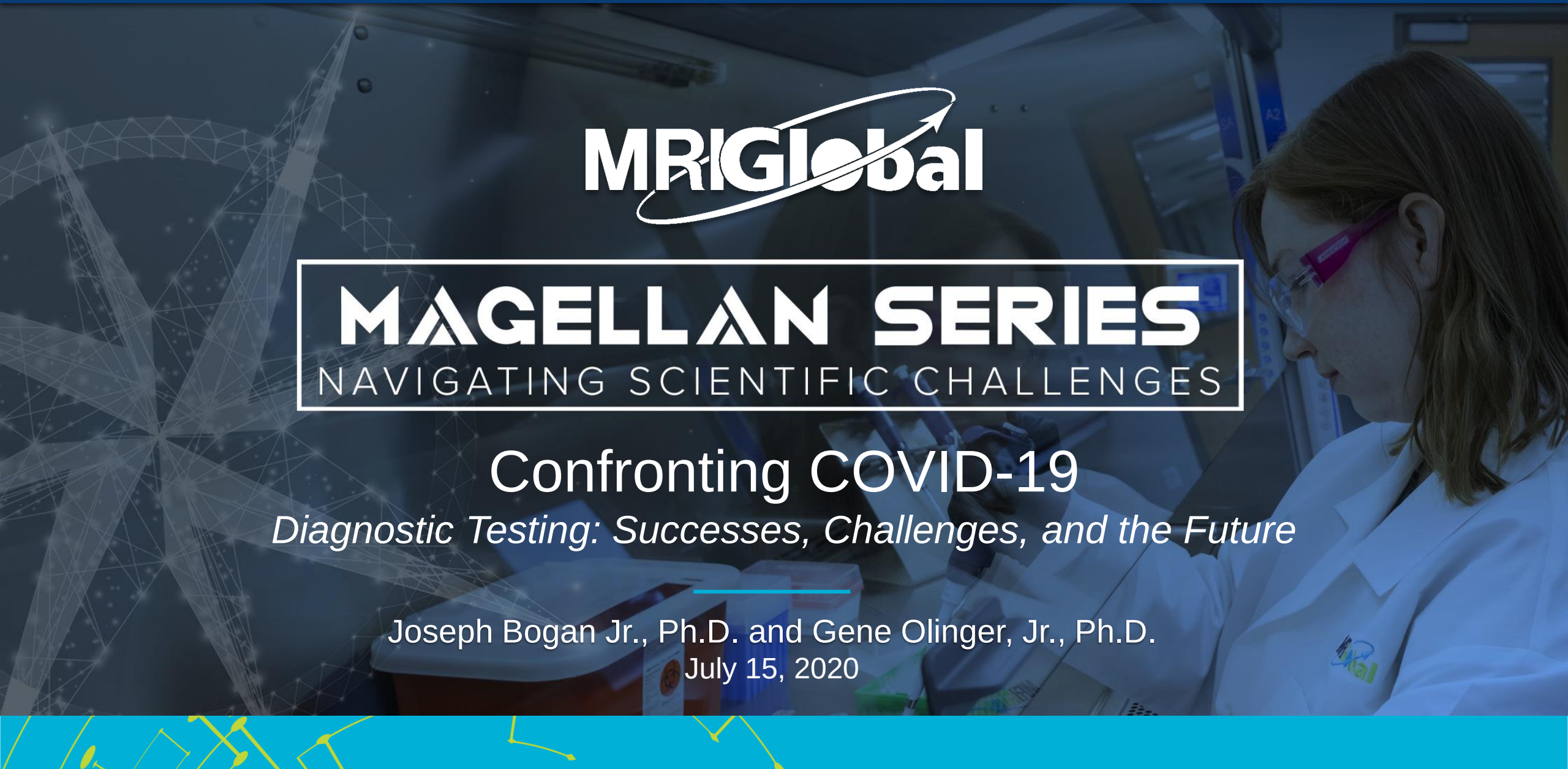


MRIGlobal

MAGELLAN SERIES

NAVIGATING SCIENTIFIC CHALLENGES

Confronting COVID-19

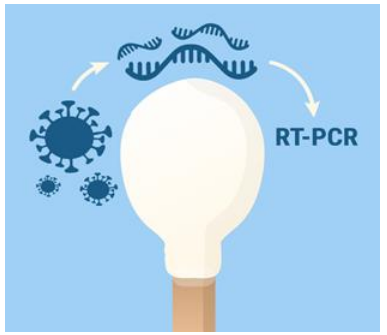
Diagnostic Testing: Successes, Challenges, and the Future

Joseph Bogan Jr., Ph.D. and Gene Olinger, Jr., Ph.D.

July 15, 2020

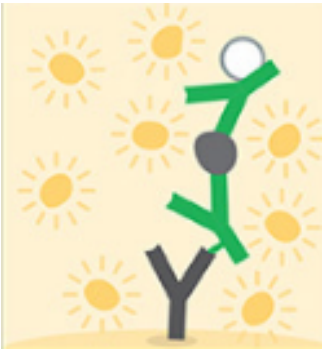
COVID-19 Diagnostics

Three Primary Types of COVID-19 Tests



Molecular Tests

- Directly detect the COVID-19 causing virus SARS-Cov-2
- Detection is through the presence/absence of SARS-CoV-2 RNA
- Viral RNA is detected through RNA amplification (primarily RT-PCR)

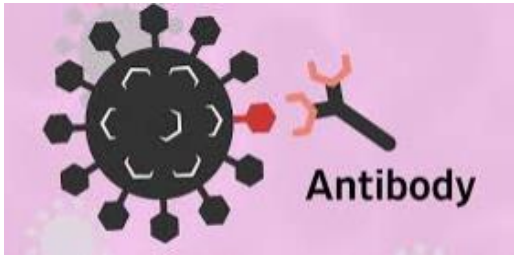


Serology/Antibody Tests

- Detect viral exposure and immunity
- Detection is through presence/absence of human IgM, IgA (exposure) and IgG (immunity)
- Human antibodies are detected with Rapid Diagnostic Tests (RDTs) or ELISAs

Antigen Tests

- Directly detect the COVID-19 causing virus SARS-Cov-2
- Detection is through the presence/absence of SARS-CoV-2 nucleocapsid protein
- Viral protein is detected with lateral flow immunofluorescent assays



COVID-19 Diagnostics

Types of COVID-19 Tests, Potential Uses and Benefits

Type of Test	Measure	Value	Beneficiary
Nucleic acid amplification test for viral RNA *(nasopharyngeal swab, oropharyngeal swab, sputum, bronchoalveolar lavage fluid, others)*	Current infection with SARS-CoV-2	• Inform individual of infection status so they can anticipate course of illness and take action to prevent transmission • Inform patient management and actions needed to prevent transmission • Inform actions needed to prevent transmission	• Individual • Healthcare or long-term care facility • Public health
Antibody detection	Past exposure to SARS-CoV-2	• Detect susceptible individuals (antibody negative) and those previously infected • Identify individuals with neutralizing antibodies • Facilitate contact tracing and surveillance	• Identify those potentially immune to SARS-CoV-2 (if tests can detect protective immunity, individuals could be returned to work) • Healthcare facilities: Experimental therapy • Public health

COVID-19 Diagnostics

Challenges

Identification of the most appropriate sample type

- What is the best sample type for the respective disease;
- Whole blood, serum, urine, stool, saliva, swabs, etc.

Determining the most appropriate time to collect samples

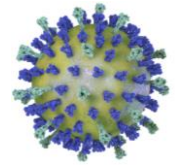
- What is the earliest time post-exposure that the biomarker is expressed and detectable?
- When is the earliest time post-exposure that the agent is present at detectable levels

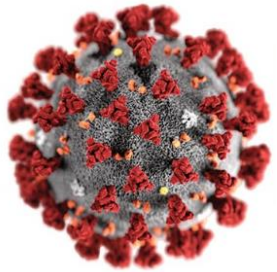
Are the biomarkers or agent targets specific to a single disease agent?

How many biomarkers or agent targets are required to make a definitive diagnosis?

Does the biomarker or agent targets only persists while the condition persists.

COVID-19 Diagnostics





Diagnostic Approaches

Pre-Symptomatic Diagnostics

Diagnostic Target:
Host Biomarkers (Antibodies, RNA, cytokines, etc.)
Agent Antigen (Protein, DNA, RNA)

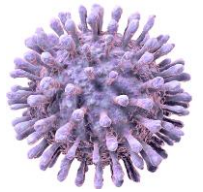
Provide promise for early detection of exposure, before signs and symptoms of disease

Employed for surveillance of at-risk/high risk populations

Diseases that have asymptomatic incubation periods during which the disease is transmissible.

Diseases that result in increased mortality rate after onset of symptoms.

Post-Symptomatic Diagnostics



Diagnostic Target:
Host Biomarkers (Antibodies, RNA, cytokines, etc.)
Agent Antigen (Protein, DNA, RNA)

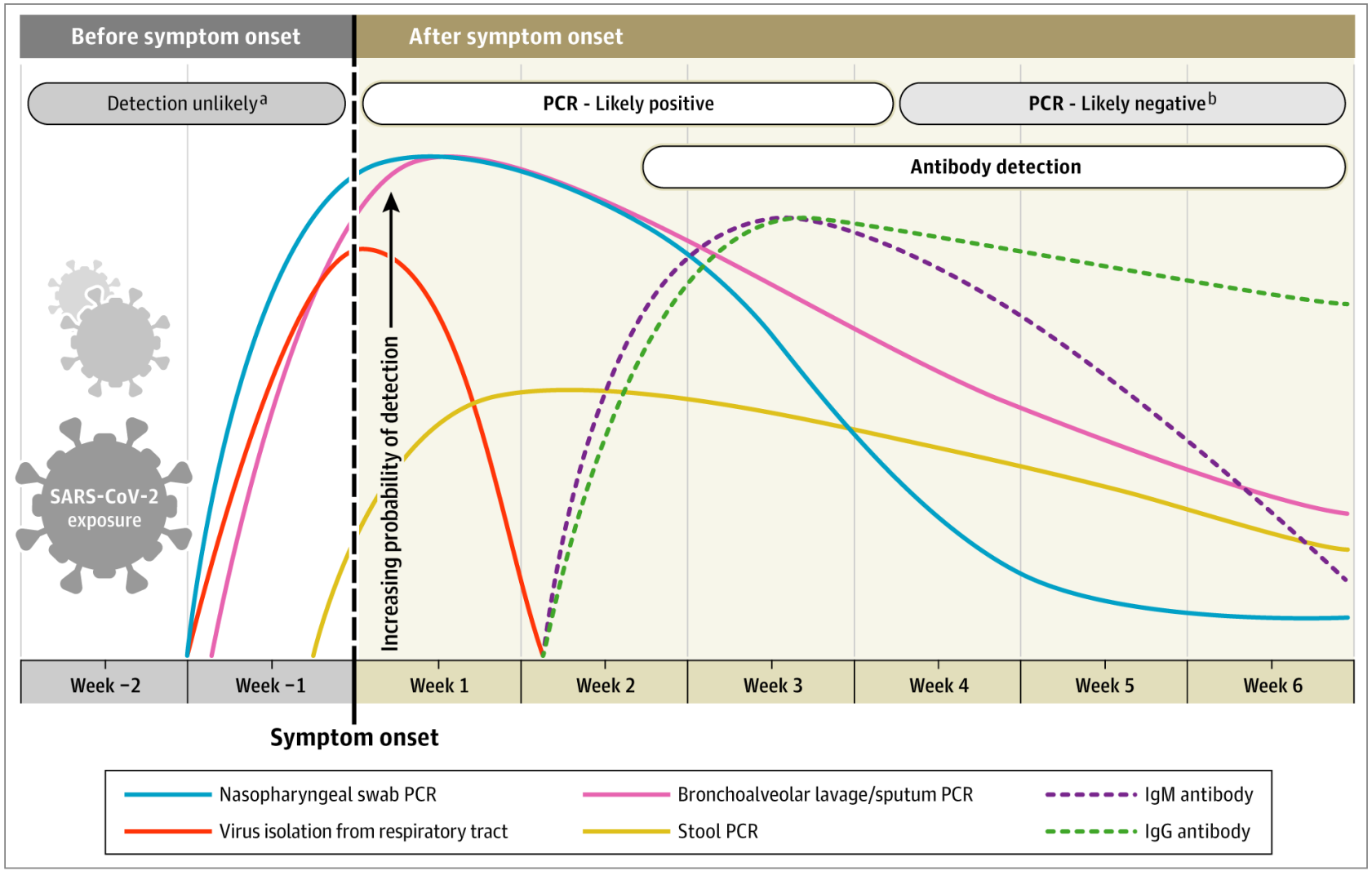
Provide promise for early detection of disease, after signs and symptoms of disease.

Employed for screening of symptomatic populations.

Differential diagnosis of diseases with “flu-like” symptoms that can be attributed to a number of infectious diseases.

Molecular based tests that target the infectious disease agent can be developed rapidly.

COVID-19 Diagnostic Stages



The Critical Role of Laboratory Medicine in COVID-19
(*Modified from: Lippi et al*, **PMID:** 32191623)

COVID-19 Diagnostics

Emergency Use Authorized Tests

In Vitro Diagnostics EUAs

On the basis of the February 4, 2020 HHS EUA determination, the Secretary of HHS then declared that circumstances exist justifying the authorization of the emergency use of in vitro diagnostics for detection and/or diagnosis of the novel coronavirus (2019-nCoV) subject to the terms of any authorization issued under section 564(a) of the Act.

On February 29, 2020, the FDA issued an immediately in effect guidance with policy specific to this public health emergency. This guidance was updated on March 16, 2020, May 4, 2020, and May 11, 2020.

Current EUA Approved COVID-19 Tests include:

- 108 Molecular Tests (104 are CLIA Highly or Moderately Complex Tests; 4 CLIA Waived Tests)
- 2 Antigen Test (Both are CLIA Waived Tests)
- 28 Serology Tests (All CLIA High or Moderately Complex Tests)

FDA U.S. FOOD & DRUG ADMINISTRATION

← Home / Medical Devices / Medical Device Safety / Emergency Situations (Medical Devices) / Emergency Use Authorizations

Test Kit Manufacturers and Commercial Laboratories Table:

Search: Show 100 entries

Date EUA Issued	Manufacturer	Diagnostic (Letter of Authorization)	Technology	Authorized Setting(s)[1]	Authorization Documents[2]	Other Documents/
05/22/2020	dba SpectronRx	Hymon SARS-CoV-2 Test Kit	Molecular	H	HCP, Patients, IFU	None
05/21/2020	BioCore Co., Ltd.	BioCore 2019-nCoV Real Time PCR Kit	Molecular	H	HCP, Patients, IFU	None
05/21/2020	SolGent Co., Ltd.	DiaPlexQ Novel Coronavirus (2019-nCoV) Detection Kit	Molecular	H	HCP, Patients, IFU	None
05/21/2020	Seasun Biomaterials, Inc.	AQ-TOP COVID-19 Rapid Detection Kit	Molecular	H	HCP, Patients, IFU	None

COVID-19 Diagnostics

Emergency Use Authorized Tests

High Complexity Molecular-based Laboratory Developed Tests:

On March 31, 2020, the FDA concluded on the totality of scientific evidence available that molecular-based laboratory developed test (LDTs) that are authorized for use by the singular developing laboratory are appropriate to protect the public health or safety (as described under the Scope of Authorization (Section II)) under section 564 of the Federal Food, Drug, and Cosmetic Act (Act) (21 U.S.C. § 360bbb-3). Under this EUA, authorized tests are authorized for use in the single laboratory that developed the authorized test and that is certified under Clinical Laboratory Amendments of 1988 (CLIA), 43 U.S.C. §263a to perform high complexity tests.

Current LDT Approved COVID-19 Tests include:

- 37 Molecular Tests/Laboratories (All High Complexity Tests performed in approved CLIA Labs)

FDA U.S. FOOD & DRUG ADMINISTRATION

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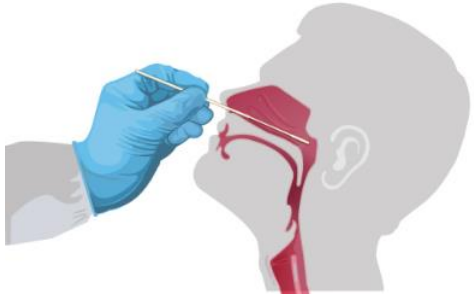
Date EUA Issued	Laboratory	Letter Granting Inclusion under EUA	EUA Summary	Other Documents
05/22/2020	Exact Sciences Laboratories	Exact Sciences SARS-CoV-2 (N gene detection) Test	EUA Summary	None
05/22/2020	Express Gene LLC (dba Molecular Diagnostics Laboratory)	Express Gene 2019-nCoV RT-PCR Diagnostic Panel	EUA Summary	None
05/22/2020	Avera Institute for Human Genetics	Avera Institute for Human Genetics SARS-CoV-2 Assay	EUA Summary	None
05/18/2020	Color Genomics, Inc.	Color SARS CoV-2 Diagnostic Assay	EUA Summary	None
05/13/2020	One Health Laboratories, LLC	SARS-CoV-2 Real-Time RT-PCR-Test	EUA Summary	None

COVID-19 Diagnostics

Diagnostic Test Components and Options



Specimen Collection

- Nasopharyngeal (NP) swab
- Oropharyngeal (OP) swab
- Nasal mid-turbinate swab
- Anterior nares swab
- Nasopharyngeal wash
- Nasal wash/aspirate
- Blood Draw (Serology)

Specimen Transport

Sterile transport tube containing 2-3 mL of either:

- Viral transport medium (VTM),
- Amies transport medium
- Sterile saline

Whole blood Serum, plasma (µl-ml)

Specimen Analysis

- RT-PCR (Viral RNA)
- Serology (Human IgA, IgM and IgG)
- Antigen (Viral Protein)

- *The objectives of the COVID-19 testing drive the selection of testing option(s)*
- *Selection of testing options ultimately involves a series of potential trade-offs*
- *Trade-offs decisions are based on available resources, population, funding, etc.*

Questions

Is a COVID-19 Diagnostic Test Required?

Does it matter which sample types or sample transport media is used?

Do all Molecular Tests perform equally well?

Which tests should be used; Molecular, Antigen, Serology?

What is the risk of a false positive or false negative result?

Do all Serology Tests perform equally well?

How frequently should testing be conducted?

What are the challenges and limitations of Molecular Tests?

What are the challenges and limitations of Antigen Tests?

What are the challenges and limitations of Serology Tests?

Resources

Coronavirus Disease 2019 (COVID-19) - Your Health

https://www.cdc.gov/coronavirus/2019-ncov/your-health/index.html

Coronavirus Disease 2019 (COVID-19) - Testing

https://www.cdc.gov/coronavirus/2019-ncov/testing/index.html

Information for Laboratories about Coronavirus (COVID-19):

https://www.cdc.gov/coronavirus/2019-nCoV/lab/index.html

Interim Guidelines for Collecting, Handling, and Testing Clinical Specimens for COVID-19:

https://www.cdc.gov/coronavirus/2019-ncov/lab/guidelines-clinical-specimens.html

The science you expect.
The people you know.

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