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Mary Kathryn Bohn, Giuseppe Lippi, Andrea R. Horvath, Rajiv Erasmus, Matthias Grimmler, Maurizio Gramegna, Nicasio Mancini, Robert Mueller, William D. Rawlinson, María Elizabeth Menezes, Maria-Magdalena Patru, Fabio Rota, Sunil Sethi, Krishna Singh, Kwok-Yung Yuen, Cheng-Bin Wang and Khosrow Adeli*, on behalf of the IFCC Taskforce on COVID-19

IFCC interim guidelines on rapid point-of-care antigen testing for SARS-CoV-2 detection in asymptomatic and symptomatic individuals

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Abstract: With an almost unremittent progression of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections all around the world, there is a compelling need to introduce rapid, reliable, and high-throughput testing to allow appropriate clinical management and/or timely isolation of infected individuals. Although nucleic acid amplification testing (NAAT) remains the gold standard for detecting and theoretically quantifying SARS-CoV-2 mRNA in various specimen types, antigen assays may be considered a suitable alternative, under specific circumstances. Rapid antigen tests are meant to detect viral antigen proteins in biological specimens (e.g. nasal, nasopharyngeal, saliva), to indicate current SARS-CoV-2 infection. The available assay methodology includes rapid chromatographic immunoassays, used at the point-of-care, which carries some advantages and drawbacks compared to more conventional, instrumentation-based, laboratory immunoassays. Therefore, this document by the International Federation for Clinical Chemistry and Laboratory Medicine (IFCC) Taskforce on COVID-19 aims to summarize available data on the performance of currently available SARS-CoV-2 antigen rapid detection tests (Ag-RDTs), providing interim guidance on clinical indications and target populations, assay selection, and evaluation, test interpretation and limitations, as well as on pre-analytical considerations. This document is hence mainly aimed to assist laboratory and regulated health professionals in selecting, validating, and implementing regulatory approved Ag-RDTs.

Keywords: asymptomatic individuals; laboratory-based immunoassays for SARS-CoV-2 detection; point-of-care immunoassays for SARS-CoV-2 detection; SARS-CoV-2 antigen rapid detection tests; severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2); symptomatic individuals.

***Corresponding author: Khosrow Adeli**, President, IFCC; Department of Paediatric Laboratory Medicine, The Hospital for Sick Children, Toronto, ON, Canada; and Department of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, ON, Canada, Phone: +1 416 813 8682, E-mail: khosrow.adeli@sickkids.ca
Mary Kathryn Bohn, Department of Paediatric Laboratory Medicine, CALIPER Program, The Hospital for Sick Children, Toronto, ON, Canada; and Department of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, ON, Canada
Giuseppe Lippi, University Hospital of Verona, Verona, Italy
Andrea R. Horvath, Department of Clinical Chemistry, NSW Health Pathology, Prince of Wales Hospital, Sydney, NSW, Australia
Rajiv Erasmus, Stellenbosch University, Cape Town, Western Cape, Republic of South Africa
Matthias Grimmler, DiaSys Diagnostic Systems, Holzheim, Germany
Maurizio Gramegna, Sentinel CH. SpA, Milan, Italy
Nicasio Mancini, Vita-Salute San Raffaele University, Milan, Italy
Robert Mueller, Abbott Laboratories, Abbott Park, IL, USA
William D. Rawlinson, Department of Virology, NSW Health Pathology, Prince of Wales Hospital, Sydney, NSW, Australia
María Elizabeth Menezes, Secretaria de Saúde do Estado de Santa Catarina, Florianópolis, Brazil
Maria-Magdalena Patru, Ortho Clinical Diagnostics, Raritan, NJ, USA
Fabio Rota, Sentinel Diagnostics, Milan, Italy
Sunil Sethi, National University Hospital, Singapore, Singapore
Krishna Singh, Siemens Healthcare USA, Malvern, PA, USA
Kwok-Yung Yuen, University of Hong Kong, Hong Kong, P. R. China
Cheng-Bin Wang, Chinese PLA General Hospital, Beijing, P. R. China

Background

There is emergent interest in clinical implementation of antigen testing for diagnosing severe acute respiratory

syndrome coronavirus 2 (SARS-CoV-2) infection. Antigen assays detect presence of viral antigen proteins in collected specimens (e.g. nasal, nasopharyngeal, saliva) to indicate current viral infection. Available assay methodology mainly includes rapid chromatographic immunoassays used at the point-of-care and laboratory-based immunoassays. Few studies have evaluated the analytical and clinical performance of laboratory-based SARS-CoV-2 antigen tests, while many assess rapid chromatographic assays [1–40]. This is not surprising, as most clinical indications (detailed throughout this guidance document) require rapid identification of SARS-CoV-2 infection at the point-of-care. Based on available evidence, this document will focus on point-of-care SARS-CoV-2 antigen rapid detection tests (Ag-RDTs), as defined by the World Health Organization (WHO).

The clinical and public health benefits of implementing Ag-RDTs for diagnosing SARS-CoV-2 infection in symptomatic (e.g. diagnostic prior to admission) and asymptomatic (e.g. surveillance and screening) individuals is debated. Proposed advantages to Ag-RDT implementation include: widespread availability as decentralized testing, rapid turnaround-time, patient stratification, potential low cost/equipment, and preventative case identification. However, concerns regarding analytical performance persist and have limited utilization. This document by the International Federation for Clinical Chemistry and Laboratory Medicine (IFCC) Taskforce on COVID-19 summarizes available data on the performance of currently available SARS-CoV-2 Ag-RDTs and provides interim guidance on: (a) clinical indications and target populations, (b) assay selection, (c) assay evaluation, (d) test interpretation and limitations, and (e) pre-analytical considerations for SARS-CoV-2 Ag-RDTs. It is aimed to assist laboratory and regulated health professionals in selecting, validating, and implementing regulatory approved Ag-RDTs. It is not meant to provide guidance on self-testing protocols by non-professionals.

Analytical and clinical performance of available SARS-CoV-2 antigen assays

Several recent reports have evaluated analytical and clinical performance of Ag-RDTs for the detection of current SARS-CoV-2 infection in different clinical settings [1–40]. Most studies assess Ag-RDT performance by comparing Ag-RDT results to results obtained from the reference standard method for SARS-CoV-2 detection, nucleic acid amplification test (NAAT), in the same or paired specimen (e.g. nasal, nasopharyngeal, oropharyngeal, saliva). A summary of available peer-reviewed evidence on SARS-CoV-2 Ag-RDT performance is provided in Supplementary Table 1. Key considerations in study interpretation include: (a) assay method, (b) patient cohort, and (c) specimen type. Most available studies evaluate Ag-RDTs in nasopharyngeal specimens collected from symptomatic patients, with fewer assessing performance in asymptomatic individuals. Based on available evidence, the sensitivity of Ag-RDTs is lower relative to NAAT-based assays [1–22, 24, 26, 27, 29–40]. Reported Ag-RDT sensitivity varies significantly depending on patient characteristics, viral load, and assay method (Supplementary Table 1). As concluded by a recent Cochrane systematic review of 58 studies evaluating SARS-CoV-2 Ag-RDTs, large differences in assay sensitivities between symptomatic (72.0%; 95% CI: 63.7–79.0%; 37 unique evaluations with 4,410 cases) and asymptomatic (58.1%; 95% CI: 40.2–74.1%; 12 unique evaluations with 295 cases) individuals have been reported [19]. Several studies have also consistently demonstrated improved assay sensitivity when considering symptomatic individuals early in disease course (e.g. <7 days post symptom onset, 78.3 and 95% CI: 71.1–84.1% vs. second week of symptoms, 51.0 and 95% CI: 40.8–61.0%) [19]. This coincides with infectious disease stage, as a well-evidenced meta-analysis showed no viable virus obtainment from samples collected 8–9 days post symptom onset [41].

Further, many reports have demonstrated Ag-RDT sensitivity is positively correlated with viral load, as determined by cycle threshold (Ct) values obtained from reference NAAT-based methods [1–10, 14, 18, 20–22, 24–27, 34, 35, 38, 40]. Ct values are commonly stratified as ≤25 and >25, demonstrating mean assay sensitivities of 94.5 and 40.7%, respectively, based on most recent Cochrane systematic review [19]. A Ct value of 30 is commonly used as a cut-point to define infection in patient specimens [42]. Recent studies have also shown inability to culture specimens with discordant results (i.e. antigen-negative, NAAT-positive), further suggesting that Ag-RDTs may be less sensitive in specimens with lower viral loads and thereby inferior infective potential [6, 13, 16, 18]. This may have implications on transmission risk and replication status (e.g. active vs. non-active infection) when taken into consideration with other factors (e.g. stage of infection, host immune response). Further studies are needed to better elucidate and define an infectious SARS-CoV-2 case. Importantly, while many studies stratify outcomes by Ct value, estimates and methods are not well standardized, complicating study interpretation. In contrast to Ag-RDT sensitivity, specificity of Ag-RDTs is reported to be very

high, almost similar to NAAT-based assays (e.g. 100% concordance). This has important implications in determination of positive predictive value (PPV) and negative predictive value (NPV) in different clinical settings and their subsequent implementation, as detailed below.

Taskforce recommendations – rapid antigen testing

[A] Clinical indications and target population

[A1] Key clinical indications for antigen testing in the identification of SARS-CoV-2

Current literature suggests that Ag-RDT performance is highly dependent on clinical setting. Most studies evaluating SARS-CoV-2 Ag-RDT performance have focused on patients with clinical suspicion of COVID-19 (e.g. exposure, symptoms) or confirmed SARS-CoV-2 infection [1, 2, 4, 5, 7–12, 14, 15, 17, 18, 20–22, 24–27, 29, 31, 35–40]. Fewer studies include asymptomatic individuals [3, 6, 13, 16, 20, 22, 25–31]. Many countries have adopted Ag-RDT protocols with different objectives and desired clinical indications in both high pre-test probability (e.g. symptomatic patients presenting to mobile testing sites or emergency departments) and more commonly, low pre-test probability settings (e.g. asymptomatic individuals at airports, schools or other public settings). Increasing uptake of Ag-RDT programs in low pre-test probability settings is not surprising given that 25–50% of SARS-CoV-2 transmission is estimated to occur in pre-symptomatic or asymptomatic individuals [43]. Current global screening and surveillance initiatives include: (a) routine screening in high-risk settings to prevent infection and transmission (e.g. Canada, USA), (b) targeted testing to release individuals from unnecessary quarantine and reduce socioeconomic harms (e.g. Germany, Belgium, Italy, Greece), (c) targeted testing in outbreak settings for more rapid contact tracing (e.g. Italy, Germany), and (d) mass testing in low and high-risk settings to prevent infection and transmission (e.g. China, Russia, Slovakia, UK) [44–46]. As evidence from government-based testing programs becomes more readily available, targeted testing protocols will be amended. Particularly, there is minimal evidence to support repeated testing (e.g. multiple times a week) in screening or surveillance settings to improve assay sensitivity, though test repetition may still be indicated in specific circumstances (e.g. recent contact with infected people, emergence of suggestive symptoms, familial cluster, etc.) [19]. Recommendations based on current evidence is provided below:

[A] Clinical indications and target population – recommendations

[A1]: Key clinical indications for Ag-RDTs in the identification of SARS-CoV-2.

Moderate-evidence supports the following clinical test indications in **high pre-test probability settings**. *Negative results* should always be followed by *confirmatory NAAT-based testing:*
- Individuals with clinical symptoms (Supplemental Table 3) of SARS-CoV-2 infection, including but not limited to individuals presenting to the emergency department or directly admitted to intensive care units and community patients.
- Pre-admission screening of patients in high probability settings.

Moderate-evidence supports the following clinical test indications in **moderate-low pre-test probability settings**. *Positive results* should always be followed by *confirmatory NAAT-based testing.*
- Individuals in workplaces or settings with high risk of transmission with no present symptoms of SARS-CoV-2 infection, including but not limited to:
  - Long term care homes/Hospitals
  - Schools (students and staff)
  - Airports
  - Open and client-facing settings (factories, offices, theatres)
- Individuals with known SARS-CoV-2 exposure in outbreak settings, but no clinical symptoms.

[B] Assay selection

[B1] Importance of assay principle, specimen type, and biosafety in assay selection

Available Ag-RDTs are commonly fluorescent or chromatographic immunoassays targeting specific viral proteins, such as the spike (S) or nucleocapsid (N) protein. As reported in Supplementary Table 2, most available Ag-RDTs target the SARS-CoV-2 N protein. Evidence supports the efficacy of N protein detection in Ag-RDTs [47–49]. Specifically, viral N protein is produced at higher levels compared to other viral SARS-CoV-2 proteins, leading to higher assay sensitivity [47–49]. However, any specific viral protein should not be considered conclusively advantageous at this time. No reports have detailed concerns regarding potential cross-reactivity in rapid antigen assay assessment with homologous proteins of seasonal endemic alpha- and betacoronaviruses. Finally, the emergence of SARS-CoV-2 variants (principally regarding, but not limited to, S protein mutations) has not been considered in available studies and should be

closely monitored for its possible effect on assay sensitivity [50]. Notably, the selective pressure placed by the increasing number of seropositive people worldwide (either post-infection or post-vaccination) is responsible of boosting higher viral mutations in the *S* gene, encoding the mature spike protein, so that using other viral antigens may be theoretically preferable.

In addition to viral protein, Ag-RDTs also vary by recommended specimen type [1–18, 24, 35–40, 51]. Nasopharyngeal specimen requirements are most common across available Ag-RDTs and have demonstrated superiority as a specimen type when compared to others (e.g. nasal, throat, oropharyngeal, or saliva) in the literature and internal manufacturer reports [4, 9, 10]. Emerging evidence regarding use of saliva as Ag-RDT specimen type in symptomatic patients is conflicting and should be re-evaluated as new studies are reported [52–54]. In addition, although biosafety risks are unlikely with Ag-RDTs, there have been concerns raised regarding lack of virus inactivation in buffers and the potential for particle spread. Manufacturer recommended handling and processing of the specimens, as well as other site and/or country recommended biosafety measures should be considered [45].

[B2] Importance of assay performance in assay selection

As detailed above, available evidence suggests sensitivity of available Ag-RDTs varies significantly depending on clinical setting and patient population [1–19, 24, 35–40]. Assay specificity has been reported as very high consistently across studies, showing near 100% concordance with NAAT-based methods [1–19, 24, 35–40]. It is essential that clinical laboratories consider assay selection in the context of the intended clinical use. Ag-RDTs can be applied in both high pre-test probability and low pre-test probability settings (see **[A1]**). In low pre-test probability settings, even Ag-RDTs with incredibly high sensitivity and specificity can result in low PPV values. Confirmatory testing protocols as recommended above can assist in improving assay performance and interpretation.

[B] Assay selection – recommendations

[B1]: Importance of assay principle, specimen type, and biosafety in assay selection
- There is insufficient evidence for selecting antigen assays based on any one specific viral antigen target (e.g. S or N).
- Clinical laboratories should adhere to manufacturer's recommendations for suitable specimen type(s) and consider that when multiple specimen types are acceptable, nasopharyngeal specimens likely provide superior performance.
- Clinical laboratories should adhere to manufacturer's biosafety recommendations and ensure that the testing environment facilitates such requirements. If manufacturers do not provide biosafety recommendations, clinical laboratories should ensure testing is conducted in a closed space and operating staff use appropriate personal protective equipment (i.e. gloves, sterile gowns, face shield, mask).

[B2]: Importance of assay performance in assay selection
- Clinical laboratories should select an antigen assay in the context of the intended clinical use (see **[C2]** below).

[C] Assay evaluation

The following recommendations provide general guidance to clinical laboratories on Ag-RDTs evaluation prior to clinical testing. This guidance is focused on verification of regulatory approved test performance, and is not meant for validation of laboratory-developed tests or validation of new tests by manufacturers. Most currently available Ag-RDTs are qualitative, and thus this guidance focuses on such assays. Individual laboratories should consider local resource availability, as well as regulatory and accreditation requirements and modify their evaluation plans accordingly.

[C1] Analytical performance verification of rapid antigen tests for SARS-CoV-2 detection

It is desirable to verify the performance of Ag-RDTs on all sample matrices that will be encountered during routine testing and are acceptable by the manufacturer. It is anticipated that many laboratories will not have direct access to suitable samples required for evaluation. This lack of access may be overcome by close collaboration with peers, or with a reference laboratory. All samples used in the evaluation should be stored under conditions that ensure high stability or tested immediately following collection, strictly following the procedures recommended by the manufacturer. A sample assay evaluation protocol is provided in Table 1 for qualitative Ag-RDTs.

[C2] Clinical performance verification of rapid antigen tests for SARS-CoV-2 detection

Before implementing Ag-RDTs into clinical care or public health initiatives, it is essential that clinical performance be verified in the context of intended use and in the target population. It is thus critical that patient characteristics (e.g. symptomatic vs. asymptomatic) are considered in assay evaluation. When clinical performance is evaluated in symptomatic patients, additional considerations include disease severity (e.g. moderate, severe or critical), timing of assessment (e.g. days since symptoms onset) and sample type (e.g. nasopharyngeal, nasal, salivary, and low

Table 1: Recommended verification of a regulatory-approved qualitative antigen assay.

Consideration	Element	Specifications
Reproducibility	Design	Prepare positive and negative quality control samples (available from commercial manufacturers). Run two times a day for a total of 10 days.
	Evaluation	Calculate reproducibility of control results (i.e. percentage of positive control specimens that return a positive result and percentage of negative control specimens that return a negative result).
	Acceptability	Reproducibility should meet the manufacturer's reproducibility claim and compare it to the laboratory's predetermined analytical requirement. Laboratories should also consider evaluating repeatability in the same specimen near the defined qualitative assay cut-off as per Section 8.3.1 of Clinical and Laboratory Standards Institute EP12-A2 guidelines, if possible, based on assay characteristics and specimen protocols.
Diagnostic accuracy	Design	Through pilot program in the desired clinical setting, run rapid antigen assay in parallel to a NAAT-based test using the same or paired specimens. Ideally, a consecutive population should be enrolled in whom testing is indicated. The pilot should continue until a minimum of 50 positive and 50 negative specimens are evaluated as per Clinical and Laboratory Standards Institute EP12-A2 guidelines. Sample size can be amended based on local resource availability and disease prevalence, particularly in low pre-test probability settings.
	Evaluation	Calculate assay sensitivity and specificity relative to reference method (NAAT-based test). Calculate NPV and PPV based on estimates derived from local pilot program.
	Acceptability	Sensitivity and specificity should meet the laboratory's ***a priori*** clinical specifications for intended case use.

respiratory tract). If these components are not considered in clinical performance verification, findings will not be transferrable to the intended clinical indication. Due to limited availability of Ag-RDT evaluation data for screening and surveillance of asymptomatic individuals, it is crucial that sensitivity and specificity estimates provided by manufacturers and in the literature are not blindly applied to local settings. Prior to verifying clinical performance, clinical laboratories should set ideal clinical performance specifications together with clinicians and policy makers that reflect the intended Ag-RDT use in the target population and clinical setting. Notably, the WHO has set a minimum performance requirement compared to a reference NAAT of ≥80% diagnostic sensitivity and ≥97% diagnostic specificity, respectively [55]. In verifying clinical performance, it would be ideal to run a pilot program in the field for a period of 2 or more weeks, wherein all Ag-RDT results are confirmed with a NAAT-based assay in the desired specimen type and the intended, consecutively enrolled population. Ag-RDT sensitivity and specificity in comparison to NAAT can then be accurately determined in the clinical indication of interest to ascertain real-life performance. Alternative testing protocols can also be compared to select the most appropriate option. Clinical and Laboratory Standards Institute (CLSI) Guidelines EP12 guidelines on evaluation of qualitative test performance recommends at least 50 positive and 50 negative specimens be evaluated in qualitative assay verification. However, given varying SARS-CoV-2 prevalence globally, this sample size recommendation may be difficult to achieve. A target number should be decided by local laboratories based on available resources and disease prevalence. One additional challenge with executing a pilot program is the need to collect parallel specimens (e.g. two specimens from the same individual at the same time) for evaluation. This can be partially overcome by collaborating with other laboratories and/or public health programs utilizing the same assay in similar patient populations to increase sample size.

[C] Assay evaluation – recommendations

[C1]: Analytical performance verification of rapid antigen tests for SARS-CoV-2 detection

- Laboratories *should verify the analytical performance* of regulatory approved rapid antigen tests, including the parameters described in Table 1, before routine use.

[C2]: Clinical performance verification of rapid antigen tests for SARS-CoV-2 detection

- Laboratories *should set clinical performance specifications* together with clinicians and policy makers that reflect the intended use of the test in the target population and clinical setting.
- Clinical performance studies *should verify if the test is fit for purpose in the local setting* by ideally conducting a field pilot program as per Table 1, depending on availability of resources.

[D] Test interpretation and limitations

[D1] Considerations for test interpretation

Given large variation and diversity in current and anticipated clinical use of SARS-Co-2 Ag-RDTs, test results must be carefully interpreted considering clinical context and diagnostic pathway. Overall, the diagnostic window of rapid antigen tests is narrower than that of conventional

molecular assays; the likelihood of detecting viral antigens is lower at the beginning and at the end of an ongoing SARS-CoV-2 infection [56]. A negative result does not definitively exclude the presence of active infection, especially given the lower reported Ag-RDT sensitivity compared to NAAT. Whether Ag-RDTs identify cases at higher likelihood of transmission remains to be definitely proven. Further studies are warranted to delineate the relationship of low Ct value and growth in viral culture with transmission risk. Implementing test protocols including confirmatory testing can be applied to avoid false negative and false positive results in settings with high or low pre-test probability [19]. Recommendations for interpretation in each of the indications described in section [A] are provided below.

[D] Test interpretation and limitations – recommendations

[D1]: Considerations for test interpretation.

High pre-test probability: Individuals presenting with clinical symptoms of SARS-CoV-2 infection.

— **Positive result**: SARS-CoV-2 antigen has been detected in the sample and the patient should be considered presumptively infected and thereby quarantined and/or treated as having COVID-19.

— **Negative result**: SARS-CoV-2 antigen has not been detected in the sample. Result should be considered preliminary. Confirmatory NAAT-based testing should be completed and results should be interpreted as per IFCC guidelines [57].

Moderate-low pre-test probability: Individuals with known exposure or in high-risk workplaces with no present symptoms of SARS-CoV-2 infection, including but not limited to long-term care homes/hospitals, schools, airports.

— **Positive result**: SARS-CoV-2 antigen has been detected in the sample. Result should be considered preliminary. Confirmatory NAAT-based testing should be completed and results should be interpreted as per IFCC guidelines [57]. Individual should be isolated until NAAT-based results are available.

— **Negative result**: SARS-CoV-2 antigen has not been detected in the sample. Patient should be considered non-infectious, though shall not abandon conventional preventive measures (face masking, social distancing, hand hygiene, etc.).

[D2] Advantages and limitations of rapid antigen tests

Advantages of Ag-RDTs for detection of SARS-CoV-2 infection include: (a) widespread availability for decentralized testing, (b) early diagnosis of pre-symptomatic individuals early in disease course when virus replication is at its highest, (c) rapid turnaround time, (d) limited need for advanced equipment and training in low resource settings, and (e) prevention of unnecessary isolation for non-infectious individuals. Limitations of such testing includes: (a) potential to miss positive cases (lower sensitivity), (b) higher risk of pre-analytical errors (see [E]), and (c) challenges associated with required confirmatory testing in low resource settings.

Proposed advantages of Ag-RDTs are uniquely suited to application of asymptomatic screening, population surveillance, and rapid patient stratification to guide patient management and prevent as well as control SARS-CoV-2 transmission. Indeed, simulation-based studies have suggested routine asymptomatic testing of SARS-CoV-2 (e.g. before travel) can reduce the number of infectious days by approximately 30%, reducing population transmission [58]. However, significant literature reports Ag-RDT sensitivity is markedly lower in asymptomatic settings, depending heavily on viral load (e.g. Ct value), days post symptom onset, and sample type [44]. Further, while some have suggested Ag-RDTs may better identify infectious SARS-CoV-2 cases and prevent unnecessary isolation of individuals with non-active viral replication and transmission as compared to NAAT (e.g. convalescent cases with persistent and lingering PCR positivity), it is still unclear if Ct values and viral culture accurately represent infectivity and transmission risk, since residual shedding of viral mRNA in the absence of viable viral particles has frequently been observed during recovery, and shall not hence be always considered straightforward evidence of an ongoing (e.g. active) infection [19, 44]. Available studies thus do not provide sufficient data to assess the ability of Ag-RDTs in the differentiation of individuals who are and are not infectious. Interestingly, emerging evidence suggests that Ag-RDT sensitivity is not only dependent on viral load but also on patient outcome, as positive Ag-RDT results had an over-fivefold higher risk of unfavorable disease progression in one study [59]. Further research is needed to confirm these findings. Finally, in addition the analytical considerations of Ag-RDT implementation, thorough discussion of pre-analytical considerations is needed (see [E]).

Taken together, it is important that clinical laboratories continue to highlight advantages and limitations when reporting Ag-RDT results and assist with the development of testing programs in collaboration with governmental public health and clinical agencies.

[E] Pre-analytical considerations

This interim guidance document details considerations for professional-use Ag-RDTs in different clinical settings. Appropriate pre-analytical procedures are critical to successful implementation of Ag-RDTs. Key pre-analytical

variables that could contribute to unnecessary errors include: inappropriate sampling, improper temperature for Ag-RDT storage and evaluation, reduced objectivity in test interpretation due to unclear band appearance, lack of proper quality control and external quality assurance procedures, inadequate staff training, and logistical challenges associated with storing results in laboratory information systems (LIS) and following up on the appropriate testing paradigm [60]. Accrediting providers of Ag-RDTs can help ensure adequate number of staff, biosafety, quality control measures, and storage and transport of kits. Clinical laboratories assisting with piloting of self-testing programs should carefully and cautiously consider the described pre-analytical variables and develop very detailed and lay training documentation, especially given non-skilled operator status.

[E] Pre-analytical considerations – recommendations

[E1]: Internal quality control and external quality assurance procedures

- Laboratories *should outline a clear internal quality control practice post-implementation* based on manufacturer's recommendations and ensure that staff is trained to carry out and report ongoing performance verifications.
- Laboratories should participate in an *External Quality Assurance Program* for SARS-CoV-2 Ag-RDTs, when possible and devise in-house programs, if needed, to provide confidence in the results produced.

[E2]: Staff training and education prior to implementation.

- Laboratories *should develop detailed standard operating procedures and in-depth training/education programs* to ensure all individuals are adequately trained on patient identification, specimen collection, quality assurance, biosafety measures, storage procedure, and test completion, interpretation and reporting prior to implementation. All new operators should be supervised for an appropriate period prior to operating alone.

Concluding remarks

Emerging evidence points toward unique advantages of rapid antigen tests for detecting SARS-CoV-2 infection provided implementation is carefully carried out in the context of intended clinical use and clinical population. Rapid antigen testing may assist global testing strategies to identify, isolate, and release SARS-CoV-2 cases earlier. However, successful implementation of rapid antigen testing protocols must closely consider technical, pre-analytical, analytical and clinical assay performance and interpret and verify test results depending on the pretest-probability of SARS-CoV-2 infection.

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