SUMMARY

Currently, the World Health Organization (WHO) does not recommend the use of rapid tests or any other diagnostic tests based on antibody or antigen detection for COVID-19 response since they have shown low sensitivity and specificity, compared to the Polymerase Chain Reaction (PCR) test. Other serological tests based on the detection of antibodies (Enzyme-linked immunosorbent assay, ELISA) have also shown low sensitivity and specificity. There is always the likelihood of false negative results (due to low sensitivity) and false positives (due to low specificity) with the use of tests different to PCR, especially those known as “rapid tests”.

Despite the obvious advantages of the PCR test which detects presence of the virus, operational considerations such as its high cost, the need for specialized equipment and additional expensive reagents, well-trained staff, and the timeframe for getting results (usually 4 to 10 hours), etc. makes PCR an unsuitable candidate for widespread surveillance testing, screening of ill individuals at ports of entry, surveillance in a public health context or other public health response settings.

Efforts to obtain accurate results with the use of technology based on the detection of antibodies (serology) or antigens have been made by international agencies, as part of the laboratory response to the COVID-19 pandemic.

The WHO has circulated a scientific brief on the use of point-of-care immunodiagnostic tests for COVID-19. It is worth mentioning the following conclusions of this technical guidance:

1. “At present, based on current evidence, WHO recommends the use of these new point-of-care immunodiagnostic tests only in research settings. They should not be used in any other setting, including for clinical decision-making, until evidence supporting use for specific indications is available.”

2. “WHO does not currently recommend the use of antigen-detecting rapid diagnostic tests for patient care, although research into their performance and potential diagnostic utility is highly encouraged.”

3. “WHO does not recommend the use of antibody-detecting rapid diagnostic tests for patient care but encourages the continuation of work to establish their usefulness in disease surveillance and epidemiologic research.”

The Caribbean Public Health Agency (CARPHA), aligned with the WHO’s recommendations, has provided several guidance documents where the use of rapid tests in the CARPHA Member States (CMS) for any purposes has been strongly discouraged. Additionally, CARPHA’s “Interim Guidance about Coronavirus Disease (COVID-19) for Ports of Entry in the CARPHA Member States”, published on March 12, 2020 offers general guidance for response to COVID-19 at ports of Entry across the Caribbean.

Notwithstanding, the current reality in most CMS indicates that the subsequent use of rapid, immunodiagnostic, point-of-care tests at points of entry and other public health settings will be inevitable.
CARPHA Interim Guidance for the Evaluation and Selection of Diagnostic Tests for the COVID-19 Response

GUIDANCE FOR THE EVALUATION AND SELECTION OF TESTS FOR COVID-19 RESPONSE

CARPHA has designed a simple, user-friendly instrument to assist national and other stakeholders in the evaluation and selection of diagnostic tests to be used for the COVID-19 response in CMS. The instrument incorporates 14 different parameters (as described below in Table 1). A scoring system will assign 0, 1 or 2 points to each parameter as met by a specific kit or testing approach. Some practical examples are provided in Annex 1.

Table 1: Parameters for the evaluation and selection of COVID-19 tests

<table>
<thead>
<tr>
<th>No.</th>
<th>Parameter</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Type of test*</td>
<td>Rapid test (antibody- or antigen-based)</td>
<td>Serology-based (ELISA)</td>
<td>PCR-based</td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td>Sensitivity</td>
<td>&lt;90%</td>
<td>&gt;90 – &lt;95%</td>
<td>&gt;95%</td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td>Specificity</td>
<td>&lt;90%</td>
<td>&gt;90 – &lt;95%</td>
<td>&gt;95%</td>
<td></td>
</tr>
<tr>
<td>4.</td>
<td>Evidence of additional performance indicators (Accuracy, precision, Negative Predictive Value, Positive Predictive Value, etc.)</td>
<td>No</td>
<td>Yes, less than 2</td>
<td>Yes, more than 2</td>
<td></td>
</tr>
<tr>
<td>5.</td>
<td>Evidence of published peer-reviewed performance</td>
<td>No data or data only presented in the product’s brochure</td>
<td>Yes, limited (up to 2 references)</td>
<td>Yes (3 or more references)</td>
<td></td>
</tr>
<tr>
<td>6.</td>
<td>Evidence of cross-reactivity with other coronaviruses (229E, NL63, OC43, HKU1), SARS, MERS, etc.</td>
<td>Yes or Unknown</td>
<td>-</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>7.</td>
<td>Food and Drug Administration (FDA) clearance</td>
<td>No FDA approval for Emergency Use</td>
<td>-</td>
<td>FDA approval for emergency use</td>
<td></td>
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<tr>
<td>8.</td>
<td>European Union (EU) clearance</td>
<td>No</td>
<td>CE or IVD</td>
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<tr>
<td>9.</td>
<td>Evidence of use and/or endorsement by WHO, PAHO or any other international public health agency</td>
<td>No</td>
<td>-</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>11.</td>
<td>Accessibility for procurement</td>
<td>No</td>
<td>Procurement possible but not a fast-track process</td>
<td>Yes, there are factors that facilitate procurement (e.g. authorized distributor in the region)</td>
<td></td>
</tr>
<tr>
<td>12.</td>
<td>Additional equipment/reagents</td>
<td>Need for additional expensive equipment/reagents</td>
<td>Some reagents or low-cost equipment needed</td>
<td>All-in-a-box kit with no need for additional expensive equipment/reagents</td>
<td></td>
</tr>
<tr>
<td>13.</td>
<td>Need for well-trained staff due to the complexity of the test</td>
<td>Yes</td>
<td>-</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>14.</td>
<td>The test or kit comes from a highly reputable company/brand</td>
<td>No</td>
<td>-</td>
<td>Yes</td>
<td></td>
</tr>
</tbody>
</table>

*For Parameter 1, if the test under review is PCR-based give an automatic score of 2 for nos. 2, 3, and 4.
RESULTS AND INTERPRETATION

1. FOR ANTIGEN DETECTION TESTS*:

Category A:
For results between 17 to 26 points (with sensitivity values >95%): The kit can be considered for screening at ports of entry, public health surveillance and other public health settings. Routinely confirmation of 10% of positive and negative results must be performed at a reference lab (e.g. CARPHA Medical Microbiology Laboratory, CMML).

Category B:
For results between 17 to 26 points (with sensitivity values between 90-94%): The kit can be considered for screening at ports of entry and public health surveillance and other public health settings but, at least 20% of the negative results should be confirmed by a national or reference laboratory (e.g. CMML) with the use of a test with sensitivity >95% (e.g. PCR)

Category C:
For results between 17 to 26 points (with sensitivity values less than 90%): The kit can only be used for specific situations where other better alternatives are not available. Examples: Remote areas with no access to a local laboratory, conveyances where the disease among passengers is suspected or reported, etc. Samples, especially those with negative results, must be sent to a regional, national or reference laboratory for confirmation (e.g. CMML). It is recommended that 30-40% of negative samples are confirmed by the reference lab.

Category D:
For scores between 11 to 16 points: The kit can be used for specific situations where other better alternatives are not available, however, at least 50% of all negative results must be confirmed by another kit or test that meets the requirements for category A or B.

Category E:
For scores between 0 to 10 points: The use of these kits must be avoided for screening at points of entry, public health surveillance or diagnostic services.

* Sensitivity is taken here as the primary parameter since the risk of false-negative results may facilitate the spreading of the disease. Notwithstanding, specificity values should be considered within the overall strategy for the selection of tests.
2.- FOR ANTIBODY DETECTION TESTS**:

**Category A:**
For results between 17 to 26 points (with specificity values >95%): The kit can be considered for screening at ports of entry, public health surveillance and other public health settings. Routinely confirmation of 10% of positive and negative results must be performed at a reference lab (e.g. CARPHA Medical Microbiology Laboratory, CMML).

**Category B:**
For results between 17 to 26 points (with specificity values between 90-94%): The kit can be considered for screening at ports of entry and public health surveillance and other public health settings but, at least 20% of the positive results should be confirmed by a national or reference laboratory (e.g. CMML) with the use of a test with sensitivity >95% (e.g. PCR)

**Category C:**
For results between 17 to 26 points (with specificity values less than 90%): The kit can only be used for specific situations where other better alternatives are not available. Examples: Remote areas with no access to a local laboratory, conveyances where the disease among passengers is suspected or reported, etc. Samples, especially those with positive results, must be sent to a regional, national or reference laboratory for confirmation (e.g. CMML). It is recommended that 30-40% of positive samples are confirmed by the reference lab.

**Category D:**
For scores between 11 to 16 points: The kit can be used for specific situations where other better alternatives are not available, however, at least 50% of all positive results must be confirmed by another kit or test that meets the requirements for category A or B.

**Category E:**
For scores between 0 to 10 points: The use of these kits must be avoided for screening at points of entry, public health surveillance or diagnostic services.

** Specificity is taken here as the primary parameter since the risk of false-positive results may facilitate the spreading of the disease. Notwithstanding, sensitivity values should be considered within the overall strategy for the selection of tests.**

REFERENCES


ANNEXES

Annex 1: Practical Examples of the COVID-19 Test Evaluation and Selection Instrument

Annex 2: CARPHA COVID-19 Test Evaluation and Selection Summary Form

ANNEX 1

Practical Examples of the COVID-19 Test Evaluation and Selection Instrument

Example No. 1:
A CMS is considering the use of the GeneXpert™ SARS-CoV-2 cartridge (Cepheid™) for screening passengers arriving at the national airport. The score assigned to this kit, using the instrument provided was:

1. Type of test: 2
2. Sensitivity: 2
3. Specificity: 2
4. Evidence of additional performance indicators (e.g. accuracy, precision, negative predictive value, positive predictive value, etc.): 1
5. Evidence of published peer-reviewed performance: 1
6. Evidence of cross-reactivity with other coronaviruses (229E, NL63, OC43, HKU1): 2
7. Food and Drug Administration (FDA) clearance: 2
8. European Union (EU) clearance: 2
9. Evidence of use and/or endorsement by WHO, PAHO or any other international public health agency: 2
10. Cost/test: 1
11. Accessibility for procurement: 1
12. Additional equipment/reagents: 0
13. Need for well-trained staff due to the complexity of the test: 2
14. The test or kit comes from highly reputable firms/brands: 2

TOTAL: 22 points

CONCLUSION: According to the categorization system, this test meets the requirements specified for Category A, and can be safely used for screening at ports of entry and for other public health settings.
Example No. 2:
A company based in a country in South-east Asia is trying to sell a low-cost rapid test for the detection of antibodies class IgM and IgG in some CMS. After the evaluation of parameters, the score obtained was:

1. Type of test: 0
2. Sensitivity: 0
3. Specificity: 1
4. Evidence of additional performance indicators (e.g. accuracy, precision, negative predictive value, positive predictive value, etc.): 1
5. Evidence of published peer-reviewed performance: 0
6. Evidence of cross-reactivity with other coronaviruses (229E, NL63, OC43, HKU1): 0
7. Food and Drug Administration (FDA) clearance: 0
8. European Union (EU) clearance: 0
9. Evidence of use and/or endorsement by WHO, PAHO or any other international public health agency: 0
10. Cost/test: 2
11. Accessibility for procurement: 1
12. Additional equipment/reagents: 2
13. Need for well-trained staff due to the complexity of the test: 2
14. The test or kit comes from highly reputable firms/brands: 0

TOTAL: 9 points

CONCLUSION: According to the categorization system, this test belongs to Category E, and its use must be avoided for screening at ports of entry and for any other public health settings.
Example No. 3:
An international reputable firm, with broad experience on diagnostic kits (including point-of-care and other rapid tests), is reaching some CMS. The company has local representation and offers an attractive kit with good levels of sensitivity and specificity and at a very reasonable cost. After the evaluation of parameters, the score obtained was:

1. Type of test: 0
2. Sensitivity: 1
3. Specificity: 2
4. Evidence of additional performance indicators (e.g. accuracy, precision, negative predictive value, positive predictive value, etc.): 1
5. Evidence of published peer-reviewed performance: 1
6. Evidence of cross-reactivity with other coronaviruses (229E, NL63, OC43, HKU1): 0
7. Food and Drug Administration (FDA) clearance: 1
8. European Union (EU) clearance: 1
9. Evidence of use and/or endorsement by WHO, PAHO or any other international public health agency: 0
10. Cost/test: 2
11. Accessibility for procurement: 2
12. Additional equipment/reagents: 2
13. Need for well-trained staff due to the complexity of the test: 2
14. The test or kit comes from highly reputable firms/brands: 2

TOTAL: 17 points

CONCLUSION: According to the categorization system, this test meets the requirements specified for Category B, and can be used for screening at ports of entry and for other public health settings with a confirmation by other test of at least 20% of the negative results.
## CARPHA COVID-19 Test Evaluation and Selection Summary Form

**Name of Test Kit:** ________________________________

**Name and Country of Manufacturer:** ________________________________

**Instructions:** Review the available literature and test kit information before completing the table below.

<table>
<thead>
<tr>
<th>No.</th>
<th>Parameter</th>
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<th>Score</th>
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<td></td>
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<td>Sensitivity</td>
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<td>&gt;95%</td>
<td></td>
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<td>3.</td>
<td>Specificity</td>
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<td>4.</td>
<td>Evidence of other performance indicators (e.g. accuracy, Precision, Negative Predictive Value, Positive Predictive Value, etc.)</td>
<td>No</td>
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<td></td>
</tr>
</tbody>
</table>

*For Parameter 1, if the test under review is PCR-based give an automatic score of 2 for nos. 2, 3, and 4.
RESULTS:

Total Score: ___________ Category: ___________

<table>
<thead>
<tr>
<th>Category</th>
<th>Category A</th>
<th>Category B</th>
<th>Category C</th>
<th>Category D</th>
<th>Category E</th>
</tr>
</thead>
<tbody>
<tr>
<td>Score</td>
<td>17 - 26 (Sensitivity &gt;95%)</td>
<td>17 - 26 (Sensitivity 90-94%)</td>
<td>17 - 26 (Sensitivity &lt; 90%)</td>
<td>11 - 16</td>
<td>0 - 10</td>
</tr>
</tbody>
</table>

CONCLUSION:

_____________________________________________________________________________

Completed by: __________________________ (Name, Title)

Date: __________________________

Authorized by: __________________________ (Name, Title)

Date: __________________________