COVID-19 Diagnostic testing: Where are we today?

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COVID-19 Diagnostic Testing

TIMELINE OF EVENTS

THE FIRST TESTS

THE UW RESPONSE

WHERE ARE WE NOW?

WHAT HAVE BEEN THE CHALLENGES?

THE ROAD TO OPENING
COVID-19 Cases as of May 10

https://coronavirus.jhu.edu/map.html
COVID19 Outbreak Timeline: Critical Events

December 31, 2019: China reports the novel SARS-2-CoV coronavirus to the World Health Organization.
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21: The first U.S. case is confirmed in a WA man who traveled from Wuhan.
30: The WHO declares global health emergency. The CDC confirms person-to-person spread of COVID-19 within the U.S.
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4: US declares public health emergency and authorizes the FDA for Emergency use Authorization (A. Azar, HHS Secretary)
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29: Washington state reports the first COVID-19 death in the U.S.
29: The Food and Drug Administration allows academic labs to develop and begin testing coronavirus testing kits while reviewing pending applications.
COVID-19 Outbreak Timeline: Critical Events

March
1: UW Virology opened for COVID-19 testing (The First Clinical Lab in the US)
13: Pres. Trump declares a national emergency, mobilizing resources. US reports 1896 cases.
16: FDA issues revised EUA policy for COVID-19 testing
17: Coronavirus now present in all 50 states
17: Washington State issues stay at home orders.
23: Nine states had stay-at-home orders by now.
26: The U.S. now leads world in coronavirus cases. 12 more states issue stay-at-home orders, totaling 21.
29: VP Pence and the COVID Task Force issue a letter to US testing labs to conform to a reporting process for all tests being conducted so FEMA can track supplies.

April
Widespread community-level transmission acknowledged

“You don’t want to wait until the last minute to start to prepare.” –Dr. Keith Jerome. NY Times, March 13, 2020
Worldwide testing rates per 100k

https://ourworldindata.org/covid-testing
https://finddx.shinyapps.io/FIND_Cov_19_Tracker
Testing data from African countries is not sufficient.
“Blood test”
AKA Serology

PCR tests detect the presence of COVID-19 virus RNA — i.e. do you have it now?

Serology tests detect the immune response to COVID-19 infection — i.e. have you ever had it?
SARS-COV-2 DIAGNOSTIC PIPELINE

We are collating an overview of all SARS-CoV-2 tests commercially available or in development for the diagnosis of COVID-19. We cannot guarantee that this is a fully comprehensive list. The below is information directly submitted by test suppliers or obtained from publicly available sources, and is not independently verified. If you have queries or updates, please contact us.

**EUA**: Emergency Use Authorization  
**HSA**: Health & Safety/Sciences Authority  
**MFDS**: Ministry of Food & Drug Safety  
**MHRA**: Medicines & Health Care Products Regulatory Agency  
**NRA**: National Regulatory Authority  
**RUO**: Research Use Only  
**TGA**: Therapeutic Goods Administration  
**WHO EUL**: World Health Organization Emergency Use Listing Procedure

<table>
<thead>
<tr>
<th>SHOW ALL</th>
<th>IMMUNOASSAYS</th>
<th>MOLECULAR ASSAYS</th>
<th>SAMPLE COLLECTION / INACTIVATION</th>
<th>DIGITAL SOLUTIONS</th>
<th>OTHER DIAGNOSTICS</th>
</tr>
</thead>
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<table>
<thead>
<tr>
<th>Status</th>
<th>Regulatory</th>
<th>FILTER</th>
<th>EXPORT TO XLS</th>
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</thead>
<tbody>
<tr>
<td>All</td>
<td></td>
<td></td>
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</tbody>
</table>

637 RESULT(S)

- [Idrop Inc. TroxyTM COVID-19 qPCR Multi Kit](#) (Korea MFDS EUA - Health Canada - Saudi FDA - Sri Lanka NMRA - CE-IVD) [Contact](#)
- [3B Biotech India Ltd TRUPCR ✶ SARS-CoV-2 RT qPCR Kit](#) (India DOG) [Contact](#)
- [3D Medicines 3Dmed 2019-nCoV RT-qPCR Detection Kit (CE-IVD)](#) [Contact](#)
- [3D Medicines ANDIS® SARS-CoV-2 RT-qPCR Detection Kit (US FDA EUA - CE-IVD)](#) [Contact](#)
314 RESULT(S)

- 1drop Inc, 1copy™ COVID-19 qPCR Multi Kit (Korea MFDS EUA - Health Canada)
- 3B BlackBio Biotech India Ltd TRUPCR® SARS-CoV-2 RT qPCR Kit (Indias)
- 3D Medicines ANDIS® SARS-CoV-2 RT-qPCR Detection Kit (US FDA EUA - Health Canada)
- 3D Medicines 3DMed 2019-nCoV RT-qPCR Detection Kit (CE-IVD)
- A'ccelerate Technology A'STAR Foritude Kit 2.0 (Singapore HSA)
- AB ANALITICA srl REAL QUALITY RQ SARS-CoV-2 (RUO)
- AB ANALITICA srl REAL QUALITY RQ-2019-nCoV (CE-IVD)
- Abacus Diagnostics GenomEra SARS-CoV-2 (RUO)
- Abbott Diagnostics Inc. ID NOW COVID-19 (US FDA EUA)
- Abbott Molecular Inc. Abbott RealTime SARS-CoV-2 EUA test (US FDA EUA - Health Canada)
- Access Bio, Inc. CareStart™ COVID-19 MDx RT-PCR (CE-IVD)
- Accuster Technologies Pvt Ltd Accuster SARS-COV2 RT-PCR test kit (CE-IVD)
- Acumen Research Laboratories Pte Ltd Acu-Corona 2.0 (Singapore HSA)
- Acumen Research Laboratories Pte Ltd Acu-Corona (RUO)
- ADALTIS srl MOLgen SARS-CoV2 Real Time RT PCR (CE-IVD)
- ADT Biotech LightStar 2019-nCoV RT-PCR Kit 1.0 (RUO)
- Advanced Biological Laboratories SA UltraGene Combo2Screen SARS-CoV-2 Assay (CE-IVD)
- Advanced Molecular Diagnostics Zena Max – SARS-COV-2 Real Time PCR Detection Kit (CE-IVD)
- AllBiotech abTES COVID-18 qPCR I Kit (Singapore HSA - CE-IVD)
- Aldatu Biosciences PANDAA qDx SARS-CoV-2 (In development)
- altona Diagnostics RealStar® SARS-CoV-2 RT-PCR Kit (CE-IVD)
- Amoy Diagnostics Co., Ltd AmoyDx® Novel Coronavirus (2019 nCoV) Detection Kit (CE-IVD)
- Amplicon Ltd AmpliTest SARS-CoV-2 (Real Time PCR) (CE-IVD)
- 3D Medicines ANDIS® SARS-CoV-2 RT-qPCR Detection Kit (US FDA EUA - CE-IVD) Contact
- Abbott Diagnostics Inc, ID NOW COVID-19 (US FDA EUA) Contact
- Becton Dickinson BioGX SARS-CoV-2 Reagents for BD MAX™ System (US FDA EUA - Health Canada - Australia TGA - Brazil ANVISA - Singapore HSA)
- BioFire Defense, LLC BioFire COVID-19 Test (US FDA EUA) Contact
- Cepheid Xpert Xpress SARS-CoV-2 (US FDA EUA - Health Canada - Australia TGA - Singapore HSA) Contact
- DiaSorin Molecular, LLC Simplexa™ COVID-19 Direct RT-PCR Kit (US FDA EUA - CE-IVD)
- Fast Track Diagnostics Luxembourg S.à r.l., a Siemens Healthineers Company FTD-114 SARS-CoV-2 (manual & lab-based NAT) (US FDA EUA - CE-IVD) Contact
- GenMark Diagnostics ePlex® SARS-CoV-2 Test (US FDA EUA) Contact
- Hologic Panther Fusion SARS-CoV-2 assay (US FDA EUA - Health Canada - Australia TGA)
- LabGenomics Co., Ltd LabGun™ COVID 19 Assay PCR Kit (US FDA EUA - CE-IVD) Contact
- LGC Biosearch technology Molecular assays, RNA extraction kit, rt-PCR reagents (China NMPA EUA - US FDA EUA) Contact
- Luminex Corp, ARIES SARS-CoV-2 Assay (US FDA EUA) Contact
- Next Pharma Inc, DiaCarta's QuantiVirus™SARS-CoV-2 Test (US FDA EUA - CE-IVD) Contact
- Novacyt/primerdesign genesig Real-Time PCR COVID-19 (US FDA EUA - CE-IVD - WHO EUL)
- QIAGEN GmbH QIAsat-Dx Respiratory Panel 2019-nCoV (US FDA EUA - CE-IVD) Contact 1 Contact 2
- Quidel Lyra SARS-CoV-2 Assay (US FDA EUA - Health Canada - CE-IVD) Contact
- Roche Molecular Diagnostics cobas® SARS-CoV-2 (for use on the cobas® 6800/8800 Systems) (US FDA EUA - WHO EUL) Contact
- Saladax Biomedical Inc, Fosun COVID-19 RT-PCR Detection Kit (US FDA EUA - CE-IVD) Contact
- SEASUN BIOMATERIALS U-TOP™ COVID-19 Detection Kit (Korea MFDS EUA - US FDA EUA - CE-IVD) Contact
- Thermo Fisher Scientific TaqPath™ COVID-19 Combo Kit (US FDA EUA - Health Canada - Australia TGA - Singapore HSA) Contact
Coronavirus disease (COVID-19) technical guidance: Laboratory testing for 2019-nCoV in humans

Overview

On this page you will find information about:
1. WHO interim guidance for laboratory testing
2. WHO interim guidance for laboratory biosafety related to COVID-19 virus
3. Molecular assays to diagnose COVID-19 virus
4. WHO reference laboratories providing confirmatory testing for COVID-19
5. Guidance for laboratories shipping specimens to WHO reference laboratories that provide confirmatory testing for COVID-19 virus
6. Laboratory Assessment Tool for laboratories implementing COVID-19 testing
7. Scientific brief Advice on the use of point-of-care immunodiagnostic tests for COVID-19

1. WHO interim guidance for laboratory testing

The purpose of this document is to provide interim guidance to laboratories and stakeholders involved in laboratory testing of COVID-19 virus.

- Read the document (updated 2 March 2020)

Diagnostic testing for COVID-19 is critical to tracking the virus, understanding epidemiology, informing case management, and to suppressing transmission. This document describes the strategic use of diagnostic testing in different transmission scenarios of the COVID-19 outbreak, from no cases to community transmission, including how testing might be rationalized when lack of reagents or...
Serology is not part of acute diagnostic testing at this time

Serology of limited use for diagnostic testing

- Specific scenarios as per clinical judgement
- e.g., NAT negative, longer duration of symptoms

The timing and level of antibodies is uncertain after SARS-CoV-2 infection, and varies between patient populations. This graphic depicts one scenario based on the limited published evidence.

Data courtesy The Royal College of Pathologists of Australasia
What have been the major challenges so far?

1. Access to Testing-
   • Tiered testing approach
   • Who to test
   • Lab Capacity/referral
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   - Slow expansion of testing
   - Regulatory process
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2. Lost time
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   - Regulatory process

3. Supply Chain Problems
   - PPE
   - sampling kits
   - lab reagents (positive control material, extraction reagents)

Courtesy University of British Columbia, Department of Pathology and Laboratory Medicine
The Road to Opening

Better data

Improvements in clinical and public health system capabilities

Effective therapeutic, prophylactic, and preventive treatments
## Serology-based tests for COVID-19

<table>
<thead>
<tr>
<th>Type of test</th>
<th>Time to results</th>
<th>What it tells us</th>
<th>What it cannot tell us</th>
<th>Approved for use in USA?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapid diagnostic test (RDT)</td>
<td>10-30 minutes</td>
<td>The presence or absence (qualitative) of antibodies against the virus present in patient serum.</td>
<td>The quantifiable amount of antibodies in the patient serum, or if these antibodies are able to protect against future infection.</td>
<td>2</td>
</tr>
<tr>
<td>Enzyme linked immunosorbent assay (ELISA)</td>
<td>1-5 hours</td>
<td>The presence or absence (quantitative) of antibodies against the virus present in patient serum.</td>
<td>If the antibodies are able to protect against future infection.</td>
<td>1 + 1 modified ELISA</td>
</tr>
<tr>
<td>Neutralization assay</td>
<td>3-5 days</td>
<td>The presence of active antibodies in patient serum that are able to inhibit virus growth ex vivo, in a cell culture system. Indicates if the patient is protected against future infection.</td>
<td>It may miss antibodies to viral proteins that are not involved in replication.</td>
<td>O</td>
</tr>
</tbody>
</table>

Early Humoral Response to SARS-CoV-2

Characteristics of plasma antibodies in patients infected with SARS-CoV-2. A, Time of appearance of IgM, IgA, and IgG antibodies to SARS-CoV-2, determined by ELISA of plasma samples obtained from inpatients with SARS-CoV-2 infection.

*Guo et al; Clinical Infectious Diseases,* March 20, 2020; [https://doi.org/10.1093/cid/ciaa310](https://doi.org/10.1093/cid/ciaa310)
These individual-level dynamics aggregate to form the population-level seroprevalence (right-top). Measures of seroprevalence may imperfectly measure past exposure to infection due to antigenic diversity of future SARS-CoV-2 viruses and cross-reactivity of endemic human coronaviruses (HCoVs) with SARS-CoV-2. Measures of seroprevalence may also be inconsistent across times as antibody levels within individuals wane.
A Word About Self Testing

- Reliable
- Accurate
- Timely

Effective diagnosis
Test Performance and Use Matters

• Sensitivity
• Specificity
• Predictive value
• Likelihood ratio
Calculations

Sensitivity = 95%
Specificity = 98%

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<tr>
<th>Disease prevalence</th>
<th>PPV</th>
<th>NPV</th>
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<tbody>
<tr>
<td>70%</td>
<td>99.08%</td>
<td>89.63%</td>
</tr>
<tr>
<td>50%</td>
<td>97.88%</td>
<td>95.28%</td>
</tr>
<tr>
<td>20%</td>
<td>92.02%</td>
<td>98.78%</td>
</tr>
<tr>
<td>5%</td>
<td>70.83%</td>
<td>99.74%</td>
</tr>
<tr>
<td>1%</td>
<td>31.79%</td>
<td>99.95%</td>
</tr>
</tbody>
</table>

→ For low disease prevalence, test specificity is paramount!