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AFRICAN SOCIETY FOR LABORATORY MEDICINE

ADVANCING THE LABORATORY PROFESSION AND NETWORKS IN AFRICA

Quality Assurance and Quality Control during emergency response

Collins Otieno Odhiambo (PhD)
ASLM

Implementation of novel laboratory diagnostics for emerging infectious diseases Workshop 19-20 May 2021

Outline

- Introduction
- Quality Assurance
- Quality Control
- External Quality Assessment
- Quality Improvement
- Summary

Introduction

- Coronavirus disease 2019 (COVID-19) pandemic, now a major public health problem across the globe
- Early detection of SARS-CoV-2 critical in limiting transmission, ensures isolation/quarantine to prevent local spread and inform intervention
- Lab diagnosis is essential element of disease surveillance for routine confirmation of infection and rapid identification of outbreak cause
- Molecular assays on nasopharyngeal swabs most commonly used as reliable tests for diagnosis

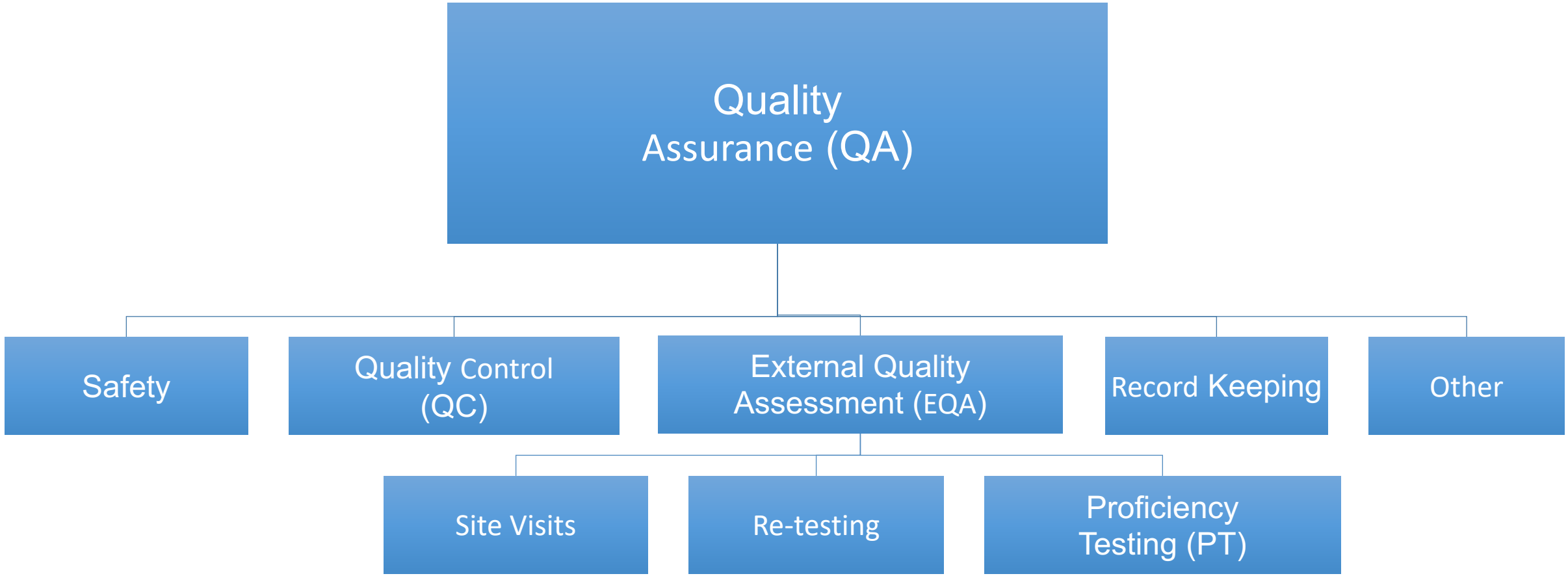
Introduction Cont…

- Most molecular assays have 100% specificity, since primers designed specifically for target gene sequences
- However, sensitivity affected by specimen quality, sampling time to symptom onset, testing errors, or other technical deficiencies
- False-positive/negative results have negative implications for disease containment efforts
- Therefore, it is critical to implement quality assurance (QA) measures in all COVID-19 testing laboratory networks

What is Quality Assurance?

- Focuses on providing confidence for the fulfilment of quality requirements
- System designed to continuously improve reliability and efficiency of laboratory testing services
- Aims to minimise error rates in all stages of laboratory testing processes (pre-analytical, analytical, and post-analytical)

Quality Assurance Activities



QA encompasses entire testing cascade

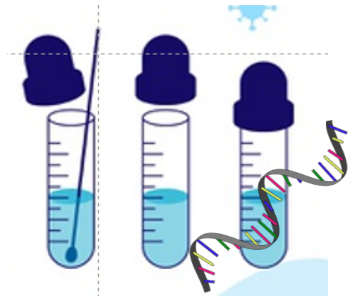
clinic | transport | Laboratory

Wrong sample collection

Sample transport in medium

RNA degradation

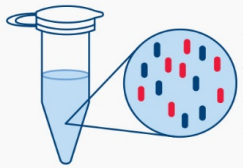
RNA extraction in lysis buffer (**extraction kit**)



RNA degradation

Nucleic acid contaminants

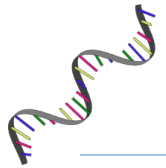
Prepare RT PCR reaction master mix (**RT PCR kit**)



- Primers
- dNTP
- Dyes
- enzymes

Bad reagents. Wrong mix

Nucleic acid contaminants



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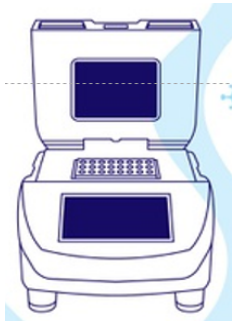
Master mix

One step RT PCR
-> **RT of RNA into cDNA + PCR reaction**
-denaturing the cDNA
-annealing the probes
-extending the probes
-measuring SARS Cov 2 DNA

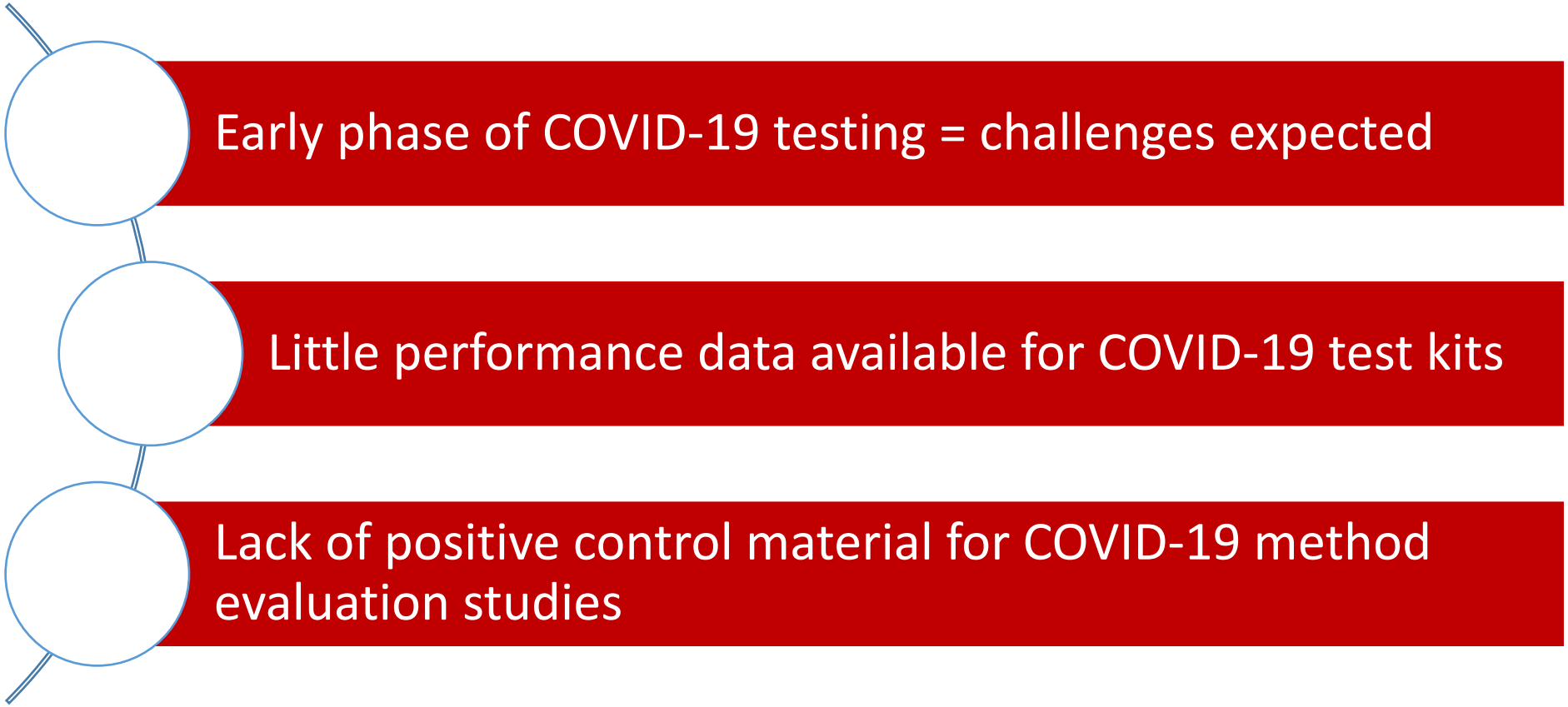


Wrong PCR cycles

Positive or negative results

Wrong interpretation

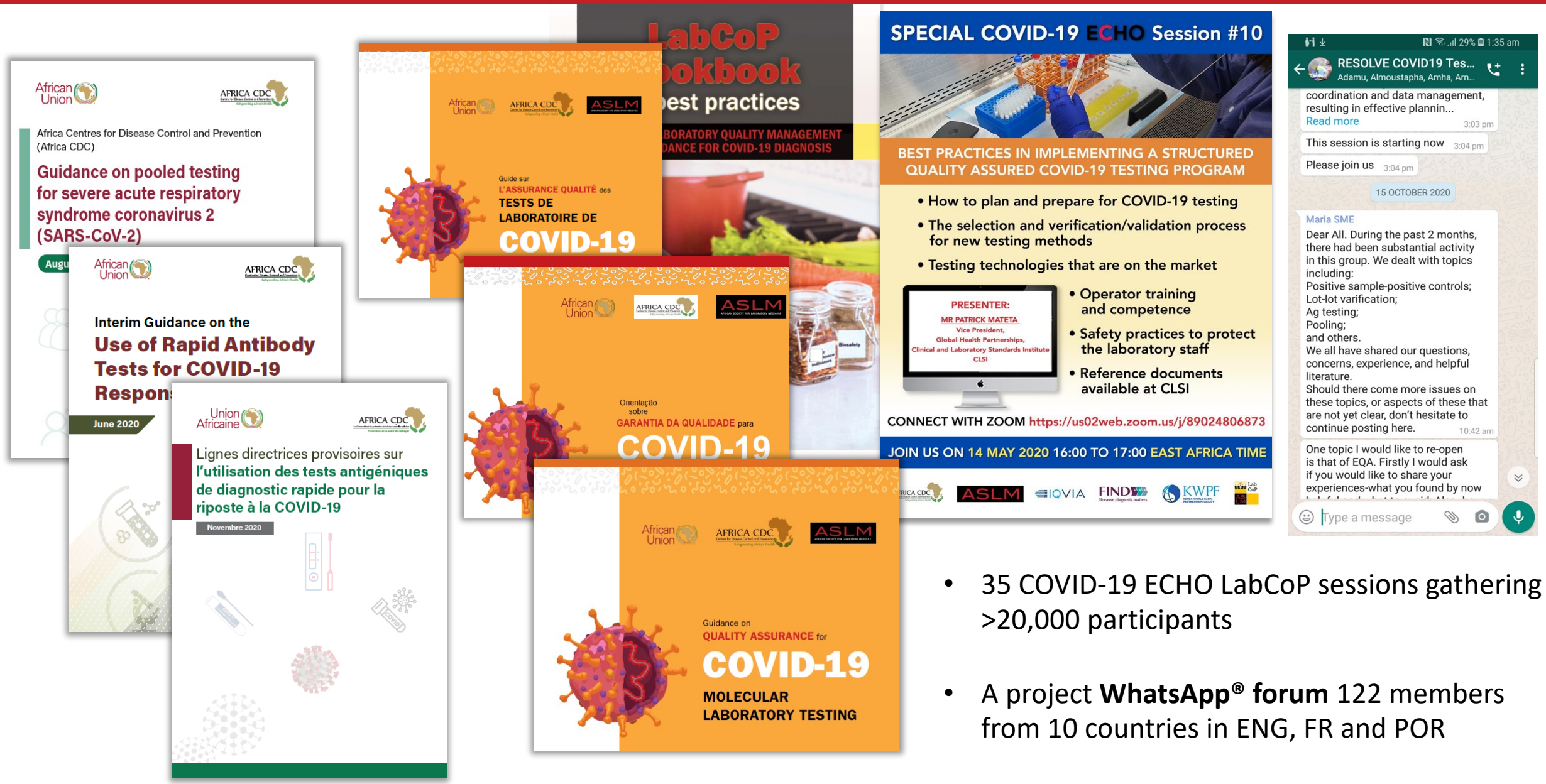
QA– COVID-19 Current Challenges



IMPORTANT: *Understanding of COVID-19 test kits is limited; Different quality paradigm exists*

- *Understand impact of governments waiving regulatory requirements to allow use of kits without complete manufacturer evidence normally required*

Guidance development and dissemination



- 35 COVID-19 ECHO LabCoP sessions gathering >20,000 participants
- A project **WhatsApp® forum** 122 members from 10 countries in ENG, FR and POR

What is Quality Control?

- Material or mechanism that monitors analytical performance of the test when used with or as part of a test system
- May monitor entire test system or only one aspect of the test
- Validates competency of testing labs by assessing sample quality and monitoring procedures, kits, and instruments against established criteria
- Includes review of results and documentation of the validity of testing methods

QC Testing Events – COVID-19 Testing

- During method evaluation
- Checking instrument integrity
- Before patient testing
- Receiving new test shipment
- Training new test operators

QC Samples – COVID-19 Testing

- Extraction positive control:
  - Used to demonstrate successful recovery of RNA and integrity of extraction reagent
  - Should be extracted and processed with each sample extraction run
- No template control (NTC):
  - Checks contamination during specimen extraction and/or plate set up
  - If any NTC reactions are positive, sample contamination may have occurred and test must be repeated with strict adherence to the testing procedures
  - Also indicates whether PCR reagents have been compromised

QC Samples – COVID-19 Testing Cont…

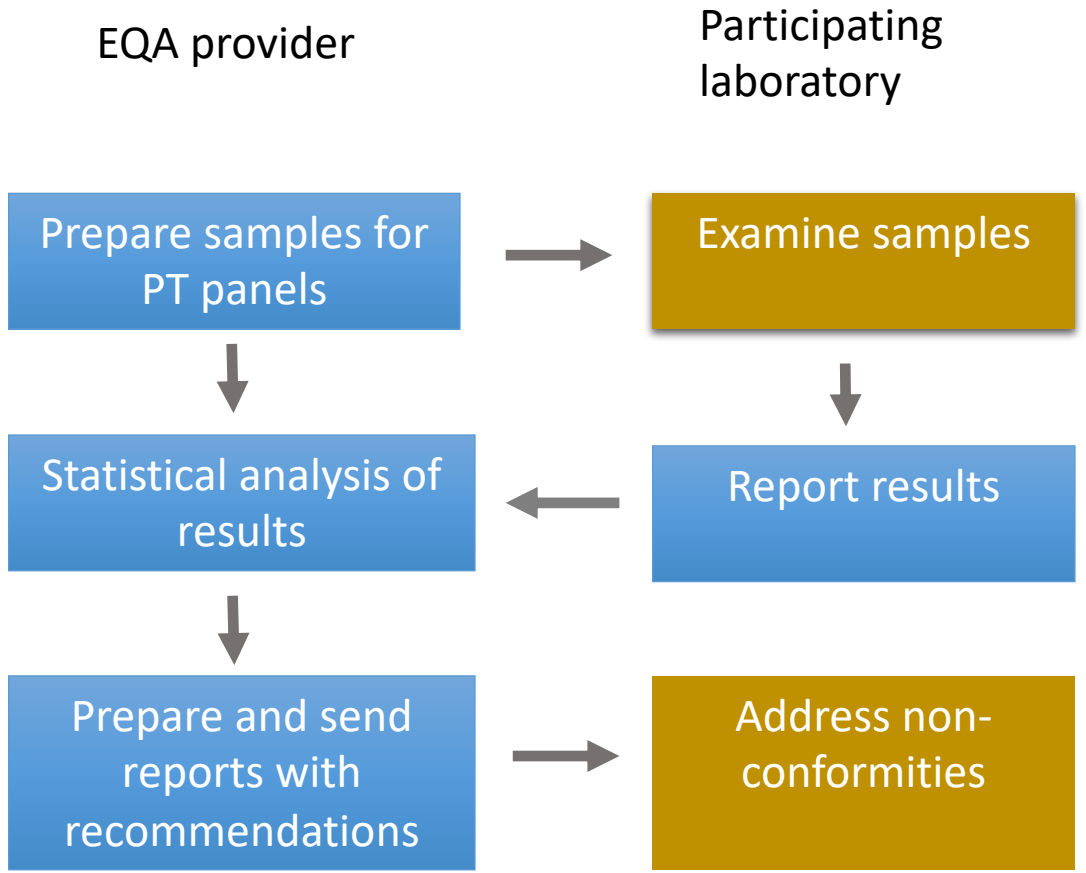
- Positive template control:
  - in vitro-transcribed SARS-CoV-2 RNA, either gene fragment or whole-genome
  - Indicates limit of detection and robustness of the assay.
  - Should be handled with caution in a dedicated nucleic acid handling area to prevent possible cross-contamination

External Quality Assessment

- Process allows testing labs assess performance by comparing results with other peer labs via panel testing and retesting
- Evaluates testing competency, performance of laboratories, reliability of testing methods, accuracy of results reports, and follow-up of unacceptable EQA results with corrective action
- Three methods applied: Proficiency testing, re-testing and onsite evaluation

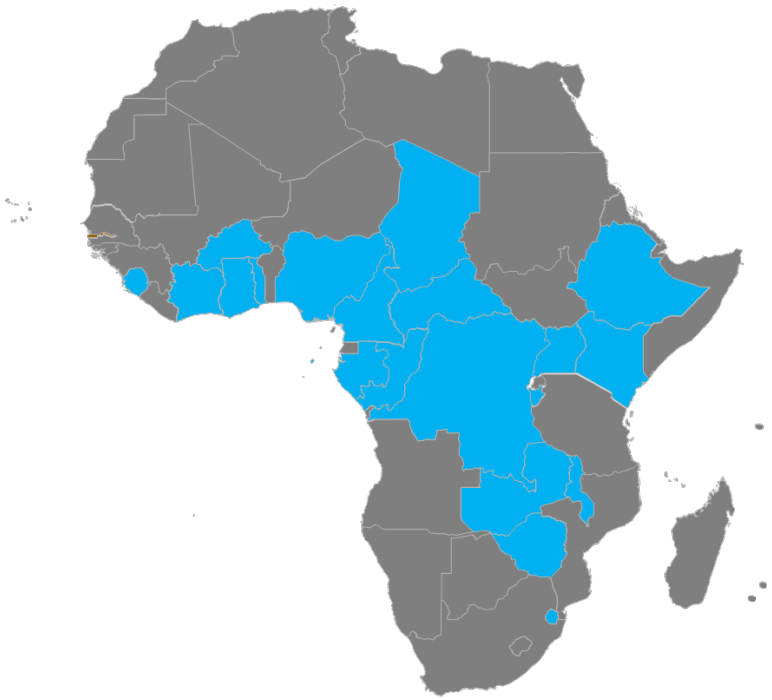
Proficiency Testing

- External provider sends a set of SARS-CoV-2 positive and negative simulated clinical samples for testing and the results of all laboratories analysed, compared, and reported back to the participating laboratories



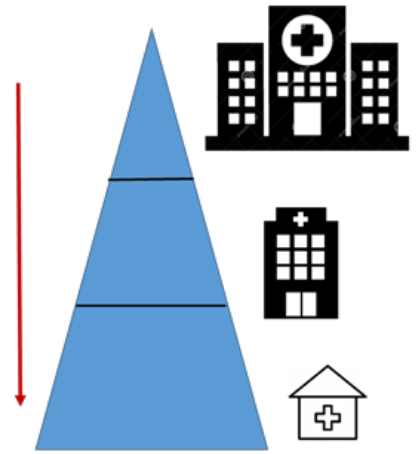
Support for External Quality Assessment: synergies

WHO EQAP
178 labs in 45 countries



ASLM
355 labs in 23 countries

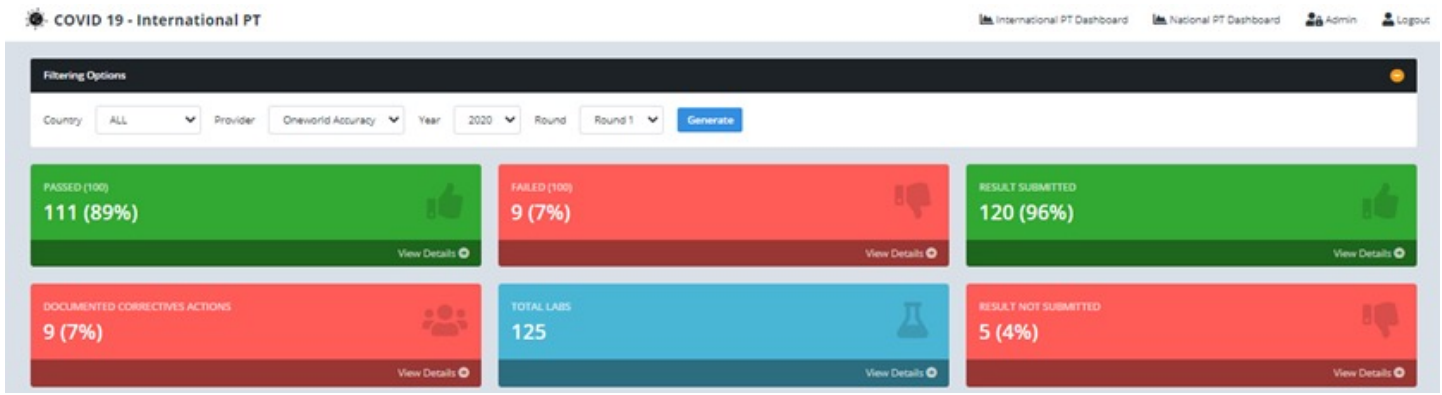
National scale up



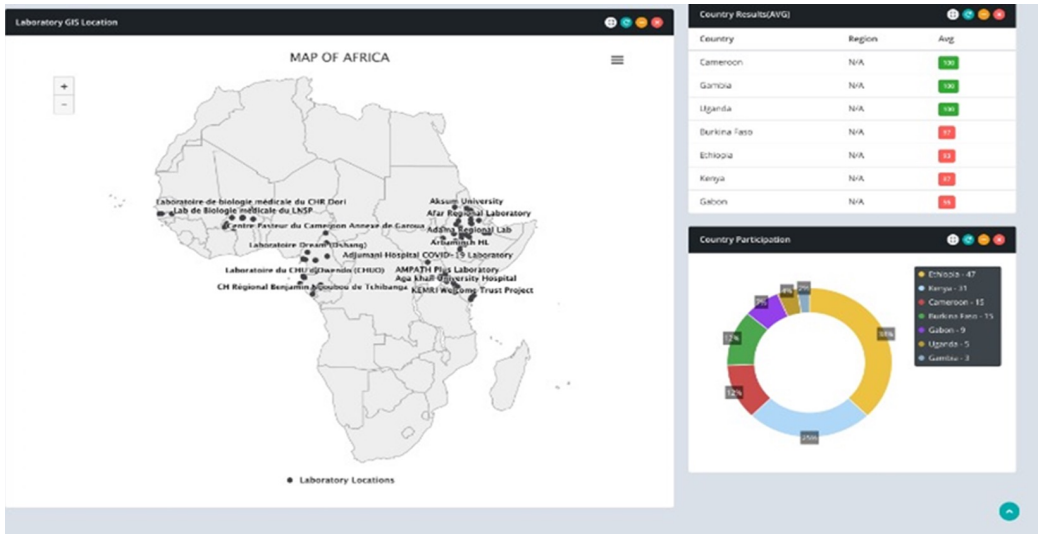
Healthcare pyramid

- In synergy with WHO:
  - WHO EQAP: reference level laboratories
  - ASLM EQAP: extension (lower lab tiers, private sector etc..)

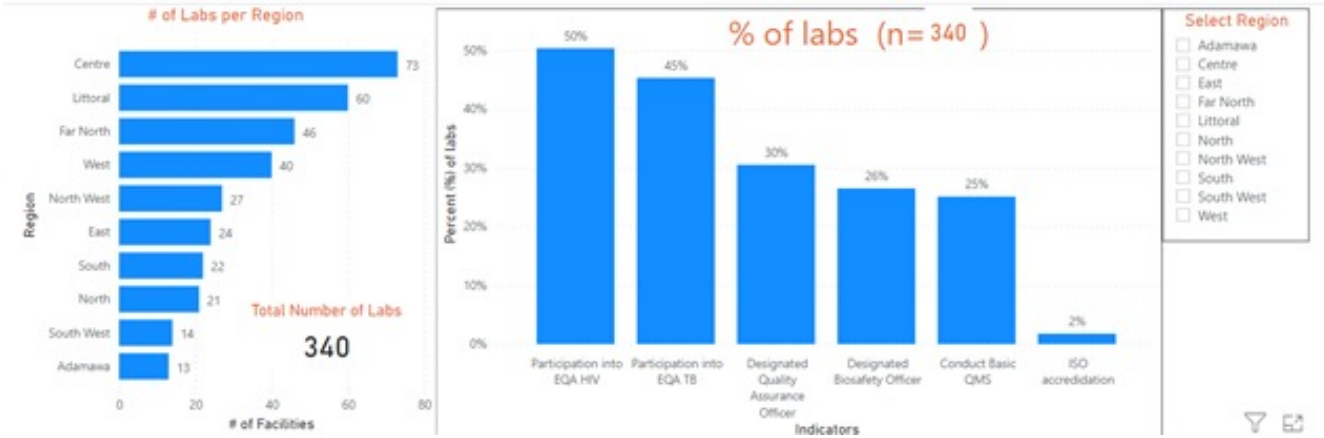
Monitoring and Evaluation : project and country level



Performance



Coverage



Integration
(country level)

Sample Re-testing

- Samples tested at one laboratory are retested at another laboratory, allowing for inter-laboratory comparison
- A laboratory's first positive sample should be sent to another testing laboratory, preferably a national or a WHO reference laboratory
- In the absence of PT, national laboratories should send 5 positive and 10 negative samples to WHO reference laboratories for retesting
- Similarly, sub-national testing laboratories should send retesting samples to their national reference laboratory

Onsite Evaluation

- Performed by experienced subject matter experts, who observe and assess the quality management systems of the COVID-19 testing laboratories across the three testing phases

- Periodic onsite evaluation may not be feasible during a pandemic

Challenges in implementing QA and possible solutions

Challenges	Mitigation measure
Unavailability of controls	Positive control: use of a confirmed positive patient sample. Negative control: use water/universal transport media/viral transport media.
Most methods are under development hence no validation data	Use methods with emergency use listing by WHO. Check https://www.who.int/diagnostics_laboratory/EUL/en/ and third party evaluated methods and perform method verification to the extent possible.
Unavailability of EQA schemes	Develop inter-laboratory comparison and send positive samples to national reference and/or WHO reference laboratories.

Applicable QA approaches

QA Approach	Internal QC	Retesting	Proficiency testing	On-site mentorship
Technology and System				
Instrument performance	YES	YES	YES	YES
Patient Identification	NO	NO	NO	YES
Sample & reagent storage	NO	NO	NO	YES
Sample transportation conditions	NO	NO	NO	YES
Inter-laboratory comparison	NO	YES	YES	YES
User				
Overall technical procedure	YES	YES	YES	YES
Sample handling	YES	NO	NO	YES
Reagent application	YES	NO	YES	YES
Sample collection	YES	NO	NO	YES
Sample application	YES	NO	YES	YES
Result intepretation	YES	YES	YES	YES
Reading and recording results	NO	YES	YES	YES

Quality Improvement

- Used to monitor routine performance of whole testing process
- Should be analyzed and reported on a regular basis (at least monthly)
- Should include the following:
  - number of specimens tested, by specimen type
  - number (%) of positive, negative and invalid test results
  - specimen rejection rate
  - number (%) of failed internal quality control results
  - EQA/PT performance (pass/fail or % score)
  - turnaround time

Summary

- Develop a structured plan for emergency testing
- Ensure the safety of your personnel
- Verify your selected tests
- Ensure effective training
- Ensure proper sample collection, handling, and transport
- Implement your tests properly

References

- Guidance on Quality Assurance for COVID-19 Molecular Laboratory Testing. https://aslm.org/resource/guidance-on-quality-assurance-for-covid-19-molecular-laboratory-testing/

- Quality Management System Considerations and Guidance for COVID-19 Molecular Testing Laboratories. https://aslm.org/resource/labcop-recipe-5-quality-management-system-considerations-and-guidance-for-covid-19-molecular-testing-laboratories/