# *In Vitro* Diagnostics (IVD) COVID-19 Testing: Supporting Patient Care and Protecting Public Health

AdvaMedDx
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# Speakers

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# About AdvaMedDx

AdvaMedDx, a division of the Advanced Medical Technology Association (AdvaMed), represents over 70 of the world's leading *in vitro diagnostics* (IVD) companies – including those manufacturing tests that are critical tools in the fight against COVID-19 – in the United States and abroad.

# Overview of COVID-19 testing workflow from patient sample to results

## Patient sample

Obtain sample
- Nasal/oral swab;
- Blood draw/finger stick; or
- Oral fluid
(Varies by test type)

## IVD tests include those run on IVD platforms in laboratories or at the point-of-care

Transfer sample

### IVD platforms

IVD platforms in small and large clinical labs, like hospital labs, run up to hundreds of tests at once

IVD platforms have easy to follow and automated workflows and integrated software to perform accurate, reliable diagnostic testing using IVD test kits

Transfer/direct sample

### IVD point-of-care

IVD point-of-care instruments, used in doctors' offices and emergency rooms, can run tests rapidly and almost anywhere

Direct sample

### IVD instrument-less point-of-care

Transportable IVD testing, single sample with rapid results, triage testing to perform almost anywhere

## Test results

Results

IVD tests on IVD platforms in clinical laboratories deliver results in 1-4 hours (molecular), and as fast as 10-60 minutes (immunoassay, such as serology/antibody)

Results

IVD point-of-care tests can deliver results in 5-45 minutes

Results

Results from a rapid point-of-care test with no instrument can be delivered in 5-30 minutes

From manufacturing of sample collection devices used by clinicians, testing platforms used by laboratories small and large, and rapid point-of-care tests and platforms, IVD manufacturing and delivering COVID-19 testing

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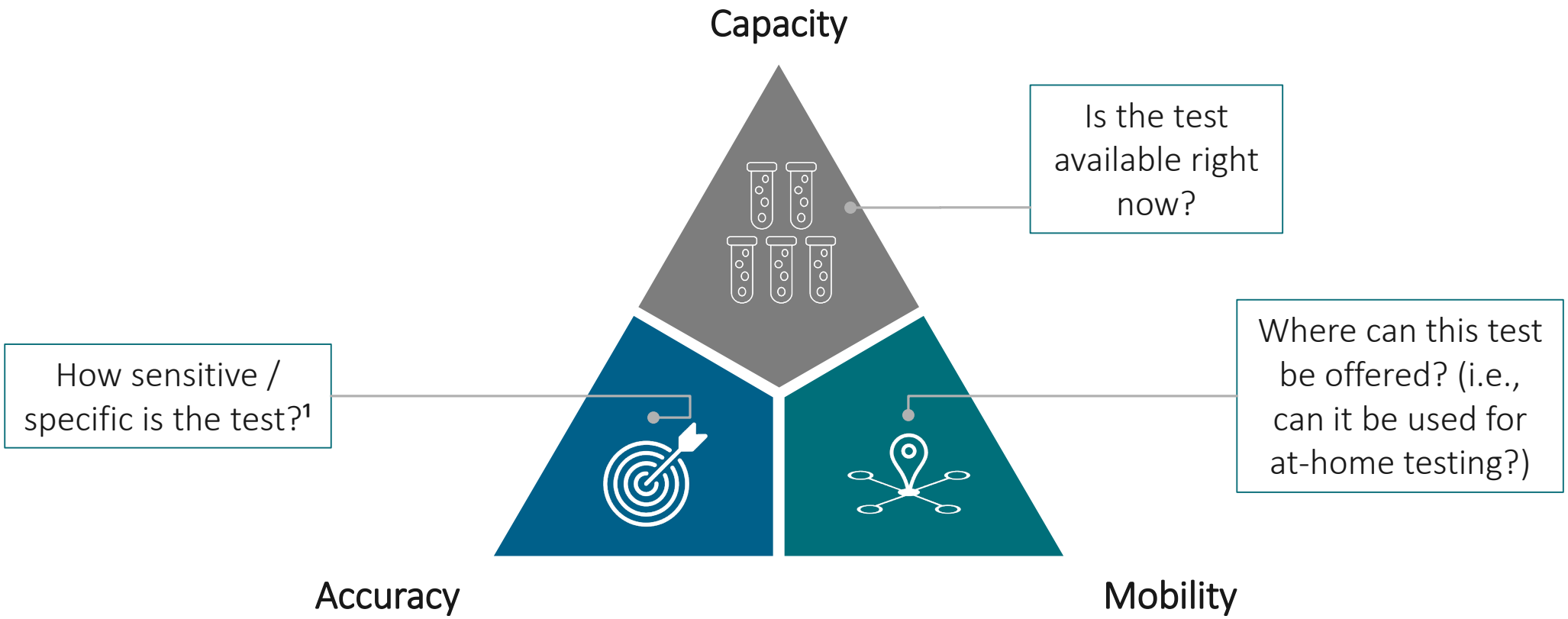
# Utilization of the full testing ecosystem to extend the reach of testing involves trade-offs




*Different types of tests are most appropriate for different use cases / patients –*
***there is no "one size fits all" testing solution***

1. Sensitivity refer to how often the test is positive when the condition of interest is present; specificity refers to how often the test is negative when the condition of interest is absent (https://www.fda.gov/regulatory-information/search-fda-guidance-documents/statistical-guidance-reporting-results-studies-evaluating-diagnostic-tests-guidance-industry-and-fda). Disease prevalence will dictate negative predictive value (NPV) and positive predictive value (PPV); also accuracy may differ in asymptomatic versus symptomatic people.

## There are three general categories of diagnostic tests most-relevant to COVID-19

Molecular Diagnostics (MDx)

Antigen testing

Serology (antibody) testing

# COVID-19 diagnostic testing : Molecular Diagnostics

## Molecular Diagnostics (MDx)

| | |
|---|---|
| What does this do? | • **Confirms** active infection |
| How does this work? | • **Detects viral RNA** (viral equivalent of DNA)<br>  - In nasal / oral swab, oral fluid |
| How quickly are results reported? | • Point-of-care tests: Can provide results in minutes, performed right at the site of care, in clinics, emergency rooms, and other settings<br>• Tests run on moderate and high-throughput platforms in hospital and reference laboratories: up to hundreds of tests can be run in 1-4 hours;  the time to send the test to the laboratory for analysis and for results to be provided to clinicians and patients can vary<br>• There are ~ 1,000 high throughput molecular platforms in the U.S. |

# Over the last month, observed molecular diagnostic capacity for COVID-19 has more than tripled


- Diagnostics manufacturers collectively shipped ~30M molecular tests during the month of April and are on track to ship 39M in May
- Typically, it can take 3-5 years to develop and bring a test to market. The diagnostics industry has dramatically hastened the pace of development and manufacturing in response to this unprecedented situation, and is committed to further innovation and expansion of testing, protecting public health

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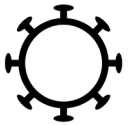
Note: Figures shown are trailing 7-day averages, rounded. Source: covidtracking.com; State COVID-19 websites. As of Apr 22, CA, OK and FL switched from reporting patients tested to total tests conducted; day-to-day variation driven in part by clearance of reporting backlog. As of May 18, 2020

# COVID-19 diagnostic testing: Antigen testing



## Antigen testing

| | |
|---|---|
| What does this do? | • Confirm active infection |
| How does this work? | • Detects viral proteins shed in human samples<br>  - In nasal / oral swab, oral fluid |
| How quickly are results reported? | • Point-of-care tests: Can provide results in minutes, performed right at the site of care, in clinics, emergency rooms, and other settings, including at-home self-tests, currently under development<br>• Tests run on moderate and high-throughput platforms in hospital and reference laboratories: up to hundreds of tests can be run in ~2 hours;  the time to send the test to the laboratory for analysis and for results to be provided to clinicians and patients can vary<br>• There are ~ 10,000 high throughput immunoassay platforms that can run antigen tests in the U.S.<br>• The first commercial antigen test, a point of care test, was authorized by FDA in early May. |

# Primary Use cases for COVID-19 molecular and antigen diagnostic tests

General population health surveillance

Continuously track & monitor spread and prevalence of disease in broad population

Diagnosis & triage of symptomatic and asymptomatic patients

Quickly diagnose and triage symptomatic patients and inform clinical care

Employer-contracted workforce testing

Build testing programs with targeted large employers to screen employees as they return to work

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# COVID-19 diagnostic testing: Serology (antibody) testing

## Serology (antibody) testing

**What does this do?**

- **Identifies** people who have been infected for which an immune response has been triggered
  - **Not used to diagnose active infection**
  - **Unclear if antibodies confer resistance**, and if so, for how long

**How does this work?**

- **Detects human antibodies** to the given pathogen (e.g. the COVID-19 virus)
  - In blood samples

**How quickly are results reported?**

- Point-of-care tests: Can provide results in minutes, performed right at the site of care, in clinics, emergency rooms, and other settings
- Tests run on moderate and high-throughput platforms in hospital and reference laboratories: up to hundreds of tests can be run in as little as 10-60 minutes;  the time to send the test to the laboratory for analysis and for results to be provided to clinicians and patients can vary
- There are ~ 10,000 high throughput immunoassay platforms that can run serology tests in the U.S.
- AdvaMedDx estimates the IVD industry is on track to ship 30M tests in May and 94M in June.

# COVID-19 diagnostic testing: Serology (antibody) testing

## Serology (antibody) testing

**What does this do?**

- **Identifies** people who have been infected for which an immune response has been triggered
  - **Can be used to diagnosis**
  - Broad testing will clarity if antibodies confer resistance, and if so, for how long

**How does this work?**

- **Detects human antibodies** to the given pathogen (e.g. the COVID-19 virus)
  - In blood samples

**How quickly are results reported?**

- Point-of-care tests: Can provide results in minutes, performed right at the site of care, in clinics, emergency rooms, and other settings
- Tests run on moderate and high-throughput platforms in hospital and reference laboratories: up to hundreds of tests can be run in as little as 10-60 minutes;  the time to send the test to the laboratory for analysis and for results to be provided to clinicians and patients can vary
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# FDA updated quality standards for serology (antibody) testing on May 4

**Policy for Coronavirus Disease-2019 Tests During the Public Health Emergency (Revised)**

**Immediately in Effect Guidance for Clinical Laboratories, Commercial Manufacturers, and Food and Drug Administration Staff**

**Document issued on the web on May 11, 2020.**

**C. Serological Tests**

FDA defines SARS-CoV-2 serological tests as tests that identify antibodies (e.g., IgG, IgM) to SARS-CoV-2 from clinical specimens. FDA recommends that the following validation studies be conducted for a SARS-CoV-2 serological assay:

- Cross-reactivity/Analytical Specificity
- Class Specificity
- Clinical Agreement Study

The clinical agreement study is intended to establish the performance characteristics (e.g., sensitivity/PPA, specificity/NPA) of the test. FDA recommends that clinical accuracy should be established on human specimens from patients with microbiologically confirmed COVID-19

https://www.fda.gov/media/135659/download

- Quality testing is not only possible – but should be expected as test results guide critical decisions about patient care and public health.
- Numerous AdvaMedDx member IVD company tests are seeking FDA authorization or have already secured authorization and are the market with 98-100% sensitivity and specificity.

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# There are 6 overarching use cases for COVID-19 diagnostic tests

*Use cases for molecular and antigen testing*

## Diagnosis & triage of symptomatic patients

Quickly diagnose and triage symptomatic patients and inform clinical care; screening for therapy development

## General population health surveillance

Continuously track & monitor spread and prevalence of disease in broad population

## Employer-contracted workforce testing

Build testing programs with targeted large employers to screen employees as they return to work

## Screening for therapy & vaccine development

Screen potential patients for clinical testing of vaccines, drug therapies in development, convalescent plasma; measure success of vaccination campaigns

## Testing for immune response

Resolve uncertain diagnosis, support case management. Identify individuals with COVID-19 antibodies, which may indicate potential resistance / immunity, assessing duration of immunity, "herd immunity"

## Population monitoring for previous exposure

Monitor populations to identify individuals who have had previous exposure(s), potentially enabling unnecessary quarantine of essential workers, return to work, lifting "stay at home" orders

*Use cases for serology (antibody) testing*

# Various components are needed to perform each type of COVID-19 diagnostic test – issues in any of these components could limit overall testing capacity

Swabs, blood collection kits, transport media, etc.

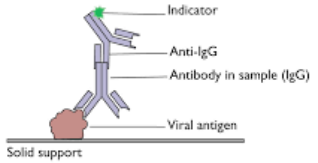
Used to collect and transport patient samples

Extraction / processing reagents

Used to extract viral RNA from patient sample

Amplification reagents

Allow for replication of viral RNA so it can be detected




Biological components

Specialized proteins / molecules used to detect antigens / antibodies

Internal / External controls

Materials used to verify the test instrument and reagents are functioning properly

Platforms / Instruments

Additional equipment needed (e.g., point-of-care devices, high-throughput machines)

*Used for*

| | Swabs, blood collection kits, transport media, etc. | Extraction / processing reagents | Amplification reagents | Biological components | Internal / External controls | Platforms / Instruments |
|---|---|---|---|---|---|---|
| Molecular diagnostics | ✓ Swabs and transport media[1] or oral fluid collection | ✓ | ✓ | | ✓ | ✓ |
| Antigen testing | ✓ Swabs and transport media[1] or oral fluid collection | | | ✓ | ✓ | ✓ |
| Serology (antibody) testing | ✓ Blood and oral fluid collection kits | | | ✓ | ✓ | ✓ Platform/instrument not needed for all rapid antigen and serology tests |

*Specialized expertise is required to make these components, and companies generally focus in offering a selection of the above – some of these components need to be tested on active viruses and patient samples*

*In addition, there are numerous potential labor-related issues to testing capacity (e.g. HCP[2] availability, lab techs, couriers to transport tests, etc.)*

1. Transport media not needed for point-of-care tests; 2. Health care provider; Note: The above represents the typical components required for each test type. Pictures are illustrative. Additionally, they may not be of products specifically intended for COVID-19 diagnostic use.
As of May 7, 2020

# The diagnostics industry has responded quickly and aggressively to the COVID-19 pandemic, and continues to do so

## Numerous tests have been brought to market…

As of mid-day, May 12th, 61 commercial COVID-19 tests have received Emergency Use Authorizations from the FDA, including:

- 50 molecular tests (3 point-of-care)
- 1 antigen test (point-of-care), days ago, with more to come
- 10 serology antibody tests

## …and manufacturers continue to innovate, leveraging established and novel technologies

May 7th: First-ever FDA-approved CRISPR-based[1] diagnostic, for use in COVID-19

May 9th: First COVID-19 antigen test approved, and additional antigen tests are in development

*Typically, it can take 3-5 years to develop and bring a test to market. The diagnostics industry has dramatically hastened the pace of development and manufacturing in response to this unprecedented situation, and is committed to further innovation and expansion of testing, protecting public health*

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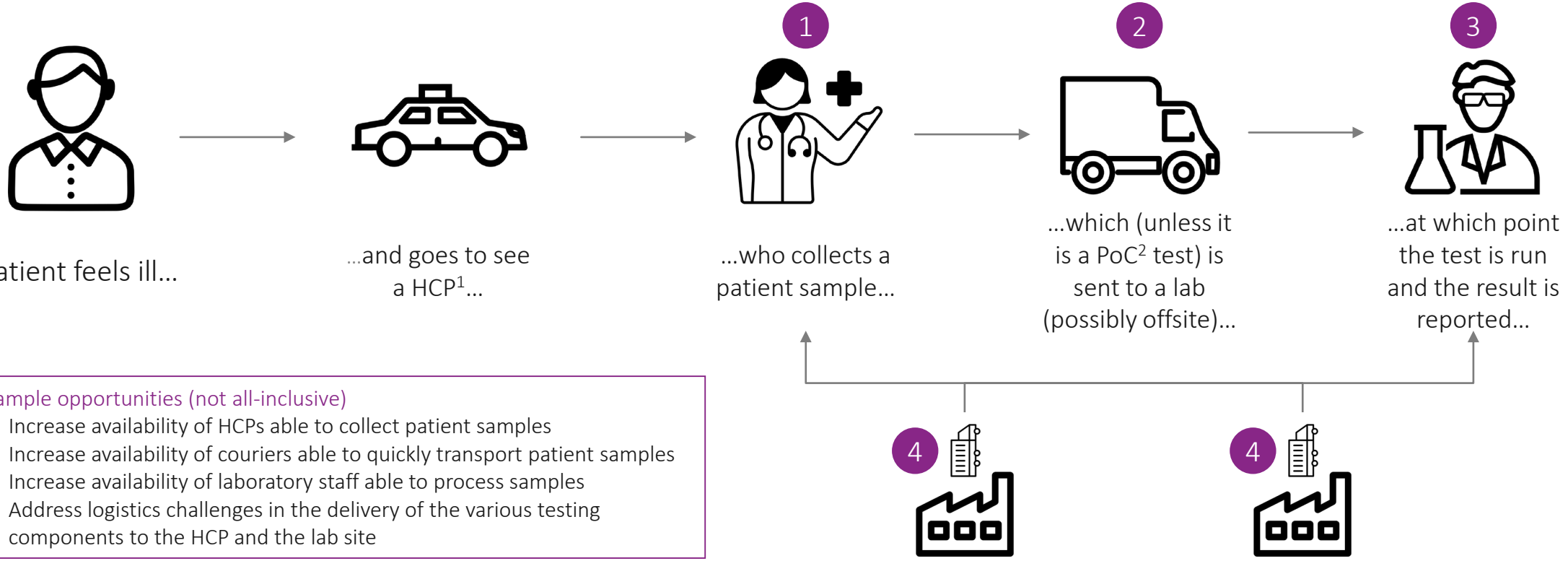
1. CRISPR stands for clustered regularly interspaced palindromic repeats – the relevant technology is more commonly used for gene-editing applications (e.g. engineering probiotic cultures, enhancing crop yield)
Source: FDA website, company websites and public announcements

Thank You

# The current testing workstream involves multiple steps and actors

Illustrative and simplified



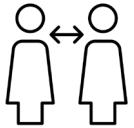

Example opportunities (not all-inclusive)

1. Increase availability of HCPs able to collect patient samples
2. Increase availability of couriers able to quickly transport patient samples
3. Increase availability of laboratory staff able to process samples
4. Address logistics challenges in the delivery of the various testing components to the HCP and the lab site

Note: Illustrative – not inclusive of all possible points of delay 1. Health care provider; 2. Point-of-care
As of May 7, 2020

# Testing is only one part of a comprehensive virus containment strategy, which includes:

Implementing COVID-19 testing

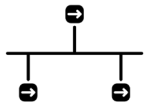


Enforcing social distancing

Leveraging contact tracing approaches

Enhancing physical protection (e.g. PPE, "closed" office structure, etc.)

Screening for relevant symptoms



Phased and considered approach to re-opening the economy

As of May 7, 2020

# Glossary

| Term | Definition/description |
|---|---|
| **Antigen** | Biological molecules that are specifically bound by antibodies |
| **EUA** | Emergency Use Authorization, mechanism for FDA to approve diagnostic and therapeutic products during an emergency; does not require clinical testing typical for approval |
| **Genome** | Genetic material of an organism |
| **Hospital lab** | Lab facilities on-site in hospitals, often scales with size of population served at hospital |
| **IgM / IgG** | Immunoglobulins or antibodies, IgM are more abundant and are the first line of defense, IgGs are responsible for long-term immunity to previously encountered viral and bacterial pathogens |
| **Immunoassay** | Test that utilizes antibodies to recognize specific antigens, including viruses; enables quick qualitative results |
| **IVD** | In-vitro diagnostic tests, clinical tests designed and manufactured by commercial supplier, can be distributed to any customer labs |
| **LDT** | Laboratory-developed tests, clinical tests that are designed, manufactured, and performed within a single lab |
| **MDx** | Molecular diagnostics, synonymous with molecular test |
| **Molecular test** | Tests that utilize biochemical techniques to detect genes and genetic products |
| **Near-patient testing** | Samples tested on instruments and in facilities near the bedside, shortening time for sample processing and test results |
| **PoC** | Point-of-care, patient samples are tested where medical care is delivered |
| **Primary / secondary immune response** | Bodily response to pathogen; primary response occurs upon first encounter, secondary response occurs upon subsequent encounters and involves immune system "memory" driven by IgG antibodies that can recognize a previous pathogen |
| **Reagents** | Individual chemicals and solutions needed to perform biochemical tests |
| **Reference lab** | Specialized, high-volume lab facilities that receive samples from other sources to test |
| **RNA** | Ribonucleic acid, basis of SARS-CoV-2 genome (vs. DNA for humans) |
| **RNA isolation kit** | Commercially available kits containing all reagents required to isolate viral nucleic acids for verification testing |
| **RT-PCR / PCR** | Reverse-transcription polymerase chain reaction, biochemical test used to detect specific genetic sequences; standard molecular diagnostic test |
| **Test kit** | Specific kit to test for SARS-CoV-2; originally only offered by CDC but has since been developed by private industry |
| **Viral load/titer** | Measure of virus quantity present in the body |