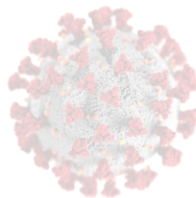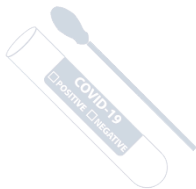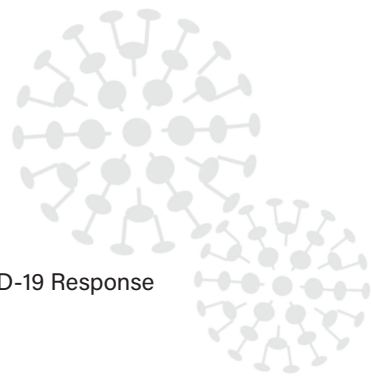# Interim Guidance on the Use of Rapid Antigen tests for COVID-19 Response

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Contents

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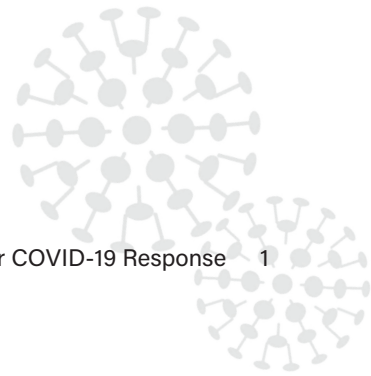
Purpose of this guidance

This document provides guidance to Ministries of Health (MOHs), laboratory personnel and implementing partners in African Union Member States on the application of rapid antigen tests to COVID-19 testing. The guidance serves as reference for policymakers, laboratory leads, implementing partners, and experts on use case scenarios and associated testing algorithms for COVID-19 antigen tests. It recommends the use of antigen tests to increase access to testing and enable timely results for persons with or without symptoms in specific settings. The document will be reviewed and updated as more evidence becomes available regarding the use of rapid antigen tests for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) from global studies and evaluation efforts.
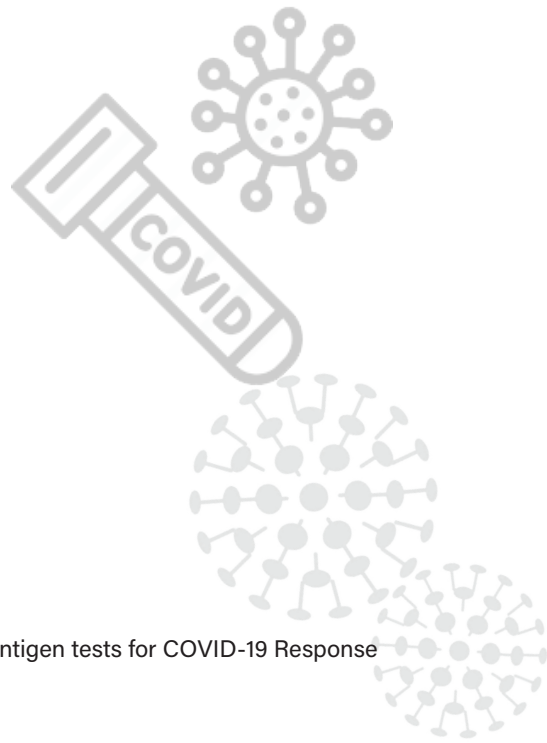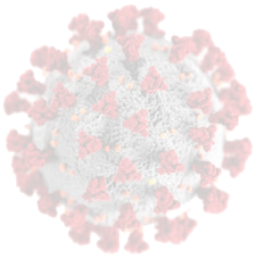
Executive summary

Key messages

- Diagnostic testing for SARS-CoV2 is vital for the control and, ultimately, suppression of COVID-19 pandemic in Africa.

- Member States should aim to test all individuals with symptoms consistent with COVID-19 as quickly as possible. This is heavily dependent on easy and timely access to testing.

- Nucleic acid amplification testing (NAAT) remains the 'reference standard' for SARS-CoV-2 diagnosis in early acute diagnosis. However, in many settings, access to these molecular tests and the provision of results in a clinically relevant timely manner limits their clinical utility.

- COVID-19 rapid antigen tests (COVID-19 Ag-RDTs) are an easy-to-use alternative to NAAT, which can provide a result in 15-30 minutes and can be used at point-of-care.

- COVID-19 Ag-RDTs have many advantages (e.g. ease of use, rapid TAT, lower cost, increased access) and may have some limitations (e.g. lower analytical performance compared to NAAT). However, the benefit of providing the result in a timely manner outweighs the analytical performance limitations of the antigen tests.

- COVID-19 Ag-RDTs can be used for the diagnosis of COVID-19 in symptomatic individuals, in individuals who have an exposure history, or are at high risk of acquiring SARS-CoV-2 infection (irrespective of symptoms).

- Use of COVID-19 Ag-RDTs is recommended for individuals with symptoms, high-risk populations, and healthcare workers/essential workers and contacts (irrespective of symptoms) in settings where NAAT is not available, or where the turnaround time for NAAT result delivery is prolonged, limiting its utility.

- Use of COVID-19 Ag-RDTs for epidemic control is also recommended in clusters or settings (e.g. workplaces, educational institutions, correctional facilities) with suspected or confirmed outbreaks to provide rapid detection and epidemic management.

- Use of COVID-19 Ag-RDTs for epidemic control is recommended for general screening in educational institutions, workplaces, high mobility areas and at points of entry for surveillance. Screening at the community level allows identification of pre-symptomatic and asymptomatic cases, while testing at port of entry creates a safe public health corridor for travel and commerce and prevents the reintroduction of SARS-CoV-2 in countries that have achieved control of the pandemic.

- Implementation and relaxation of mitigation strategies (e.g. lockdowns, closure of educational institutions/workplaces) should be guided by key indicators such as the number of new cases within the last 14 days and the percentage of positive tests within the last 14 days.

- Support systems are critical to maximize the impact of COVID-19 Ag-RDT implementation and include providing comprehensive training and supervision, engagement in quality assurance activities, establishing clear roles for both COVID-19 Ag RDTs and RT-PCR within the new testing strategy, capturing and integrating testing data to inform evidence-based decisions, and continuously learning and updating testing strategies based on information gained domestically and across the broader African Union region.
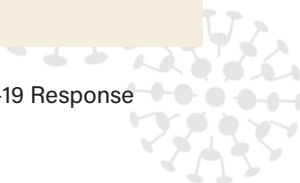
Background

Testing is part of the first line of defence against COVID-19, enabling early identification and isolation of cases to slow transmission, the provision of targeted clinical care to those infected, and protection of health systems operations.[1] Current evidence indicates that Member States have limited capacity to run nucleic acid amplification testing (NAAT) assays and turnaround time for testing by NAAT methods is more than two days, limiting clinical utility of testing. Speed of testing and reporting of results to individuals and public health authorities for isolation and contact tracing is essential to maximize the impact of diagnostics.

There are two types of COVID-19 rapid diagnostic tests (RDTs): antigen (Ag) tests which directly detect SARS-CoV-2 viral antigen(s) and antibody (Ab) tests which detect one or more types of antibodies against the virus produced by the host immune response.[2] RDTs can be used outside of laboratory conditions, at/ or near the point of care. They are easy to use, provide rapid results and do not require any expensive equipment. **Ag-RDTs can be considered as alternatives to NAAT for direct detection of SARS-CoV-2 virus for diagnosis of early COVID-19.** The guidance in this document refers only to **COVID-19 Ag-RDTs**.

COVID-19 Ag-RDTs directly detect SARS-CoV-2 antigens, most often the nucleocapsid, in respiratory secretions, which are produced as the virus replicates. Therefore, like NAAT, COVID-19 Ag-RDTs are useful for the detection of active infection. Currently available COVID-19 Ag-RDTs use nasopharyngeal samples or anterior nares (nasal) samples but may be suitable for use with other sample types in the future, once more data are available.

COVID-19 Ag-RDTs are a critical tool to scale-up testing in the fight against COVID-19. COVID-19 Ag-RDTs can make testing more widely available in decentralized settings, extend the reach of existing testing programmes, significantly decrease turnaround times, and ultimately meet the testing demand in Member States. While increasing testing capacity through Ag-RDTs, access to accurate real-time data should remain a priority so that testing can be used to make evidence-based decisions regarding national policies and public-health control measures.

(Endnotes)

[1]World Health Organization. COVID-19 Strategy Update. 14 April 2020 (https://www.who.int/publications/i/item/covid-19-strategy-update---14-april-2020, accessed 24 November 2020).
[2]FIND. Rapid diagnostic tests for COVID-19 (https://www.finddx.org/wp-content/uploads/2020/05/FIND_COVID-19_RDTs_18.05.2020.pdf, accessed 24 November 2020).

General recommendations for the use of COVID-19 Ag-RDTs

Currently, in the absence of accessible specific treatment for COVID-19, the primary goal of diagnostic testing is to inform and reduce transmission. Given the infectious period of SARS-CoV-2 (10 days), which can start in the 1-3 days before the development of symptoms, and extend 5-7 days after onset of symptoms, there is a need for fast turnaround of results, ideally same visit, to begin isolation of cases and initiate tracing of contacts. Thus, antigen tests offer a high value in informing healthcare workers and individuals about a diagnosis at point-of-care for immediate action (triage/isolation) and inform community-level response (surveillance). Furthermore, COVID-19 Ag-RDTs allow decentralization of SARS-CoV-2 testing, as they do not require complex infrastructure, thus increasing testing coverage. This can raise confidence of policymakers to institute adaptive responses at local or regional level.

To appropriately implement COVID Ag-RDTs, the following factors should be considered:

- Only COVID-19 Ag-RDT that meets the minimum performance requirements of sensitivity ≥ 80% and specificity of ≥ 97% in relation to NAAT, as set in the WHO TPP, should be used.
- Introduction of high specificity tests (>99%) is preferred in all settings but is of particular importance in low prevalence settings and general screening applications.
- COVID-19 Ag-RDT should be deployed as a first-line test in contexts where NAAT is not available or where turnaround times are too long for clinical utility (e.g. >24 to 48 hours).

COVID-19 Ag-RDT with high specificity (>99%) can be deployed in any setting but may be of increased importance in settings where the consequences of a false positive are impactful, either due to needs for epidemic management or economic consequences. Proper interpretation of antigen results within these use cases is important for clinical management of cases and for assessing the SARS-CoV-2 epidemic. The accuracy of results depends largely on the context within which the results are interpreted. Therefore, the management of results within a given setting should consider the tolerance and consequences of misdiagnosis, either false positive or false negative.
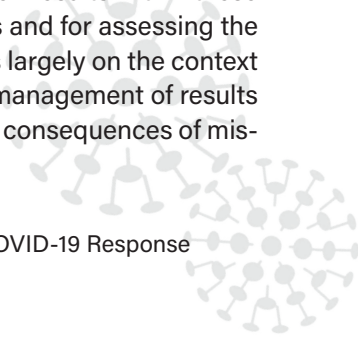
Diagnosis in populations with known risk exposure

The goal of testing within these populations and use cases is to manage the epidemic, in addition to the provision of clinical care where needed. Target populations include:

- Individuals with symptoms
- Frontline healthcare workers and essential workers (symptomatic and asymptomatic)
- High-risk populations in areas with confirmed/suspected outbreak (includes the elderly, people with comorbidities, and populations in closed settings such as prisons, care homes, etc)
- Contacts of confirmed cases (symptomatic and asymptomatic).

Although the recommended testing algorithm for these target populations is the same, the rationale for testing differs for individuals with symptoms, and individuals at high exposure risk (independent of the presence of symptoms). Diagnosis of symptomatic individuals enables individual clinical management and helps achieve epidemic control. By contrast, diagnosis of individuals with high exposure risk is primarily focused on epidemic control, as many of such individuals currently show no symptoms and may be asymptomatic or pre-symptomatic.

In all these populations, positive results are more likely to be true positives and can be interpreted as likely SARS-CoV-2 infection: appropriate individual, clinical management, and prevention and control measures should be followed. However, a negative test implies that the infection is unlikely if there are no clinical signs or epidemiological connection to SARS-CoV-2 and these individuals should be managed as negative; symptomatic individuals who test negative should be evaluated for other potential causes of illness, such as other upper respiratory tract infections and/or febrile diseases. If there are clinical and/or epidemiological indications for COVID-19, then individuals who test negative should be re-tested with COVID-19 Ag-RDT, and if still negative should be treated as presumptive positive. Where NAAT is available and confirmation is desired, manage as a presumptive while awaiting results (Figure 1).
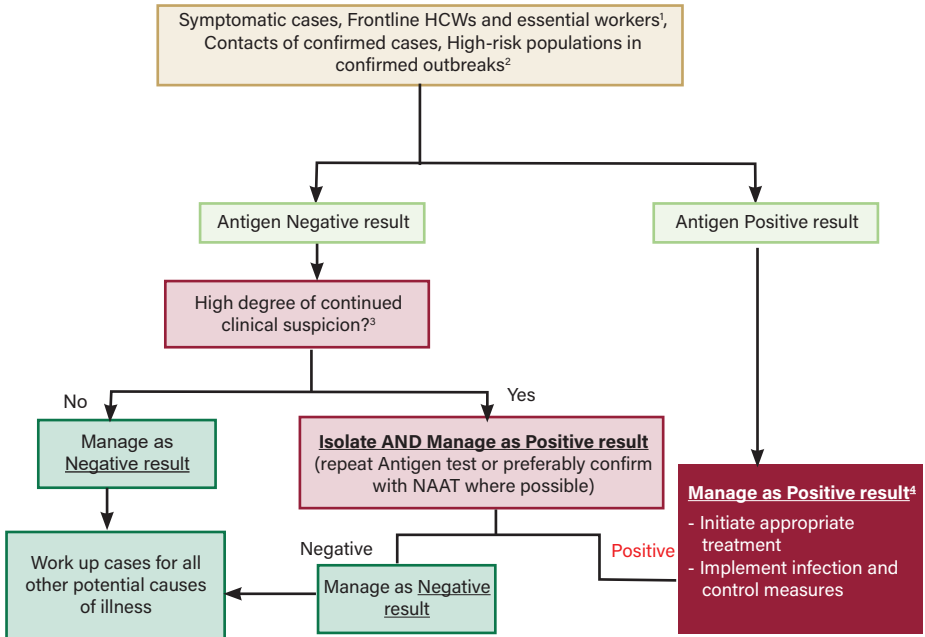
Figure 1: *Algorithm when testing populations with higher suspicion of positivity, including: (1) individuals with symptoms, (2) frontline healthcare workers and/or essential workers, (3) contacts of confirmed cases, (4) high-risk populations in confirmed outbreaks*

[1]*Symptomatic & asymptomatic;* [2]*Includes the elderly, people with comorbidities, and/or populations in closed settings (prisons, care homes, etc.);* [3]*As determined by clinician based on patient clinical history. As per WHO "Continued clinical suspicion can, for example, be the absence of another obvious aetiology, the presence of an epidemiological link, or suggestive clinical finding (e.g. typical radiological signs)." Special considerations for contacts (see below);* [4]*Special considerations for healthcare workers and frontline workers (see below).*

Special considerations for contacts

For close contacts, a negative result may not imply that there is no infection as they can still be in the pre-infectious phase, thus they should be considered as high-degree clinical suspicion and isolated accordingly.

Special considerations for healthcare workers and frontline workers (including laboratory staff)

In areas where community spread has been detected, healthcare workers and/or frontline workers should be screened regularly because they face an increased risk of contracting and spreading SARS-CoV-2. It is recommended that the algorithm for "populations with known risk or exposure in suspected or confirmed outbreak" (Figure 1) should be used. **Where there is community spread, frequent (twice weekly), routine testing (independent of the presence of symptoms) is recommended to prevent outbreaks and to reduce case numbers[1].**

Where there is limited-to-no suspected or confirmed outbreak, once a week routine asymptomatic testing should suffice[4]. When healthcare workers and/or frontline workers are screened regularly in areas where there are limited-to-no suspected or confirmed outbreaks, a positive result should be interpreted with caution due to low likelihood of positive results. In these individuals, re-test with Ag-RDT or preferably confirm with NAAT where possible. If neither is possible, then isolate the individual and manage as a presumptive positive case.

(Endnotes)

[4]Chin ET, Lo NC, Huynh BQ, Murrill M, Basu S. Frequency of routine testing for SARS-CoV-2 to reduce transmission among workers. medRxiv [Preprint]. 2020 May 6:2020.04.30.20087015. doi: 10.1101/2020.04.30.20087015. PMID: 32511523; PMCID: PMC7273291.
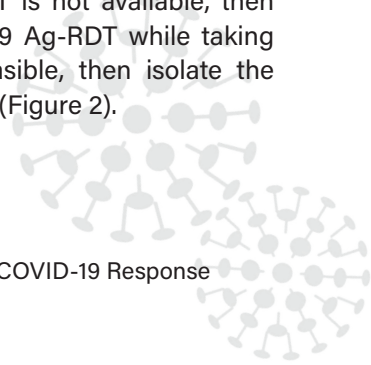
Screening in general population with unknown or low exposure risk

The goal of testing within the general population is to allow for opening of economic/social activities safely while minimizing the risk of new outbreaks. The target populations include:

- Travelers crossing borders/points of entry
- Teachers, students and administrative staff at educational institutions
- Factory workers, government employees and private sector employees at workplaces
- In-patients at hospitals admitted for other conditions than COVID-19 (e.g. elective surgeries, other illnesses, etc.)
- Other general populations (e.g. random community screening, surveillance).

Screening at border points of entry and among in-patients enables early identification of new cases and seeks to prevent new clusters and outbreaks from forming. By contrast, testing in educational institutions and workplaces allows for these critical services to remain open and limit the introduction of COVID-19 into these semi-closed settings. Together, these screening priorities allow for a safe re-opening of economies, educational systems, and social activities and can be used to inform the introduction or relaxation of various public health mitigation strategies.

Due to expected low prevalence in these populations during non-outbreak scenarios, false-positive results are more likely to occur. Accordingly, negative results are likely to be true negatives and can be interpreted as unlikely to be SARS-CoV-2 infection, and should be managed accordingly. However, a positive result means COVID-19 infection is possible, but confirmation, preferably with NAAT, should be considered where possible. If NAAT is not available, then consider the possibility of re-testing with a COVID-19 Ag-RDT while taking appropriate public health precautions, or, if not feasible, then isolate the individual and manage as a presumptive positive case (Figure 2).
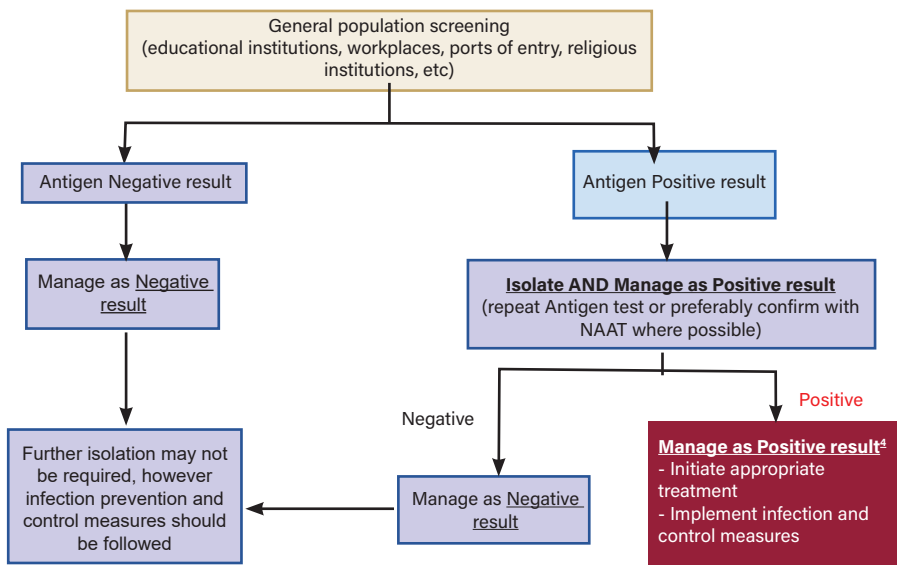
Figure 2: *Algorithm for general screening of persons (irrespective of symptoms) in settings with unknown or low community transmission, including in schools, workplaces, ports of entry or houses of worship, etc.*

Special considerations for screening in semi-closed settings

Educational institutions provide safe place not just for learning but also for the development of social and emotional skills. Workplaces provide critical services and are important for economic activity. However, both settings are considered high-risk environments for transmission and potential outbreaks, due to the close and prolonged contact among large groups of people, especially in indoor environments. An unmitigated outbreak in these settings can have a substantial impact not just for the affected individuals, but also on their households and the wider community. To facilitate safe reopening of educational institutions and workplaces, public health measures to prevent SARS-CoV-2 infection are needed such as wearing of masks, physical distancing, hand hygiene, cleaning and disinfection, and frequent testing. **Within these settings, where there is limited-to-no suspected or confirmed outbreak, once a week routine asymptomatic testing is recommended to prevent outbreaks and reduce case numbers[4].**

Public health indicators for decision-making to inform mitigation strategies

COVID-19 Ag-RDTs have many advantages, including ease of use, rapid turnaround time, and lower cost, compared to NAAT, allowing testing to be broadly accessible across the nation. Broader access to testing allows mitigation strategies to be applied and tailored to local jurisdiction levels rather than at national level.

To mitigate the SARS-CoV-2 epidemic, countries have implemented wide-scale restrictions, including closure of borders, educational institutions and workplaces. As Member States achieve success in bringing SARS-CoV-2 transmission under control, quantitative thresholds will be needed to inform when to adjust (loosen or reinstate) these measures. One quantitative measure that can be considered to guide decision-making is the positivity rate. Test positivity rate provides valuable information about the current level of SARS-CoV-2 transmission in the community, as well as to help assess whether testing levels are keeping up with levels of disease transmission.

A high positivity rate suggests the need for implementation of mitigation strategies and increased restrictions to control the epidemic. A high positivity rate may also indicate that testing is not being implemented widely enough, and thus suggests increasing testing coverage to identify mild symptomatic, asymptomatic and contacts in order to control the epidemic.

In May 2020, WHO recommended a benchmark threshold positivity rate of 5%: if rates fall below this threshold for at least two weeks, governments should consider loosening restrictions, or reinstating targeted restrictions if rates remain above this threshold[5]. There are growing discussions to lower the benchmark threshold of positivity rate to 3%; however, Member States may lower or increase the threshold further based on success in bringing SARS-CoV-2 transmission under control.

(Endnotes)

[5]World Health Organization. Public health criteria to adjust public health and social measures in the context of COVID-19: annex to considerations in adjusting public health and social measures in the context of COVID-19, 12 May 2020 (https://apps.who.int/iris/handle/10665/332073, accessed 24 November 2020)
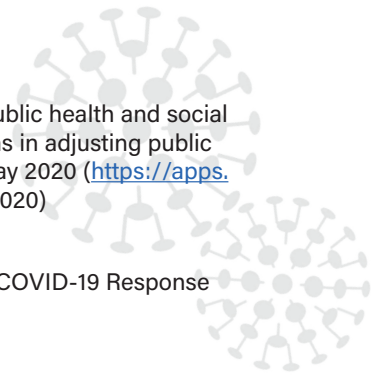
Assessing test quality and performance to guide selection

Member States should carefully choose the appropriate test depending on intended use and setting. Tests that have been assessed through a national Emergency Use Authorization (EUA) and/or the WHO Emergency Use Listing (EUL) procedure should be prioritized for SARS-CoV-2 testing. The list of tests that have been given EUA by the USA FDA can be found here: https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations#covid19ivd; those approved for emergency use in IMDRF jurisdictions can be found here: https://extranet.who.int/pqweb/key-resources/documents/imdrf-collated-table; and information on the WHO EUL procedure, including lists of tests that have received WHO EUL can be found here (https://www.who.int/diagnostics_laboratory/EUL/en/).

The requirements for EUA may vary substantially among countries and are less rigorous than the regulatory approval procedures in non-emergency scenarios.

While test thresholds of ≥80% sensitivity and ≥97% specificity are recommended, existing evaluations may have been performed on very small sample sizes, which result in wide confidence intervals. As reliable and accurate data can only be gathered after an appropriate sample size is used for evaluations, preliminary data should be considered with caution. Additional factors should be considered when selecting tests, including company experience and distribution/supply networks, affordability, range of validated sample types, requirements for additional equipment or infrastructure, and simplified workflows.

Implementation considerations

Role of existing RT-PCR programmes

Appropriate introduction of COVID-19 Ag-RDTs must also consider a continuing role of RT-PCR within the COVID-19 testing programme. RT-PCR may be positioned in settings where turnaround times allow for clinical utility (<48 hours) or where confirmatory testing is desired following initial COVID-19 Ag-RDT screening. In settings where cases are very low or non-existent, RT-PCR can continue to be used to confirm the first new cases to identify new or emerging outbreaks. Both tests will continue to play key roles in the testing programme and RT-PCR should be positioned to maximize the strengths of COVID-19 Ag-RDTs while still contributing to appropriate diagnosis of results.

Training

Training and supervision are critical components of COVID-19 Ag-RDT quality assurance. COVID-19 Ag-RDTs may be considered 'easy to use' but that does not negate the need for training and supervision, especially as these tests are decentralized and often offered in remote settings. A training curriculum has been developed by Africa CDC and ASLM as a key resource to ensure appropriate and accurate training, and countries should plan for the need for both significant training or new sampling and testing personnel as well as ongoing supervision and monitoring of the implementation. Africa CDC and ASLM training materials can be accessed here: https://aslm.org/courses/covid-19-antigen-training-materials/.

Quality assurance

Ensuring quality test results is a cornerstone for a successful implementation of COVID-19 Ag-RDTs. Key pillars for monitoring quality assurance include procurement of high-quality and suitable products, good transport and storage, verification of quality prior to deployment (if appropriate quality control samples are available), training and supervision of end-users, and a system to monitor, communicate and address concerns. Countries should ensure periodic verification of new consignments or lots prior to testing and external quality assessment procedures through the use of both proficiency

testing panels and/or re-testing with a defined frequency established for each. Additional resources on appropriate quality assurance for COVID-19 Ag-RDTs will be made available through Africa CDC here: https://aslm.org/wp-content/uploads/2020/12/Quality Assurance Framework-for-SARS-CoV-2 Antigen-Rapid-Testing-for-diagnosis-of-COVID-19-Web.pdf

Data use

Timely, detailed COVID-19 testing and surveillance data from the COVID-19 testing programmes will be vital for the public health response. COVID-19 Ag-RDT testing data are a fundamental part of this landscape. All cases managed as positive result should be referred to the contact tracing programme to ensure timely testing and isolation/quarantine of contacts. All results, including valid and invalid, should be included in the national surveillance data, and where possible, RT-PCR and COVID-19 Ag-RDT test results should be disaggregated for better oversight of the testing programme. Countries should make real-time data availability a priority so they can use evidence-based metrics to drive national policy.

Continuous learning

Countries should apply this guidance to their country settings taking into close consideration the local context, national and regional priorities, and the continuously changing state of the epidemic at the sub-national level. This guidance will be updated as additional evidence becomes available from countries that are implementing the strategies.
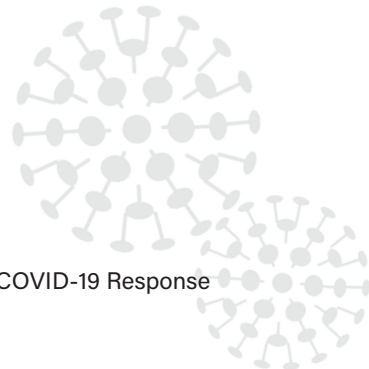
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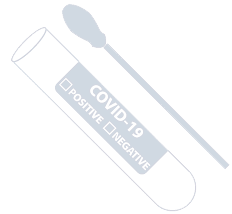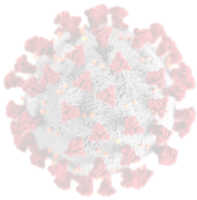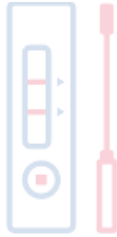
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World Health Organization. Public health criteria to adjust public health and social measures in the context of COVID-19: annex to considerations in adjusting public health and social measures in the context of COVID-19, 12 May 2020 (https://apps.who.int/iris/handle/10665/332073, accessed 24 November 2020)