October 2020 | Issue 23

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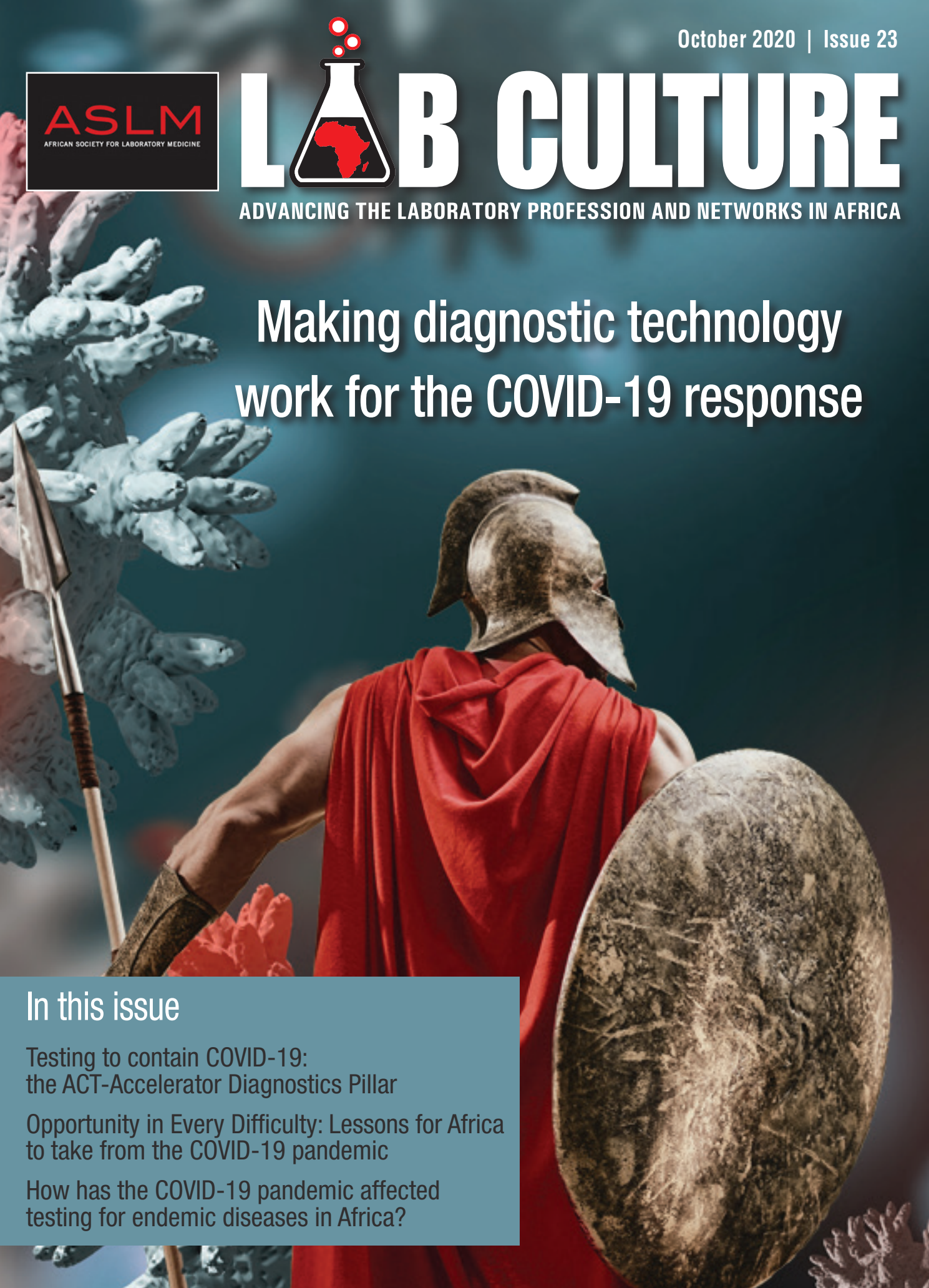
AFRICAN SOCIETY FOR LABORATORY MEDICINE

LAB CULTURE

ADVANCING THE LABORATORY PROFESSION AND NETWORKS IN AFRICA

Making diagnostic technology work for the COVID-19 response



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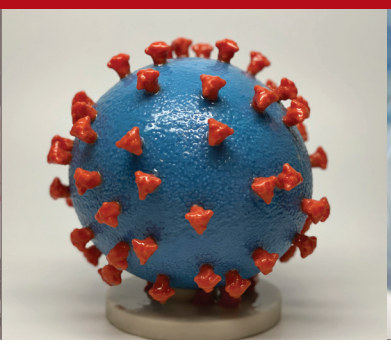


October 2020 | Issue 23

LAB CULTURE

ADVANCING THE LABORATORY PROFESSION AND NETWORKS IN AFRICA

FEATURED TOPIC

Q & A

DEPARTMENTS

Contribute to *Lab Culture*

ASLM is currently accepting article and photo submissions for upcoming issues of ***Lab Culture***. We publish timely, informative, inspirational articles relevant to the unique challenges faced by laboratories in resource-limited settings. We are interested in articles on the critical aspects of laboratory medicine, best practices, success stories, leaders in the field, industry news, etc.

To submit article or photo proposals, please contact the Editor at newsletter@aslm.org.

Lab Culture. Established along with ASLM in 2011 as a member newsletter, ***Lab Culture*** relaunched in 2017 as ASLM's magazine for laboratory medicine in Africa. Dedicated to bringing timely, informative articles relevant to the unique challenges faced by African laboratories, ***Lab Culture*** seeks to be Africa's premiere resource for laboratory professionals and other stakeholders working on with the continent. Published six times a year as a digital edition, ***Lab Culture*** includes features on critical aspects of laboratory medicine and best practices in resource-limited settings, success stories from the continent, industry news, and more.

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Lab Culture is produced in partnership with *Medical Laboratory Observer.*

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COVID-19 Diagnostics

by Dr Collins Otieno

Laboratory diagnosis is key to the coronavirus disease 2019 (COVID-19) 'test-trace-isolate' response strategy, which has to date relied on molecular testing as the most reliable method for identifying infected persons. With guidance and support from Africa CDC, WHO and other partners, Africa has stepped up to the plate and quickly ramped up its COVID-19 testing capacity from 2 to 43 countries capable of performing PCR testing for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), within a couple of months of the outbreak.

Continuing to scale up COVID-19 diagnostic capacity to meet the growing demand for testing, requires consolidated knowledge acquired at the central level combined with a coordinated decentralization of testing at the sub-national level. These efforts require access to technology, funding and guidance in a rapidly evolving scientific, political and epidemiology context.

In vitro diagnostic manufacturers are playing a critical role in enabling countries to expand their COVID-19 testing capacities: indeed, molecular testing instruments usually dedicated to HIV and tuberculosis programs constitute a unique opportunity to be repurposed for COVID-19 response. Meanwhile, the development, evaluation and validation of new technologies that allow more practical COVID-19 screening and confirmation strategies are awaited in order to meet the demand for testing at the community level and relieve pressure on molecular biology laboratories.

For this reason, ASLM invited manufacturers of COVID-19 diagnostics to provide technical information and address questions related to their tests and required supplies in a series of special COVID-19 ECHO sessions, and as part of the Laboratory Systems Strengthening Community of Practice (https://aslm.org/what-we-do/labcop/). Manufacturers responded enthusiastically to this invitation and were given the floor to present their most recent and promising technologic innovations with potential to contribute to the COVID-19 response. While there is an overwhelming number of COVID-19 testing solution available, ASLM gave priority to manufacturers who had obtained Emergency Use Authorization either from the United States Food and Drug Administration or the World Health Organization and/or who had their test kits independently validated by FIND.

The ECHO sessions and webinars gave a unique opportunity for interaction between

Continued on page 5

manufacturers, policy makers, front-line healthcare providers, scientists and members of civil society from the African continent and beyond.

The online dialogue generated a wealth of best practices, recommendations and other valuable resources. This dialogue not only allowed countries to make informed decisions on what to procure as they expanded testing within their countries, but also supported manufacturers in their efforts to make reagents and testing instruments as relevant as possible to African settings.

In this issue of *Lab Culture,* manufacturers of COVID-19 diagnostic products are given an opportunity to elaborate further on the technical and field performance of their products. Additionally, key stakeholders and opinion leaders were asked to provide their unique perspectives on the challenges, opportunities and concerns around COVID-19 testing implementation at a continental and global level. We hope that this information will help relevant authorities in decision making to combat the current pandemic, while maintaining the gains already made in achieving global health targets like the UNAIDS 95:95:95 targets to end the AIDS epidemic.

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African Society for
Laboratory Medicine

Opportunity in Every Difficulty

Lessons for Africa to take from the COVID-19 pandemic

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Over the course of 2020, the world has been turned upside down by a novel viral pathogen, severe acute respiratory syndrome coronavirus 2 or SARS-CoV-2. WHO has declared coronavirus disease 2019 (COVID-19), the disease caused by SARS-CoV-2, as a pandemic. While governments struggle to control the spread of the disease and shield those who are most vulnerable to prevent deaths, all of us have started to live with what we now call the 'new normal' of frequent hand washing, wearing face masks and social distancing. Travel and mass gatherings, such as concerts, trade shows and scientific conferences, are now an uncertainty.

The pandemic has taken its toll in Africa, as it has in other regions of the world. However, its lasting legacy will be the positive effect that it has on making health systems in African countries more resilient, with strengthened laboratory infrastructure to provide surge capacity for testing and improved logistics and specimen transport systems for commodities needed as part of the pandemic response. The pandemic has highlighted the importance of a connected diagnostic system that links data from networks of point-of-care testing sites to central laboratory information systems for real-time surveillance of COVID-19 cases and contact tracing.

There are many lessons learnt[1], but two important ones are: 1) the critical role of public health education, so that everyone plays their part in helping to control the spread of the virus, and 2) self-reliance with regard to commodities such as diagnostics.1 Development and manufacturing of diagnostics in Africa is now a reality, thanks to several initiatives. In Morocco, the Moroccan Foundation for Advanced Science (MASCIR), through its startup Moldiag, has developed a nationally and internationally validated SARS-CoV-2 qRT-PCR test kit with a manufacturing capacity of one million tests per month. Incas Diagnostics, through a partnership with Kwame Nkrumah University of Science and Technology in Ghana, has developed a rapid diagnostic test that detects COVID-19 antibodies within 15-20 minutes. The Kenya Medical Research Institute is manufacturing a rapid testing kit that detects SARS-CoV-2 antigen from swab samples. It is also manufacturing 200 000 litres per day of virus transport media for swab sample transportation from the field to centralized laboratories for PCR testing. In Senegal, the Institut Pasteur de Dakar is working with the Diatropix initiative, which promotes access to diagnostics and whose core members include the Foundation of Innovative and New Diagnostics, Foundation Mérieux, Institut de Recherche et Développement, France. They have developed a 10-minute COVID-19 rapid diagnostic test for $1 (United States dollars) per test in partnership with United Kingdom-based Mologic.

Besides the development of diagnostics tests for COVID-19, distribution of reagents, consumables and kits, and digital platforms for medical supplies have completed the ecosystem to provide countries with the needed support to scale up testing for a better response to the pandemic. In the light of the creativity and vibrant activity that the COVID-19 pandemic has generated in Africa's laboratory systems so far, one can be optimistic about the transformational opportunity the pandemic can bring to Africa's health systems. We can seize this opportunity through mediation of the famous quote from Sir Winston Churchill: 'A pessimist sees the difficulty in every opportunity; an optimist sees the opportunity in every difficulty.'

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Testing to contain COVID-19: the ACT-Accelerator Diagnostics Pillar

Lessons for Africa to take from the COVID-19 pandemic

Heidi Albert, BPharm (Hons), MPH, PhD

FIND (Foundation for Innovative New Diagnostics)

South Africa

The COVID-19 pandemic has thrust testing and diagnostic laboratory services into the global spotlight. Aggressive, sustained testing is the cornerstone of the test-trace-isolate strategies that are central to today's COVID-19 response and critical to mitigating both the health and economic impact of the pandemic.

Effective testing strategies rely on quick turn-around of results from reliable, accurate tests. Alongside test-trace-isolate in the general population, tests are the first line of defence to protect health workers from infection. At a programme oversight level, testing provides critical information for disease surveillance and targeted interventions for communities most in need. It can also help weak health systems manage scarce resources such as hospital beds.

Looking forward, effective testing will also underpin the success of future COVID-19 vaccines and therapeutics. Test data are already informing clinical trials that are currently underway. Once therapies or vaccines become available, diagnostics will enable roll out strategies and help ensure our most vulnerable populations can be reached first.

Leadership from the African Union has been largely praised for its pandemic response, building on experience from frequently faced epidemics on the continent, ranging from Ebola to Lassa fever, and of course SARS. We have previously highlighted that if you don't test, you are blinded. Africa was quick off the mark to start building capacity for SARS-CoV-2 testing, convening regional training sessions as early as the start of February 2020 in Senegal. Rwanda is a notable example of a country that coupled a strong diagnostics component with public health measures to successfully control the disease.[1]

Yet despite its widely accepted importance, COVID-19 testing has been a critical point of failure in the pandemic response in many countries. In low- and middle-income countries (LMICs), the challenges are drastically magnified: FIND analysis shows that testing levels in LMICs are just 10% of those in high-income countries. In low-income countries it is less than

ACTaccelerator
ACCESS TO COVID-19 TOOLS

Diagnostics- Led by The Global Fund and FIND- is focused on reaching **500 million people** by mid-2021 in low- and middle-income countries with simple, affordable, high-quality and **rapid tests to detect infection** and contain the spread of the disease.

The tools developed will benefit the whole world.

Act Now. Act Together. Act to end COVID-19.

1%. The reasons for these challenges span the whole diagnostic value chain, from affordable, accurate rapid tests simply not existing, to LMICs losing out in a worldwide supply chain war.

The Access to COVID-19 Tools Accelerator (ACT-Accelerator)[2] was launched at the end of April 2020, to put a focus on equity in the global response. The ACT-Accelerator brings together governments, health organizations, scientists, businesses, civil society and philanthropists with the goal of ending the pandemic as quickly as possible through the accelerated development, equitable allocation and scaled up delivery of tests, treatments and vaccines, thereby protecting health systems and restoring societies and economies in the near term.

Building on decades of experience fighting other epidemics and infectious diseases, FIND and the Global Fund are co-convening the ACT-Accelerator Diagnostics Pillar, focused on accelerating innovation and overcoming the technical, financial and political obstacles that stand in the way of equitable access to effective and timely testing.

The pillar has been set up to achieve impact in three main areas:

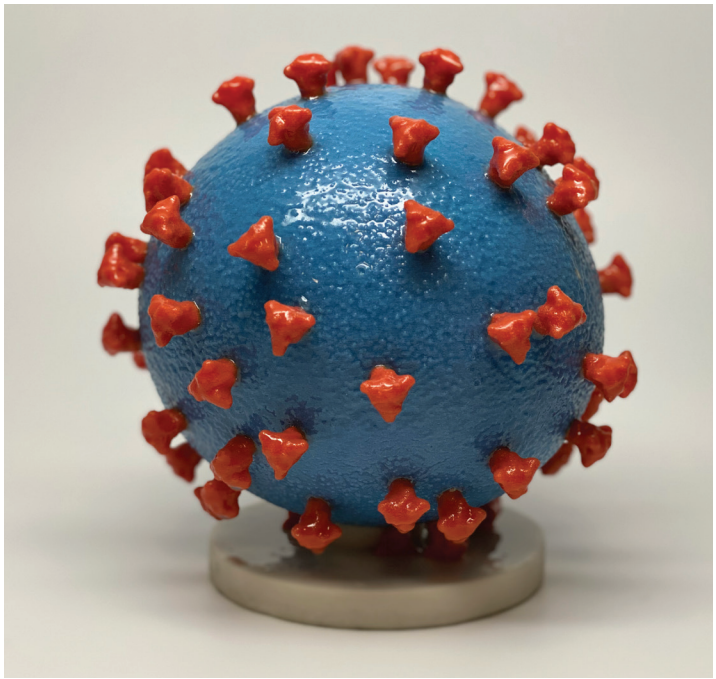
1. All countries should be able to deploy affordable, quality point-of-care tests.

2. LMICs should be supported to put in place effective test-trace-isolate strategies.

3. Disruption of core health services should be minimized.

Over 30 partners from around the globe are engaged, including representatives from academia, industry, regulators, civil society, funders, international organizations and country representatives. Four main working groups have been put in place:

- **Research and development of tests and digital tools** – to fill gaps in research and development
- **Market readiness –** engaging in market-shaping interventions to stimulate rapid, massive scale-up
- **Supply** – powering supply and distribution, with additional support for LMICs
- **Country preparedness –** building the capacity of countries' health infrastructures to enable uptake of tests



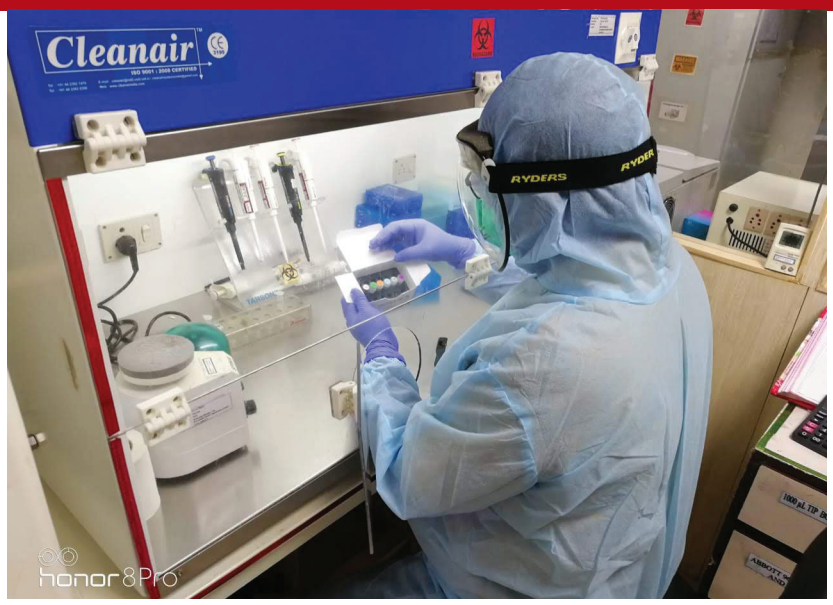
These are complemented by cross-cutting working groups:

- **Data foundation and modelling**
- **Strategic private sector engagement**
- **Advocacy and community engagement**

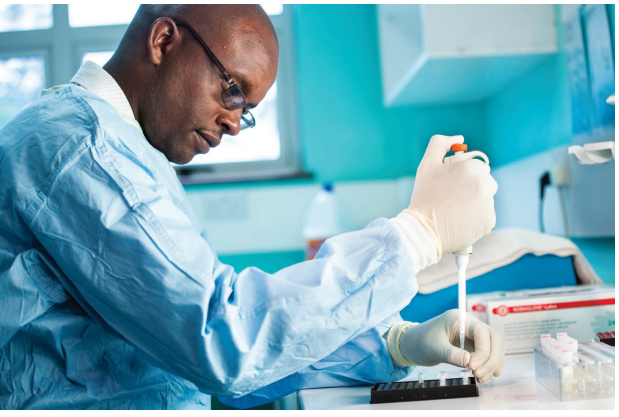
Africa CDC is co-leading the country preparedness working group, alongside the Pan-American Health Organization. Work is progressing on laboratory strengthening and healthcare worker training, and operational research – including innovative delivery models – is underway to support country policies.

On 28 September 2020, the Diagnostics Pillar announced that 120 million affordable, quality antigen rapid diagnostic tests (Ag RDTs) would be made available for LMICs through manufacturer volume guarantees, alongside WHO policy guidance on the use of these tests, catalytic funding to assist governments to deploy them and an initial US$50 million procurement fund from the Global Fund.

With the lockdowns restricting travel, learning and capacity building have had to shift online, and as part of the working group efforts, FIND teamed up with the ASLM and the London School of Hygiene and Tropical Medicine to develop free online training courses that are hosted on the FutureLearn platform. These courses are designed for ministry of health officials, laboratory professionals, clinicians and anyone involved in laboratory testing and diagnosis for COVID-19, with a focus on LMICs. Over 16 000 learners from 186 countries signed up for the first course on *COVID-19 Diagnostics and Testing,* with subsequent runs now ongoing,[3] including a version



in French that was developed in partnership with Fondation Mérieux.[4] An invitation-only course on *Laboratory Training*



for COVID-19 Molecular Testing has been run in partnership with the Nigeria Centre for Disease Control and the National Tuberculosis and Leprosy Control Program, Nigeria Ministry of Health, and an open-access version was made available on 13 July 2020.[5] With support from ASLM, this training has been translated to French, and in partnership with Africa CDC, laboratory professionals from more than 20 countries, including West and Central Africa, will be invited to join trainings in both languages, combined with additional capacity building support and mentorship being deployed to drive scale up of testing.

Significant fundraising is ongoing to support the ACT-Accelerator Diagnostics Pillar activities. A full investment case has been developed and published,[6] which estimates that $6 billion is needed in the next 12 months to ensure the right test is available to all who need it through driving research and development, shaping an effective market for products, building country laboratory capabilities and procuring 500 million tests for LMICs who are unable to shoulder the costs of test procurement. US$300 million has been pledged so far.

There is a long way to go, but it is clear that diagnostics and testing are – and will remain – central to the COVID-19 exit strategy. Ensuring that laboratories have the capacity to meet this unprecedented demand is critical. If you would like more information on FIND or the ACT-Accelerator Diagnostics Pillar, including support or guidance on laboratory matters, please contact info@finddx.org.

Keywords: Diagnostics, COVID-19, testing, capacity building

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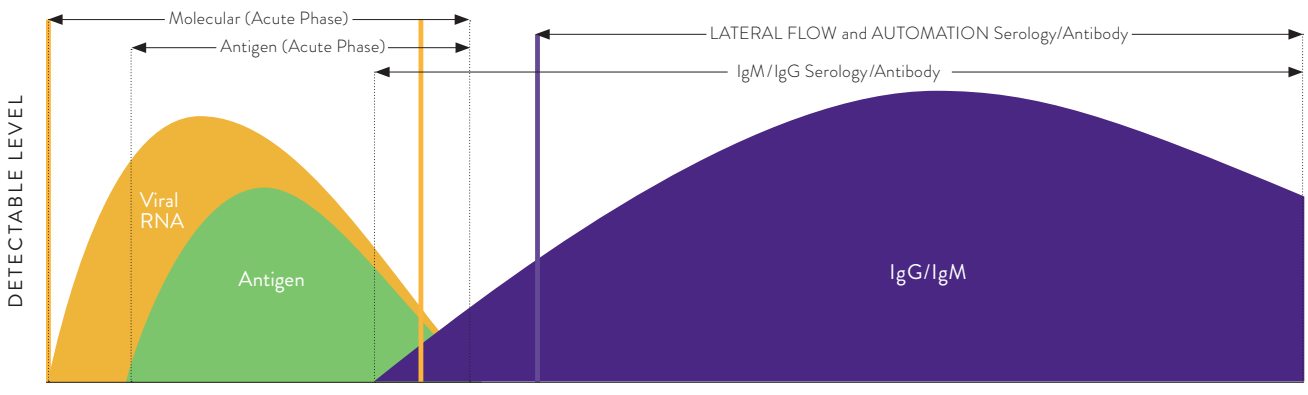
COVID-19 TESTS
WHEN YOU NEED THEM

Whether you were recently infected with SARS-CoV-2 or have recovered from an exposure, Abbott tests span the COVID-19 infection.

THE INFECTION CYCLE OF A VIRUS[1]



This is general to viral infections and not specific to SARS-CoV-2

Approximately 0 to 14 days	Approximately 2 to 14 days	Approximately 14 days to months
Viral RNA multiplies	Viral antigens increase	Body produces antibodies to fight reinfection
MOLECULAR TESTS	ANTIGEN TESTS	SEROLOGY IgG TESTS
***m*2000 RealTime System™** **Alinity®**	*Abbott is evaluating a potential antigen test for the future.	**ARCHITECT® *i*1000SR and *i*2000SR** **Alinity® i**
		SEROLOGY IGG/IGM TEST
		Panbio® COVID-19 IgG/IgM Rapid Test Device

*The Panbio™ COVID-19 Ag Rapid Test has since received WHO EUL

**SARS-CoV-2 IgM is now available on the Architect and Alinity analysers and have CE and FDA EUA approvals.

1. Developing a National Strategy for Serology (Antibody Testing) in the United States. Johns Hopkins, April 22, 2020
Current performance of COVID-19 test methods and devices and proposed performance criteria, European Commission, 16 April 2020

NOTE: This is a typical viral load patient response and is not specific to COVID-19

Disclaimers: Time periods listed for each phase of infection are general estimates and not indicative of a person's immune reaction to SARS-CoV-2. These tests have not been FDA cleared or approved. These tests have been authorized by FDA under EUAs for use by authorized laboratories and have been authorized only for the detection of nucleic acid from SARS-CoV-2 or detection of IgG antibodies against SARS-CoV-2, and not for any other viruses or pathogens. These tests are only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of *in vitro* diagnostic tests for detection and/or diagnosis of COVID-19 under Section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.

PRODUCT MAY NOT BE AVAILABLE IN ALL MARKETS AND IS SUBJECT TO REGULATORY APPROVAL IN REGULATED COUNTRIES.

The SARS-CoV-2 assays that run on the *m*2000 RealTime System™, Alinity® m, Panbio® COVID-19 IgG/IgM Rapid Test Device, ARCHITECT® *i*1000SR and *i*2000SR, and Alinity® i have CE marking.

WHO Prequalification of *in vitro* diagnostics and the Collaborative Registration Procedure

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Introduction

Access to high quality diagnostic tests is a key component in effectively identifying and monitoring disease. However, current processes to determine the quality, safety and performance of an in vitro diagnostic (IVD) test can also create barriers to access, increasing the time it takes for products to be available in the laboratory or at a community testing site. For IVDs that have already undergone stringent review for performance and safety, repetitive analysis aimed at quality assurance to inform national adoption or registration can cause delay without additional benefit. National regulatory processes have been identified as one of the areas that contribute to delayed access to quality-assured IVDs in many World Health Organization (WHO) Member States. Finding a balance between robust evaluation of an IVD and the regulatory requirements needed to protect public health and safety is a constant challenge. WHO is committed to supporting national regulatory authorities and respective national reference laboratories that conduct performance evaluations to optimize available resources and utilize reliance principles (where appropriate) to facilitate access to quality-assured IVDs at the country level.

WHO prequalification of IVDs

For a decade, WHO has provided a Prequalification of IVD service designed to assess the quality, safety and performance of IVDs for priority diseases, considering needs and challenges in resource-limited settings. The current scope of prequalification IVD assessment (Table 1) encompasses over 100 IVDs on the WHO list of prequalified in vitro diagnostic products.[1] Prequalification assessment of an IVD follows a standardized procedure that incorporates a review of the manufacturer's documentation for the IVD (product dossier), a laboratory performance evaluation, inspection of manufacturing site(s) and a labelling review. All aspects of the assessment are based on internationally recognized standards, as well as WHO guidelines and specifications. Where there is evidence of an IVD having been assessed by regulatory authorities applying stringent standards, an abridged assessment may be conducted to streamline the prequalification process and avoid unnecessary duplication of effort. The focus of prequalification IVD assessment is the suitability of the product for use in resource-limited settings, with particular attention to aspects such as usability, stability across a broad range of environmental conditions, risk management, manufacturing capacity and recommended specimen types.

IVDs that meet requirements are listed on the WHO website along with a public report that summarizes the results from the assessment. To maintain a prequalification listing, manufacturers must comply with post-qualification obligations, including annual reporting on the IVD, notification of any reportable changes to the product or the quality management system under which the product is manufactured, and periodic re-inspection of manufacturing facilities. The WHO prequalification listing is a mark of quality assurance that is used by the United Nations, international procurers and Member States to identify IVDs that meet WHO specifications.

The Collaborative Registration Procedure for IVDs

The Collaborative Registration Procedure (CRP) for WHO prequalified products aims to accelerate product registration by sharing information between WHO prequalification and national regulatory authorities (NRAs). Manufacturers often face repetition of work as they seek registration through NRAs in multiple countries. The CRP can reduce these duplicative efforts by building a collaboration among WHO, NRAs and manufacturers, enabling NRAs and manufacturers to leverage WHO's prequalification evidence of IVD quality, performance and safety, while maintaining strict confidentiality on the information shared by each participant. To utilize the CRP, NRAs sign a confidentiality undertaking with WHO to ensure the information shared on the assessment of the IVD is used only for reaching a regulatory decision and is not made public. For the manufacturer of a prequalified IVD, participation in the CRP is voluntary; if a manufacturer consents to this procedure to facilitate in-country registration, they provide written consent authorizing WHO to share assessment reports with the NRA. Under the CRP, it is mandatory for the manufacturer to submit to the NRA the same version of the IVD as that which was prequalified by WHO.

Once a CRP agreement is in place for an IVD, WHO shares with the NRA the confidential prequalification assessment reports for the product dossier, the laboratory performance evaluation and the manufacturing site inspection via a secure internet-based platform. The NRA will then follow its internal procedures to reach a regulatory decision using the information provided by WHO as well as data submitted directly by the manufacturer (Figure 1). It is strongly recommended that the NRA verifies that the product submitted for registration is the same as the WHO prequalified IVD. Review of WHO assessment information should be conducted by NRA staff with appropriate expertise to determine that the evidence provided supports the intended use of the IVD. It is anticipated that the assessment information provided by WHO will satisfy the NRAs requirements for product quality, performance and safety, reducing the need for additional evaluation studies. It is through reliance on or recognition of the WHO prequalification assessment that the efficiencies of CRP are gained. By applying the CRP, national resources used to perform full IVD assessments can be directed towards products that are not within the scope of WHO prequalification. When CRP is used in this way, there is a two-fold benefit: quality-assured IVDs can reach the market more quickly, and the effort needed to thoroughly evaluate IVDs can be focused on products that have not already undergone robust WHO assessment.

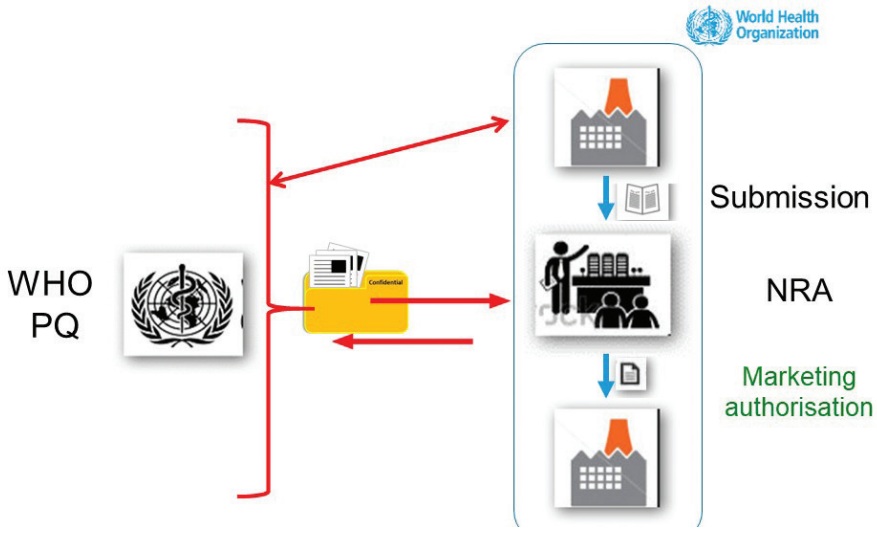

Figure 1

CRP pilot for IVDs

A one-year pilot project aiming at introducing the CRP for IVDs was implemented in 2019. Five countries participated in the pilot – Cameroon, Côte d'Ivoire, Ethiopia, Nigeria and Tanzania – and three of the five were able to use the CRP to register prequalified IVDs in a shorter timeframe than the usual procedure. In all five countries, opportunities for optimizing the CRP process at the country level were identified by participants. The pilot project has encouraged examination of the current national registration procedures for IVDs, bringing a clearer understanding of the regulatory burden and the duplication of existing processes.

Lessons learned from the pilot project have been used in the development of the draft *Guidelines for Collaborative Procedure between the World Health Organization (WHO) and National Regulatory Authorities in the assessment and accelerated National Registration of WHO-Prequalified In Vitro Diagnostics*,[2] which is now undergoing public consultation.

Main findings from the pilot:

- The following benefits of applying CRP were observed:

  o Shorter regulatory approval times (target timeline: within 90 days),

o Reduced workload for NRA experts and

o Reduced need for in-country evaluations based on acceptance of WHO prequalification performance evaluation and related assessment reports.

Table 1: Products currently eligible for prequalification assessment

Analyte / Pathogen	Intended Use (Technology)
HIV-1, HIV-2	Diagnosis (RDT, EIA, NAT) Self-testing (RDT) Monitoring (Flow cytometer, NAT)
HCV	Diagnosis (RDT, EIA) Monitoring (NAT)
HBsAg	Diagnosis & Monitoring (RDT, EIA)
Malaria parasites	Diagnosis (RDT)
HPV	Diagnosis (NAT)
G6PD enzyme	Detection of enzyme deficiency (RDT)
Toxigenic *Vibrio cholerae*	Outbreak Detection & Surveillance (RDT)
Treponema pallidum (syphilis)	Screening & Aid to diagnosis (RDT)

- The best CRP results were observed in countries or NRAs where there is a clear regulatory pathway or where regulatory structures for IVDs exist. In the absence of clearly defined country registration pathways, it may not be possible to meet the target CRP registration timeline of 90 days.
- Inadequate capacity of the NRA experts to assess technical files and reports led to delays in processing of applications and subsequent product registration.
- Variability in registration requirements among participating NRAs increased workload to the manufacturer applying for IVD registration. For example, mandatory submission of product samples and or a free sale certificate, or requiring additional performance evaluation instead of leveraging on PQ performance evaluation reports.
- Delays in registration were also triggered by suboptimal communication within NRAs staff and between NRAs and their external CRP stakeholders.

Based on the findings of the pilot CRP stipulated above, it is crucial that NRAs establish a regulatory framework for IVDs based on the recommendations provided in the WHO Global Model Regulatory Framework as a foundation to effectively utilize CRP and improve access to high quality IVDs when needed. Another important element is strengthening communication, collaboration and cooperation among NRA stakeholders both within NRAs and with external stakeholders. Getting quality-assured IVDs to end users can be accelerated by coordinated action among manufacturers, regulatory bodies, laboratories and healthcare facilities in settings of intended use. Activities that support a robust regulatory system, such as capacity development for NRA experts and harmonized regulatory requirements for IVDs within NRAs, should also be prioritized.

Participate in CRP to accelerate access to IVDs

The CRP for IVDs is an innovative mechanism designed to accelerate registration and facilitate timely availability of IVDs. Based on the experience gained in the pilot CRP for IVDs, streamlining regulatory frameworks for IVDs and NRAs' readiness to implement the CRP procedure are the keys to success. The direct benefit from participation in CRP is the efficient registration of quality-assured IVDs, with predictable timelines and simpler post-registration maintenance. Further operational benefits include national registration data being harmonized with WHO's prequalification registration; the availability of WHO assessment, inspection and performance evaluation outcomes to support national decisions; and a reduced regulatory burden for assessment of prequalified IVDs, freeing up time to focus on IVDs that have not previously undergone extensive evaluation. Most importantly, CRP facilitates improved access to quality-assured IVDs where they are most needed – at laboratories and community testing sites.

Countries interested in utilizing CRP as a pathway to accelerating the availability of prequalified IVDs can find information on the WHO website.

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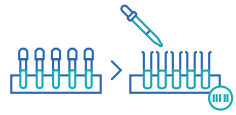
How antibody tests help to detect those already infected with SARS-CoV-2

1. The **human blood sample** is taken and sent to the **lab for analysis.**

2. **Trained lab professionals** prepare the sample. First the **red blood cells are separated to obtain serum/plasma** through centrifugation.

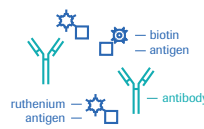


3. Small amounts of serum/plasma are **pipetted into a special sample tube.** To ensure correct identification and traceability each tube carries a **unique barcode.**

4. The tube is **loaded onto a fully automated analyser.** The system begins the identification of antibodies in the sample.

3 reagents are used to process a reaction. Reagents are complex mixtures of biochemicals. The manufacturing of quality reagents at industrial scale is technically demanding.

An antigen, like SARS-CoV-2, is a molecule or molecular structure that triggers an immune response resulting in antibody production.



4a. The sample is incubated with a mix of **laboratory synthesised reagents.** One contains a SARS-CoV-2 specific antigen carrying a **"biological bulb"** (ruthenium-label) and another contains a SARS-CoV-2 specific antigen equipped with a **"biological anchor"** (biotin-label).

4b. **If SARS-CoV-2 antibodies** are **present** in the sample, a **double-antigen-sandwich** complex is **formed.**

4c. The **sandwich complexes** are attracted via the biological anchor onto **paramagnetic beads.**

4d. These complexes enter the measuring cell of the analyser. A current is applied to an electrode, consequently **it becomes magnetic.** All **paramagnetic beads** carrying the complexes **get bound to the magnetic surface.**

Electrochemiluminescence (ECL) is a kind of luminescence produced during electrochemical reactions in solutions.

4e. Now the detection takes place. A **special solution** is added and the **biological flashlight turns on.** The **light indicates** the presence of **Anti-SARS-CoV-2 antibodies** in the sample.

5. Lab professionals **analyse, control** and **approve** the **test results** before they go into the computer based lab information **system.**

6. These **results** are made available to the **healthcare provider** to enable more **informed decisions.**

Pan-African EQA Initiative for COVID-19 Testing

As each country in Africa monitors their efforts to mitigate the COVID-19 pandemic, the question of when to return to work and resume normal activities is one of the most critical issues they face. Molecular, antibody and antigen tests have an important role in these complex calculations. Results from these tests can identify who has been infected, who has developed antibodies that may protect them from future infection, who is still at risk and who can be a suitable donor of blood to make convalescent plasma to treat those seriously ill from COVID-19.

It is clearly important to ensure that these tests, many of which were brought to market quickly under emergency use authorizations, are accurate and reliable. The fact that the United States Food and Drug Administration (FDA) recently identified a number of antibody tests that 'should not be distributed' as not meeting their evaluation criteria[1] underscores the need for ongoing external quality assessment (EQA) and raises concerns about the uptake of underperforming tests, especially through grey markets.

This article introduces an initiative to implement comprehensive pan-African EQA for COVID-19 testing that could deliver better health outcomes for hundreds of millions of people at a very modest cost.

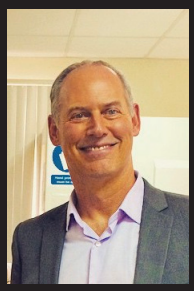
EQA Implementation Model

Several years ago, our group, Oneworld Accuracy, was invited to participate in a Request for Proposal to build laboratory capacity for HIV/AIDS testing, including EQA, in a network of 57 countries. Public health groups in each country would serve as national EQA providers in accordance the World Health Organization (WHO) manual for organizing a national EQA programme for health laboratories and other testing sites.[2] EQA providers had to be able to start quickly, collaborate as peers, easily add more programs and participants and be on a track to attain accreditation by their national accreditation bodies under ISO/IEC 17043:2010 Conformity assessment - General requirements for proficiency testing.[3] We were tasked to create a step-wise, costed plan. While the proposal we participated in was not successful, one legacy is the project model we created.

The project model has six key variables.

1. **EQA programmes.** We created sets of EQA programmes mapped to associated medical tests and disease entities. We started with HIV/AIDS and have since added malaria, tuberculosis, antimicrobial resistance, diabetes, renal disease, cardiovascular diseases and now COVID-19.

2. **Sample set strategy.** For each programme, we asked whether it was advantageous to make sample sets in-country following a structured training programme or procure them centrally using a group-purchase model. Sample sets that can be made with standard laboratory equipment and used in programs with quantitative non-peer-group assessments are generally more suited for in-country production. The benefit, of course, is eliminating the cost and complexity of importing them from international sources. Bacteriology to cover the pathogens



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Oneworld Accuracy (www.1wa.org) is an accredited EQA provider based in Vancouver, Canada. They operate with a social enterprise commitment to make EQA globally sustainable. They have 20 years' experience training national EQA providers around the world. In Africa, they have worked with more than 30 current and aspiring national EQA providers comprised of public health agencies, national reference laboratories and laboratory oversight bodies.

in the WHO Global Antimicrobial Resistance Surveillance System[4], HIV rapid testing and early infant diagnosis are examples of this category. Sample sets that are more complex to manufacture and are used in programmes with qualitative peer-group assessments are generally more suited for central procurement. Most chemistry and haematology programs are examples of this category.

3. **Health facilities.** We estimated the number and type of health facilities in each country from WHO data[5] and added their World Bank income grouping.[6] Where data were missing for countries, we made a population-adjusted estimate using a proxy country with comparable gross domestic product per capita. Wherever possible, we updated WHO data with curated data from government or other sources.

4. **Participation rates.** We estimated the percentage of each type of health facility that would participate in the various programme sets.

5. **On-boarding.** We created a function to sequentially on-board EQA providers and have them expand their programmes and participants over time.

6. **Shipping.** We created an algorithm to calculate the costs of shipping pre-kitted EQA sample sets from a central point to each EQA provider for transhipment to their participants. This is based on a test event calendar with the fewest shipments, each with the most sample sets.

We used this project model to answer two simple, but compelling questions with respect to EQA for COVID-19 testing in Africa. *How much would it cost? How would it be organized?*

Table 1 outlines a suggested set of EQA programs for molecular, antibody and antigen testing, all with three test events annually. Molecular and antigen EQA have two samples per test event. Antibody EQA has six samples per test event to properly cover IgA, IgM and IgG. To provide a more comprehensive, rigorous quality regime, we also included companion internal quality control (IQC) for each EQA programme and validation for molecular EQA. IQC and validation are currently being provided on a sample-only basis. The plan is to extend the informatics system[7] beyond EQA to include IQC and validation. Unified informatics, encompassing these core quality processes, will significantly enhance quality oversight of COVID-19 testing by a pan-African Scientific Advisory Board (SAB) described below and EQA providers and facilitate quality improvement by participants.

Table 2 estimates the number and type of health facilities and the percentage of each that would participate in the programme set outlined in Table 1. These estimates are starting points only. We invite input from government and other curated sources to improve and refine these estimates.

We estimate in Table 3 that it would cost about $7 million United States dollars (USD) for the health facilities in Table 2 to participate in almost 11 000 subscriptions of the programs outlined in Table 1. This amount does not include antibody IQC and antigen IQC, which are expected to be operational in the second quarter of 2021. We offer this estimate as

Table 1 - COVID-19 Program Set

Description	Program Name	Format	Status
molecular EQA	SARS-CoV-2 Molecular	3 test events x 2 samples	Operational / accredited
molecular validation	SARS-CoV-2 Molecular Validation	8 positive and 4 negative in swabs or liquid	Operational
molecular IQC	SARS-CoV-2 Molecular QC	10 positive or negative in swabs or liquid	Operational
antibody EQA	SARS-CoV-2 Serology	3 test events x 6 samples	Operational / accredited
antibody IQC	SARS-CoV-2 Serology QC	Under development	Projected to be operational Q2 2021
antigen EQA	SARS-CoV-2 Antigen	3 test events x 2 samples	Projected to be operational / accredited Q4 2020
antigen IQC	SARS-CoV-2 Antigen QC	Under development	Projected to be operational Q2 2021

Notes

Program details are available at www.1wa.org.

We suggest molecular validation be done once at the outset of testing to validate test platforms and operators.

We suggest molecular IQC be done at least weekly with positive and negative controls.

Table 2 - Health Facilities in Africa

		Estimated Participation Rates						
		Molecular			Antibody		Antigen	
Health Facility	Estimated N	EQA	Validation	IQC	EQA	IQC	EQA	IQC
Regional hospitals	550	100%	50%	100%	50%	50%	0%	0%
Provincial hospitals	1,448	75%	75%	75%	50%	50%	25%	10%
District hospitals	4,282	0%	0%	0%	10%	10%	5%	2%
Health centres	61,029	0%	0%	0%	5%	5%	2%	0%
Health posts	28,582	0%	0%	0%	0%	0%	0%	0%
	95,891							

Table 3 - Estimated COVID-19 Program Delivery Cost (USD)

Program Name	Subscriptions	Cost
SARS-CoV-2 Molecular	1,636	433,805
SARS-CoV-2 Molecular Validation	1,361	629,925
SARS-CoV-2 Molecular QC	1,636	2,936,369
SARS-CoV-2 Serology	4,479	2,161,431
SARS-CoV-2 Serology QC	-	-
SARS-CoV-2 Antigen	1,797	476,385
SARS-CoV-2 Antigen QC	-	-
	10,908	6,637,915
Shipping to central facility in each country		438,000
Total		7,075,915

an invitation for discussion. Naturally, a model is only as good as its inputs. We think there is significant room to refine the inputs, particularly health facilities and their participation rates.

Costing Details

Programme costs consist of the cost of sample sets and informatics fees. Informatics fees defray the cost of developing, hosting and improving the informatics system as a shared resource by all EQA providers and cover all associated training and support for EQA providers, each of whom is supported by a dedicated account manager. The project amount also includes estimated shipping costs based on three shipments per calendar year of pre-kitted sample sets to EQA providers in all African countries, who then tranship them to their participants.

Staff and overhead costs for EQA providers and the cost of shipping sample sets from EQA providers to their participants are not included in this project amount. Having said that, the supporting informatics system significantly reduces the workload on EQA provider staff. Participants enter their own EQA test results, obviating the need for manual, error-prone entry by EQA provider staff. Moreover, the informatics system automates notices to participants of upcoming shipments, results deadlines, missing results and delivery of performance reports. The net impact is improved turn-around time and operating efficiencies that enable staff to shift their efforts from largely clerical tasks to helping their participants improve their testing quality.

We expect that actual project costs will be less for several reasons. Eleven countries account for about 80% of the total COVID-19 tests conducted in Africa - South Africa, Morocco, Ethiopia, Egypt, Ghana, Kenya, Nigeria, Rwanda, Uganda, Mauritius and

Cameroon.[8] The initial focus of this initiative should obviously be on these countries. Moreover, antibody and antigen tests are still in early stages of development and commercialization and it could be a while before they are widely adopted in Africa, particularly at the point of care. We also believe there is considerable room, through negotiation and organization, to reduce sample set and shipping costs. In this regard, we have obtained 'most favoured nation' provisions with the sample manufacturers to secure the best possible pricing.

Moreover, antibody EQA is an obvious candidate for in-country production of sample sets. Molecular and antigen EQA are less likely candidates for in-country production as they require more sophisticated production techniques. Internal quality controls are also are less likely candidates for in-country production as they are generally treated as in vitro diagnostic devices and are subject to significantly more regulation than EQA sample sets.

Finally, this project amount includes almost $3 million USD for molecular IQC - 44% of the total programme costs. Since most, if not all, laboratories doing molecular testing are already separately purchasing IQC, it would instructive to compare the aggregate of their IQC costs versus those in the project model. There may well be significant IQC savings given the group purchase economics underlying IQC in this project.

Feasibility

If this project has modest costs, is it operationally feasible? In a word, yes.

African EQA providers would deliver a harmonized set of programmes (test event formats, sample sets, calendar, informatics system). These would include the WHO Regional Office for Africa (AFRO), WHO Regional Office for the Eastern Mediterranean (EMRO) and the many existing national EQA providers, including those in the 11 countries that perform 80% of the testing. Regional EQA providers, ideally designated by the African Society for Laboratory Medicine (ASLM) and the Africa Centres for Disease Control and Prevention (Africa CDC), could provide EQA programs in countries not ready for national EQA. We believe that there is also a role for a pan-African EQA provider, perhaps ASLM, to cover any potential regional gaps. This EQA project could also engage a set of reference laboratories from the African Public Health Laboratory Network, ASLM collaborating centres and Africa CDC.

Oversight would be provided by a SAB, ideally with representation from ASLM, Africa CDC, WHO-AFRO, WHO-EMRO and other key public health groups. The SAB would design and iterate the programme set to meet clinical standards, review performance data after each test event with EQA providers and participants and develop online educational / remedial courses for participants.

In summary, we believe that this project is eminently feasible. It requires modest funding, can commence with very short lead times and can scale seamlessly. Importantly, it maximizes African intellectual resources – SAB, EQA providers, reference laboratories, participants, in-country producers of sample sets and even informatics. Project uptake would enable us to recruit African developers to accelerate the informatics roadmap to create open-source modules freely available to public health stakeholders to contribute to EQA sustainability in Africa. Perhaps most importantly, this project can build durable quality infrastructure within Africa that can be deployed for future viral outbreaks and other pressing public health issues such as HIV/AIDS, tuberculosis, malaria and antimicrobial resistance.

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2 World Health Organization (WHO) manual for organizing a national EQA programme for health laboratories and other testing sites. https://www.who.int/hiv/pub/toolkits/manual-external-quality-assessment-testing/en/

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5. World Health Organization (WHO) country data. https://www.who.int/data https://www.afro.who.int/countries

6. World Bank income grouping. https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups

7. The OASYS informatics system is multi-tenant, enterprise-scale, cloud-ready EQA informatics system currently localized in English, French, Spanish, Italian and Turkish. The system is developed and hosted by Oneworld Accuracy and made available to public health EQA providers globally. The system roadmap includes further localizations with Portuguese and Arabic, integration with open-source help desk software, CRM (customer relationship management) software and LMS (learning management system) and connection with open-source LIMS/LIS (laboratory information management systems / laboratory information systems).

8. Our World in Data; selecting African countries. https://ourworldindata.org/coronavirus

SARS-CoV-2 antibody testing in Africa: Specificity to ensure reliable results

Detection of mature antibodies is key

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Introduction

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is a major global crisis. On 11 March 2020, the World Health Organization (WHO) declared COVID-19 a pandemic, and it has become one of the deadliest pandemics in the last century. The COVID-19 pandemic has disrupted the lives of billions of people in Africa and elsewhere, nearly overwhelming healthcare systems and pushing the global economy to the brink of collapse. The quest for effective treatments and a preventive vaccine starts with – and depends on – the broad availability of fast, accurate and reliable testing.

Scalable and affordable diagnostic tests are an essential service in the delivery of healthcare in low- and middle-income countries and have become an indispensable tool in clinical practice. In vitro diagnostic testing plays a vital role in determining who may have contracted COVID-19, ensuring that healthcare professionals can work safely and that quality care and treatment is available to all those who need it. The focus is on helping to flatten the curve and lowering the rate and spread of infection, by providing governments and healthcare institutions with actionable test results. High quality diagnostics aid more accurate disease identification, leading to more appropriate patient care on the continent.

Principal uses of NAT, antigen and serology testing for SARS-CoV-2

Testing for SARS-CoV-2 involves either:

- Nucleic acid tests (NATs) to detect viral RNA directly, or antigen testing, to detect viral proteins directly, determining if someone is currently infected with the virus, or
- Detection of the immune response (antibodies), determining whether someone has been infected and developed antibodies in response to viral infection.

NATs or antigen tests are generally used for testing of symptomatic patients and can detect SARS-CoV-2 infection up to one week before symptoms appear (Figure 1).[1]

Antibodies against SARS-CoV-2 generally target the viral spike (S) and nucleocapsid (N) proteins, and are typically detectable 8 days post symptom onset (Figure 1, Figure 2).[1,4, 6-11]

For many other infections, immunoglobulin M (IgM) appears before immunoglobulin G (IgG), but in the case of SARS-CoV-2, IgM and IgG appear around the same time, with the IgG response maintained >30 days following symptom onset/ PCR positivity; IgM is maintained during that period, but starts to decline afterwards.[3,4,12-15] Hence, there are important open questions around IgG maturation and differences in early-appearing IgGs versus those detected later post exposure.

Anti-SARS-CoV-2 assays will be useful for: prevalence screening, disease surveillance, contact tracing, vaccine studies and to support return to work strategies. However, currently we do not know: [2,16-18]

- Whether antibodies confer reliable immunity
- The duration of any immunity
- At which point a positive antibody test means immunity (e.g. NAT negative, antibody positive)

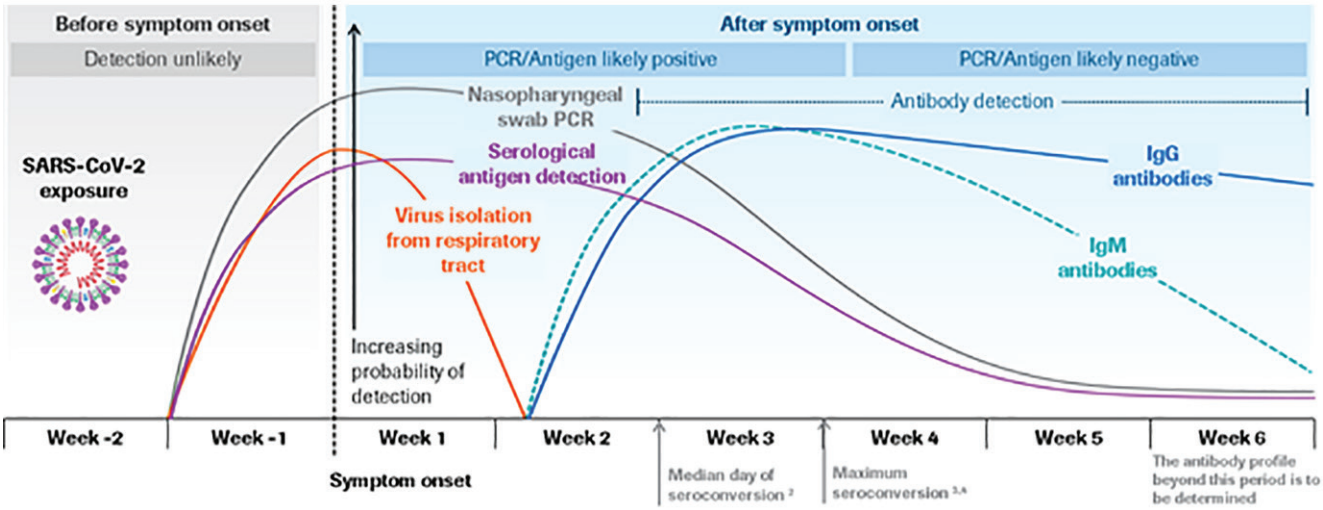

Figure 1. Estimated course of molecular and serological biomarkers during SARS-CoV-2 infection (adapted from references 2-5).

Requirements for serology testing: high specificity, high sensitivity, and no cross-reactivity

A key requirement of an antibody test is high specificity. Highly specific antibody tests will correctly identify someone who has not been infected and will be unlikely to give a false-positive result (Figure 3).

High specificity is key. For SARS-CoV-2, false-positive results could lead to individuals believing that they have some immunity, and this could put them at greater risk of infection, possibly infecting others, and resulting in an over-estimation of infection rates within a population, particularly in low-prevalence areas.

Sensitivity is important. The detection of early antibodies may not be useful for serosurveillance of SARS-CoV-2, versus correct detection of mature antibodies, which is more likely to provide correlation with putative immunity. The most sensitive serology test, that detects the earliest antibody response, may also detect immature antibodies that are less specific.

Hence reducing specificity in favor of sensitivity does not make sense for anti-SARS-CoV-2 testing.

Cross-reactivity must be minimal. Although SARS-CoV-2 infection only emerged in 2019, there are endemic coronaviruses which may cause potentially cross-reactive false-positive antibody results.[16,19] Additionally, the SARS-CoV-2 N and S proteins have

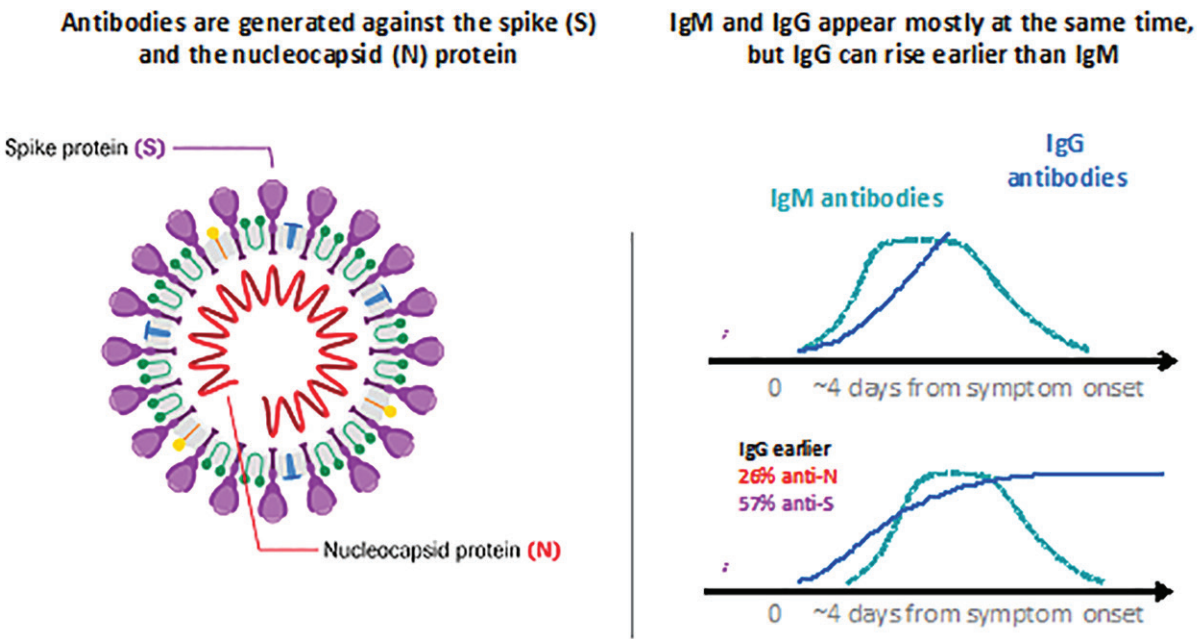

Figure 2. Antibody response during SARS-CoV-2 infection. 3,5,12

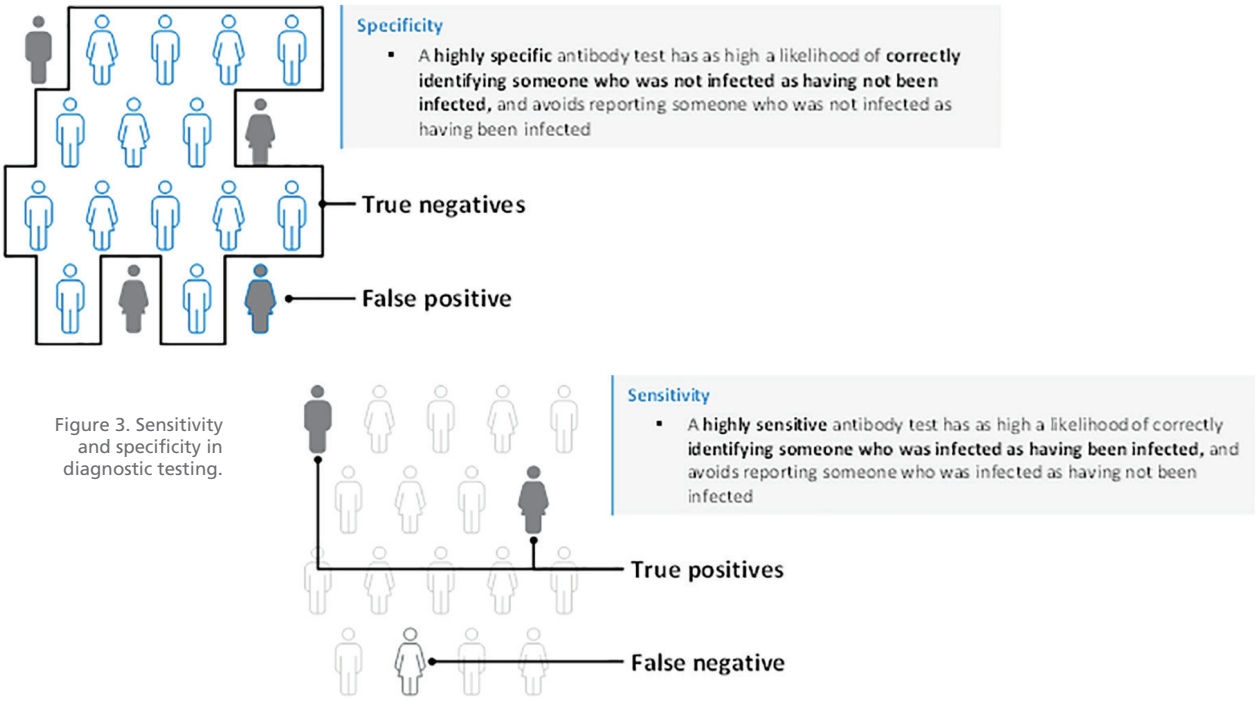

Figure 3. Sensitivity and specificity in diagnostic testing.

90% and 72% homology to the N and S proteins of SARS-CoV, respectively.[16,20]

Cross-reactivity with endemic coronaviruses could reduce the specificity of an antibody test.

Detection of mature antibodies is key to ensuring a highly specific serology test

Detection of mature antibodies is key to ensuring assay specificity. As mature antibodies evolve, they become more effective at tagging the virus for destruction by cytotoxic T cells. Also, antibodies develop that have neutralizing activity, either blocking the virus from entering the cell (neutralizing anti-S antibodies) or binding to the viral capsid, blocking the uncoating of the viral genome (neutralizing anti-N antibodies; Table 1).[3,12,21-23]

Which antibodies should an assay detect to ensure specificity?

For SARS-CoV-2, antibodies against both the viral N and S antigens have been shown to correlate with neutralizing activity, which has also recently been confirmed for the Roche Elecsys® Anti-SARS-CoV-2 assay.[16,24,25] Hence targeting mature antibodies against the N antigen ensures a test that is both highly specific and highly sensitive towards those antibodies most likely to correlate with greatest neutralizing activity.

Elecsys® Anti-SARS-CoV-2 assay performance

In a total of 10 453 samples assessed using the Elecsys Anti-SARS-CoV-2 assay, there were 21 false-positive samples and an overall specificity of 99.80%26. The 95% lower confidence limit was 99.69% (Table 2).

Antibody main types	Early/immature	Mature	Neutralizing
Description	• Appear in early infection phase • Do not effectively recognize the virus	• Appear in convalescent phase • **Effectively recognize the virus**	• Appear in the convalescent/immunity phase • **Effectively neutralize the virus**
Examples	IgA, IgM, early/immature IgG	Late/mature IgGs	Neutralizing antibodies (subset of mature IgGs)
Relevance/purpose	Initial host response to start understanding the virus	Host memory of the virus for future recognition	Render the virus ineffective against the host
All neutralizing antibodies are mature BUT not all mature antibodies are neutralizing antibodies			

Table 1. Antibody types that evolve during infection.

Cohort	N	Reactive	Specificity % (95% CI)
Diagnostic routine	6305	12	99.81% (99.67–99.90%)
Blood donors	4148	9	99.78% (99.59–99.90%)
Overall	10 453	21	99.80% (99.69-99.88%)

Table 2. Diagnostic specificity of the Elecsys® Anti-SARS-CoV-2 assay.

Conclusions

• A positive antibody response will indicate that a person has previously been infected with SARS-CoV-2, and may be used to understand the spread of infection in the population, contact tracing, for vaccine studies, and for supporting return to work strategies.[2,20,27]

• High specificity is needed for an antibody test to be used effectively in these settings; false positive results may lead to an increased risk to people/communities who believe they already have some immunity.

• The Elecsys® Anti-SARS-CoV-2 assay has a high specificity, as assessed in >10 000 samples, which can provide confidence that the PPV of the test will be high in the relevant prevalence settings, including those with lower infection rates.

• Additionally, due to the in-solution double-antigen sandwich assay format of the Elecsys® Anti-SARS-CoV-2 antibody test, it preferentially targets highly specific mature antibodies appearing later post exposure. This provides the added benefit of high sensitivity for the antibodies most likely to be correlated with a neutralizing effect.

Uses for serology testing: in depth

What can an antibody test tell you?[2,8]

Note: Some information contained in this article is taken from rapidly published articles which have not been peer reviewed

Keywords: COVID-19, neutralizing, antibodies, test, testing, Africa, SARS-CoV-2

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Fully automated high-throughput solutions for the detection of SARS-CoV-2 in respiratory specimens

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Germany

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first identified in December 2019 and has quickly become a worldwide pandemic with over 17.6 million cases of coronavirus disease 2019 (COVID-19) by the beginning of August 2020.[1]

Despite SARS-CoV-2 being a worldwide pandemic, Africa was the last continent affected by it. The first COVID-19 patient was confirmed in Egypt on14 February 2020, with the first case in sub-Saharan Africa reported in Nigeria on 27 February 2020 in an Italian patient who had flown to Nigeria two days earlier.[2] According to the African Centres for Disease Control and Prevention (CDC), as of 3 August 2020 there were over 945 000 confirmed cases in 52 African countries, including 503 000 cases in South Africa alone.[3] The arrival of the 'winter flu season' in southern Africa and the high burden of infectious diseases and chronic diseases (e.g., cardiovascular, respiratory) are major factors in this pandemic for the continent.

All coronaviruses are known to be involved in zoonotic transmission between a wide variety of animals and humans. SARS-CoV-2 as well as SARS-CoV and MERS-CoV can cause severe disease, whereas seasonal coronavirus HKU1, NL63, OC43 and 229E are associated with mild symptoms.[2] Coronaviruses target mainly the respiratory and gastrointestinal tracts, and viral shedding can occur from these sites. Transmission and subsequent infection can occur through aerosols (e.g., sneezing, coughing), fecal-to-oral routes and contaminated surfaces.[4]

The rapid identification of infected individuals and their isolation is essential to minimize the spread of the disease.

Several companies manufacturing clinical diagnostic tools have developed molecular assays for the direct detection of the viral genome of SARS-CoV-2 through nucleic acid amplification test (NAAT) methods. Most NAATs are highly sensitive and specific methods for the detection of SARS-CoV-2 in respiratory specimens. As an increase in testing capacity is critically needed to manage current testing demands, fully automated, scalable and high-volume testing solutions (>1000 results in 24 hours) are required.[5]

In the early stages of the outbreak, laboratories around the world tried to convert their manual, laboratory-developed tests for the detection of SARS-CoV-2 to their existing automated high-throughput platforms. In late February 2020, investigators from the Hannover Medical School in Germany demonstrated feasibility to detect SARS-CoV-2 using Hologic's Panther® Fusion system.[6] The group adapted two published PCR-protocols through the instrument's Open Access capability to quickly respond to the emerging threat.[7]

On 16 March 2020, the United States Food and Drug Administration (FDA) granted Emergency Use Authorization (EUA) for Hologic's first molecular SARS-CoV-2 assay on their Panther Fusion platform, enabling laboratories to provide results in approximately three and a half hours and process up to 1000 coronavirus tests in a 24-hour period.[8] Other manufacturers (e.g. Biofire, BD, Cepheid) also received FDA EUA for their automated solutions at that time.

Despite the urgency to have a fully automated and high-throughput solution for SARS-CoV-2 available, the overall quality of an assay regarding its

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† The Aptima SARS-CoV-2 assay:
- Has not been FDA cleared or approved;
- The test has been authorized by FDA under an EUA for use by authorized laboratories;
- The tests has been authorized only for the detection of nucleic acid from SARS-CoV-2, not for any other viruses or pathogens; and
- The test is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of *in vitro* diagnostic tests for detection and/or diagnosis of COVID-19 under Section 564(b)(1) of the Act, 21 U.S.C.§ 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.

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Table 1: Panther Fusion SARS-CoV-2 Performance Relative to Expected Results for Swab Specimen

		Contrived Specimen Expected Result	
		Positive	Negative
Panther Fusion SARS-CoV-2 Assay	Positive	69	0
	Negative	0	109

Positive Percent Agreement: 100% (94.7% – 100%)
Negative Percent Agreement: 100% (96.6% – 100%)
Overall Agreement: 100% (96.6% – 100%)

Source: Aptima SARS-CoV-2 Package insert

specificity and sensitivity cannot be compromised. High specificity minimizes the number of individuals detected as false positive, whereas high sensitivity reduces the number of individuals that are detected as false negative.[9]

In accordance with several county-specific recommendations, most molecular assays that detect SARS-CoV-2 follow a dual target strategy where two different SARS-CoV-2-specific genes or gene regions are detected and amplified. This mitigates the risk of a false-negative test result due to a mismatch or mutation in one of the gene targets, as mutations in several genes of SARS-CoV-2 are already observed.[10]

Early data on the Hologic Panther Fusion SARS-CoV-2 assay showed a 100% agreement on assay performance relative to expected results in contrived specimens.[11]

A study by Zhen et al.[12] benchmarked the analytical and clinical performance of four commercially available molecular SARS-CoV-2 assay that received FDA EUA using nasopharyngeal swabs from symptomatic COVID-19 patients. The authors concluded that all assays yielded comparable results; however, Hologic's SARS-CoV-2 was one of the assays that outperformed the other assays on limit of detection (LoD). The clinical correlation was in line with the performance on the LoD: 'Hologic's SARS-CoV-2 on the Panther Fusion was one of the assays that detected correctly all samples deemed positive.'

In early June 2020, Hologic received FDA EUA clearance and the CE-mark for their second assay for the novel coronavirus. The Aptima® SARS-CoV-2 assay utilizes the large, existing global installation base of Hologic's Panther instrument with the ability to produce and distribute millions of tests each month. Unlike many other manufacturers Hologic produces their Aptima SARS-CoV-2 assay at different production sites to circumvent logistical challenges regarding the availability of assay reagents and required consumables. A recent study on the performance characteristics of this high-throughput automated assay showed a 100% sensitivity in clinical nasopharyngeal swab specimen with a specificity of 98.7%.[13]

Serological analysis, or 'antibody testing', of COVID-19 patients to detect antibodies against SARS-CoV-2 is complicated, because coronavirus-induced antibody responses are highly variable and

Table 2: Clinical performance comparison of four EUA molecular assays for the detection of SARS -CoV -2 (modified)

Molecular Assay		Reference Standard [a] Positive	Reference Standard [a] Negative	(± 95% CI) [bc] Kappa (κ)[d]	(± 95% CI) [bc] PPA	(± 95% CI) [bc] NPA
Vendor C	Positive	51	1[e]	0.98 (0.94-1)	100% (0.93-1)	98% (0.89- 0.99)
	Negative	0	52			
Vendor D	Positive	51	0	1.0 (0.99-1)	100% (0.93-1)	100% (0.93-1)
	Negative	0	53			
Vendor G	Positive	49	0	0.96 (0.91- 1)	96% (0.87- 0.99)	100% (0.93- 1)
	Negative	2[f]	53			
Hologic	Positive	51	2[g]	0.96 (0.91- 1)	100% (0.93- 1)	96% (0.87-0.99)
	Negative	0	51			

Source: Zhen W, Manji R, Smith E, Berry GJ. Comparison of Four Molecular In Vitro Diagnostic Assays for the Detection of SARS-CoV-2 in Nasopharyngeal Specimens. J Clin Microbiol. 2020 Jul 23;58(8):e00743-20. doi: 10.1128/JCM.00743-20. PMID: 32341143; PMCID: PMC7383517. (modified)

short-lived.[14] Several public-and private partnerships are in place to dramatically accelerate the development and validation of potential vaccines against SARS-CoV-2, and first clinical trials are underway.[15] These vaccines will play a critical part in overcoming the pandemic by reducing mortality, morbidity and hopefully transmission of the virus. However, until vaccines against SARS-CoV-2 are available and, most importantly, are widely administered, fully automated high-throughput solutions to detect individuals with a SARS-Cov-2 infection are required. These solutions empower laboratories to rapidly rise to the diagnostic challenge and deliver results that are needed by clinicians and the patients they serve.

The views and opinions expressed in his article are those of the author and do not necessarily reflect the opinion of Hologic Inc. or any of its affiliated companies.

Keywords: SARS-CoV-2; Hologic; Panther; Aptima; Automation; COVID-19

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Maintaining HIV Early Infant Diagnosis and Viral Load Monitoring during the COVID-19 Pandemic

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The ongoing COVID-19 pandemic is a serious global health threat affecting 213 countries and territories and impacting global prevention and treatment progress against other infectious diseases, such as HIV. It has become evident that the COVID-19 pandemic will remain a significant concern for the near, and possibly longer, future and that sustained efforts are required to limit transmission even in areas initially successful in outbreak control. Reliable and high-quality COVID-19 testing is fundamental to mitigating spread; in Africa, nearly 9 million tests have been conducted so far and countries are continuing to ramp up testing capacity.

The COVID-19 pandemic has exposed vulnerabilities in national healthcare systems and created strains even in well-resourced settings. In Africa, these demands are even more acutely felt given workforce and infrastructure constraints. In addition, sub-Saharan Africa has 25.7 million people living with HIV and 16.4 million people on antiretroviral therapy (ART). People living with HIV do not have substantially increased risk for acquisition or death from COVID-19; however, if concerted efforts are not made to mitigate COVID-19-related interruptions in health services and supplies, the effects could reverse hard-won gains in the HIV epidemic. In a Global Fund survey, 80% of HIV programs reported service delivery disruptions, with 21% of programs describing high to very high critical disruptions.[1] To avert COVID-related ART interruptions, global and national interventions have been instrumental in providing patients with continuous ART supplies through multi-month dispensing and community-based ART distribution. However, decreased access to other life-saving HIV services could also have a detrimental impact, especially given the probable long-term effects on commodities, the healthcare work force and communities.

The need to rapidly scale-up SARS-CoV-2 diagnostic testing has led to adaptation and use of PCR instruments, supplies, and personnel normally used for HIV viral load and early infant diagnosis (EID) testing, making access to these essential tests particularly vulnerable. In the Global Fund Survey, viral load testing was the second most common service disrupted (after HIV testing),[1] and a recent study in Kenya showed turn-around time for viral load results increased from 1–2 weeks to several months due to diversions of laboratory resources for COVID-19 testing.[2] As demand for COVID testing accelerates, these issues will likely become even more acute. Without focused efforts to adapt laboratory systems to the new realities of concurrent HIV and COVID epidemics, we risk a dangerous situation in which we fall short of meeting the diagnostic needs for both diseases. To create a sustainable and effective system for the near future, laboratory leaders and clinical program managers should work together to determine how to address the diagnostic needs for the COVID-19 pandemic, while also maintaining essential HIV laboratory services such as viral load and infant virologic testing. This will require a thoughtful approach to determine appropriate prioritization of testing for people living with HIV and HIV-exposed infants.

More specifically, there will need to be reprioritization and operational strategies at the country national level to get the right tests to the right places and to people most in need. In Africa, this could mean the more highly populated urban areas that can accelerate the spread of the virus. We have already seen tremendous efforts by partners, such as Unitaid, to quickly reshape their programs to accommodate COVID testing, while also trying to maintain EID and viral load (VL) point-of-care (POC) testing. We should continue to look to

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the existing footprint of diagnostics, in particular POC testing, and how to optimize their testing capacity, strategically place new COVID-19 diagnostic innovations where needed, and most importantly, consider all the short and long-term implications to the healthcare and laboratory systems when flooding country programs with new tests during emergencies. In an article by Cnops et al., the authors question 'what lessons did we learn from the Ebola outbreak?'. There was an urgency to bring in new diagnostics, changing the laboratory network for a short period of time, and then what happened to all those devices?[3] Where are they now for the next outbreak? There should be continual, smart, far-sighted investments in the healthcare infrastructure to prepare us for the next outbreak but also maintain essential services, with consideration on how to quickly optimize the existing health system to meet fluctuating demands.

VL monitoring: At the facility and program level, providers and managers should re-assess VL testing guidance to help reduce the volumes of VL tests submitted to laboratories overstretched with competing COVID-19 testing demands. Routine VL monitoring can be safely delayed for patients stable on ART, but providers should be directed to ensure that VL testing is maintained for children, pregnant and breastfeeding women, adults with documented non-suppression on their last VL test and other groups at high risk for virologic failure (e.g., adolescents and youth, marginalized populations) to identify those failing treatment. To mitigate concerns and risks related to COVID-19, decentralized specimen collection should be provided as much as possible.

Early infant diagnosis: EID and prompt ART can reduce infant mortality by 76% and the progression of HIV by 75%. In the absence of ART, the mortality rate for HIV-positive infants is 20% by age 3 months.[4] Thus, infant virologic testing and linkage to ART for those positive for HIV infection is a life-saving and time-sensitive intervention that must not be delayed. Programs and laboratories should ensure that collection and processing of infant virologic testing specimens is maintained as a priority.

Africa has spent the past 20 years establishing laboratory systems to address the HIV epidemic and has invested heavily in building laboratory capacity with high throughput molecular instruments to scale-up access to routine VL monitoring and EID. To further increase access and alleviate bottlenecks, African countries also lead the globe in use of innovative technologies such as POC testing for both EID and VL. UNICEF's procurement

Testing considerations to manage COVID-19 and maintain essential EID and VL testing services

EID

- Testing must be maintained with no delays in test turn-around times and no lack of access
- Utilize/optimize POC testing to increase testing coverage and minimize bringing potentially high-risk populations into contact with COVID-19
- Consider platforms with connectivity capability to enable digital reporting of results

COVID-19

- Implement appropriate testing strategies to reduce transmission6
- Testing should include high through-put, near POC, and lateral flow assays for diagnosis and surveillance

VL

- Possibly delay testing for stable patients on ART to decrease testing volumes and minimize potential COVID-19 exposure for patients and staff
- Consider how to utilize and optimize POC instruments for VL testing; particularly POC platforms that cannot perform COVID-19 testing
- Consider platforms with connectivity capability to enable digital reporting of results

of POC tests for HIV EID and VL testing has grown substantially since 2015 to reach 445 342 tests by 2019.[5] We are currently underutilizing POC testing but must consider how to leverage the experiences and instruments to ensure access to VL and EID.

Some countries are considering plans to alleviate national laboratory testing backlogs by moving most EID and VL testing to POC platforms (e.g., mPIMA) at the community level where healthcare workers are already equipped for this type of service. Decentralization of EID and VL testing to community-level POC instruments would free up capacity on high throughput and near-POC platforms (e.g., GeneXpert) at hospitals and district clinics that will likely have the highest burden of COVID-19 patients.

During the pandemic, all modalities for diagnosis and surveillance of COVID-19 should be explored to curb transmission. However, we cannot divert resources from HIV services in Africa, as this would amplify fractures in health systems and expand the costs of managing both critical situations at a time when resources are increasingly scarce. As Winnie Byanyima, Executive Director of UNAIDS, said, 'There is a risk that the hard-earned gains of the AIDS response will be sacrificed to the fight against COVID-19, but the right to health means that no one disease should be fought at the expense of the other.' [7,8]

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Key challenges of training for lab safety and COVID-19 effects

Brenda Silva

Medical Laboratory Observer

Senior Editor

Traditionally, best practices in lab safety have included wearing personal protective equipment (PPE) while performing lab procedures in such a way as to prevent the risk of injury or transmission of infectious diseases to lab personnel. Today, lab safety includes the same practices plus new issues and challenges that lab directors must address, such as hiring and training a sufficient number of incoming lab personnel to replace staff members who are aging out into retirement.

Along with ensuring necessary workforce positional needs are met, training and proficiency of all new lab personnel are top priorities, just as in the past. However, with the emergence of SARS-CoV-2 and COVID-19, current learning curves in clinical labs also must incorporate procedural proficiencies that prepare all lab staff in the event of another pandemic in the future.

Lab workforce shortage

Before lab directors create or streamline training programs for additional lab personnel, their work begins with finding qualified candidates to fill key positions within the clinical lab. Current research highlights a workforce shortage among lab personnel, with some positions left unfilled for months.[1]

Brittany Vaughn, MHA, MLS(ASCP)SM, Global Healthcare Consultant at BD, located in Franklin Lakes, NJ, reports that "Laboratories are experiencing staffing vacancy rates that exceed the number of new graduates; coupled with high retirement rates due to an aging working population, this creates a substantial workforce shortage crisis."[1]

She continued, "The workforce profile of many laboratories looks like an inverted bell curve, with a large number of technologists just starting out their career and an even larger number of highly experienced technologists preparing for retirement in the next five to 10 years. As those retirement-ready technologists move on to their next stage of life, labs commonly face challenges finding and hiring experienced and qualified replacements. It is not uncommon for certified laboratory positions to go unfilled for months due to this workforce shortage, particularly those seeking a degree of specialty experience or positioned on less-desirable overnight shifts."

Effective training and proficiency

For labs fortunate enough to find qualified additions to their staff, the most important task at hand becomes training them. Training programs, regardless of the area of specialty, are typically only as successful as the communication of an instructor and the competence of a student. In the clinical lab, both instructor and student look to their training for safety within the lab and for helping patients waiting for a diagnosis.

Luann Ochs, MS, Product Development Manager at the Clinical and Laboratory Standards Institute (CLSI), located in Wayne, PA, pointed out that "Proper training of laboratory workers is essential to producing accurate results for patient care and is the lab's first line of defense against errors. Robust training and competence assessment programs are an essential element of a quality management system and are required by all laboratory

accreditors. Although laboratory managers know the importance of training for good quality results, competence assessment is one of the top 10 deficiencies seen by major accreditors in the U.S.[2] Clearly, for many laboratories, more work needs to be done in this area."

Training and competence assessment

According to CLSI's document QMS03, Training and Competence Assessment,[3] "people are the most valuable resource of the organization. Effective training and competence assessment programs ensure personnel are knowledgeable and competent in their assigned roles and responsibilities."

As such, the QM303 CLSI document lists three recommendations for effective training and competence assessment programs:

Ensure personnel performance results in consistent, predictable, and high-quality outcomes.

Ensure performance of assigned job tasks remains constant.

Verify that personnel have and can demonstrate the necessary knowledge, skills, and behaviors to perform their respective duties.

Ochs adds, "And while everyone knows that training is needed for newly hired personnel, it's also important to ensure effective training whenever organizational or technological changes occur that affect work processes, and when any employee repeatedly demonstrates performance problems. Competence should be assessed not only following a training exercise, but also periodically to ensure continued performance. Competence should also be assessed when processes or responsibilities change, as well as when any retraining needs are identified."

According to the QMS03, "an effective training and competence assessment program can decrease the risk of a nonconforming event that could lead to an undesired patient outcome and could also have adverse financial consequences."

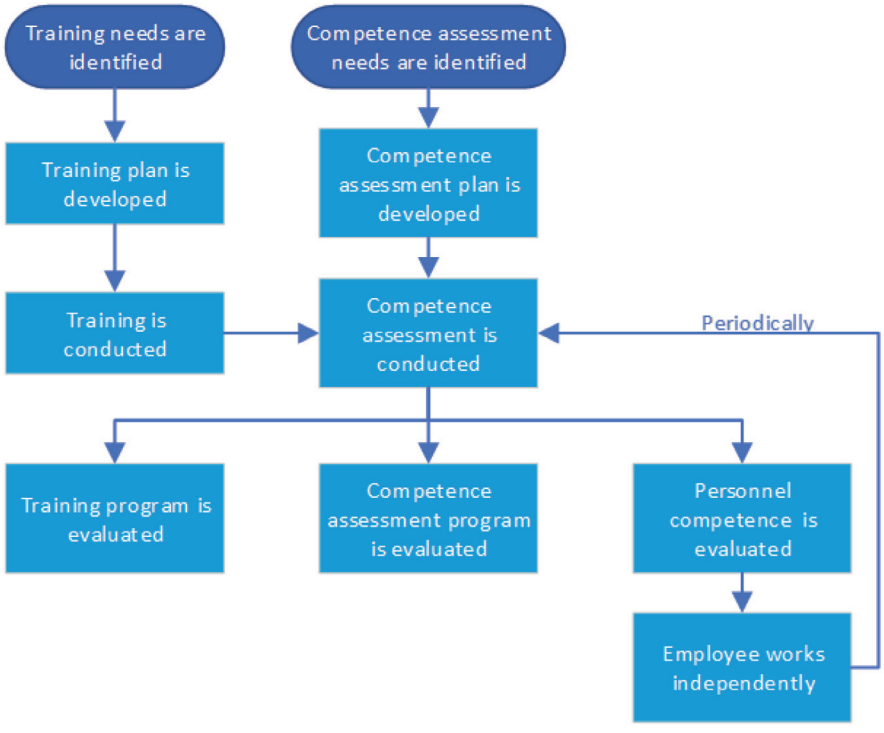

Figure 1: The inter-relationships between training and competence assessment

Source: CLSI

Challenges of training methods

When it comes to the best training methods for lab personnel, all staff members may not respond the same way to the same methods. It is up to the lab manager to realize this and work with new hires to find a training method that allows the required training to take place in a way that benefits both the lab manager and the new staff member.

Vaughn from BD asserts, "Hiring new graduates and trainable individuals can be a prerequisite for a steeper learning curve, resulting in increased training efforts, which more often than not are short cut due to a lack of time due to the staffing challenges. There are, however, a couple of different approaches available in a laboratory manager's toolbox to counteract this downward spiral:

Defining a clear career pathway for non-certified employees within the lab to encourage advancement into a technologist role through partnership with an MLS or MLT teaching program, or by providing an opportunity to gain the necessary full-time clinical experience required to qualify for alternate certification routes through the American Society for Clinical Pathology (ASCP). The respective employees would contractually guarantee to remain employed by the laboratory for a set amount of years, if the laboratory sponsors their education. Having defined career pathways can create a steady feed of employees to pull

from as retirements and other openings present themselves.

(When considering this approach, it is important for laboratories to support their employees by providing access to education and training for the scientific theory behind the work they are doing as well as teaching how the work performed ties into the greater picture of patient care.)

Adopting new automated technology in the laboratory will free up resources to be reallocated into full- or part-time training roles, allowing for greater and more focused attention on the training process.

Bringing experienced technologists back after retirement, or incentivizing them to stay on longer prior to retirement, by offering part-time training roles to bridge the knowledge gap and allow them to pass on the baton.

Exploring new training methods that allow the trainees to access training content from their mobile devices will appeal to different training styles, as well as allow the trainings to be executed more frequently. Video-recorded training is a successful method for ensuring consistency of material shared with students."

Effects of COVID-19 on lab safety

With almost a year of dealing with SARS-CoV-2 and COVID-19 on a daily basis, it would seem that lab personnel have a good understanding of the virus and its subsequent disease. However, the reality is that there is still much to learn from this pandemic that continues to be responsible for infections and deaths every day around the world.

Reminding clinicians about the risk of COVID-19 transmission, CLSI's Ochs points out that "Although the general transmission of COVID-19 is typically through respiratory droplets, laboratory workers are at risk of infection through aerosolization, splattering, and splashing of laboratory specimens. This can occur whenever samples are being handled, but especially when samples are being opened and prepared for testing. Precautions must be taken to prevent exposure from accidental sample contact."

> "Proper training of laboratory workers is essential to producing accurate results for patient care and is the lab's first line of defense against errors."
> -- Luann Ochs, MS

According to another CLSI document, M29, Protection of Laboratory Workers From Occupationally Acquired Infections, "facial barrier protection should be used if there is a reasonably anticipated potential for splattering or splashing blood or body substances or any liquid suspected of containing infectious agents." It goes on to say that "a plastic face shield provides the best facial protection,"[4] and that splashguards may serve as an acceptable alternative to plastic face shields, but neither face shields nor splashguards are protective enough when it comes to aerosols. When aerosols are a concern, respirators are needed, or all work can be performed within a biological safety cabinet (BSC).

Ochs summarizes, "The M29 guideline encourages labs to be prepared for dealing with infectious agents by preparing a biological hazard assessment before a hazard actually occurs. Factors to consider include possible routes of transmission, including portals of entry through which pathogens can enter the body; possible agents that could be encountered and their pathogenicity; and the work environment, including the facility, procedures, and the availability and use of PPE. All of these factors contribute to the overall level of hazard to which an individual laboratory worker may be exposed."

"In addition, according to M29, negative factors in the laboratory environment can affect the behavior of staff (e.g., poor workflow, poor housekeeping, insufficient space in the BSC). The nature of the work itself (e.g., high stress, high volumes of samples and workload, lack of time for adequate training or attainment of competency, repetitive nature of routine procedures) can lead to a false perception of safety. This perception can lead to complacency and unknowingly increase the risk of exposure (e.g., disruption of air barrier in the BSC, assumptions that PPE are performing properly),[4] she added.

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CLSI currently offers the following documents on its website to help with the COVID-19 pandemic. The documents are free of charge and only require an email to download. Once logged in, a summary of the documents is available, with each description including a"How is this helpful for COVID-19?" tip. Further information can be found here: https://clsi-covid-19.org/Login.aspx.

CLSI EP19 ED2:2015

A Framework for Using CLSI Documents to Evaluate Clinical Laboratory Measurement Procedures, 2nd Edition

This report uses the "measurement procedure lifecycle" framework to aid users of CLSI evaluation protocols documents during establishment and implementation of measurement procedures developed by both commercial manufacturers and clinical laboratories, i.e., for laboratory-developed tests.

How is this helpful for COVID-19?

EP19 explains when you need to validate a test and when you need to verify a test. It also lists all CLSI documents that can help you either verify or validate a new test in your laboratory.

CLSI GP36 A:2014

Planning for Laboratory Operations During a Disaster; Approved Guideline

This document provides guidance for laboratory and healthcare leadership for development, implementation, and sustainment of effective emergency preparedness plans (all hazards) supporting nonanalytical components of clinical and public health laboratory services that may pertain to various natural and manmade disasters.

How is this helpful for COVID-19?

This document will help you develop and implement emergency preparedness plans.

CLSI MM22 A:2014

Microarrays for Diagnosis and Monitoring of Infectious Diseases; Approved Guideline

This document provides guidance for the laboratory development and use of qualitative nucleic acid microarray methods for the diagnosis and monitoring of infectious diseases. It also presents recommendations for validation and verification, quality control, and interpretation of results.

How is this helpful for COVID-19?

This guideline will help you understand how to validate or verify a new microarray test.

CLSI POCT07 A:2010

Quality Management: Approaches to Reducing Errors at the Point of Care; Approved Guideline

This document presents the core infrastructure for a standardized error tracking system with the primary goals of reducing risk and increasing quality of point-of-care testing, while accumulating standardized data for benchmarking use.

How is this helpful for COVID-19?

This document will help you identify and eliminate errors in your point-of-care testing programs.

CLSI QSRLDT-2015

Quality System Regulation for Laboratory-Developed Tests: A Practical Guide for the Laboratory

This practical guide, compiled with the help of experts from the in vitro diagnostics industry, is intended for the laboratory that is creating laboratory developed tests that may be subject to the U.S. Food and Drug Administration (FDA) regulations, specifically the Quality System Regulation (QSReg), 21 CFR Part 820.

How is this helpful for COVID-19?

This guide will help you meet FDA requirements for a laboratory developed test.

Is responding to the COVID-19 pandemic an opportunity or a threat to achieving universal health coverage?

As the COVID-19 pandemic has spread across the world, one worry foremost on the minds of many public health professionals in Africa is how testing and treatment for priority diseases like HIV/AIDS, tuberculosis and malaria would be maintained in the context of mounting the health system response against the COVID-19 threat.

ASLM recently conversed with a leading expert on these issues, Prof Madhukar Pai, MD, PhD, FCAHS, the Canada Research Chair in Epidemiology and Global Health at McGill University in Montreal, Canada, for his perspective, especially in the area of diagnostics.

ASLM: Since the COVID-19 pandemic has been officially recognized by the WHO, Africa has worked hard to surge the testing capacity for the SARS-CoV2 virus. Only 2 laboratories were capable of conducting molecular diagnostic for COVID-19 in February 2020. By late June 2020, the World Health Organization reported all African countries had laboratory capacity to test for SARS-CoV-2.

What is your general opinion on the COVID-19 diagnostic capacity on the continent? Do you think that we have learnt from the Ebola Epidemic?

Madhukar Pai: As I wrote in a recent article at Forbes, outbreaks and emergencies have a way of exposing weaknesses in health systems and governance.[1] The COVID-19 pandemic has clearly exposed how countries have neglected global health diagnostics for decades. In a crisis, everyone is scrambling to scale-up testing capacity, and most nations are struggling. We cannot build up laboratory capacity overnight. We need to invest in laboratories and diagnostics as a key component of universal health coverage (UHC). In fact, without diagnostics, UHC is not feasible.[2]

I hope this pandemic will force all countries to develop their own national essential diagnostics lists (EDL) (adapted from the WHO EDL), and ensure access to essential tests at various levels of the health system.[3]

The Ebola outbreaks in Africa should have been used as a warning sign to ramp up diagnostic and laboratory capacity. But apparently this has not happened – most countries in Africa still have very low COVID-19 testing rates. Africa simply cannot continue to neglect diagnostics and laboratories. Donors and funders cannot continue to emphasize vaccines and drugs, without investing in diagnostics. And we cannot afford to think about diagnostics only during outbreaks and emergencies. That is myopic, unsustainable, and, frankly, detrimental to the UHC agenda.

ASLM: You recently shared your concerns about the 'covidization' of funding and resources, while other infectious disease remain extremely prevalent. Can you elaborate on the implication of skewing our attention to the COVID-19 pandemics?

MP: Yes, as I have written, during this pandemic, researchers, universities, funders, philanthropies, journals, and journalists have all pivoted, en masse, to COVID-19. Everyone is 'covidized', and that worries me.[4] Yes, we do need to control COVID-19, but we cannot afford to neglect other major priorities in health. Because of COVID-19, there are massive setbacks in our efforts to end tuberculosis, malaria and AIDS.[5] So, we must not stop testing for these major killer diseases, and ensure continuity of routine, essential health services. We cannot take away funding from other priorities to fight COVID-19. We must advocate for new funding to deal with the COVID-19 crisis. And all health research cannot be about COVID-19.

A big concern that is emerging now is that diagnostic companies are facing a huge demand for their COVID-19 tests. This is understandable and I hope they will rise to the occasion and meet the demand. But if this means diagnostic companies will drastically reduce manufacture of other tests (like tuberculosis, AIDS, malaria), then that worries me a lot.[6] We need diagnostic

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companies to continue meeting their global health obligations and not de-prioritize other disease areas, especially diseases that may be less profitable for industry.

ASLM: In your opinion, what should be done differently to increase the capacity of laboratory systems and networks of Africa can meet the current and upcoming health challenges? What should be the new role of organizations like Africa CDC and ASLM should do? How can countries act differently?

MP: I think a key lesson from this pandemic is that UHC cannot be a luxury or privilege. It is a fundamental and non-negotiable universal human right. I hope all African countries will commit to making UHC a reality by 2030, in line with the Sustainable Development Goals. When countries develop their UHC benefits packages, they must explicitly include and budget for essential tests, along with essential medicines. If this is done, we should see good progress with increasing diagnostic capacity within countries.

It is good to see diagnostics get a lot of attention during this pandemic. But we cannot think about testing only during a crisis. What we need is a long-term, strategic, well-resourced alliance of all key stakeholders, to make sure essential diagnostics are available, affordable, and accessible in all low and middle-income countries, at all tiers of the health system, during all periods (not just during outbreaks). Stakeholders include country governments, WHO and other key United Nations agencies, donors, diagnostics industry, academics, non-governmental organizations, and civil society. To convene stakeholders, we need honest broker agencies. That is where I see agencies like ASLM and Africa CDC come in. If they can coordinate and align various stakeholders in Africa, we can make sure essential diagnostics reach everyone who needs them.

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Prof Pai did his medical training and community medicine residency in Vellore, India. He completed his PhD in epidemiology at UC Berkeley, and a postdoctoral fellowship at the UCSF. He serves on the SAGE-IVD committee of WHO, Geneva; Scientific Advisory Committee of FIND, Geneva; and Access Advisory Committee of TB Alliance, New York. He serves as the Chair of the Public-Private Mix (PPM) Working Group of the Stop TB Partnership. He is on the editorial boards of Lancet Infectious Diseases, PLoS Medicine, and BMJ Global Health, among others. His research is mainly focused on improving the diagnosis and treatment of tuberculosis, especially in high-burden countries like India and South Africa. His research is supported by grant funding from the Gates Foundation, Grand Challenges Canada, and Canadian Institutes of Health Research. He has more than 300 publications. He is recipient of the Union Scientific Prize, Chanchlani Global Health Research Award, Haile T. Debas Prize, and David Johnston Faculty & Staff Award. He is a member of the Royal Society of Canada, and a Fellow of the Canadian Academy of Health Sciences.