U.S. FOOD & DRUG ADMINISTRATION & Devices

FDA's Response to COVID-19: Diagnostics

Timothy Stenzel, M.D., Ph.D., Director

Toby Lowe, Associate Director for Regulatory Programs

Office of In Vitro Diagnostics and Radiological Health (OIR)

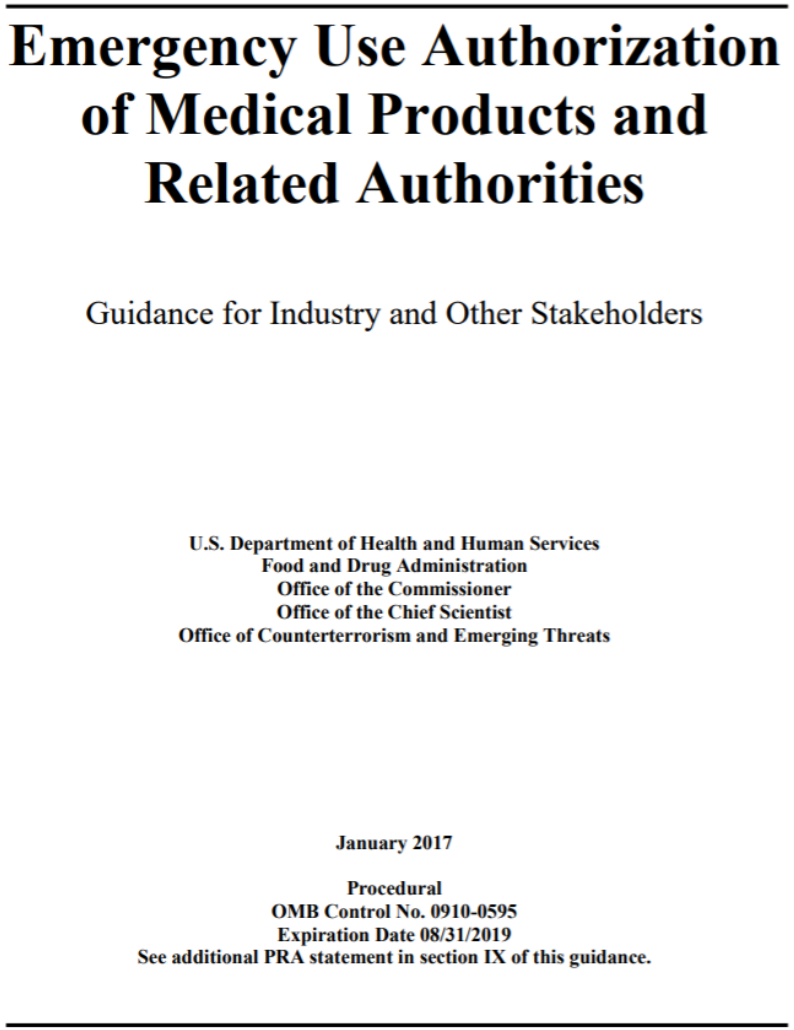
November 19, 2020

Emergency Use Authorization Authority

- Section 564 of the FD&C Act
  - The FDA Commissioner may allow unapproved medical products or unapproved uses of approved medical products to be used in an emergency to diagnose, treat, or prevent serious or life-threatening diseases or conditions caused by chemical, biological, radiological, and nuclear (CBRN) threat agents, including emerging infectious diseases, when there are no adequate, approved, and available alternatives.
- Requires a determination and declaration by the HHS Secretary that there exists a public health emergency or significant potential of a public health emergency
- Declaration under section 564 authorizes FDA to issue emergency use authorizations (EUAs)

FDA-Internal Use Only

General EUA Guidance Document



Emergency Use Authorization of Medical Products and Related Authorities

Guidance for Industry and Other Stakeholders

U.S. Department of Health and Human Services
Food and Drug Administration
Office of the Commissioner
Office of the Chief Scientist
Office of Counterterrorism and Emerging Threats

January 2017

Procedural
OMB Control No. 0910-0595
Expiration Date 08/31/2019
See additional PRA statement in section IX of this guidance.

Criteria for Issuance:

- Serious or life-threatening disease or condition caused by agent
- Product **"may be effective"** to diagnose, prevent or treat the condition (lower level of evidence than "effectiveness" standard)
- Known and potential benefits outweigh known and potential risks
- No adequate, approved, and available alternative; unavailable includes insufficient supplies of the approved alternative

Prior Public Health Emergencies (PHEs)

- 2013 - Avian Influenza A (H7N9)
- 2013 - Middle East Respiratory Syndrome Coronavirus (MERS-CoV)
- 2014 - Ebola Virus
- 2016 - Zika Virus

February 29 Testing Guidance

FDA NEWS RELEASE

Coronavirus (COVID-19) Update: FDA Issues New Policy to Help Expedite Availability of Diagnostics

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For Immediate Release:

February 29, 2020

Español

Today, as part of the U.S. Food and Drug Administration's ongoing and aggressive commitment to address the coronavirus outbreak, the agency issued a new policy for certain laboratories seeking to develop diagnostic tests for coronavirus in order to achieve more rapid testing capacity in the U.S.

www.fda.gov

Recommendations:

- Validating newly developed SARS-CoV-2 tests prior to clinical use
- Notifying FDA when clinical use of a validated test begins
- Confirming the first 5 positive and negative samples with an EUA authorized test
- Indicating in test reports that the test has been validated but independent review by FDA is not yet complete
- Submitting an EUA within 15 days of initiating testing
- Steps to take if any specimens fail confirmatory testing or if FDA is unable to authorize the EUA

March 16 Testing Guidance

FDA STATEMENT

Coronavirus (COVID-19) Update: FDA Provides More Regulatory Relief During Outbreak, Continues to Help Expedite Availability of Diagnostics

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For Immediate Release:

March 16, 2020

Statement From:

Commissioner of Food and Drugs - Food and Drug Administration
Stephen M. Hahn M.D.

Today, as part of our ongoing and aggressive commitment to address the coronavirus outbreak, the FDA updated a policy originally issued on Feb. 29 on diagnostic testing for coronavirus (COVID-19) in order to achieve more rapid testing capacity in the U.S. We believe the unprecedented policy set forth in today's updated guidance, which addresses laboratories and commercial manufacturers, will

www.fda.gov

Updated Recommendations:

- Expanded February 29, 2020 policy to commercial developers of diagnostic tests
- Introduced new policy allowing states to oversee tests developed by labs in their jurisdictions
- Introduced new policy for serology tests without an EUA where:
  - ❖ Validated &
  - ❖ notification to FDA &
  - ❖ certain limitations appear in labeling (ex. cannot use to diagnose or exclude active infection)

Serology Testing

Important Information on the Use of Serological (Antibody) Tests for COVID-19 - Letter to Health Care Providers

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The U.S. Food and Drug Administration (FDA) recommends that health care providers continue to use serological tests intended to detect antibodies to SARS-CoV-2 to help identify people who may have been exposed to the SARS-CoV-2 virus or have recovered from the COVID-19 infection. Health care providers should also be aware of the limitations of these tests and the risks to patients and the community if the test results are used as the sole basis to diagnose COVID-19.

The FDA is not aware of an antibody test that has been validated for diagnosis of SARS-CoV-2 infection. While the FDA remains open to receiving submissions for these tests for such uses, based on the underlying scientific principles of antibody tests, the FDA does not expect that an antibody test can be shown to definitively diagnose or exclude SARS-CoV-2 infection.

FDA STATEMENT

Coronavirus (COVID-19) Update: Serological Test Validation and Education Efforts

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For Immediate Release:

April 18, 2020

Statement From:

Commissioner of Food and Drugs - Food and Drug Administration
Stephen M. Hahn M.D.

Every step we have taken as part of our approach to COVID-19 testing has been a careful balancing of risks and benefits in order to meet the urgent public health needs as we combat this new pathogen. We have moved quickly and thoughtfully, and we are continuing to learn and adapt based on the real-world experience and data we're seeing. In the meantime, frontline health care workers who are making life-and-death decisions every day in their fight against this novel coronavirus need to have all the information possible to make educated decisions about which test to use to help identify individuals who have developed an

May 4 Testing Guidance

Insight into FDA's Revised Policy on Antibody Tests: Prioritizing Access and Accuracy

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By: Anand Shah, M.D., Deputy Commissioner for Medical and Scientific Affairs, and Jeff Shuren, M.D., Director, Center for Devices and Radiological Health

Updated Recommendations:

- Commercial developers of serology tests should submit an EUA to FDA within 10 business days of notification or publication of the guidance, whichever is later
- Policy maintained for serology tests developed by labs
- Policy maintained for diagnostic tests

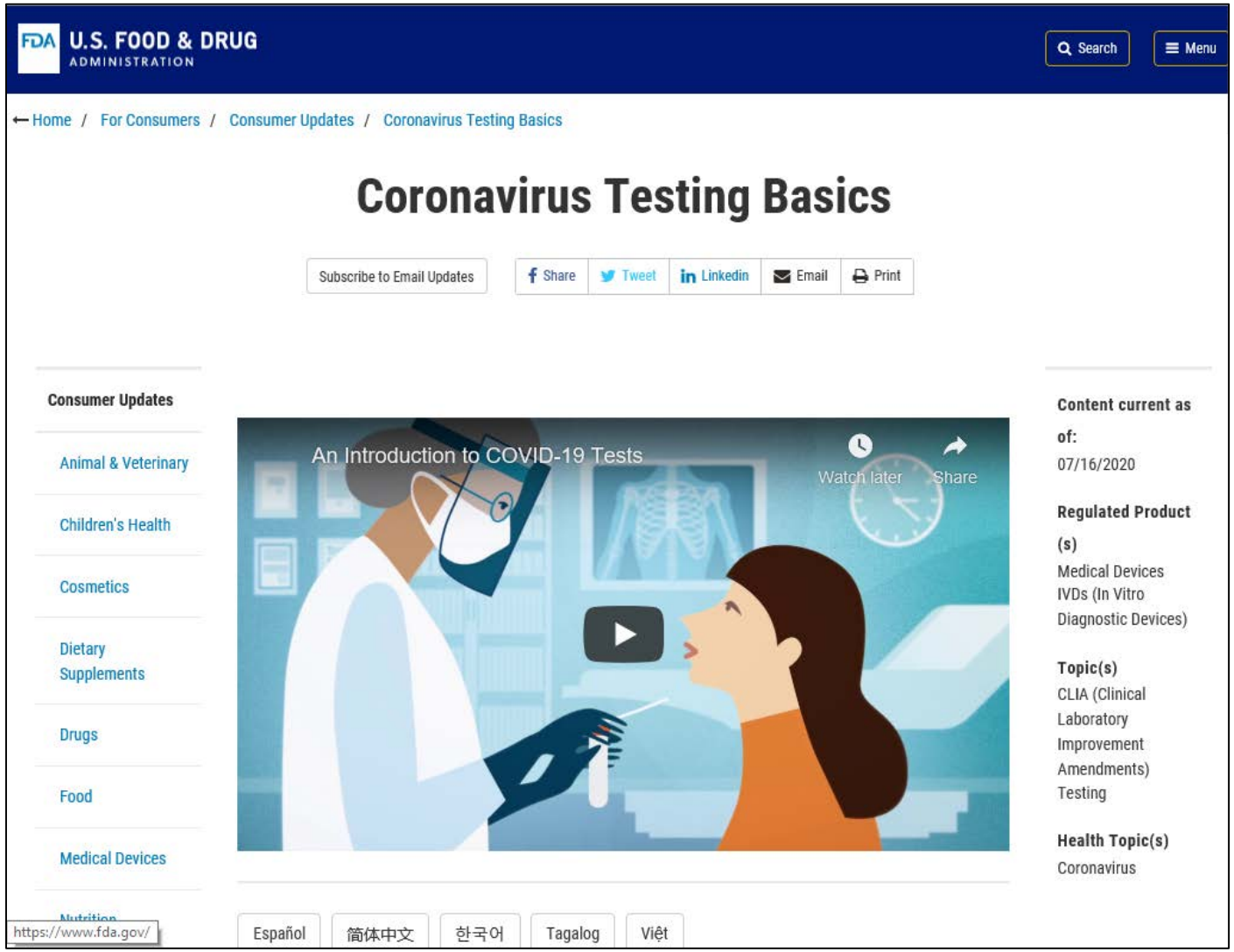
May 11 Testing Guidance

1. Molecular Diagnostic Template for Laboratories
2. Molecular Diagnostic Template for Commercial Manufacturers
3. Antigen Template for Manufacturers
4. Serology Template for Commercial Manufacturers
5. Serology Template for Laboratories
6. Home Specimen Collection Molecular Diagnostic Template
7. Template for Manufacturers of Molecular and Antigen Diagnostic COVID-19 Tests for Non-Laboratory Use

Updated Recommendations:

Announced availability, on FDA website, of template laboratories may use to facilitate preparation, submission & authorization of EUA for molecular diagnostic test

Outreach

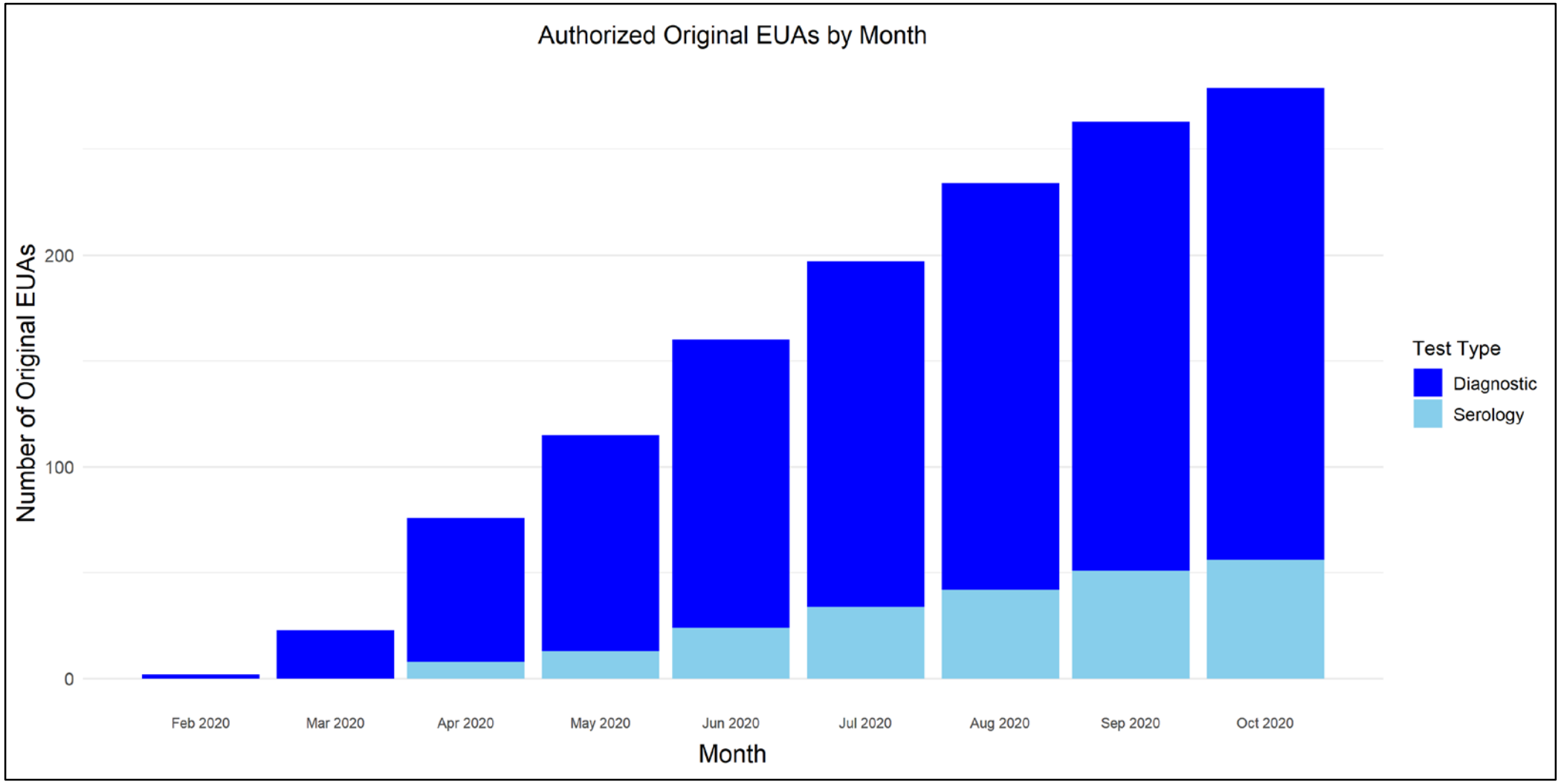


- 34 Virtual Town Halls (40,000+ participants)
- FAQs on Testing for SARS-CoV-2
- Safety Communications
- Resources for Patients, Healthcare Providers, and Developers
- COVID-19 Diagnostics Mailbox (170,000+ inquiries)

Growing US Testing Menu

- First molecular test authorized (CDC)
- First commercial molecular test authorized (Roche)
- First molecular point of care (POC) test authorized (Cepheid)
- First SARS-CoV-2 / flu panel authorized (QIAGEN)
- First serology test authorized (Cellex)
- First molecular home collection test authorized (LabCorp)
- First molecular saliva home collection test authorized (Rutgers University)
- First antigen POC test authorized (Quidel)
- First pooling test authorized (Quest)
- First asymptomatic screening test authorized (LabCorp)
- First POC serology test authorized (Assure)
- First at-home molecular diagnostic test authorized (Lucira)

EUA Authorizations

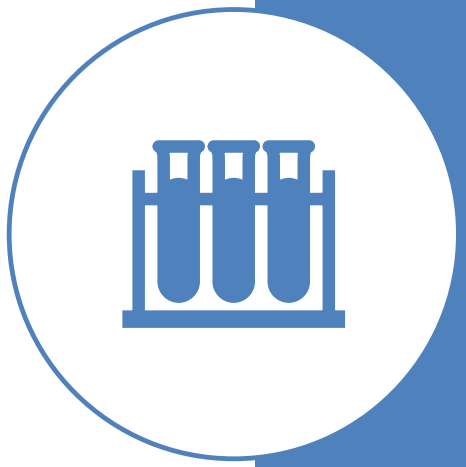


Approximately 600 Tests Allowed to Market Based on Guidances

Authorized tests under EUAs: 288

- Molecular Diagnostic Tests: 223
- Antibody Tests: 58
- Antigen Tests: 7

EUA Supplements: Over 200



**Data current as of 11/16/20*

Transparency: Relative Test Performance

Diagnostic Reference Panel Results

SARS-CoV-2 Reference Panel Co

fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/sars-cov-2-reference-panel-comparative-data

Table 2. Sensitivity* Mean Estimates of the EUA authorized SARS-CoV-2 molecular diagnostic tests using the FDA SARS CoV-2 Reference Panel

A - Swabs in Transport Media**

Swabs are collected and transported in media as per the Instructions for Use of each EUA. If several specimen types are authorized, nasopharyngeal (NP) swabs were recommended to use. The clinical matrix is spiked following the FDA-proposed dilution protocol and tested.

Search:

Product LoD (NDU/mL***)	Developer	Test
180000	Diatherix Eurofins Laboratory	SARS-CoV-2 PCR Test
180000	Luminex Corporation	ARIES SARS-CoV-2 Assay
180000	QIAGEN GmbH	QIAstat-Dx Respiratory SARS-CoV-2 Panel
18000	Acupath Laboratories, Inc	Acupath COVID-19 Real-Time (RT-PCR) Assay
18000	Avellino Lab USA, Inc.	AvellinoCoV2 test
18000	Infectious Diseases Diagnostics Laboratory (IDDL), Boston Children's Hospital	Childrens-Altona-SARS-CoV-2 Assay
18000	Centers for Disease Control and Prevention (CDC)	CDC 2019-nCoV Real-Time RT-PCR Diagnostic Panel (CDC)
18000	Color Genomics, Inc.****	Color Genomics SARS-CoV-2 RT-LAMP Diagnostic Assay
18000	Eli Lilly and Company	Lilly SARS-CoV-2 Assay
18000	Enzo Life Sciences, Inc.	AMPIPROBE SARS-CoV-2 Test System
18000	Gravity Diagnostics, LLC	Gravity Diagnostics COVID-19 Assay (370KB)

https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/sars-cov-2-reference-panel-comparative-data

NIH/NCI Serology Validation Results

open.fda.gov/apis/device/covid19serology/

U.S. FOOD & DRUG ADMINISTRATION

U.S. Department of Health and Human Services Food and Drug Administration

openFDA

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Independent Evaluations of COVID-19 Serological Tests

Serology tests detect the presence of antibodies in the blood when the body is responding to a specific infection, like COVID-19. In other words, the tests detect the body's immune response to the infection caused by the virus rather than detecting the virus itself. In the early days of an infection when the body's immune response is still building, antibodies may not be detected. This limits the test's effectiveness for diagnosing COVID-19, and this is one reason serology tests should not be used as the sole basis to diagnose COVID-19. Serology tests could play a role in the fight against COVID-19 by helping healthcare professionals identify individuals who may have developed an immune response to SARS-CoV-2. In addition, these test results can aid in determining who may donate a part of their blood called convalescent plasma, which may serve as a possible treatment for those who are seriously ill from COVID-19. However, to use serology tests properly, it is important to understand their performance characteristics and limitations. Moreover, studies are underway to address questions that will better inform the appropriate use of these tests, such as whether the presence of antibodies conveys a level of immunity that would prevent or reduce the severity of re-infection as well as the duration for which immunity lasts.

Key Facts

Source of the data:	Independent testing by US Government Laboratories
Changes to the source data:	openFDA may change some field names and converts the data into JSON, which is a widely used machine readable format.
Time period covered in this API:	2020 to present
Frequency of API updates:	Intermittently

Responsible use of the data

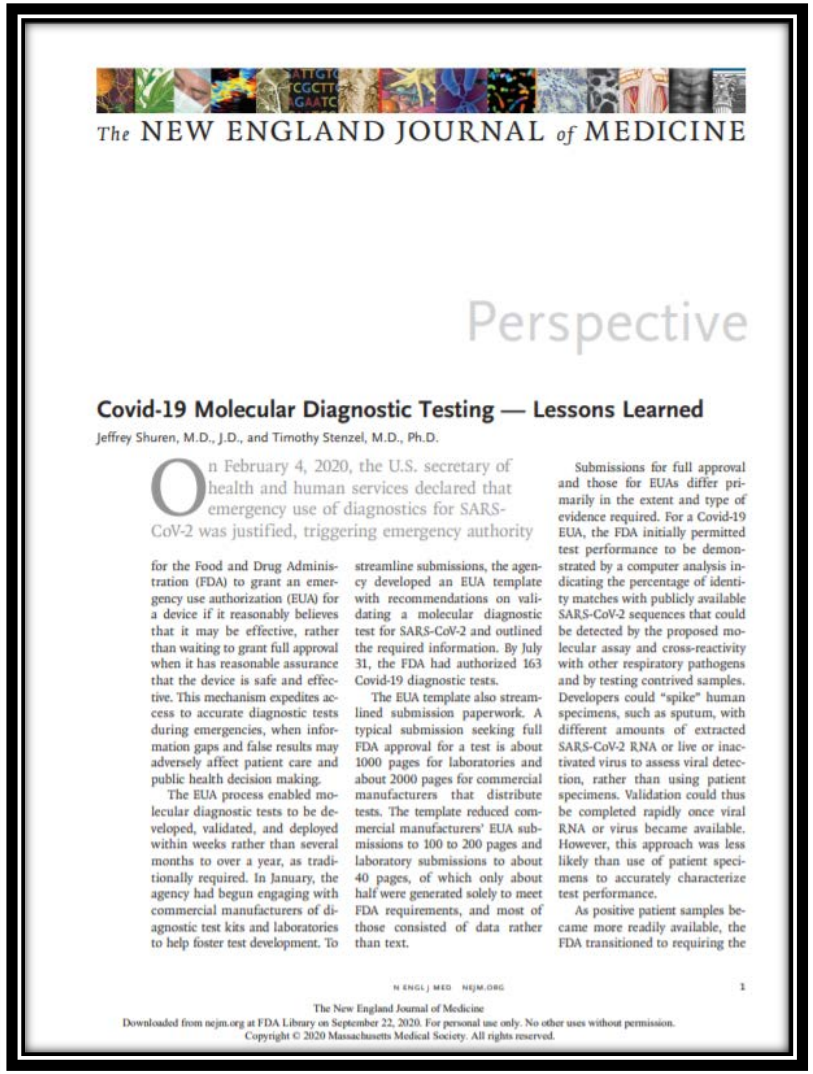
Do not rely on openFDA to make decisions regarding medical care. Always speak to your health provider about the risks and benefits of FDA-regulated products. We may limit or otherwise restrict your access to the API in line with our Terms of Service

https://open.fda.gov/apis/device/covid19serology/

Lessons Learned re Molecular Testing

1. U.S. government & international partners should establish plan for sharing clinical specimens as soon as public health threat emerges

2. Authorize a small number of well-designed, well-developed, and validated tests run on common high-throughput platforms, followed by a few point-of-care tests



The NEW ENGLAND JOURNAL of MEDICINE

Perspective

Covid-19 Molecular Diagnostic Testing — Lessons Learned

Jeffrey Shuren, M.D., J.D., and Timothy Stenzel, M.D., Ph.D.

On February 4, 2020, the U.S. secretary of health and human services declared that emergency use of diagnostics for SARS-CoV-2 was justified, triggering emergency authority for the Food and Drug Administration (FDA) to grant an emergency use authorization (EUA) for a device if it reasonably believes that it may be effective, rather than waiting to grant full approval when it has reasonable assurance that the device is safe and effective. This mechanism expedites access to accurate diagnostic tests during emergencies, when information gaps and false results may adversely affect patient care and public health decision making.

The EUA process enabled molecular diagnostic tests to be developed, validated, and deployed within weeks rather than several months to over a year, as traditionally required. In January, the agency had begun engaging with commercial manufacturers of diagnostic test kits and laboratories to help foster test development. To streamline submissions, the agency developed an EUA template with recommendations on validating a molecular diagnostic test for SARS-CoV-2 and outlined the required information. By July 31, the FDA had authorized 163 Covid-19 diagnostic tests.

The EUA template also streamlined submission paperwork. A typical submission seeking full FDA approval for a test is about 1000 pages for laboratories and about 2000 pages for commercial manufacturers that distribute tests. The template reduced commercial manufacturers' EUA submissions to 100 to 200 pages and laboratory submissions to about 40 pages, of which only about half were generated solely to meet FDA requirements, and most of those consisted of data rather than text.

Submissions for full approval and those for EUAs differ primarily in the extent and type of evidence required. For a Covid-19 EUA, the FDA initially permitted test performance to be demonstrated by a computer analysis indicating the percentage of identity matches with publicly available SARS-CoV-2 sequences that could be detected by the proposed molecular assay and cross-reactivity with other respiratory pathogens and by testing contrived samples. Developers could "spike" human specimens, such as sputum, with different amounts of extracted SARS-CoV-2 RNA or live or inactivated virus to assess viral detection, rather than using patient specimens. Validation could thus be completed rapidly once viral RNA or virus became available. However, this approach was less likely than use of patient specimens to accurately characterize test performance.

As positive patient samples became more readily available, the FDA transitioned to requiring the

The New England Journal of Medicine
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3. Need a common legislative framework to ensure all clinical tests accurate & reliable

4. Clinical community should understand test performance & how to use that information in patient care.

* "COVID-19 Molecular Diagnostic Testing – Lessons Learned," New England Journal of Medicine (NEJM), Dr. Jeffrey Shuren & Dr. Timothy Stenzel, September 9, 2020

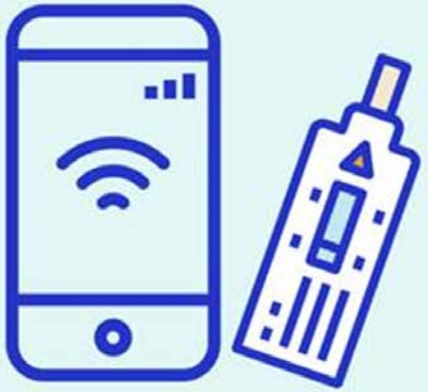
Established COVID-19 Response In Vitro Diagnostics Shortages Team

- Focus on IVD shortages from specimen collection through test reagents and equipment.
- Developing a tool to help laboratories and commercial manufacturers resolve shortage issues (e.g. swabs, transport media and extraction reagents)
- Helping coordinate military airlifts of millions of swabs
- Establishing/maintaining multiple communications channels with other government agencies (DoD, DOE, HHS, BARDA), manufacturers, distributors and laboratories

COVID-19 AT-ANYWHERE DIAGNOSTICS

Design-a-thon

Developing digital solutions for data capture, harmonization, and reporting from diagnostic tests



#COVIDdesignathon

The Design-a-thon is a public-facing, open-innovation technology sprint with industry that aims to develop device-integrated software for automatic data capture and wireless transmission directly from in vitro diagnostic devices (IVDs).

GOAL 1: The Design-a-thon brings together **public and private sector innovators** to develop software/digital health tools that **integrate with IVDs.**

GOAL 2: Build an **HHS interface** that will exemplify the **design principles** and provide device/systems-agnostic "docking" between HHS Protect and various reporting systems, called **"Wireless Automated Transmission for Electronic Reporting Systems" (WATERS).**

- Future State: By setting the design principles, the Design-a-thon will establish and align diagnostics data reporting **standards** for **every single core data element defined under CARES**, which have been defined by HHS (including **technological specifications**) for lab-based and non-lab-based tests.

Happening NOW through Nov. 30

Participate in the Design-a-thon at: Waters.Crowdicity.com

We're Constantly Working on COVID Testing Options

Nearly 300 Tests Authorized

FDA Performance Recommendations

Home Use: 80% Sensitivity (physician ordered)
90% Sensitivity (purchased OTC)

Diagnostic Prescription POC Tests: 80% Sensitivity

https://thehill.com/opinion/healthcare/515628-fda-were-constantly-working-on-covid-testing-options

Thank You