# Use of COVID-19 IgG and IgM Rapid Diagnostic Test (RDT) Kits for Mild and Asymptomatic At-Risk COVID-19 Cases

## *Evidence Summary*

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| *Publication Date* | 13 April 2020 |
| *Adopted Report* | Use of COVID-19 IgG and IgM Rapid Diagnostic Test (RDT) Kits for Mild and Asymptomatic At-Risk COVID-19 Cases Rapid Review (published 25 March 2020) |
| *Summary Length* | 9 pages |
| *Prepared by* | Health Technology Assessment Unit, Health Regulation Team, Department of Health (Philippines) |
| *Contact details* | hta.philippines@gmail.com \| 8-875-7734 loc. 260 or 258 |

# Section 1.

## General information of the proposed health technology (HT)

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| **Product name** | IgG/IgM Rapid Diagnostic Test Kits |
| **Product description** | An immunographic test kit which can detect IgM and IgG simultaneously in the human blood within 15 minutes |
| **Technical specification** | It has a gold nanoparticle-based immunographic test kit with a plastic backing, sample pad, conjugate pad, an absorbent pad and NC membrane. |
| **Indication** | Used in the rapid detection of COVID-19 |
| **Global Medical Devices Nomenclature (GMDN)** | not provided |
| **Universal Medical Device Nomenclature System (UMDNS)/ ASEAN medical device nomenclature** | not provided |
| **Does the proposed medical service include a registered trademark component with characteristics that distinguishes it from other similar health components?** | **Description of registered trademark:** not provided<br><br>**Origin of IP Office Application:** not provided |

# Section 2.

## Background

The World Health Organization (WHO) declared the novel coronavirus disease (COVID-19) caused by severe acute coronavirus 2 (SARS-COV-2) a global pandemic. The most common symptoms are fever, sore throat, malaise and dry cough. The symptoms are usually mild and begin gradually. It can spread from person-to-person through small droplets when coughing or sneezing. As of 06 April 2020, it has affected more than 209 countries and regions with at least 1,136,851 cases and 62,955 deaths worldwide. Locally, there are over 3,246 cases and 152 deaths.

Currently, there are no known treatments for COVID-19. As a response to this pandemic, the Department of Health has implemented a triage algorithm in conducting diagnostic testing for patients with suspected cases of COVID-19. Patients presenting with acute respiratory illness may be classified as (1) person under investigation or (2) person under monitoring, depending on the patient's history of exposure, pre-existing conditions and travel history. The algorithm does not recommend diagnostic testing for patients presenting with mild symptoms (with or without travel history to any area with local transmission of COVID-19 or close contact to a confirmed COVID-19 case but no symptoms within 14 days) and those considered asymptomatic high-risk patients, thus creating public clamor for mass testing.

## Policy Question

***Should the Philippine government introduce COVID-19 IgG and IgM RDT kitsin detecting COVID19 cases among mild and asymptomatic at-risk cases versus no testing?***

# Section 3.

## Selection Criteria

### 3.1. Inclusion Criteria

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| **Population** | Mild and asymptomatic at-risk COVID-19 patients<br><br>Mild at-risk COVID-19 cases - patients with history of exposure and have no comorbidities, non-elderly, and show only mild clinicalsymptoms (i.e., fever, dry cough, fatigue, sputum production, sore throat, headache, myalgia or arthralgia, chills, nausea and vomiting, nasal congestion, diarrhea)<br><br>Asymptomatic at-risk COVID-19 cases - patients with history of exposure and have no comorbidities, non-elderly, and shows no clinical symptoms (i.e., fever, dry cough, fatigue, sputum production, sore throat, headache, myalgia or arthralgia, chills, nausea and vomiting, nasal congestion, diarrhea, difficulty of breathing) |
| **Intervention/Exposure** | COVID-19 IgG and IgM RDT kits |
| **Comparator** | **Clinical accuracy**: RT-PCR<br><br>**Cost-Effectiveness**: No testing |

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| **Outcomes** | Clinical efficacy/ effectiveness: Sensitivity, Specificity<br>Cost-effectiveness: cost case detected<br>(such as but not limited to the outcome measures listed above) |
| **Study Designs** | Health technology assessments, systematic reviews (SRs), meta-analyses, primary diagnostic accuracy studies, economic evaluations, guidelines and protocols |

## 3.2. Exclusion Criteria

Articles were excluded if they did not meet the selection criteria outlined in Table 1 or they were duplicate publications.

# Section 4.

# Research Questions and Key Findings

## 4.1. COVID-19 Testing Guidelines and Protocols

***What are the evidence-based guidelines for the use of COVID-19 IgG and IgM RDT kits among mild and asymptomatic at-risk cases? What are the current COVID-19 testing protocols among healthcare systems?***

According to the WHO Interim Guidance published on March 22, 2020 titled, Laboratory testing strategy recommendations for COVID-19, “Serological assays will play an important role in research and surveillance but are not currently recommended for case detection and are not included in the rapid review. The role of rapid disposable tests for antigen detection for COVID-19 needs to be evaluated and is not currently recommended for clinical diagnosis pending more evidence on test performance and operational utility. “ An exhaustive UptoDate® search of the various guidelines of the countries revealed that only South Korea allows for testing of mild and asymptomatic at-risk cases but using RT-PCR, while the other countries/territories like Canada, USA, United Kingdom, Europe, Australia and China recommend self-quarantine for those with mild and asymptomatic cases. Some countries offer free testing for mild and asymptomatic cases; however, those are only under special cases and for patients with higher risk. Singapore offers free testing for mild casesfor health workers and known contacts of COVID-19 positive patients, while Thailand offers free testing for mild cases for patients with recent travel history to crowded places. Currently, RDT kits for Covid-19 IgG and IgM are only registered at the European Union under a CE-IVD registration. Based on the search, no country has included these kits as a nationwide testing strategy.

## 4.2. Clinical Efficacy or Accuracy of COVID-19 IgG and IgM RDT kits

***What is the accuracy of COVID-19 IgG and IgM RDT kits in detecting COVID19 cases among mild and asymptomatic at-risk cases versus gold standard testing?***

There was only one accuracy study found in this review (Li et al, 2020), which shows that COVID-19 IgG and IgM RDT has a specificity of 90.63% and sensitivity of 88.66%. However, based on the appraisal, there were considerable flaws observed in the study design. The positive predictive value of the test appears to be very high because the prevalence of COVID-19 in the study is greater than 75%. The likelihood of a false-negative result from immunoassays, in general, must be considered given that strong evidence on the real accuracy of immunoassay for COVID-19 is yet to be established. Further, the analytical specificity and sensitivity have not yet been determined as stated by the authors. In addition, the cross-reactivity with other coronaviruses and flu viruses as well as the detection limit has not yet been ascertained. It was noted that while the study authors suggest a potential application of the test kit in testing asymptomatic patients, study results do not provide any evidence on the clinical characteristics of the sampled patients, thus being unable to identify its accuracy with regards to screening of asymptomatic and mild cases.

## 4.3. Cost-effectiveness of COVID-19 IgG and IgM RDT kits

***Does COVID-19 IgG and IgM RDT kits represent value for money (in terms of cost per additional case detected) in detecting COVID19 among mild and asymptomatic at-risk cases versus no testing?***

There was no relevant evidence regarding the cost-effectiveness of COVID-19 IgG and IgM RDT kits, to date; therefore, no summary to support its cost-effectiveness or efficiency can be provided. It has to be noted, however, that testing for pre-symptomatic persons, in general, is costly and difficult to implement in consideration to access, adherence, awareness, and training.

# Section 5.

# Ethical, Legal, Social, and Health System Impact

## 5.1. Ethical, Legal and Social Impact

From a social point of view, the higher likelihood of false negative results from this may undermine the social distancing policy that is being advocated nationally and ethically put the tested individuals, their families and contacts at unjustified risks. No relevant evidence was found regarding the ethical and legal implications of IgG/IgM RDT kits.

## 5.2. Health system impact

In general, mass testing is considered to be costly and can be challenging for a variety of reasons including accessibility, adherence, awareness, and training requirements.

# Section 6.

## Recommendation

The HTA Council **does not recommend at this time the use of IgM/IgG Rapid Diagnostic Test (RDT) Kits as a sole screening and diagnostic tool for COVID-19**, pending further scientific evidence on its accuracy. The Council is continuously on the watch for future evidence on its utility. However, **a parallel multi-site clinical trial is highly recommended** to be spearheaded by the Research Institute for Tropical Medicine (RITM) and designated healthcare facilities. Only those who will enroll in the RITM-led clinical trial research should have access to the rapid antibody-based test kits procured with government funds. In addition, the test kits to be funded by the government should be those that can differentiate between IgG and IgM.

The Council also recommends the exploration of studies using serology based RDTs but only in specific population groups for public health purposes, as recommended by WHO to inform public health policies. Another potential use is for monitoring and serologic survey to determine immunogenicity of COVID-19.

For local Government Units (LGUs) that are responding to a public clamor for expanded testing to cover specific population groups with higher exposure, please be advised that **the antibody-based testing itself is not recommended as a diagnostic test for COVID-19**. The antibody-based testing **must be used together with the Reverse Transcriptase Polymerase Chain Reaction** (RT-PCR) test and needs a **health expert for interpretation of results**. Moreover, the expanded testing should be part of a research activity, which requires systematic data collection. The Food and Drug Administration (FDA) certification is **not a permit for unrestricted public use**. In case the COVID-19 IgG and IgM RDT kits will be utilized by government and private institutions, there should be capable health teams (e.g., education, training and experience in infectious disease and public health) at the local government unit (LGU) level, possibly at the provincial/chartered city level to perform the test, in close coordination with RITM or other subnational hospitals also performing the RT-PCR test.

Further, the HTA Council supports the **Philippine Society for Microbiology and Infectious Diseases (PSMID) guidelines**, as quoted below:

1. Only Food and Drug Administration (FDA) approved kits should be used.
2. A COVID-19 antibody test CANNOT be used as a stand-alone test to definitively diagnose COVID-19 and CANNOT be used for mass testing, but only for monitoring patient status.

3. This should only be used in people who had onset of symptoms for at least 5 days (i.e. for IgM) and 21 days (i.e. for IgG).
4. Anyone who tests positive for IgM should be tested with an RT-PCR to confirm the positive test.
5. A negative IgM test DOES NOT rule out COVID-19 and the symptomatic patient should REMAIN ISOLATED and swabbed using RT-PCR for confirmation.
6. IgG-only positive individuals without RT-PCR should be labeled as presumptive past COVID-19 and not be officially counted as confirmed unless there is a further validation test in the future, or if validated with a PRNT (Plaque reduction neutralization test) or viral culture by a third party. If a patient is symptomatic, an RT-PCR should be done, and the patient should be quarantined. If a patient is asymptomatic, there is no need to test using an RT-PCR.
7. The IgG antibody can be used as an adjunct test to clear quarantined patients who remain asymptomatic at 14 days post discharge. The presence of antibodies typically indicates viral clearance. If IgG is positive, the patient can be released from self-quarantine. If IgG is negative, a repeat RT-PCR should be performed.
8. ONLY medical doctors can prescribe and interpret the use of the antibody-based test kits. These kits will not be available over the counter. In accordance with the FDA Advisory 2020-498 “Purchase and Administration of FDA Approved COVID-19 Rapid Antibody Test Kits” released on 01 April 2020, this product must be acquired using a prescription issued by a licensed physician and procured from a DOH licensed hospital or pharmacy.

# Section 7.

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