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
• 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
• 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)
QA encompasses entire testing cascade

**Clinic**
- Wrong sample collection
- RNA degradation

**Transport**
- Sample transport in medium
- RNA extraction in lysis buffer (extraction kit)
- Prepare RT PCR reaction master mix (RT PCR kit)
- Nucleic acid contaminants

**Laboratory**
- 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

- Positive or negative results
- Master mix
- Wrong PCR cycles
- Wrong interpretation
- Bad reagents
- Wrong mix
- Nucleic acid contaminants
- QC
- EQA
- Template control
Early phase of COVID-19 testing = challenges expected

Little performance data available for COVID-19 test kits

Lack of positive control material for COVID-19 method evaluation studies

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
• 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
• 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
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

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

WHO EQAP
178 labs in 45 countries

ASLM
355 labs in 23 countries
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

<table>
<thead>
<tr>
<th>Challenges</th>
<th>Mitigation measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Most methods are under development hence no validation data</td>
<td>Use methods with emergency use listing by WHO. Check <a href="https://www.who.int/diagnostics_laboratory/EUL/en/">https://www.who.int/diagnostics_laboratory/EUL/en/</a> and third party evaluated methods and perform method verification to the extent possible.</td>
</tr>
<tr>
<td>Unavailability of EQA schemes</td>
<td>Develop inter-laboratory comparison and send positive samples to national reference and/or WHO reference laboratories.</td>
</tr>
<tr>
<td>QA Approach</td>
<td>Internal QC</td>
</tr>
<tr>
<td>-------------------------------------</td>
<td>-------------</td>
</tr>
<tr>
<td><strong>Technology and System</strong></td>
<td></td>
</tr>
<tr>
<td>Instrument performance</td>
<td>YES</td>
</tr>
<tr>
<td>Patient Identification</td>
<td>NO</td>
</tr>
<tr>
<td>Sample &amp; reagent storage</td>
<td>NO</td>
</tr>
<tr>
<td>Sample transportation conditions</td>
<td>NO</td>
</tr>
<tr>
<td>Inter-laboratory comparison</td>
<td>NO</td>
</tr>
<tr>
<td><strong>User</strong></td>
<td></td>
</tr>
<tr>
<td>Overall technical procedure</td>
<td>YES</td>
</tr>
<tr>
<td>Sample handling</td>
<td>YES</td>
</tr>
<tr>
<td>Reagent application</td>
<td>YES</td>
</tr>
<tr>
<td>Sample collection</td>
<td>YES</td>
</tr>
<tr>
<td>Sample application</td>
<td>YES</td>
</tr>
<tr>
<td>Result interpretation</td>
<td>YES</td>
</tr>
<tr>
<td>Reading and recording results</td>
<td>NO</td>
</tr>
</tbody>
</table>
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
