

Advice on the use of point-of-care immunodiagnostic tests for COVID-19

Scientific brief

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In response to the growing COVID-19 pandemic and shortages of laboratory-based molecular testing capacity and reagents, multiple diagnostic test manufacturers have developed and begun selling rapid and easy-to-use devices to facilitate testing outside of laboratory settings. These simple test kits are based either on detection of proteins from the COVID-19 virus in respiratory samples (e.g. sputum, throat swab) or detection, in blood or serum, of human antibodies generated in response to infection.

WHO applauds the efforts of test developers to innovate and respond to the needs of the population.

However, before these tests can be recommended, they must be validated in the appropriate populations and settings. Inadequate tests may miss patients with active infection or falsely categorize patients as having the disease when they do not, further hampering disease control efforts. **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.**

WHO continues to evaluate available immunodiagnostics tests for COVID-19 and will update this scientific brief when necessary.

Rapid diagnostic tests based on antigen detection

One type of rapid diagnostic test (RDT) detects the presence of viral proteins (antigens) expressed by the COVID-19 virus in a sample from the respiratory tract of a person. If the target antigen is present in sufficient concentrations in the sample, it will bind to specific antibodies fixed to a paper strip enclosed in a plastic casing and generate a visually detectable signal, typically within 30 minutes. The antigen(s) detected are expressed only when the virus is actively replicating; therefore, such tests are best used to identify acute or early infection.

How well the tests work depends on several factors, including the time from onset of illness, the concentration of virus in the specimen, the quality of the specimen collected from a person and how it is processed, and the precise formulation of the reagents in the test kits. Based on experience with antigen-based RDTs for other respiratory diseases such as influenza, in which affected patients have comparable concentrations of influenza virus in respiratory samples as seen in COVID-19, the sensitivity of these tests might be expected to vary from 34% to 80%.¹

Based on this information, half or more of COVID-19 infected patients might be missed by such tests, depending on the group of patients tested. These assumptions urgently require further study to understand whether they are accurate. Additionally, false-positive results – that is, a test showing that a person is infected when they are not – could occur if the antibodies on the test strip also recognize antigens of viruses other than COVID-19, such as from human coronaviruses that cause the common cold. If any of the antigen detection tests that are under development or commercialized demonstrate adequate performance, they could potentially be used as triage tests to rapidly identify patients who are very likely to have COVID-19, reducing or eliminating the need for expensive molecular confirmatory testing.

With the limited data now available, **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.**

Rapid diagnostic tests based on host antibody detection

There is another, more common type of rapid diagnostic test marketed for COVID-19; a test that detects the presence of antibodies in the blood of people believed to have been infected with COVID-19.²⁻⁵ Antibodies are produced over days to weeks after infection with the virus. The strength of antibody response depends on several factors, including age, nutritional status, severity of disease, and certain medications or infections like HIV that suppress the immune system.⁶⁻⁸ In some people with COVID-19, disease confirmed by molecular testing (e.g. reverse transcription polymerase chain reaction: RT-PCR), weak, late or absent antibody responses have been reported.^{6,7,9} Studies suggest that the majority of patients develop antibody response only in the second week after onset of symptoms.^{2,6,7,10-14} This means that a diagnosis of COVID-19 infection based on antibody response will often only be possible in the recovery phase, when many of the opportunities for clinical intervention or interruption of disease transmission have already passed. Antibody detection tests targeting COVID-19 may also cross-react with other pathogens, including other human

coronaviruses.^{7,15,16} and give false-positive results. Lastly, there has been discussion about whether RDTs detecting antibodies could predict whether an individual was immune to reinfection with the COVID-19 virus. There is no evidence to date to support this.

Tests to detect antibody responses to COVID-19 in the population will be critical to support the development of vaccines, and to add to our understanding of the extent of infection among people who are not identified through active case finding and surveillance efforts, the attack rate in the population, and the infection fatality rate. For clinical diagnosis, however, such tests have limited utility because they cannot quickly diagnose acute infection to inform actions needed to determine the course of treatment. Some clinicians have used these tests for antibody responses to make a presumptive diagnosis of recent COVID-19 disease in cases where molecular testing was negative but where there was a strong epidemiological link to COVID-19 infection and paired blood samples (acute and convalescent) showing rising antibody levels.

Based on current data, **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](#).**

Next steps

- Molecular (e.g. PCR) testing of respiratory tract samples is the recommended method for the identification and laboratory confirmation of COVID-19 cases. COVID-19 molecular diagnostic products are being evaluated for quality and safety through the [WHO Prequalification Emergency Use Listing Procedures](#) and through a collaboration with the Foundation for Innovative New Diagnostics (FIND). WHO guidance documents for detection of COVID-19 have been published: WHO Guidance on [Laboratory testing for COVID-19 in suspected human cases](#). In addition, guidance on how testing might be rationalized when lack of reagents or testing capacity necessitates prioritization of certain populations or individuals for testing is also [available](#).
- To inform WHO policy on the use of immunodiagnostic rapid tests for COVID-19, WHO is working with our global laboratory expert network, and closely reviewing the results of laboratory and clinical studies planned and implemented by reference laboratories, academic groups and non-governmental organizations.
- Target product profiles for desired COVID-19 diagnostics to inform research and development efforts are in development.
- WHO will continue to work with research groups, other agencies, and Member States to develop and interpret data that might indicate specific areas where such tests can be useful for clinical management of cases, epidemiologic understanding, and/or infection control.

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WHO continues to monitor the situation closely for any changes that may affect this interim guidance. Should any factors change, WHO will issue a further update. Otherwise, this scientific brief will expire 2 years after the date of publication.

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