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Current Status and Future Perspective of Rapid Diagnostic Kits / Vaccine against COVID-19

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ABSTRACT

Coronavirus disease 2019 (COVID-19), which causes serious respiratory illness such as pneumonia and lung failure, was first reported in Wuhan, the capital of Hubei, China. The etiological agent of COVID-19 has been confirmed as a novel coronavirus, now known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which is most likely originated from zoonotic coronaviruses, like SARS-CoV, which emerged in 2002. Rapid diagnostics, vaccines and therapeutics are important interventions for the management of the 2019 novel coronavirus (2019-nCoV) outbreak. Currently, various diagnostic kits to test for COVID-19 are available and several repurposing therapeutics for COVID-19 have shown to be clinically effective. In addition, global institutions and companies have begun to develop vaccines for the prevention of COVID-19. Here, we review the current status of, diagnosis, and vaccine development for COVID-19.

KEYWORDS: *COVID-19, diagnostics, vaccine, shipment*

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Purpose of the document:

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. On 30 January 2020, the World Health Organization (WHO) declared the COVID-19 (SARS-CoV-2) outbreak as a Public Health Emergency of International Concern (PHEIC), and shortly thereafter called for research on point of care diagnostics for use at the community level. In response, numerous point-of-care in-vitro diagnostics (IVDs) are in development or have entered the market. Most of them detect COVID-19 antigens or antibodies in a so-called "Rapid Diagnostic Test" (RDT) design.

Diagnostic Kits:

1. 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. 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%. 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.

2. 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. 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. 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. The majority of patients develop antibody response only in the second week after onset of symptoms. This means that a diagnosis of COVID-19 infection based on antibody response will often only be possible in the recovery phase.

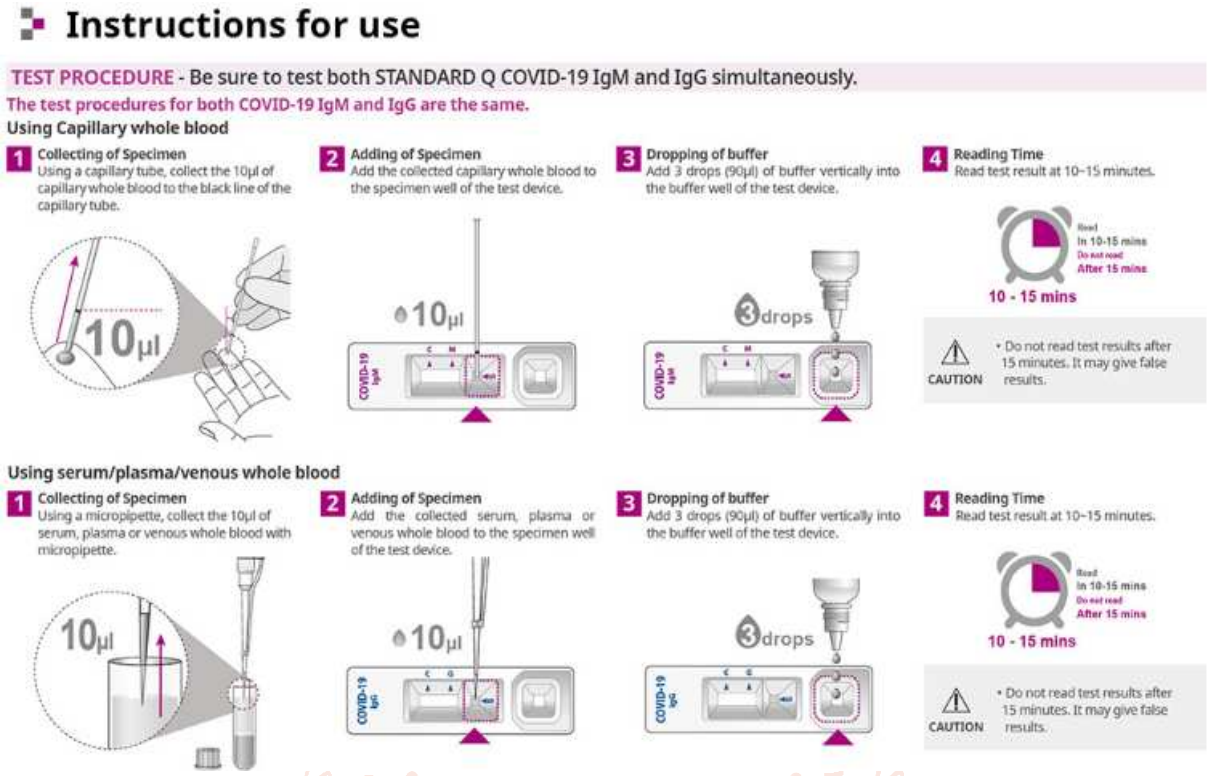

Fig: Test procedures for both COVID-19 IgM and IgG antibodies found in sample.

3. Abbott ID NOW COVID-19:

Abbott ID NOW COVID-19 is a portable, light-weight (3kg), small toaster sized COVID-19 test device, which can be used in various locations including physician's office, clinic or mobile units. The test is an automated assay that delivers positive results in just five minutes and takes only 13 minutes to show the negative results, using the ID NOW™ molecular platform. The ID NOW™ molecular platform of the test is an instrument-based, isothermal system for rapid qualitative identification of infectious diseases. Its isothermal nucleic acid amplification technology facilitates accurate test results in few minutes. The test detects nucleic acid from the RNA of SARS-CoV-2 virus present in nasal, nasopharyngeal or throat swabs, as well as the swabs eluted in viral transport media, collected by the healthcare providers from the suspected Covid-19 patients.

Abbott ID NOW COVID-19

The Covid-19 test system comprises a sample receiver, a test base, a transfer cartridge and the ID NOW instrument. Sample receiver contains elution or lysis buffer. The test base has two sealed reaction tubes, each with a lyophilised pellet, while the transfer cartridge sends the eluted sample to the test base.

The sample receiver and test base are placed into the ID NOW instrument, with the specimen kept in the sample receiver. The sample then transports to the test base via transfer cartridge for target amplification. The ID NOW instrument eventually performs heating and mixing activity to detect the virus and furnish the results. The package also contains external patient swabs, as well as positive control and negative control swabs.

Diagnostic kits available in NIV Pune:

Till date, 23 antibody based rapid tests have been validated at NIV Pune, and the following were found to be satisfactory. 9 of these kits are manufactured in India.

S.No.	Kit Detail	*Lot no./Batch no.
1.	SARS-CoV-2 Antibody test (Lateral flow method): Guangzhou Wondfo Biotech, Mylan Laboratories Limited (CE-IVD) M R Roofs Private Ltd Abbott Laboratories Cadila Healthcare Limited (Zydus Cadila)	 W19500309 W19500302 W19500351 W19500338
2.	COVID-19 IgM IgG Rapid Test: BioMedomics (CE-IVD)	20200226
3.	COVID-19 IgM/IgG Antibody Rapid Test: ZHUHAI LIVZON DIAGNOSTICS (CE-IVD)	CK2003010410
4.	New Coronavirus (COVID-19) IgG/IgM Rapid Test: Voxtur Bio Ltd, India	PCCV200301S
5.	COVID-19 IgM/IgG Antibody Detection Card Test: VANGUARD Diagnostics, India	RCOVID200301T
6.	Makesure COVID-19 Rapid test: HLL Lifecare Limited, India	CVCT030420 CVCT0204203 CVCT0104202
7.	YHLO iFlash-SARS-CoV-2 IgM and IgG detection kit (additional equipment required): CPC Diagnostics	20200206
8.	ACCUCARE IgM/IgG Lateral Flow Assay kit: LAB-CARE Diagnostics (India Pvt. Ltd)	CVC 200401
9.	Abchek COVID-19 IgM/IgG Antibody Rapid Test: NuLifecare	NUL/COV-19/R&D/001
10.	One Step Corona Virus (COVID-19) IgM/IgG Antibody Test: ALPINE BIOMEDICALS	A10420 A20420
11.	COVID 19 IgM/IgG Rapid Test Kit; Medsource Ozone Biomedicals (ver 2.0)	COV-002
12.	Immuno Quick Rapid Test for Detection of Novel Coronavirus (COVID-19) IgM/IgG Antibodies: Immuno Science India Pvt. Ltd	E142001
13.	Standard Q Covid -19 IgM/IgG Duo test – One Step Rapid Antibody test: SD Biosensors	E054002 E054004
14.	COVID-19 IgG/IgM Rapid Test Kit Rafael Diagnostic: BMT Diagnostics	COV20030059 COV20030059-1

Current Status of Vaccines:

Vaccines are the most effective strategy for preventing infectious disease since they are more cost-effective than treatment, and reduce morbidity and mortality without long-lasting effects. Vaccines are the most effective strategy for preventing infectious disease since they are more cost-effective than treatment, and reduce morbidity and mortality without long-lasting effects. Nonetheless, there are social, clinical and economic hurdles for vaccine and vaccination programmes, including (a) the willingness of the public to undergo vaccination with a novel vaccine, (b) the side effects and severe adverse reactions of vaccination, (c) the potential difference and/or low efficacy of the vaccine in populations different from the clinical trials' populations and (d) the accessibility of the vaccines to a given population (including the cost and availability of the vaccine). The following describes the current status of vaccine development against COVID-19 through various approaches:

1. Recombinant Subunit Vaccine:

In general, subunit vaccines are advantageous over other types of vaccines in that they are highly safe and have fewer side effects by inducing the immune system without introducing infectious viruses. Subunit-based vaccine development studies have also reported enhancement of T cell immune responses and generation of high titer neutralizing antibodies in vivo. Clover Biopharmaceuticals is testing a recombinant subunit vaccine based on the trimeric S protein (S-Trimer) of the SARS-CoV-2. The S protein contains three S1 heads and a trimeric S2 stalk. Clover Biopharmaceuticals confirmed the generation of a nativelike trimeric viral spike in mammalian cell culture-based expression system and the detection of antigen-specific neutralizing antibodies in the sera of fully-recovered COVID-19 patients.

2. DNA Vaccine:

DNA vaccines represent an innovative approach by direct injection of plasmids encoding the antigens, accompanied with a wide range of immune responses. Recently, various DNA vaccine platforms have been developed to improve the efficacy of vaccines by using electroporation to deliver plasmids and adding adjuvant to enhance the immune responses. This vaccine platform has advantages that can produce therapeutic antibodies and activate immune cells by delivering the vaccines intradermally into the patient. Inovio Pharmaceuticals is preparing for phase I trials in the U.S.A. and China with support from the Coalition for Epidemic Preparedness Innovations (CEPI).

3. mRNA Vaccine:

mRNA vaccines are rapidly developing technologies to treat infectious diseases and cancers. mRNA-based vaccines contain mRNAs encoding the antigens, which are translated at the host cellular machinery by vaccination. mRNA vaccines have advantages over conventional vaccines, by the absence of genome integration, the improved immune responses, the rapid development, and the production of multimeric antigens. Moderna's mRNA vaccine is designed in silico, which enables the rapid development and evaluation of vaccine efficacy. Moderna Inc. is preparing a phase I study with financial support from CEPI.

4. Other Vaccine Approaches:

Genexine Inc. is developing a COVID-19 vaccine using Hyleukin-7 platform technology. Hyleukin-7 platform enhances the immune responses by fusion of interlekin-7 (IL-7) to hyFc, designed to hybridize IgD and IgG4 for long-acting effects of Fc fusion proteins. IgD has a flexible hinge structure that maximizes biological activity of Fc-fusion protein. IgG4 has an unexposed junction site that minimizes adverse immunogenicity by preventing antibody-dependent cellular cytotoxicity (ADCC) and complement-dependent cytotoxicity (CDC). Genexine Inc. has reported the improved vaccine efficacy showing the accumulation of pulmonary T cells and the increase of plasma cytoid dendritic cells by treatment of Fc-fused IL-7 in influenza A virus infection model.

Shipment of Specimens to WHO Reference Laboratories:

WHO has established a shipment mechanism to expedite and cover the costs of the shipment of clinical samples from patients with suspected COVID-19 from the country of collection to one of the WHO reference laboratories providing confirmatory molecular testing for COVID-19. Instructions are outlined in this guidance document. This mechanism, which is similar to the Global Influenza Surveillance and Response System (GISRS) Shipping Fund Project (SFP), uses contracted couriers (World Courier and, in some circumstances, HAZGO) for shipping.

Process and documentation required for shipment:

A. For each shipment, laboratories should complete the booking form: https://www.who.int/docs/defaultsource/coronaviruse/booking-form-2019-ncov-world-courier.pdf), and email it to World Courier, Switzerland (opsgva@worldcourier.ch) with copy to all WHO staff listed on the form. In countries where World Courier does not operate, WHO will contact HAZGO, which will be instructed to transport the sample.

B. The designated courier or a local agent representative will contact the shipping laboratory to arrange collection as soon as possible, along with any other instructions. The agent will provide all packaging, labelling, and paperwork required to comply with international transport regulations. Dry ice will also be provided if the laboratory requests "frozen" shipment on the booking form. For advice on shipment temperatures, see Annex I. Clinical (non-propagated) samples from suspected or confirmed COVID-19 cases are assigned to UN 3373, Biological Substance, Category B, unless the countries of origin, transit, or destination have issued national recommendations defining them otherwise.

C. The shipping laboratory will be required to provide the following paperwork before the agent can accept the package for shipment:

- The completed booking form;
- A packing list or invoice indicating the recipient's address, number of packages, and details of contents, including their weight and value;
- An export permit for the originating country, if relevant;
- An import permit for the recipient country, if relevant;
- Any other document required by national regulations for importing infectious substances;
- A House Airway Bill (HWB) provided by the courier's agent. NB: The courier's local shipping agent can provide assistance on export documentation upon request.

D. Include your WHO regional laboratory focal point in the email with the booking form. If you do not know the name of the focal point, please contact the logistics emergency support team (José Rovira: roviraj@who.int, or Christian Fuster, fusterc@who.int), indicating WHO/Shipment/COVID-19 and the name of the shipping country in the subject line.

Recommended conditions for international shipment of specimens referred for COVID-19 testing (1,2,3,4)				
Specimen type	Temperature for storage until shipment	Expected duration of shipment	Recommended shipment temperature*	Shipment category**
• Nasopharyngeal and oropharyngeal swab (+ VTM or sterile saline #)	2–8 °C	≤ 12 days	2–8 °C	Biological Substance, Category B – UN 3373 / Packing Instructions P650 (5,6).
		> 12 days	−70 °C (dry ice)	
• Serum • Whole blood • Urine • Stool	2–8 °C	≤ 5 days	2–8 °C	
		> 5 days	−70 °C (dry ice)	
• Bronchoalveolar lavage (+VTM §) • (Endo)tracheal aspirate (+VTM §) • Nasopharyngeal aspirate or nasal wash (+VTM §) • Sputum	2–8 °C	≤ 2 days	2–8 °C	
		> 2 days	−70 °C (dry ice)	
• Tissue from biopsy or autopsy including from lung (+ VTM or sterile saline)	2–8 °C	≤ 24 hours	2–8 °C	
		> 24 hours	−70 °C (dry ice)	

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