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

AdvaMedDx

Presentation and Discussion with
Republican Members of the
House Energy and Commerce Committee

June 19, 2020

Speakers

Agim Beshiri, MD, Senior Medical Director of Medical and Scientific Affairs, Abbott Diagnostics

Doug Bryant, President and CEO
Quidel Corporation

Richard Frank, MD, PhD, Chief Medical Officer
Siemens Healthineers

Alan Wright, MD, MPH, Chief Medical Officer
Roche Diagnostics

Danelle Miller, JD, VP, Global Regulatory Policy and Intelligence
Roche Diagnostics

Susan Van Meter, Executive Director
AdvaMedDx

Sarah Killeen, VP Government Affairs,
AdvaMed

Duane Wright, JD, VP Government Affairs,
AdvaMed

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.

IVD industry products range from patient sample collection devices, testing platforms used by laboratories small and large, to rapid point-of-care tests and platforms, and more

Patient sample

OR

Transfer sample

Transfer/direct sample

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

IVD platforms

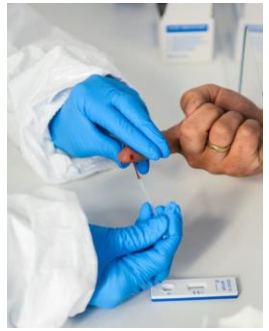
IVD point-of-care instruments

Results

Test results

Direct sample

Results



IVD instrument-less point-of-care →

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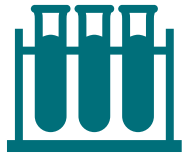
Utilization of the full testing ecosystem is necessary to address patient and public health needs



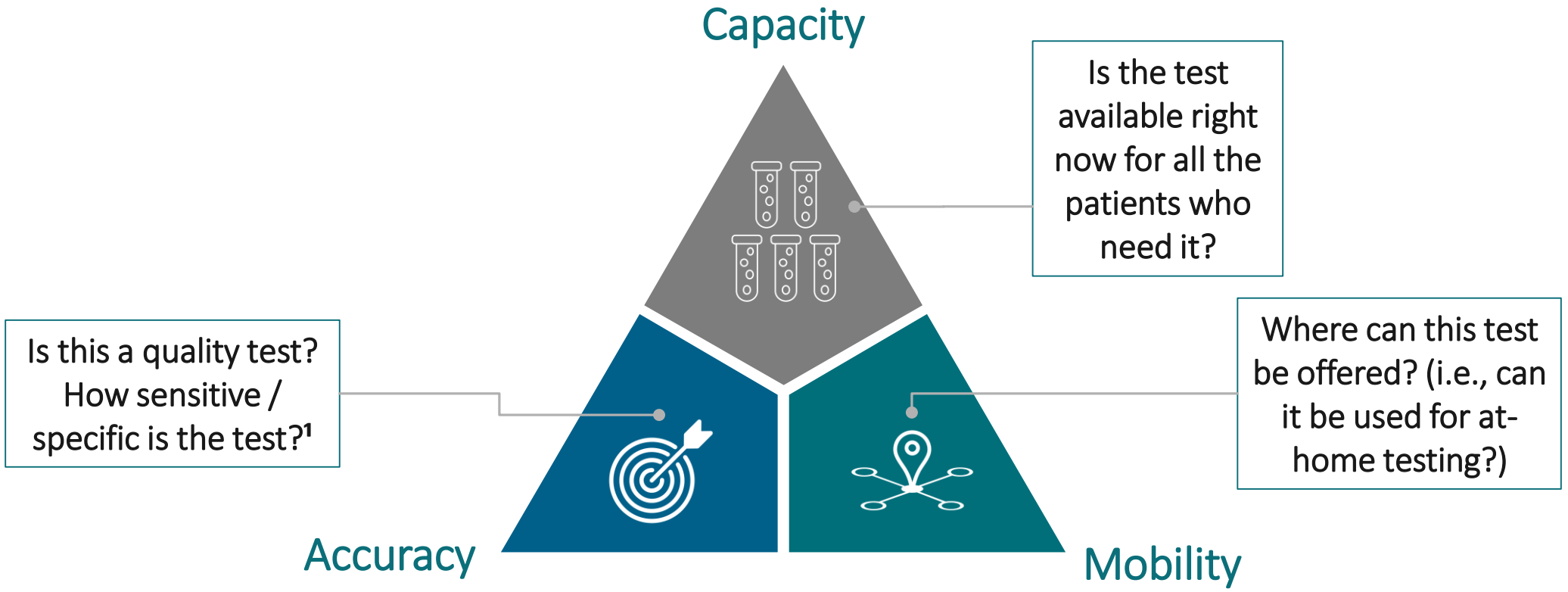
Leveraging all types of COVID-19 diagnostic testing (molecular, antigen, serology/antibody), in parallel and repeat testing …

… across lab-based and point-of-care modalities …

…as essential tools to support patient and public health, whenever and wherever patients present for care, or individuals seek to secure clarity on their COVID-19 status.

We thank the Committee for your leadership in legislating coverage for testing, bolstering of laboratory capacity and strong support for health care providers

Utilization all modalities of molecular, antigen and serology/antibody testing 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

There are 6 overarching and complimentary 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 for both symptomatic and asymptomatic individuals

Employer-contracted workforce testing

Enable voluntary testing programs 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

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

Population monitoring for previous exposure

Monitor populations to identify individuals who have had previous exposure(s), which can limit unnecessary quarantine of essential workers, or facilitate return to work/lifting "stay at home" orders'

Use cases for serology (antibody) testing

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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) - 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
How many lab platforms are there?	• Tests run on moderate and high-throughput platforms in **hospital and reference laboratories**: up to thousands of tests can be run and 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. • **There are ~ 1,000 high throughput molecular platforms in the U.S.**

Over the past several weeks, observed molecular diagnostic capacity for COVID-19 has more than tripled

- Since March 12, **sixty-three Emergency Use Authorizations** (EUA) has been secured by **diagnostics manufacturers** from the FDA for molecular tests

- **Diagnostics manufacturers collectively shipped to laboratories ~30M molecular tests during the month of April, ~39M in May and are on track again to ship ~39M tests in June**

- 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 June 1, 2020

COVID-19 diagnostic testing: Antigen testing

Antigen testing

What does this do?	• Confirms active infection
How does this work?	• Detects viral proteins shed in human samples - 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 • There are ~ 65,000 point-of-care analyzers in the U.S. that can run 40-50 tests per hour • The FDA has thus far authorized <u>one</u> commercial antigen test, a point-of-care test
How many point-of-care and lab platforms are there?	• **Laboratory tests**: Tests run on moderate and high-throughput platforms in **hospital, public health 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 • There are ~ 10,000 high throughput immunoassay platforms that can run antigen tests in the U.S. • FDA has <u>not</u> yet authorized a commercial, laboratory-based antigen test

COVID-19 diagnostic testing: Antigen testing

- At present, there is one commercial antigen test on the market. This point-of-care test was authorized by the FDA in early May.
- We anticipate additional point-of-care and laboratory based commercial, antigen testing to come onto the market in the weeks and months ahead

- Companies are developing tests – discovering the right antibody necessary for development; validating tests with curated, positive samples; bringing tests through the FDA for EUA.

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
- Antibodies are detectable in the blood long after the virus is no longer detectable
- Antibodies are detectable in people even if their infection did not cause symptoms
- Used in surveillance, case management, find donors of convalescent plasma, resolve uncertain diagnosis
- Use cases expand, eg to avoid quarantine of 1st responders, when antibodies proven to confer immunity

How does this work?

- **Detects human antibodies** to a 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, with results in as little 15 minutes, running up to 50 tests per hour
- There are 50,000+ immunoassay, point-of-care analyzers in the U.S.

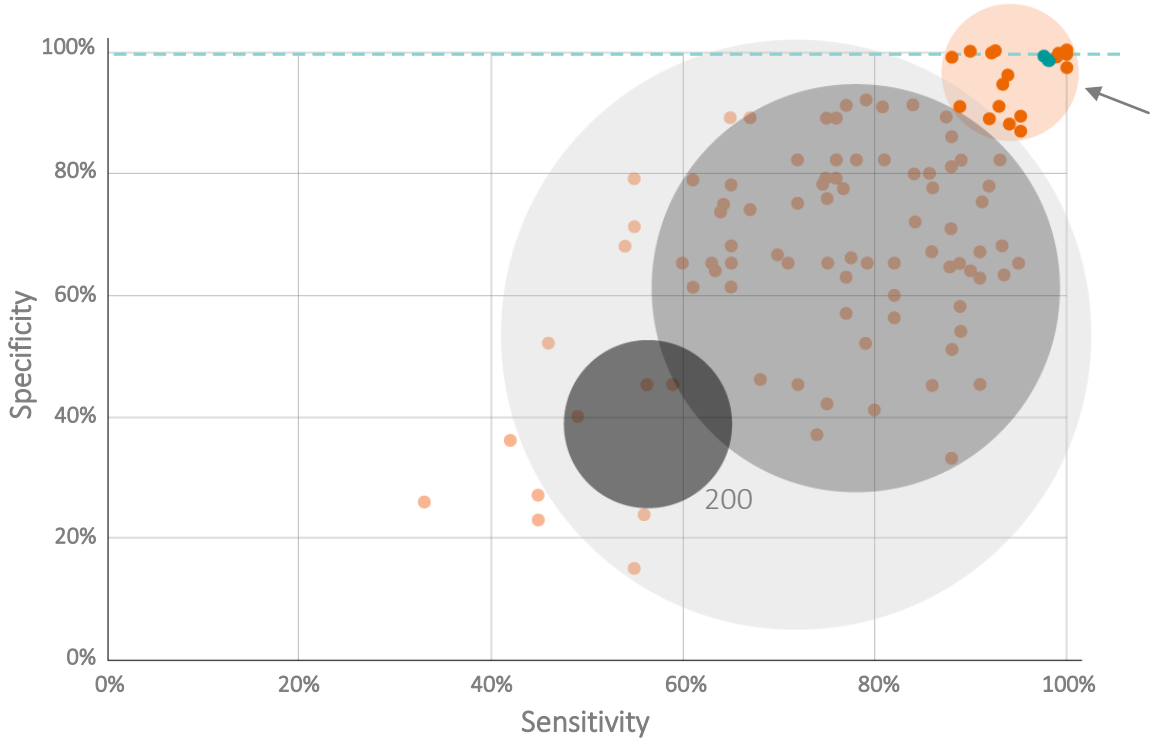
How many point-of-care and lab platforms are there?

- High throughput platforms in hospital and reference laboratories can run **hundreds of tests, with result in as quickly as 10 – 60 minutes**; equipment operates automatically around the clock. 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.

Quality and accuracy first

With lives at stake, test accuracy is paramount to minimize risks for communities and employees
There are numerous tests that claim to detect antibodies to the SARS-CoV-2 virus; **only a few are highly accurate.**

A good antibody test is one that in clinical studies used in the FDA authorization process demonstrate specificity of 99.5% or above, which has good performance even in populations with low disease prevalence[1].



20 Antibody tests with FDA EUA,
12 have >99.5% specificity[2]

Data as of June 15, 2020

200 = Total number of antibody tests in the market

38 = Number of tests withdrawn from the market

142 = Tests without FDA EUA

Data as of June 15, 2020

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1. According to CDC
2. https://www.fda.gov/medical-devices/emergency-situations-medical-devices/eua-authorized-serology-test-performance

Diagnostics manufacturers are providing quality serology testing at tremendous scale

- **AdvaMedDx members that have received FDA EUAs are:**
  - Abbott,
  - Bio-Rad,
  - Ortho Clinical Diagnostics,
  - Roche Diagnostics, and
  - Siemens Healthineers

- Demonstrating that **quality testing** is not only possible – but **should be expected** as test results to guide critical decisions about patient care and public health
- FDA modified its guidance on serology / antibody testing on May 4 to require all commercial manufacturers secure an EUA to be on the market

- AdvaMedDx estimates the IVD industry is on track to ship 30M tests in May and **94M in June** for laboratory based testing; laboratory capacity is huge; millions of tests can be completed daily

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Use cases for molecular and antigen testing

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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.

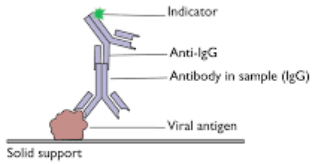
Used to collect and transport patient samples

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.)

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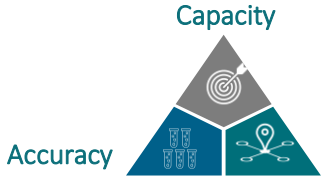
1. Transport media not needed for point-of-care tests; 2. Health care provider; Note: The above represents the typical components required for each test type. Pictures are illustrative. Additionally, they may not be of products specifically intended for COVID-19 diagnostic use.
As of May 7, 2020

Until we have an effective treatment or a vaccine, to utilize the full testing ecosystem . . . .

Leveraging all types of COVID-19 diagnostic testing (molecular, antigen, serology/antibody), in parallel and repeat testing . . .



. . . across lab-based and point-of-care modalities . . .

...as essential tools to support patient and public health, whenever and wherever patients present for care, or individuals seek to secure clarity on their COVID-19 status.

. . . .broad coverage and reimbursement and flexibility in where sample collection and/or testing can occur are key to communities reopening as safely as possible:

- Broad coverage and reimbursement policy that accounts for parallel and repeat testing: Patients may seek care / clarity on their COVID-19 status prior to symptom onset, with symptoms, post-symptomatic, or never having experienced symptoms but with a suspicion of exposure
  - Clinicians need the full toolkit of all COVID-19 diagnostic tests – molecular, antigen and serology/antibody – to best guide patient care and support population health
- Flexibility to allow for expansion of where sample collection for laboratory based testing and/or point of care testing can take place, i.e., non-traditional sites, including voluntary testing programs in schools, houses of worship, places of employment, home-based self-collection and/or self-testing
  - Maximizing access to testing ensures we are using the best tools we have to support patient and populations health and we strive to achieve a new normal until a meaning therapeutic or a vaccine is widely available

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 June 15th, 82 commercial COVID-19 tests have received Emergency Use Authorizations from the FDA, including:

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

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

Early May: First-ever FDA-authorized CRISPR-based[1] diagnostic, for use in COVID-19

Mid June: First COVID-19 New Generation Sequencing (NGS) test authorized

On the horizon: T-cell based testing

…and industry will continue to innovate to support patient care and public health throughout this emergency and beyond

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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

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