as there are many parameters that no one has yet combined into a functioning dashboard. Since every big project can be broken down into smaller, more manageable components, we have identified the following suggested components for this dashboard: Third, EQA providers should prioritize remedial

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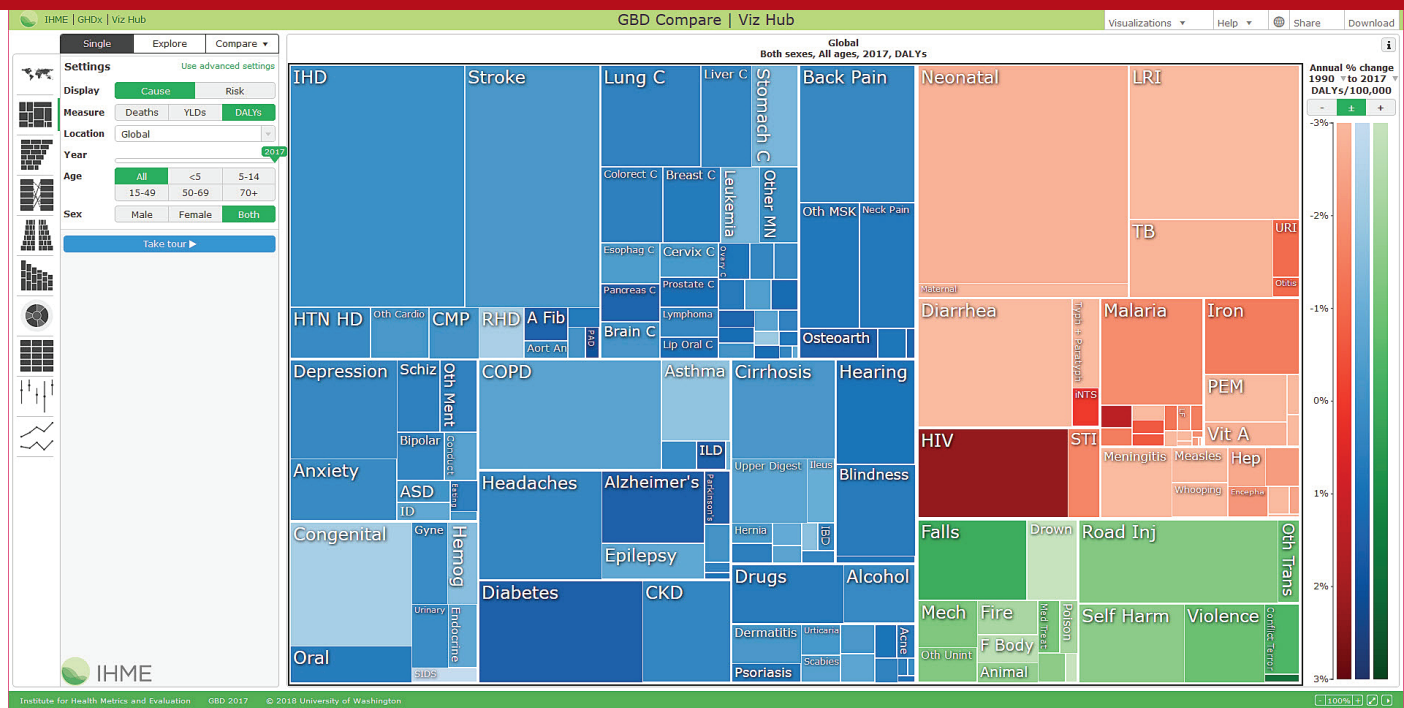
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Gerd Altmann from Pixabay

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GBD Compare Tool landing page from the IHME website

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components, we have identified the following suggested components for this dashboard:

- (1) Link curated data on local burden of disease from IHME,
- (2) Wap disease burden to specific tests and associated EQA programs,
- (3) Add participants' test menus and test volumes,
- (4) Properly cost EQA programmes,
- (5) Include standard troubleshooting checklists by discipline,
- (6) Access data from IQC, SLIPTA and other quality processes to inform remedial follow-up and
- (7) Develop cogent ROI models for EQA with healthcare economists.

We believe this project lends itself to an agile, iterative, collaborative approach to create an open source, online dashboard to assist EQA providers and funders to allocate scarce EQA funding to maximize public health impact. We invite discussion from those interested in participating in this potentially transformative project.

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Fleming Fund Regional EQA Grants for Africa and Asia:

Comparing approaches to implementation

Background

The Fleming Fund is a United Kingdom-based aid programme to help low- and middle-income countries to generate, share and use antimicrobial resistance (AMR) data. In 2018, Round 2 of its Regional Grants was launched, focused on strengthening the quality of diagnostics for AMR by supporting improvements in external quality assessment (EQA) of laboratory testing, training, quality diagnostics, and policy and advocacy in Africa and Asia. Specifically, the grant aims to strengthen the quality of pathogen identification and antimicrobial susceptibility testing (AST) by increasing the coverage, availability and uptake of EQA programmes for AMR across One Health sectors in both regions.

The African Society for Laboratory Medicine and the Technical University of Denmark are leading consortiums of international organizations in the implementation of the grants in Africa (EQuAFRICA) and Asia (EQAsia), respectively.

Implementing actions were developed from the outcomes of mapping exercises on the coverage, availability and uptake of EQA programmes across One Health sectors, conducted during the initiation phases of the grants and complimented by comprehensive stakeholder consultations (**Figure 1**). Embedded in both implementation strategies are three strategic objectives:

- Strengthen the availability and coverage of EQA programmes for pathogen identification and AST focusing on the 11 priority pathogens of the World Health Organization's Global Antimicrobial Resistance Surveillance System and the Food and Agricultural Organization of

the United Nations, across One Health sectors in Asia and sub-Saharan Africa.

- Increase demand and uptake of EQA for AMR programmes under One Health, in National Reference Laboratories and Centres of Excellence
- Establish/strengthen capacity for the establishment of national EQA programmes.

This article provides a comparative overview of the implementation strategies of the Africa and Asia grants

Increasing coverage of EQA for AMR programmes in Asia and Africa

The Africa Approach: Implement an Africa-coordinated EQA programme operated through regional providers

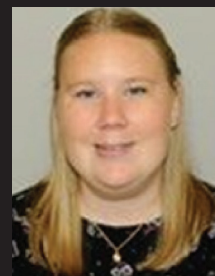
To address the lack of EQA providers in sub-Saharan Africa, EQuAFRICA, the Africa Centre for Disease Control and Prevention, South Africa's National Institute for Communicable Diseases, Public Health England, and the Technical University of Denmark are leveraging the existing regional capacity at South Africa's National Institute for Communicable Diseases, whilst establishing three additional regional EQA providers across One Health sectors. The Institute Pasteur Dakar in Senegal, the Institute Pasteur Abidjan in Côte d'Ivoire and Amref Health Africa in Kenya were selected after a careful assessment of centres of excellence already providing EQA proficiency testing panels in various regions of Africa, or who had the potential to do so.

The four selected providers are being strengthened by EQuAFRICA in all aspects of EQA programme establishment and management. Strengthening activities



Beatrice van der Puije, MSc

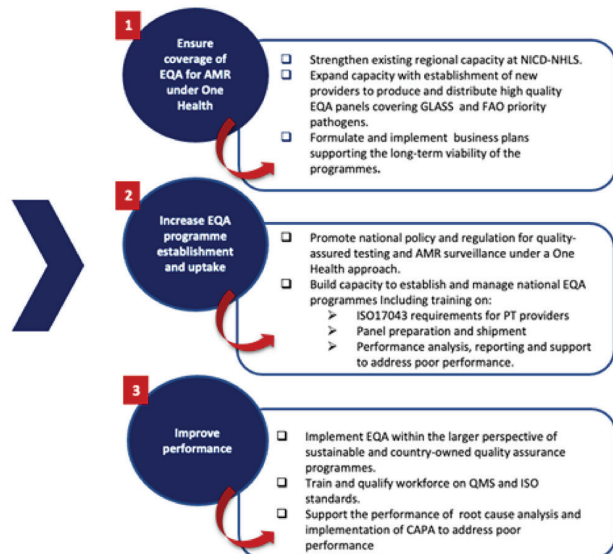
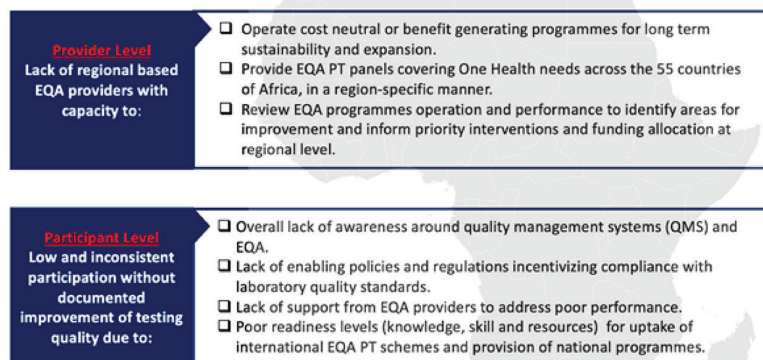
African Society for Laboratory Medicine, Ethiopia



Rikke Braae, MSc

Technical University of Denmark (DTU)

A



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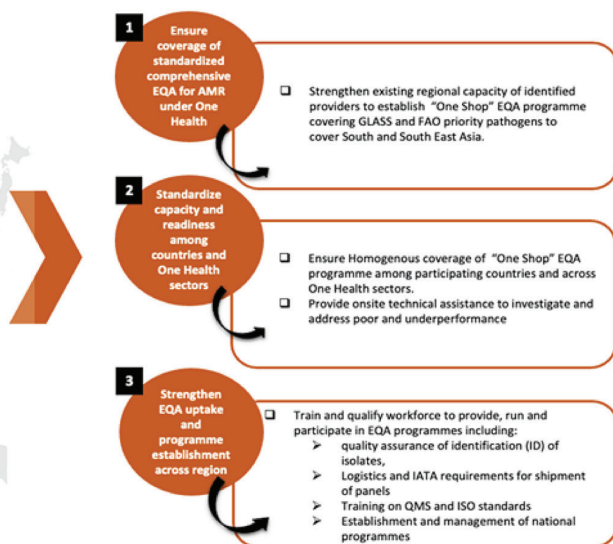


Figure 1. Outcomes of mapping exercises and implementation strategies. A) EQuAFRICA exercises and strategies, which included a focus on performance improvement. B) EQuAsia exercises and strategies, which included startardizing capacity and readiness among countries.

include the delivery of a package of training workshops, secondments, technical assistance and mentorship covering:

- Knowledge and expertise in bacteriology: including pathogen identification and AST.
- Establishment, operation and management of EQA programmes including: ISO17043:2010 requirements for EQA providers, panel manufacturing, shipping panels with adherence to International Air Transport Association certification, results evaluation and reporting, provision of support to participants, and use the programme informatics system.

- Quality management systems and requirements for implementation under ISO15189:2012, ISO17025:2017.

A training and qualification package developed by the Clinical Laboratory and Standards Institute intends to provide certification of the competence of the EQA providers and will be complemented with ISO17043 accreditation. Beyond the training packages, resources will be provided to support the recruitment of key personnel (e.g., microbiologist, information technology experts and administrative staff) and the provision of all necessary

equipment, hardware, supplies and consumables, necessary for the full establishment and management of the programmes. **Figure 2** shows the proposed structure configuration and functions of the EQuAFRICA EQA Programme, which initially will target AMR national reference laboratories in priority countries with a minimum of two events per year.

The Program Steering Committee is led by the Africa Centres for Disease Control and Prevention and includes the World Organization for Animal Health, the United Nations' Food and Agriculture Organization, and the World Health Organization's Regional Office

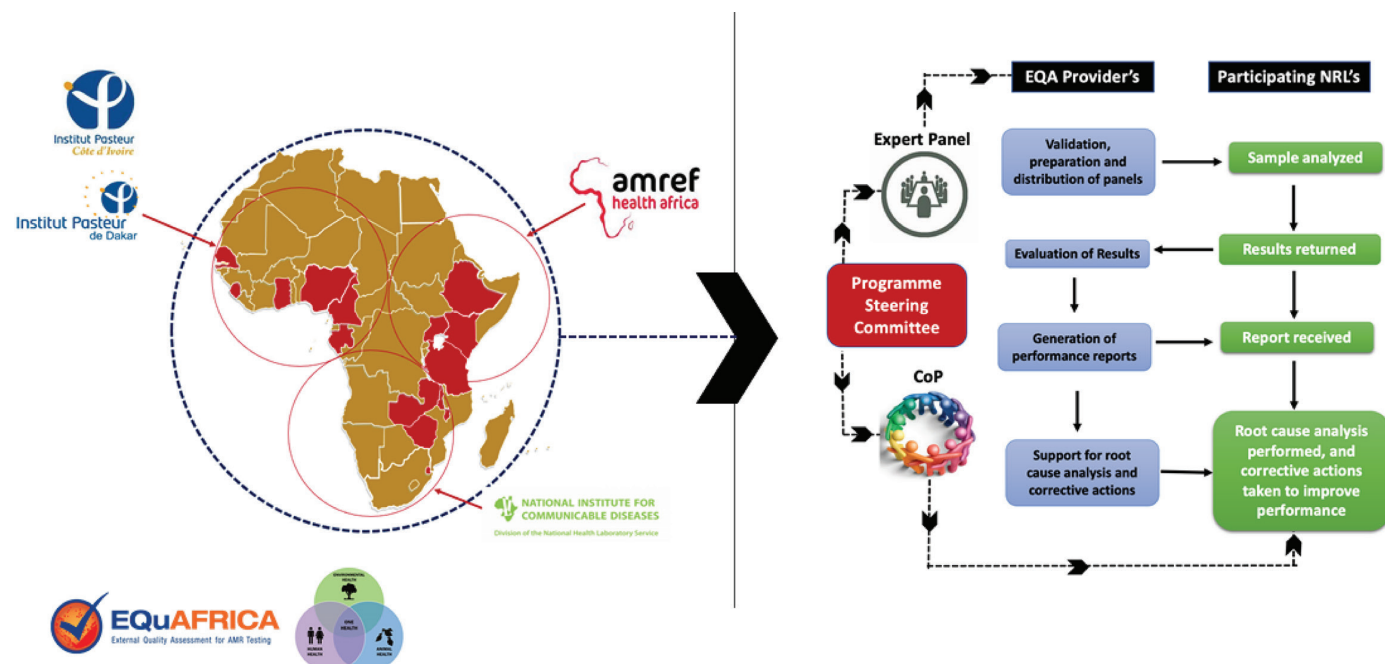


Figure 2. EQuAFRICA programme structure, configuration and functions.

for Africa. The Program Steering Committee is responsible for the overall management, design and implementation of the EQA programme, including proficiency testing panel composition, frequency of distribution and performance criteria. An expert panel within the Program Steering Committee provides technical assistance and guidance to the EQA providers.

Additionally, an EQuAFRICA Community of Practice is being set up to facilitate the exchange of knowledge and best practices to participating laboratories and serve as a resource centre to support laboratory performance improvement. The E-PT tool is web-based, open-source EQA informatics system funded by the United States Centers for Disease Control

and Prevention, which has been selected as the informatics package to manage the EQuAFRICA PT programme. The system, which was developed for HIV viral load and early infant diagnosis proficiency testing programmes, will be further developed to perform all basic functions of EQA programme management and be operable for the EQA providers without

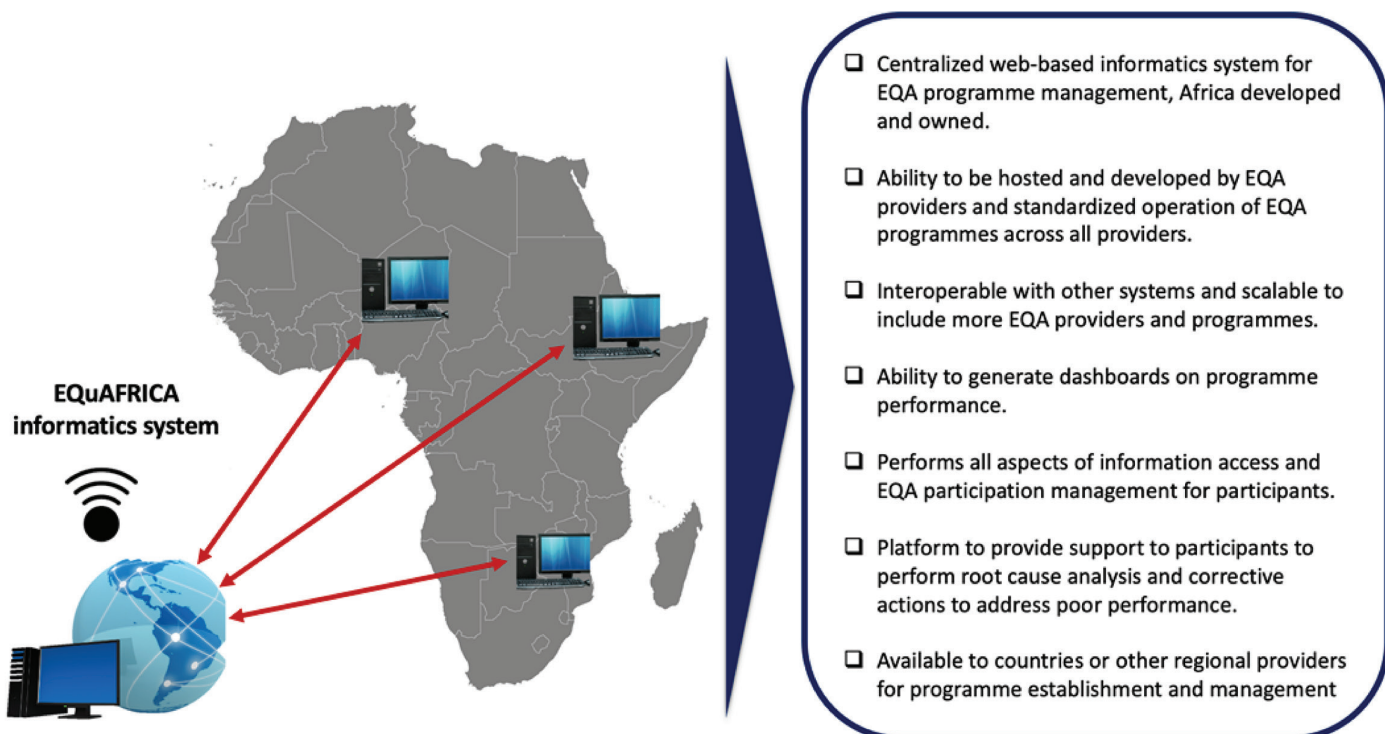


Figure 3. EQuAFRICA informatics system.

EQAsia

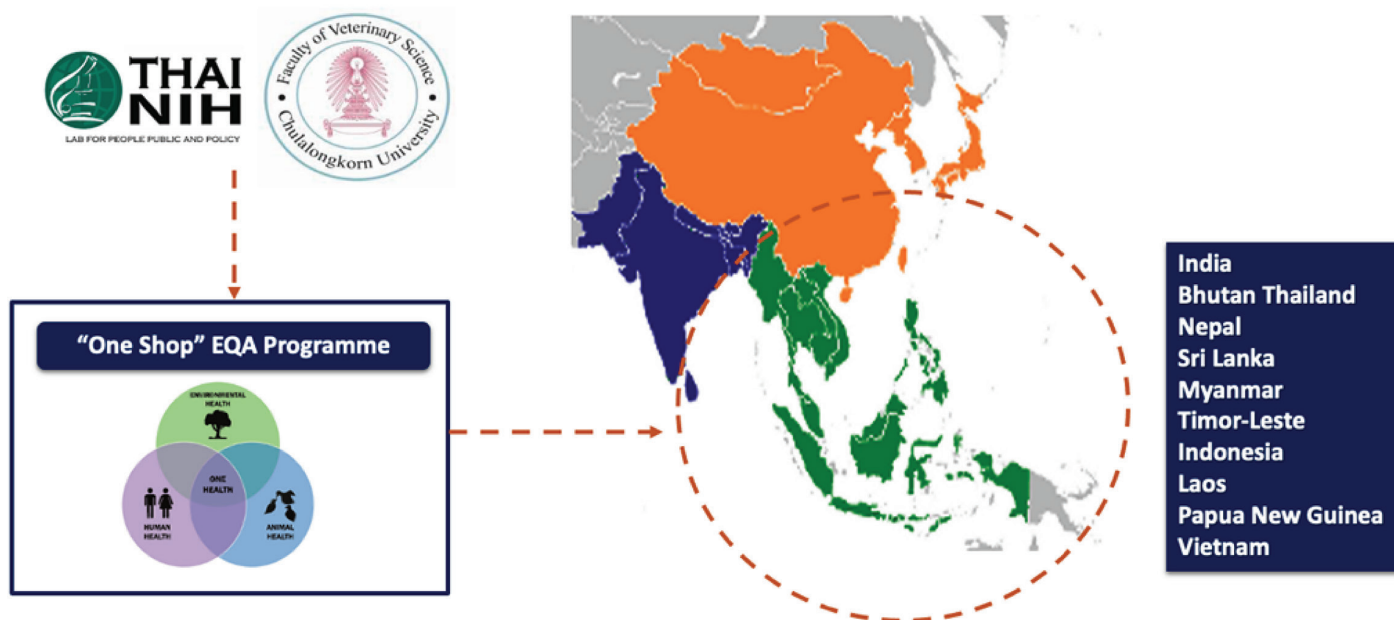


Figure 4. EQAsia programme structure.

additional costs. A key feature is the scalability of the system to multiple EQA providers and different EQA schemes (Figure 3). Actionable dashboards are being programmed as part of the package that will be made available at no cost to organisations and countries within the region, who want to establish EQA programmes. Additionally, a business plan and investment case are being established for providers to operate at a cost-neutral or benefit-generating level, which will contribute to the long-term sustainability of the programmes.

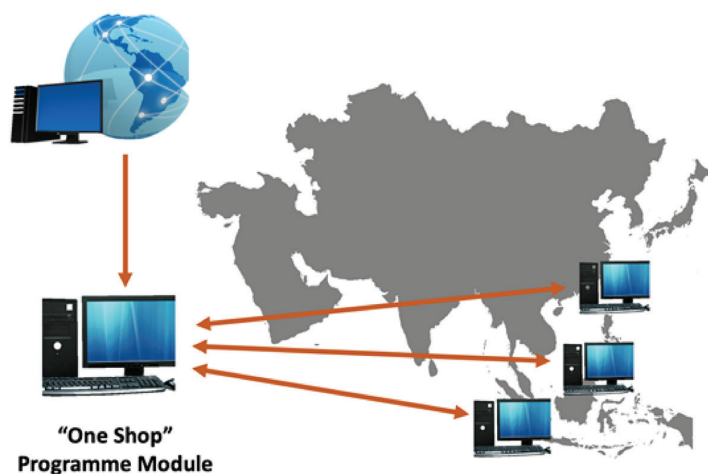
The Asia Approach: Standardize provision of EQA with 'One Shop' programme for AMR

With multiple providers already present across the region, EQAsia is focusing on strengthening the provision of a quality, comprehensive and standardized programme across One Health sectors to address gaps in the content and comprehensiveness of available programmes. EQAsia will strengthen

existing capacity within two identified centres of excellence in Thailand, the National Institute of Health and the Faculty of Veterinary Science at Chulalongkorn University, to provide a state-of-the-art 'One-Shop' EQA programme, free of charge for the South-East Asian region. The programme will be designed to enable laboratories to select and participate in relevant proficiency tests for both pathogen identification and AST. Panel options will include all World Health Organization's Global Antimicrobial Resistance Surveillance System and United Nations Food and Agriculture Organization priority pathogens. This includes a matrix EQA to assess participants' ability to detect extended-spectrum β -lactamase- and carbapenemase-producing *Escherichia coli* in food and ceacal samples from domestic animals. In the One-Shop EQA programme, laboratories will also be able to choose which organisms in the provided EQA they find relevant and have the capacity to participate in (Figure 4).

The One-Shop EQA programme will be supported by an informatics module developed, hosted and managed by the Technical University of Denmark within its existing system (Figure 5). The module will allow users to sign-up to or deselect the EQA offered based on relevance and capacities, as well as capturing methodologies used for both identification of the species, and AST by either minimum inhibitory concentration determination or disk diffusion. Reporting page(s) will allow users to enter results directly, including results from the testing of Clinical Laboratory and Standards Institute reference strain(s). The EQA administrators for the Technical University of Denmark and the providers will have access to all data and be able to customize reports by section and country to obtain an overview of the participants' performance, as well as identify underperformance and users in need of follow-up in the form of capacity building or site visit(s). 'Super-user' rights to the system can be granted

DTU EQA Informatics System



- ❑ Module developed for “One Shop” EQA programme on existing system hosted by DTU
- ❑ Participants registration directly unto system.
- ❑ DTU act as EQA administrators for regional EQA programme and NIH and CU - “super-users” within each OH sector .
- ❑ Super-user”-rights can be granted to individual country NRLs, allowing them to re-use the EQA panels for launching nation-wide EQAs for local and regional laboratories providing monitoring data for the country surveillance of AMR
- ❑ Performs all aspects of information access and EQA participation management for participants.

Figure 5. EQAsia informatics system.

to individual country National Reference Laboratories, allowing them to re-use the EQA panels for launching nation-wide EQAs for local and regional laboratories that provide monitoring data for the country surveillance of AMR. Keeping the programmes free to ensure participation is a priority for EQAsia. Regional and local

donors, including current funders for capacity development in the Asian region, will be identified to contribute to a long-term sustainability plan.

Strengthening EQA proficiency testing establishment, uptake and performance

Both grants seek to increase the demand for EQA proficiency testing by advancing the implementation of quality management systems at both the facility and tiered network level, and by consolidating knowledge and skills around the processing, reporting and corrective actions of EQA with targeted training packages, technical assistance

Acknowledgements



EQuAFRICA Consortium



EQAsia Consortium



Technical University of Denmark



and mentorship. In Africa, a customizable blueprint for the development of National Laboratory Quality Standards and Policies with a focus on quality management system implementation and EQA participation, will seek to address a lack of enabling policies and regulations incentivizing compliance with laboratory quality standards to further encourage the demand and uptake of EQA proficiency testing.

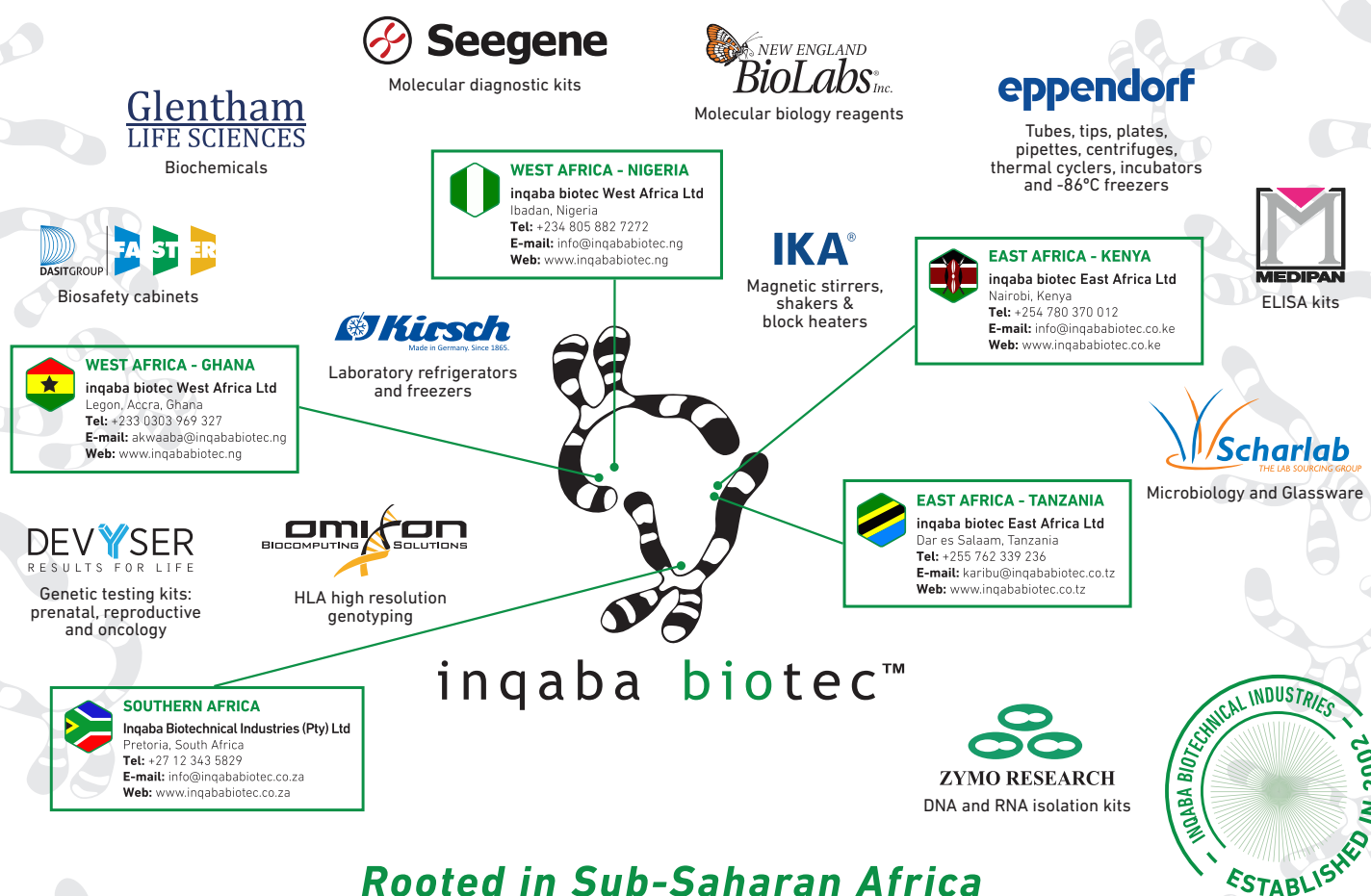
Support to participating facilities to address poor performance will be led by the community of practice established under the EQuAFRICA Program Steering Committee. Providers will also track the performance of corrective and preventive actions with a digital root-cause-analysis form. Annual workshops hosted by the EQA providers will allow feedback

sharing and determination of areas for improvement and provide a platform for participants to collaborate and communicate on EQA challenges and successes. Supportive assessment visits will be the main intervention under EQAsia. Onsite performance assessments will be conducted to identify potential areas for corrective and/or preventive action and guidance provided for the performance of corrective and preventive actions and quality management procedures for continuous quality improvement. Supporting documents such as EQA protocols, guidelines on how to maintain the quality control reference strains, and tutorials (document and tutorial videos) on how to navigate the EQA informatics system, will be provided

to participating sites to further strengthen their performance.

Summary

In addressing the objectives of this grant, the theory of action and approaches of the Africa and Asia consortiums vary in key areas, such as programme establishment, regional ownership and sustainability strategies. There are synergies in approaches to increasing the uptake and establishment of regional and national programmes, with almost identical training packages and infrastructure capacity building activities. Moving forward, engagement and knowledge exchange to share achievements, challenges and lessons learnt during the cause of implementation will be a priority to ensure the achievement of the three core objectives.



Rooted in Sub-Saharan Africa

Offering quality products and services for COVID-19 and general diagnostics

Expansion of SARS-CoV-2 testing through public-private partnership in Uganda

Coronavirus disease 2019 (COVID-19) was characterized as a pandemic shortly after it was first reported in December 2019. Since then, it has spread to over 190 countries worldwide, causing more than 1.5 million deaths with over 66 million confirmed cases as of 7 December 2020 (<https://www.worldometers.info/coronavirus/>). The first case of COVID-19 in Uganda was reported on 21 March 2020 and, over the last 9 months, over 647 471 samples have been tested, 23 200 cases identified and 207 deaths reported as of 6 December 2020 (<https://www.health.go.ug/covid/>).

The rapid growth in the country's testing needs initially focused on points of entry, including land, water and airports, and later on clustered community transmission. This necessitated a quick expansion of SARS-CoV-2 molecular testing capacity from national reference laboratories to subnational level laboratories, including public, private and research laboratories across the country. This structured decentralization started at the national reference laboratories including Uganda Virus Research Institute (UVRI), Uganda National Health Laboratory Services (UNHLS) and Makerere University–Mulago hospital laboratory. Later, sub-national COVID testing mobile laboratories at points of entry and other parastatal, research and private laboratories were added.

To support effective scale up to include parastatal, research and private laboratories, the Ministry of Health, with support from partners, identified laboratories with the capability to support the national COVID-19 response through safe and quality-assured testing. Twelve additional laboratories were identified, and taken through a 'COVID-19 testing accreditation' process that included internal assessment, external assessment,

training on COVID-19 testing, one-time proficiency testing with UVRI and setting up the results management system for successful laboratories prior to their activation.

The partnership between the Ministry of Health and the identified institutional, research and private laboratories was based on the understanding that a collective response was needed to fight COVID-19. The Ministry of Health and identified laboratories agreed on a cost-sharing mechanism. Laboratories agreed to cover costs related to equipment management, including placement, servicing and repair, staff wages, utility bills and overhead cost. The government was required to provide support through ongoing technical assistance, provision of reagents and supplies required for testing and biosafety, and risk allowances for staff.

Whereas the MoH is working on a long-term position, guidance and solution to this, in the interim, implementing partners were encouraged to step in so that the scale up of testing services were not interrupted given the rapidly growing demands. The Africa Centre for Disease Control and Prevention (CDC) / African Society for Laboratory Medicine (ASLM) Resolve Surge COV19 Testing Project is a 6-month project funded by Resolve to Save Lives, an initiative of the global public health organization Vital Strategies. The Project received a formal request from the Uganda Ministry of Health to complement support to one of the laboratories identified for expanded COVID-19 testing.

This identified laboratory is a department within the Mildmay Uganda establishment, a Christian-based NGO with four entities including Mildmay Hospital, Mildmay Institute of Health Sciences, Mildmay Uganda Research Center, and the Projects arm providing health systems strengthening. The Mildmay Uganda



Francis Ocen,

African Society for Laboratory Medicine, Ethiopia



Emmanuel Omony,

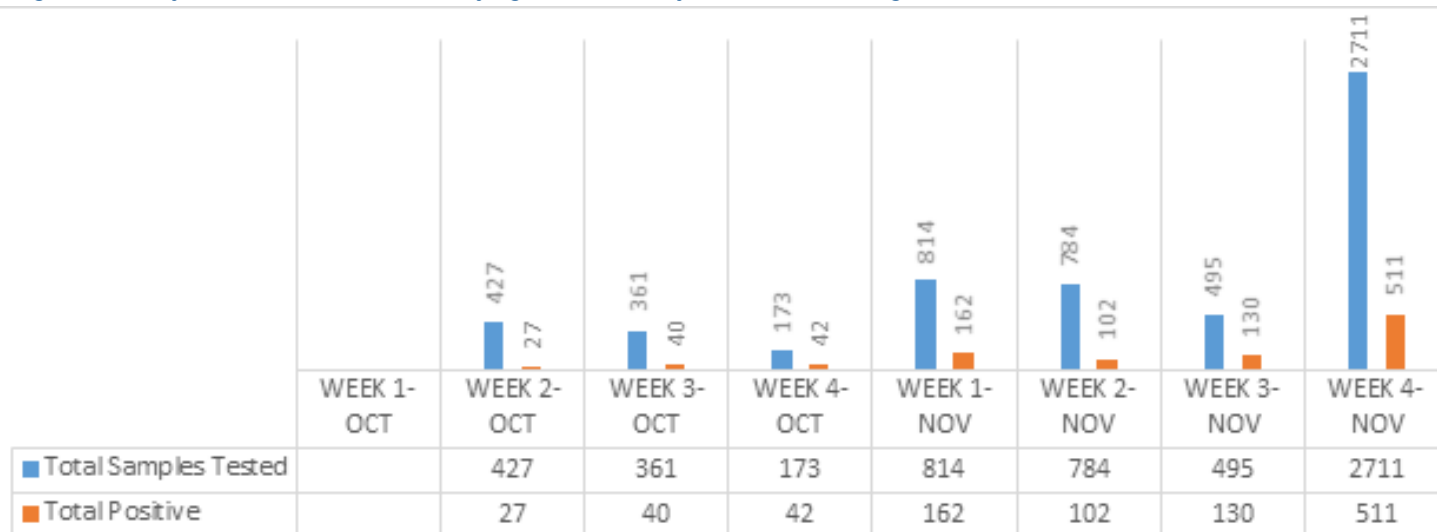
Mildmay Uganda



Susan Nabadda,

Ministry of Health, Uganda

Figure 1. Weekly test statistics for the Mildmay Uganda Laboratory from October through November 2020.



Laboratory, is internationally accredited to ISO: 15189:2012 by the South Africa National Accreditation Systems (SANAS). The laboratory has supported the Ministry of Health as a backup laboratory for HIV viral load testing and early infant diagnosis since 2016 and it was therefore easy to bring the laboratory on board to support COVID-19 testing.

The Mildmay Uganda Laboratory had two testing platforms available that could easily be repurposed for COVID-19 testing: the ABBOTT M2000 (Abbott Laboratories, Abbott Park, Illinois, United States) and the GeneXpert system (Cepheid, Sunnyvale, California, United States), as well as reagents and supplies available from the Ministry of Health. The Africa CDC/ASLM Resolve Surge COV19 Testing Project accepted

the request from the Ministry of Health to provide additional support to cover risk allowance for seven laboratory staff, stationery, training and enrolment into an international external quality assurance scheme.

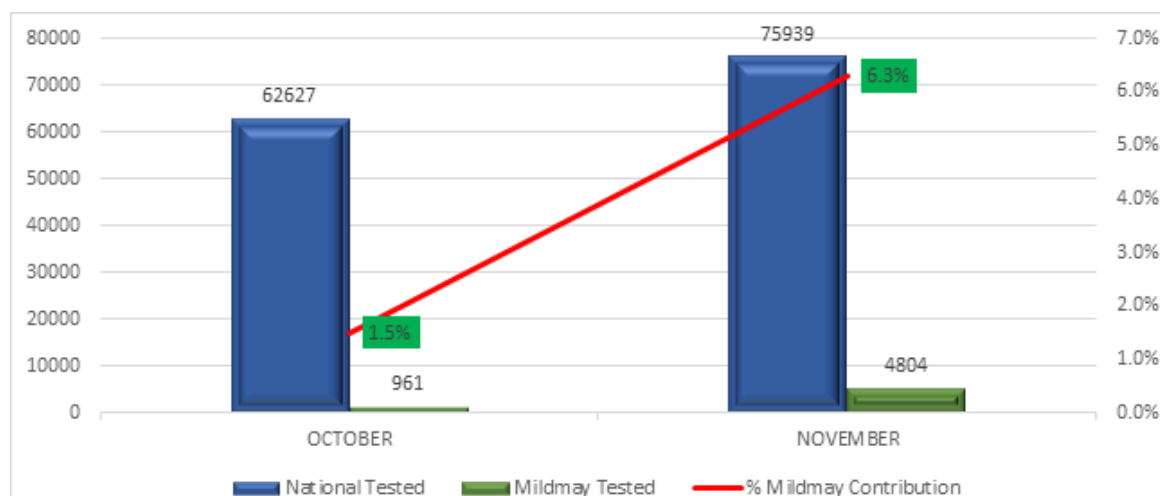
Due to the scale down in COVID-19 testing by reference laboratories to adequately support other programs, including HIV viral load testing, and increasing community spread, the Mildmay Uganda Laboratory is now operating 24 hours a day and continues to fill what would otherwise be a testing gap. A palpable increase in test volume occurred from an average 1000 tests per month in October 2020 to over 4000 tests in November 2020. The test demand increased from an average 320 per week in October to 1200 per week by November

2020 representing a 275% increase in weekly test volume from the first week of support (week 2 in October) and the fourth week of November. Altogether, the Mildmay Uganda Laboratory performed 5765 tests over the period of this support with 1014 new COVID-19 cases identified, representing over 6% of all tests performed in the country (**Figure 2**).

With increased testing needs as a result of widespread community transmission in the country, taking advantage of available laboratory services capacity at research and private institutions through public-private partnerships in Uganda is one way to ease pressure on current testing laboratories. Additionally, these research and private laboratories are positioned to activate a second dimension to their scope by providing direct support to the public

sector. Once such laboratories are demarcated and supported to attain required levels of performance, they naturally form part of the nation's response infrastructure to future epidemics.

Figure 2. Contribution of the Mildmay Uganda Laboratory to national COVID-19 testing.



Providing care to more patients when and where it is needed the most.

Aptima® HIV-1
Quant Dx Assay

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Patient Safety Monitoring in International Laboratories (pSMILE)

Introduction

International travel, teaching, and improving laboratory quality worldwide may not describe the responsibilities of most laboratory professionals, however, the Johns Hopkins University (JHU) Patient Safety Monitoring in International Laboratories (pSMILE) Medical Technologists have taken their clinical laboratory training and skills beyond the bench.

JHU-pSMILE is a National Institutes of Health (NIH) resource designed to evaluate and develop the capability of laboratories to participate in National Institute of Allergy and Infectious Diseases (NIAID) supported prevention, vaccine and therapeutic clinical studies conducted in developing countries.¹ The program ensures the integrity and reliability of laboratory tests for monitoring safety and efficacy of experimental products investigated in studies funded by the Division of AIDS (DAIDS). The pSMILE program has been operating at the Johns Hopkins University (JHU) School of Medicine, Department of Pathology

since the inaugural contract was awarded in 2004.

The four core functions of pSMILE are:

- Monitoring laboratories' compliance with Good Clinical Laboratory Practices Standards (GCLP)
- Monitoring the ability of laboratories to reliably perform protocol-specified laboratory testing
- Providing laboratories with various means of assistance, guidance and training to address and prevent recurrence of deficiencies in GCLP and/or Proficiency Testing (PT) to improve quality of laboratory operations, and
- Hosting and maintaining a computerized data management system and document library that includes laboratory performance data and guidance and resource documents.

The JHU-pSMILE team has developed processes, standard operating procedures (SOPs) and

software systems to accomplish these four core functions. Over the past sixteen years, the program has grown into an organization that is internationally recognized for their Quality Assurance methods. In July of 2020, JHU-pSMILE was awarded International Organization for Standardization (ISO) 9001:2015 certification. The ISO 9001:2015 standard ensures that products and services meet the needs of clients through an effective quality management system. As part of the ISO 9001:2015 certification process, JHU-pSMILE developed and implemented a quality management system to improve overall performance and maintain a high-level of quality and strong customer service.

Throughout the 16-year history of the program, the team has supported 285 laboratories in 31 different countries (**Figure 1**), providing expert laboratory assistance for patient-safety testing. Currently, pSMILE actively supports 144 international laboratories in 18 countries



Figure 1

Continent	Country	# Labs
Africa	Botswana	5
	eSwatini	1
	Ethiopia	2
	Kenya	11
	Malawi	7
	Mozambique	1
	Senegal	2
	South Africa	66
	Tanzania	6
	Uganda	15
	Zambia	1
	Zimbabwe	5
Asia	Cambodia	9
	China	4
	India	14
	Philippines	2
	Thailand	24
	Vietnam	2
	Switzerland	1
Europe	Costa Rica	3
	Dominican Republic	1
	Haiti	2
	Jamaica	2
	Mexico	1
	Panama	3
	Puerto Rico	1
	United States	16
	Argentina	8
	Brazil	39
South America	Colombia	2
	Ecuador	3
	Peru	14

including: 30 in South America, 39 in East Africa, 41 in South Africa, 7 in Southern Africa, two in the Caribbean, 25 in Asia and one in Europe. Laboratories are selected for pSMILE support because they are performing NIAID-sponsored research for HIV/AIDS and its related co-infections and co-morbidities. Research protocols are administered through HIV Clinical Trials Networks such as the AIDS Clinical Trials Group (ACTG), International Maternal Pediatric Adolescent AIDS Clinical Trials Network (IMPAACT), HIV Prevention Trials Network (HPTN), HIV Vaccine Trials Network (HVTN), and Microbicide Trials Network (MTN). pSMILE also supports non-network studies funded by DAIDS. JHU-pSMILE has also been called upon to assist with emerging infectious diseases such as the Zika virus outbreak in 2016 and the SARS CoV2 pandemic in 2020.

pSMILE overview

The pSMILE resource is managed by the NIH Division of AIDS by a Contracting Officer's Representative (COR) who administers and directs all activities. At JHU, pSMILE activities are led by a Principal Investigator and a Project Manager who oversee daily operations and staff including:

- Ten registered Medical Laboratory Scientists who serve as International QA/QC Coordinators
- A Program Officer managing financial accounting and invoicing
- A Programmer Analyst providing website development and management
- An Administrative Coordinator performing administrative and clerical functions and
- Information Technology Consultants providing targeted specialties and expertise as needed

This dedicated team of professionals comes from diverse cultural backgrounds and speak multiple languages, providing a unique basis of understanding and pertinent global sensitivity that are beneficial for the pSMILE international mission. Members of the current JHU-pSMILE team have worked in the field of Pathology and Laboratory Medicine ranging from 12 to 40 years in both the United States and globally, and have a combined total of greater than 200 years of laboratory experience. JHU-pSMILE Coordinators are credentialed by a range of Clinical Laboratory certifying bodies including the American Society for Clinical Pathology (ASCP), American Medical Technologists (AMT), and the Department of Health Education and Welfare (HEW). JHU-pSMILE also has a team member who holds certification from the American Society for Quality (ASQ) as a Certified Quality Process Analyst (CQPA). The team members' laboratory experience is as varied as their educational and cultural backgrounds, ranging from large university hospital laboratories, commercial laboratories, international research and clinical laboratories, doctor's office laboratories and more. They also have a wide range of knowledge and practical experience covering nearly every specialty in the clinical laboratory including: Chemistry, Hematology, Immunology, Flow Cytometry, Serology, Microbiology, Mycobacteriology, Histology/ Cytology, and Blood Bank. Team members also possess advanced degrees such as Masters in Business Administration (MBA), Masters in Distance Education (MDE), and Master of Science (MS) in Biotechnology

JHU-pSMILE Coordinator training

In order to develop the skills

required to be a JHU-pSMILE Coordinator, new employees complete a rigorous training program. They receive training on all pSMILE internal procedures and are mentored by assigned trainers who are experienced members of the JHU-pSMILE team. By using a virtual education platform, training is standardized, comprehensive, and inclusive of all pSMILE tasks including proficiency testing review, laboratory audit review and creation of remediation action plans, instrument validation, and international laboratory visits. Since this job is unlike many in the clinical laboratory profession, it typically takes about a year to complete the training of a new pSMILE Coordinator.

pSMILE Coordinator responsibilities

The day-to-day work of a JHU-pSMILE Coordinator typically involves a few key tasks that almost always provide an exciting challenge. pSMILE's approximately 144 global laboratories are divided amongst Coordinators for everyday activities, including evaluating, analyzing and reviewing proficiency testing data, assisting with audit remediation, reviewing instrument validation and assisting with other laboratory quality issues. Coordinators also work with laboratory sites to track PT shipments as well as resolve shipping and results submission problems.

Each international laboratory is required to complete the same level of Proficiency Testing as required for US laboratories. pSMILE provides PT surveys, evaluates results, and follows up with a written review. Coordinators also work with laboratories on resolving PT failures with resolutions documented as part of an Investigation Report (IR). Many pSMILE laboratory sites

participate in College of American Pathologists (CAP) PT programs. However, over the years, PT programs from other countries have also been utilized since they may provide better peer groups for international laboratories, or may be better suited to assays being performed in international settings. A good example is Tuberculosis (TB) testing. Since TB is more prevalent internationally than in the United States, comprehensive and robust PT material is not readily available domestically. JHU sources PT panels from Germany (INSTAND) and France (IQLS) to ensure adequate PT coverage for TB culture, identification and drug susceptibility testing (DST). Additionally, there are TB diagnostic methods that are widely used outside of the United States, such as the HAIN Line Probe Assay (LPA) and Cepheid GeneXpert Ultra. pSMILE utilizes panels from the South Africa-based SmartSpot Quality PT provider because they have developed panels that are specifically customized and validated for these methods. In the case of Interferon Gamma Release Assays (IGRA), JHU-pSMILE discovered that the US-based PT was inadequate to cover the assay as it is utilized in network studies. More rigorous coverage was found utilizing panels produced by UKNEQAS based in Sheffield, England. Other PT providers such as One World Accuracy (OWA) from Canada are utilized because they bundle all PT panels together and ship three times per year. This approach has proven to be helpful for sites who have frequent problems with tracking shipments, import permits and customs. pSMILE also provides PT when products are not available commercially or are insufficient. For example, in response to a lack of commercially available PT, JHU-pSMILE developed vaginal wet mount microscopy PT utilizing

digital images available through an online training program. This PT program assures the ability of laboratories to identify *Trichomonas Vaginalis* and vaginal clue cells, a critical component of one of the research protocols supported by pSMILE.

A laboratory audit performed by an independent DAIDS contractor is an entry point for new laboratories. Audits are generally performed annually for established laboratories and are based on DAIDS GCLP guidelines, which are very similar to CAP accreditation checklists. Audit reports are then sent to pSMILE for review and preparation of an Action Plan (AP) that guides the laboratory through the process of correcting each documented deficiency. This can sometimes be a lengthy process involving many emails and web-based meetings between the pSMILE Coordinator and the site. The resolution of the Action Plan also provides opportunities for sites to improve their processes as well as for pSMILE Coordinators to engage in formal and informal teaching and training.

Coordinator day-to-day work is interspersed with other responsibilities and challenges. Each Coordinator generally participates in several internal and external committees working on a wide range of topics and projects. Internal committee charges include developing resources, designing pSMILE.org website content, developing and testing software, developing protocols for instrument validation, and preparing conference and other educational materials. pSMILE also has an internal Quality Assurance Committee that focuses on regulatory compliance, accreditation (such as ISO 9001), and the monitoring of pSMILE internal processes to ensure quality. External committees include JHU

Pathology Department committees such as the Diversity Committee or Annual Educational Symposium Committee. Team members also serve on research protocol working groups and participate in cross-network projects.

Tools of the Trade

JHU-pSMILE Coordinators utilize a unique array of competencies. Extensive clinical laboratory experience is complemented with computer skills using software programs such as Microsoft Excel, Word, Teams, PowerPoint and SharePoint. Coordinators also use method validation tools such as EP Evaluator and a web-based SOP management tool, Zavanta. Additionally, JHU hosts and maintains multiple software systems that aid in managing all aspects of pSMILE functions and workflow. These novel, easy access web applications were developed in-house from the ground up and include electronic document repositories, automated filing systems, and online data warehouses customized for optimal functionality and utility. There are three primary software tools:

1. Oversight Masterlist (OSML), a SQL database designed to organize and track laboratory-specific information. This is an internal application accessible only by pSMILE staff members. Examples of the comprehensive information stored for each laboratory includes the location, contact information for leadership personnel, network affiliation and DAIDS oversight staff, and laboratory accreditation status. Additional PT-specific information includes PT provider registration numbers and orders, shipping details, and email distribution lists for proficiency testing review. Audit action plan progress is also tracked in this database.
2. pSMILE.org website, a document

repository that not only stores and posts laboratory-specific documents but also contains an extensive library of guidance and open-access resource documents. Resources include templates for SOPs and forms, checklists, Excel spreadsheets for calculations used in method validation studies, published articles, and web links. All JHU-pSMILE staff are encouraged to develop resources to populate the library. A committee of staff members keeps the resources organized based on the Clinical Laboratory Standards Institute (CLSI) '12 Quality System Essentials' format and continually reviews and updates these resources to ensure all information is current and relevant for laboratory use.

3. AutoSMILE, a tool built at JHU, is a database and web-based user interface for automating the review of laboratory proficiency testing data. This system provides proficiency testing reviews, summaries, and schedules that meet regulatory requirements that govern clinical trials such as the European Medicines Agency (EMA) and Food and Drug Administration (FDA). JHU has established a relationship with each of the proficiency testing providers to arrange for secure electronic transfer of proficiency testing data that is uploaded to AutoSMILE. JHU-pSMILE Coordinators are able to verify the providers' evaluation of the data and supply evaluations for results that are ungraded. The system derives a score based on the overall evaluation and determines whether the laboratory needs to complete an investigation report for unacceptable results. The system then generates a review report that the Coordinator can edit as needed and emails it to all stakeholders, including the laboratories, network personnel, and DAIDS representatives. A valuable feature of AutoSMILE is the

ability to track and assess laboratory PT performance over several years. The database generates an Excel spreadsheet for each laboratory that summarizes performance of each protocol analyte over the previous three years.

The system also produces Excel reports that track shipping schedules for proficiency testing samples. These schedule reports track dates of Coordinator review and the status of any required investigations. The AutoSMILE system is currently directly accessible only by pSMILE staff, however an external interface allows NIH and network personnel to review and add comments to a monthly PT Exceptions Report. Also in development is an external interface to allow laboratories to complete PT investigation reports online. This enhancement is currently in beta testing.

The AutoSMILE software has been extensively validated to ensure that data integrity is maintained and the system complies with Good Clinical Laboratory Practice (GCLP) standards. AutoSMILE not only allows for the efficient use of Coordinators' time; the automated process also improves accuracy of transcription, standardizes the review of PT data, and provides timely and uniform reports to stakeholders.

International travel and teaching

Interfacing with the international laboratories on a daily basis is key to the success of the pSMILE mission. Strong communication skills are needed and cultural sensitivity goes a long way in establishing a connection and fostering collaboration. E-mail, telephone, and web-based conferencing are standard daily channels of communication; however, Coordinators are able

to travel to selected laboratories throughout the year, averaging stays of a one to three week duration. Laboratories are located primarily in developing, resource-constrained countries and personal safety while traveling is a priority. Coordinators typically travel in pairs and most days are spent in the laboratories, working side by side with our international counterparts to resolve problems, offer possible solutions, and sharing our knowledge to help improve quality in the laboratory. Each laboratory visit focuses on specific objectives. These may include instrument validation, assessment of laboratory testing capacity and methods, TB laboratory assessments, laboratory audit remediation, instrument/method troubleshooting, and other special assignments from the NIH sponsor. Training sessions to larger groups are often held while on-site, providing continuing education opportunities for both bench technologists and management staff. We also help and mentor laboratories to become accredited by agencies such as CAP, South African National Accreditation System (SANAS), and ISO 15189. The work we accomplish during these trips is rewarding and we are proud that laboratories that we have supported are recognized as having high standards of quality by the NIH, clinical trials networks, and other regional laboratories.

Team members also participate in regional and international meetings and conferences that provide an opportunity to collaborate with researchers in the field of HIV/AIDS. JHU-pSMILE team members have provided educational seminars and presentations on a wide variety of topics related to laboratory quality assurance. Presentations have included such topics as method validation, evaluation of QC ranges, technical assistance for novel TB

methods, and HIV proficiency testing. The JHU-pSMILE team has also given many presentations on laboratory safety, audit preparation, and developing Quality Management Systems. Additionally, the JHU-pSMILE team has been able to participate in and contribute to research studies and publications.¹⁻³

Summary

The pSMILE program at JHU is a collaborative effort that ensures the quality of testing in international laboratories conducting clinical trials and studies. Although pSMILE was established to assist laboratories performing HIV/AIDS research, we are flexible enough

to mobilize quickly to assist with emerging infectious diseases such as Zika and SARS CoV2. pSMILE has provided an opportunity for interesting, fulfilling, and challenging alternative career paths in a non-laboratory, clinical research setting. The pSMILE resource, connecting the NIH Division of AIDS and the Johns Hopkins University, has enabled us to use our experience, skills, and education as laboratorians to go Beyond the Bench.

Acknowledgements

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Authors on the JHU team:

Column 1

Column 2

Column 3

Column 4:



Column 1:

Bre'Shey Jones
Administrative Coordinator
Afton Dorasamy BSc(Hons), MS(HPCSA)
International QA/QC Coordinator
Mark Swartz MBA, MT(ASCP)
SMILE Project Manager
Amy Rada BS, MLS (ASCP)CM
International QA/QC Coordinator

Column 2:

Arden Bongco BS, MT (AMT), RT
International QA/QC Coordinator
Peggy Coulter MDE, BS, MT(HEW)
Sr. International QA/QC Coordinator
Anne Leach BS, MT(ASCP)
Sr. International QA/QC Coordinator

Column 3:

Heidi Hanes BS, MT(ASCP) SH
Sr. International QA/QC Coordinator
Roderick Julius
Sr. Programmer Analyst
Kelly Feehely BS, MT (ASCP) MS, LCPC
International QA/QC Coordinator
Eunhee Rim MBA, BSc (Hons)
Program Officer II

Column 4:

Mandana Godard MBA, MS, MT (ASCP)
International QA/QC Coordinator
Lori J. Sokoll, Ph.D.
Professor of Pathology and Principal Investigator
Orlanda Maforo HBMLS, ASQ CQPA
Sr. International QA/QC Coordinator