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IN THIS ISSUE

Point of Care: Are Rapid Immunodiagnostic Tests for COVID-19 Ready for Prime Time?

The success of treatment, quarantine and, ultimately, return to normalcy, all hinge on the development and dissemination of tests capable of not just accurate but rapid detection of COVID-19 coronavirus. Among the most promising solutions are point-of-care (POC) molecular-based immunodiagnostic tests that detect SARS-CoV-2 antibodies. On March 21, the Cepheid Xpert Xpress SARS-CoV-2 test became the first POC COVID-19 detection assay to receive Emergency Use Authorization (EUA) from the US Food and Drug Administration. More POC test approvals followed in rapid order, including assays from Abbott, Mesa Biotech and the combination of Becton Dickinson and BioGX. And dozens more are in the pipeline and likely to gain EUA in the coming months, if not weeks.

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Emerging Tests: Serology Testing Critical to COVID-19 Survival & Post-Crisis Transition

There are two kinds of people who have SARS-CoV-2 antibodies in their systems: Those who are currently infected with COVID-19 (both symptomatic and asymptomatic), and those who were infected but have recovered. Being able to identify and distinguish between these two groups will go a long way in determining how and how soon people can emerge from self-isolation and the world can go back to normal. That is why so many are investing so much hope and energy in serology testing. Here is an overview of the FDA's strategy to promote serology testing for COVID-19.

Importance of Serology COVID-19 Testing

Antibodies remain in the body long after the infection they were created to fight disappears. The principle method being used to diagnose COVID-19, reverse transcriptase polymerase chain reaction (RT-PCR) testing, detects viral material that is present during a

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Hip-hip-hooray! 'Right?

Well, maybe not so much, at least to some critics.

The cloud to the silver lining is that POC COVID-19 antibody testing is unproven. So, even as the FDA admits them into the US market, the World Health Organization (WHO) says they shouldn't be used for clinical decision making.

The Diagnostic Challenge

Most of the current COVID-19 tests, including the US Centers for Disease Control and Prevention (CDC) that received the initial EUA from the FDA, are based on reverse transcriptase polymerase chain reaction (RT-PCR) detecting genetic material from the SARS-CoV-2 virus from respiratory samples taken with a throat or nasal swab. The way it works: SARS-CoV-2 is an RNA virus, which must be converted to DNA at the laboratory using the RT enzyme. Laboratories then add specific sequences of DNA (primers) capable of recognizing complementary virus sequences, so that another enzyme—typically a modified form of Taq polymerase—can make a copy of a short length of viral DNA. The process is repeated over 20 to 30 cycles to expand the amount of DNA that can be detected.

The good news about RT-PCR detection is its accuracy, with both sensitivity and specificity rates of 90 percent and above. The bad news about the method is that it takes a long time and usually must be carried out at a testing laboratory away from the site of care. The hours and days patients must await their test results is not only agonizing but ill-suited to the logistics and dynamics of social distancing which calls for rapid identification of those who are healthy and those who need to be in isolation.

POC Immunodiagnostic Tests

The POC immunodiagnostic tests utilize the same basic methodology as the laboratory assays. But several of the steps are automated and performed at an accelerated pace on small, portable platforms that can be used right at the doctor's office, hospital or other care setting—and even a patient's home—without being transported to an off-site laboratory. As a result, test results can be generated in under an hour as the patient waits.

But there is also a fly in the ointment, namely, test accuracy. The other key difference between RT-PCR and rapid immunodiagnostic testing is that the latter detects COVID-19 indirectly. Rather than detecting viral genetic material, rapid tests target the patient's immune response by detecting antibodies against the virus or virus antigens. The problem is that antibodies develop several weeks after an infection. This lag between time of testing and time of antibody development can result in false negatives, especially for asymptomatic cases or patients in the earliest

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stage of the disease. And because antibodies can remain in the body years after the infection goes away, people who do not have the virus may still test positive.

The WHO Response

This tradeoff between POC immunodiagnostic testing speed and lack of accuracy is forcing policy makers and public health officials around the world to make some difficult decisions. As noted above, the US seems to be all in on rapid tests, at least for as long as the COVID-19 pandemic lasts. But the WHO is not so sure.

On April 8, the organization issued a scientific briefing saying that POC immunodiagnostic SARS-CoV-2 tests should not be used for clinical decision-making "until evidence supporting use for specific indications is available." Before such tests can be recommended, "they must be validated in the appropriate populations and settings," according to the WHO. "Inadequate tests may miss patients with active infection or falsely categorize patients as having the disease when they do not, further hampering disease control efforts."

Molecular RT-PCR testing "of respiratory tract samples is the recommended method for the identification and laboratory confirmation of COVID-19 cases," according to the WHO. But the organization did endorse use of POC immunodiagnostic tests for epidemiological research. "Tests to detect antibody responses to COVID-19 in the population will be critical to support the development of vaccines, and to add to our understanding of the extent of infection among people who are not identified through active case finding and surveillance efforts, the attack rate in the population, and the infection fatality rate," according to the WHO.

Antigen Detection Tests for Triage

However, the WHO does see a limited treatment role for another kind of POC testing, i.e., rapid diagnostic tests (RDTs) that detect the presence of viral proteins, or antigens, expressed in a sample from the respiratory tract by the SARS-CoV-2 virus. "If any of the antigen detection tests that are under development or commercialized demonstrate adequate performance, they could potentially be used as triage tests to rapidly identify patients who are very likely to have COVID-19, reducing or eliminating the need for expensive molecular confirmatory testing," the WHO said.

The caveat: Based on experience from their use for other respiratory diseases such as influenza, how well antigen-based RDTs work may vary from 34 percent to 80 percent, based on factors such as:

- The time from onset of illness;
- The concentration of virus in the specimen;

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- The quality of the specimen collected;
- How the specimen is processed; and
- The precise formulation of the reagents in the test kit.

"Based on this information, half or more of COVID-19 infected patients might be missed by such tests, depending on the group of patients tested," the WHO added. "These assumptions urgently require further study to understand whether they are accurate."

In addition, the WHO warned of false positives that may result if the antibodies on the test strip also recognize antigens of viruses other than COVID-19, such as from human coronaviruses that cause the common cold.

Takeaway

At a time where diagnostic speed is of the essence, testing laboratories are at the limits of their capacity and reagents are in short supply, these POC tests detecting SARS-CoV-2 antibody seem like the perfect solution. And test makers have responded by adapting their previous pathogen detection assays to COVID-19. But, as the WHO reminded us, there is also a major risk in relying on these tests unless and until they are proven accurate enough for use in clinical decision-making.

FDA WATCH

Agency Clears Dozens of New COVID-19 Diagnostic Tests in Record Time

The US Food and Drug Administration (FDA) has taken a lot of heat for wasting precious time in responding to the COVID-19 emergency. While this criticism is fair, it is also true that the agency has made up for at least some of that lost time since getting its response strategy in order. In previous public health emergencies, approval for commercial laboratory tests to diagnose a pathogen has taken months, if not years. Eight weeks was the fastest on record. The first commercial test for COVID-19, from Roche, was approved just six weeks into the emergency. And since then literally dozens of new tests have received FDA Emergency Use Authorization (EUA), a total that grows literally every day. Here is the latest count as of April 17, 2020.

COVID-19 LABORATORY TESTS RECEIVING FDA EMERGENCY USE AUTHORIZATION

((S) = Serology Test)

Date	Manufacturer(s)	Test Receiving EUA
Feb 4	CDC	2019 Real Time RT-PCR Diagnostic Test Panel
March 2	New York State	Wadsworth Center, New York State Department of Public Health's New York SARS-CoV-2 Real-time Reverse Transcriptase (RT)-PCR Diagnostic Panel
March 13	Roche	Cobas SARS-CoV-2 Test
March 15	Thermo Fisher Scientific	TaqPath COVID-19 Combo Kit for qualitative detection of SARS-CoV-2 nucleic acid
March 16	LabCorp	COVID-19 RT-PCR test
March 16	Hologic	Panther Fusion SARS-CoV-2 assay for use on firm's Panther Fusion system
March 17	Quidel	Lyra SARS-CoV-2, RT-qPCR assay for qualitative detection of nucleic acid from SARS-CoV-2
March 18	Abbott	Abbott RealTime SARS-CoV-2 EUA run on firm's PCR-based m2000 RealTime System
March 19	Quest Diagnostics	SARS-CoV-2 rRT PCR test
March 19	GenMark Diagnostics	ePlex SARS-CoV-2 Test run on firm's ePlex system
March 20	DiaSorin Molecular	Simplexa COVID-19 Direct assay run on firm's Liason MDX real-time PCR instrument
March 21	Cepheid	Xpert Xpress SARS-CoV-2 point-of-care test
March 23	Primerdesign	COVID-19 Genesig Real-Time PCR assay
March 24	Mesa Biotech	Accula SARS-CoV-2 test
March 24	BioMérieux	BioFire COVID-19 test run on firm's BioFire FilmArray system
March 24	PerkinElmer	New Coronavirus Nucleic Acid Detection Kit
March 25	Quidel	Expanded EUA for Lyra SARS-CoV-2 assay
March 27	BGI Americas (BGI Genomics US sub)	BGI Real-Time Fluorescent RT-PCR Kit
March 27	Luminex	NxTag CoV Extended Panel
March 27	Abbott	SARS-CoV-2 point-of-care test
March 30	Qiagen	QiaStat-Dx Respiratory SARS-CoV-2 Panel, first "syndromic" testing product to be deployed in US
March 30	NeuMoDx	NeuMoDx SARS-CoV-2 Test Strip for use on NeuMoDx 288 Molecular + NeuMoDx 96 Molecular systems
April 1	Yale New Haven Hospital Clinical Virology Laboratory	SARS-CoV-2 RT-PCR test
April 2	Cellex	qSARS-CoV-2 IgG/IgM Rapid Test, first coronavirus serology test to get EUA clearance(S)
April 2	Ipsum Diagnostics	COV-19 IDx, an RT-PCR-based SARS-CoV-2 test
April 3	Becton Dickinson + BioGX	Sample-Ready hospital SARS-CoV-2 assay for use on BD Max system

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FDA Watch: COVID-19 Laboratory Tests Receiving FDA Emergency Use Authorization, *from page 5*

Date	Manufacturer(s)	Test Receiving EUA
April 6	ScienCell Research Laboratories	ScienCell SARS-CoV-2 Coronavirus Real-time RT-PCR Detection Kit
April 6	Co-Diagnostics	Logix Smart Coronavirus COVID-19 Test
April 6	Luminex	Aries SARS-CoV-2 Assay
April 6	Massachusetts General Hospital	MGH SARS-CoV-2 assay
April 6	Infectious Disease Diagnostics Laboratory at Children's Hospital of Philadelphia	SARS-CoV-2 RT-PCR Test
April 6	Diagnostic Molecular Laboratory at Northwestern Medicine	SARS-CoV-2 Assay
April 7	Gnomegen	COVID-19 RT-Digital PCR Detection kit for diagnosing SARS-CoV-2
April 8	Viracor Eurofins Clinical Diagnostics	Viracor SARS-CoV-2 molecular assay
April 8	Becton Dickinson	BD MAX ExK TNA-3 kit run on the BD Max system
April 9	Stanford Health Care Clinical Virology Laboratory	SARS-CoV-2 assay
April 9	DiaCarta	QuantiVirus PCR diagnostic (Dx) test for COVID-19
April 13	Rutgers Clinical Genomics Laboratory	First approved molecular COVID-19 test for use with saliva samples
April 13	University of North Carolina Medical Center	UNC Health SARS-CoV-2 real-time RT-PCR test
April 13	Atila Biosystems	iAMP COVID-19 Detection Kit
April 13	Specialty Diagnostic Laboratories	Test for qualitative detection of a region in SARS-CoV-2 ORF1a/b gene
April 13	Orig3n	Novel Coronavirus Test for qualitative detection of two regions in SARS-CoV-2 nucleocapsid gene
April 14	Integrity Labs	Probe-based molecular test for SARS-CoV-2 detecting N1 and N2 targets from CDC Prevention assay kit
April 14	Baptist Hospital Miami	Probe-based real-time RT-PCR assay detecting the CDC N2 target
April 15	Ortho Clinical Diagnostics	Vitros Immunodiagnostic Products Anti-SARS-CoV-2 Total Reagent Pack and Calibrators(S)
April 15	Chembio Diagnostics	DPP COVID-19 serological point-of-care test and analyzer providing numerical readings for IgM and IgG antibody levels(S)
April 15	Boston Children's Hospital	Childrens-Altona-SARS-CoV-2 assay
April 16	Mount Sinai Laboratory	COVID-19 ELISA IgG Antibody Test(S)
April 16	Maccura Biotechnology	Fluorescent PCR-based SARS-CoV-2 test kit
April 16	Hackensack University Medical Center	CDI Enhanced COVID-19 test
April 16	CirrusDx Laboratory	Assay detecting SARS-CoV-2 nucleocapsid gene

The Business of Testing: New COVID-19 Revenues Not Enough to Offset Declines in Elective & Screening Tests

That line from Charles Dickens' *A Tale of Two Cities* about the best of times and the worst of times is especially apt with what testing laboratories in the US and around the world are experiencing. For laboratories performing COVID-19 testing, it is the best of times, with test volumes running at unprecedented levels. For other laboratories that lack the capabilities for COVID-19, it is just like being in the restaurant, travel, retail and other businesses hemorrhaging revenues as a result of pandemic disruption. And while cancer and other acute care laboratories are still carrying on, the laboratories suffering the most are the ones that perform routine and elective tests that most consumers are putting off until the COVID-19 crisis ends.

₵oronaviru$ Economics

Smaller regional and community laboratories, particularly, are facing challenges. According to National Independent Laboratory Association (NILA) Administrator **Mark Birenbaum** based on conversations with NILA members, many of these laboratories are reporting drops in testing volume ranging between 40% to 90%. Laboratories which do primarily "non-essential" testing, he says, are seeing drops between 60 to 90%, while laboratories with clients that do "essential" testing are enduring drops of around 40%. Certain specialty laboratories, like those serving the in vitro fertilization space, have shut down completely, he adds.

Even the giant corporate laboratories are feeling the impact. On March 3, Quest Diagnostics filed a Current Report on Form 8-K with the Securities and Exchange Commission to outline the impact of the pandemic on its operating results, cash flows and financial condition and withdraw its previously announced guidance for full year 2020. The company disclosed that during the last two weeks of March, volumes declined in excess of 40%; and that is *inclusive* of COVID-19 testing.

"Federal, state and local governmental policies and initiatives designed to reduce the transmission of COVID-19 have resulted in, among other things, a significant reduction in physician office visits, the cancelation of elective medical procedures, customers closing or severely curtailing their operations (voluntarily or in response to government orders), and the adoption of work-from-home or shelter-in-place policies, all of which have had," stated Quest in its Form 8-K, "and we believe will continue to have, an impact on the Company's operating results, cash flows and financial condition."

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The Business of Testing: New COVID-19 Revenues Not Enough to Offset Declines in Elective & Screening Tests, *from page 7*

COVID-19 Testing Gains Not Offsetting Declines in Other Testing

On its March 31 Form 8-K, Quest noted that in response to the COVID-19 pandemic it has made substantial investments to expand the amount of COVID-19 testing available to the country and is currently doing more than 30,000 COVID-19 tests per day. However, even with that level of testing, the company still expects a decline in overall volume.

In addition, Birenbaum notes that many independent laboratories cannot make up the lost volume with COVID-19 testing; and even if they could, there are issues with the reimbursement rates. To do the testing, you must be a Level 2 laboratory, he explains. That means that Level 1 laboratories cannot do it.

Even if you are a Level 2 laboratory, you must have certain platforms to run COVID-19 tests. Laboratories that do not have those platforms would need to spend between $250,000 to $1 million or more to obtain the required equipment, Birenbaum says.

And even if you are a Level 2 laboratory and even if you do have all the necessary equipment for COVID-19, you would still face formidable challenges, starting with obtaining the test kits. According to Birenbaum, some laboratories are being told by their vendors that they will not be able to get new shipments of kits for two months. Obtaining swabs for collecting patient samples has also been a challenge for some laboratories, as has supplying the required personal protective equipment (PPE), above all, N95 respiratory filtering masks. And do not forget the staffing challenges posed by pandemic.

But that is not all. Even if a laboratory is able to overcome all of these hurdles and provide COVID-19 testing, there is the further problem of getting reimbursed enough to cover costs. Until recently, pricing put out by local Medicare Administrative Contractors put reimbursement for the Centers for Disease Control (CDC) test at around $36 and reimbursement for non-CDC versions at around $51—not enough to cover costs for most laboratories.

On April 15, CMS announced that it was raising the reimbursement rate to $100, but Birenbaum suggests that even that increase may not be enough to cover the costs for most laboratories. This is particularly true for laboratories that have to make capital expenditures like purchases of new equipment to run COVID-19 tests. And reimbursements from private payors are not much better, particularly insofar as the new CARES Act bans insurers from charging COVID-19 patients the usual cost-sharing payments for laboratory testing.

Takeaway

For all but a few testing laboratories, pandemic is bad for business. And that, in turn, is bad for patients. As long as Medicare and other reimbursement rates remain far below what is necessary to maintain healthy margins, let alone support costly capital improvements, many laboratories are choosing not to perform COVID-19 testing. In addition to limiting patient access, this puts an enormous strain on the testing laboratories that are already up to their neck in meeting the demands for COVID-19 testing.

The COVID-19 Crisis: Easy & Rapid Testing Remains Unavailable to Most Physicians

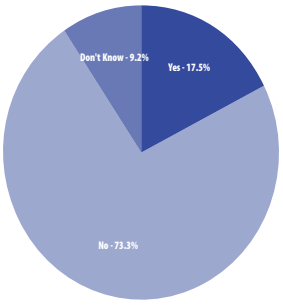
New laboratory tests to detect COVID-19 are clearing the Food and Drug Administration and reaching the US market faster and in volumes greater than anybody would have ever dared to expect. But so far at least, it still does not seem to be enough to satisfy the urgent demand for COVID-19 testing. That is the troubling conclusion of a new survey from Harvard Medical School, the Rand Corporation and Doximity, a professional medical network of which 70% of all US physicians are members

Quick and Easy Testing Remains Elusive

Conducted at the end of March 2020, the survey "Physicians Views on the Coronavirus Pandemic Response," included 2,600 physicians. Half of the respondents said they have treated at least one patient with potential COVID-19 symptoms. When asked whether they were "currently able to test their patients for COVID-19 quickly and easily," 73.3% of those physicians who reported treating at least one potential COVID-19 case answered "no."

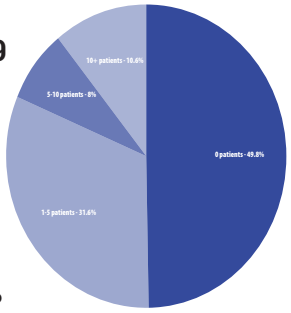
Are you currently able to test your patients for COVID-19 quickly and easily?

- **Yes - 17.5%**
- **No - 73.3%**
- **Don't Know - 9.2%**



How many patients have you treated with possible COVID-19 symptoms, but have not been able to test for COVID-19

- **0 patients - 49.8%**
- **1-5 patients - 31.6%**
- **5-10 patients - 8%**
- **10+ patients - 10.6%**



Some of the other noteworthy survey findings:

- Close to 50% of the physicians surveyed said they believed patients are avoiding testing due to financial and health insurance concerns;
- Over 77% reported that they do not believe their hospital/clinic has adequate medical supplies and equipment if the pandemic worsens;

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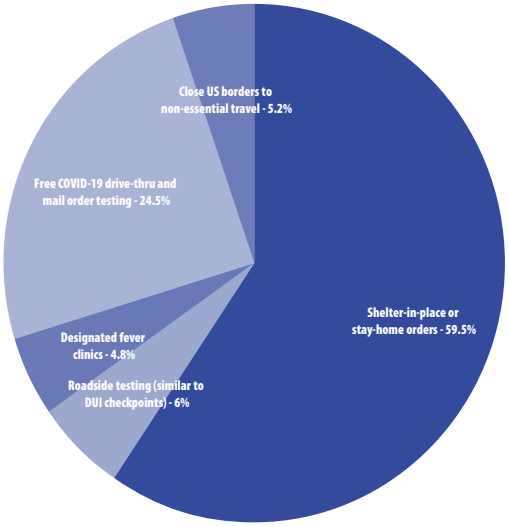
- Close to 70% believe that the government has not taken appropriate measures to support the medical supply chain and ensure that their hospital/clinic has the medical supplies it needs to address the pandemic;
- Close to 60% did not believe that there were enough precautions in place in their clinic to protect them from infection while treating COVID-19 patients;
- 70% did not believe the government is responding adequately to the pandemic;
- Nearly 60% believed social distancing, closing schools and travel restrictions were an appropriate reaction to the potential risks of COVID-19;
- Nearly 60% believe the stay-at-home or shelter-in-place orders would do the most to "flatten the curve," while nearly 25% believed free COVID-19 drive through and mail in testing would do the most; and
- Over 50% reported increasing their use of telemedicine in response to the pandemic.

From observing your patient habits, which of the following US policy actions would "flatten the curve" the most?

- **Shelter-in-place or stay-home orders - 59.5%**
- **Roadside testing (similar to DUI checkpoints) - 6%**
- **Designated fever clinics - 4.8%**
- **Free COVID-19 drive-thru and mail order testing - 24.5%**
- **Close US borders to non-essential travel - 5.2%**



Takeaway

*"The findings highlight the difficult road ahead for healthcare providers confronting the coronavirus pandemic," said **Chris Whaley**, Ph.D., lead author and Policy Researcher at the RAND Corporation in a **press release**. "We hope this insight on physician experiences and concerns surrounding the pandemic will help design appropriate and immediate policy response." It is also worth noting that much has happened since the survey, including the adoption of the CARES Act and the COVID-19 acceleration of the testing pipeline. Regrettably, the physician outlook from an anecdotal basis seems to remain less than optimistic.*

Pandemic & Progress: First Saliva COVID-19 Test Secures FDA Approval

One of the toughest parts of COVID-19 laboratory testing is the sample collection process. A swab must be inserted into each nostril, one at a time, to the nasopharynx at the back of the nasal cavity, followed by gentle scraping of the tissue to obtain the needed respiratory samples. The process poses at least three challenges:

- It is uncomfortable for patients;
- It requires a qualified health care professional to perform; and
- It directly exposes the professional to risk of infection thus requiring the use of personal protective equipment (PPE), including respiratory masks that are in short supply.

There must be a better way.

Spit Over Swab

On April 13, the US Food and Drug Administration (FDA) granted Emergency Use Authorization (EUA) to the first COVID-19 test cleared for use on saliva samples. The Rutgers Clinical Genomics Laboratory TaqPath SARS-CoV-2 Assay test is based on the Thermo Fisher Scientific Applied Biosystems TaqPath COVID-19 Combo Kit previously approved for the detection of specific genomic regions of the SARS-CoV-2 nucleocapsid gene, spike gene and ORF1ab region in nasopharyngeal swab, nasopharyngeal aspirate, and bronchoalveolar lavage specimens. But it has now been modified for use on additional specimen types, including saliva.

The test runs on the Thermo Fisher Applied Biosystems QuantStudio 5 Real-Time PCR System equipped with software v1.3 or the Applied Biosystems ViiA7 Real-Time PCR System with the Applied Biosystems QuantStudio 5 software v1.3. All the patient has to do is spit into a tube. However, it is not a home test. Under the terms of the EUA, the testing must still take place in a healthcare setting under the supervision of a qualified professional. But in addition to being less invasive, spitting significantly reduces the risk of infection to the sample taker, freeing up the use of desperately needed PPE and eliminating the use of swabs, which are also in short supply due to the COVID-19 crisis.

Takeaway

The EUA was provided under the FDA's Policy A COVID-19 pathway for tests developed by high-complexity CLIA laboratories which allows for use only by the laboratory that develops them. Accordingly, the new saliva test can be performed only at Rutgers University Cell and DNA Repository (RUCDR) laboratories in New Jersey. However, you can expect other laboratories and test makers to develop their own versions of COVID-19 saliva tests in the very near future.

Emerging Tests: Serology Testing Critical to COVID-19 Survival & Post-Crisis Transition, *from page 1*

current infection. By contrast, blood-based serology tests indicate whether a person had COVID-19 but since recovered. In addition to furnishing invaluable data about particular populations, the capability to identify healthy individuals who carry COVID-19 antibodies and are thus presumably safe to "let out" is integral to the coming challenge of gradually peeling back social distancing.

FDA Regulation of Serology Testing

Not surprisingly, fostering the development of safe and reliable serology tests is one of the key elements of the US Food and Drug Administration's (FDA) COVID-19 emergency response strategy. After initially resisting the idea, the agency agreed to loosen its regulatory control over new diagnostic tests for COVID-19, allowing high-complexity and commercial laboratories to develop and provide their own tests immediately after validating them without waiting for FDA Emergency Use Authorization (EUA). The agency organized the four different regulatory pathways into separate "Policies." Among these, the least rigorous is "Policy D," which allows commercial manufacturers and high-complexity laboratories to provide validated tests without having to apply for an EUA at all.

Serology tests can also be cleared via Policy C, a slightly more rigorous pathway requiring the manufacturer or laboratory to launch tests intended for use at the point of care, upon validation without an EUA, provided that it notifies the FDA immediately and submits an EUA application within 15 business days.

Are Manufacturers Taking Advantage of Policy D?

Of the 74 COVID-19 serology tests that have passed or are currently in these pathways (as of April 17, 2020), only four have received EUA. That leaves 70

assays without FDA clearance. While getting serology tests immediately to the front lines is of critical importance, the FDA is also wondering if it might have gone a bit too far in lowering its guard.

COVID-19 Serology Tests with FDA Emergency Clearance

As of April 17, four COVID-19 serology tests have received EUA clearance from the FDA (listed in chronological order of approval date):

- **Cellex's** qSARS-CoV-2 IgG/IgM Rapid Test, a lateral flow immunoassay detecting IgG and IgM in blood serum, plasma, or venipuncture whole blood specimens in 15 minutes;
- **Chembio Diagnostics'** DPP COVID-19 serological point-of-care test and analyzer providing numerical readings for IgM and IgG antibody levels from a finger stick blood drop in 15 minutes;
- **Ortho Clinical Diagnostics'** high-throughput Vitros Immunodiagnostic Products Anti-SARS-CoV-2 Total Reagent Pack and Calibrators capable of processing up to 150 tests per hour;
- **Mount Sinai Laboratory's** COVID-19 ELISA IgG Antibody Test detecting human IgG antibodies in serum and plasma.

The source of the concern are the claims being made by some firms that the serology tests they are providing under Policy D, the EUA-less pathway: i. have FDA approval; or ii. can diagnose COVID-19. On April 7, FDA Commissioner **Steven Hahn** issued a statement warning against such false claims and indicating that "the FDA will take appropriate action against firms making false claims or marketing tests that are not accurate and reliable."

A week later, the agency once more cited the false claims issue. "We continue to see problematic claims and uses of serology tests, particularly those . . . under pathway D," noted **Timothy Stenzel**, director of FDA's Office of In Vitro Diagnostics and Radiological Health during the agency's weekly town hall. "These devices are only for high-complexity labs; they are not to be used in moderate complexity labs or in point-of-care, near-patient settings, nor in the home."

The Accuracy Challenge

The other big concern is with the sensitivity and specificity COVID-19 serology tests that have passed through Policy D. The problem is that serology tests are especially vulnerable to specificity issues that can produce false positive results, leading people who are still susceptible to COVID-19 into falsely believing they are immune.

Thus, the FDA finds itself in the very strange position of having to assess whether the results of tests it allowed into the US market "can be relied upon and can have a level of accuracy that indicates that they are fit for use in the United States," according to Stenzel. In response, the agency has formed a voluntary interagency validation protocol that is open to all

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developers of serology tests in the Policy D pipeline. The agency is asking developers to send their point-of-care test kits and any instrumentation that might be needed to a central laboratory for validation. Meanwhile, the agencies are creating a panel of sera and plasma to independently evaluate test performance. "We have been receiving test kits from some of these developers and we believe testing will begin in the very near future," Stenzel noted.

CLIA Categorization of Serology Tests

The other element of the test regulation strategy that the FDA has to create on the fly due to the emergency is CLIA categorization of serology tests that go through the different pathways. In the recent town hall, Stenzel offered some clarification.

Tests with EUA clearance: Stenzel noted that tests that receive EUA are authorized for use in specific environments. Thus, for example, the Cellex serology test can be used by laboratories with CLIA authorization to perform moderately complex testing. EUA-cleared tests for use at the point of care are deemed to be CLIA-waived tests.

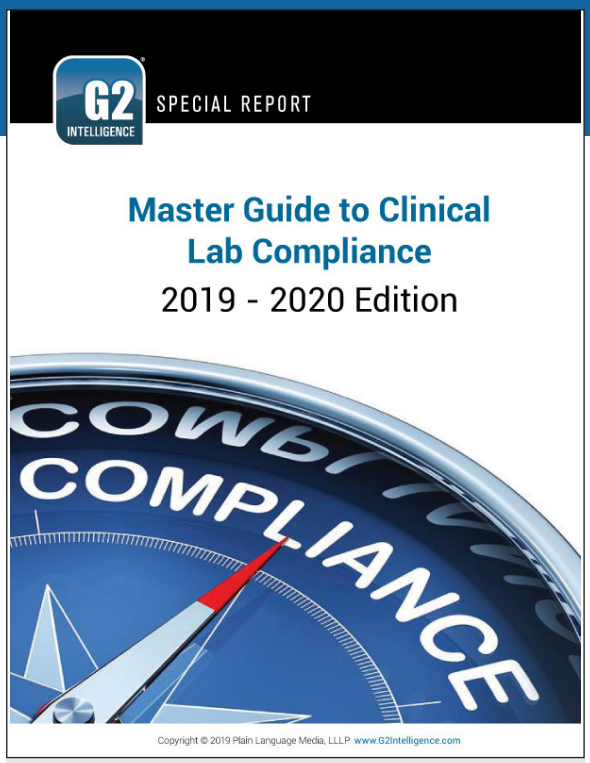
Non-EUA Policy D tests: Stenzel also clarified that tests that go through Policy D have not undergone FDA review and thus have not received a CLIA categorization. Result: By default, these tests revert to highly-complex test status.

Takeaway

These are extraordinary times and, like everybody else, the FDA has to make its strategy on the fly. The agency's test-now-and-regulate-later approach helps satisfy the desperate need for COVID-19 testing but also carries significant risks, including false claims by test makers and, more significantly, accuracy and reliability of test results. It remains to be seen how the FDA catches up with the runaway train of its own making.

Protect Your Lab against Growing Legal Risk!

Master Guide to Clinical Lab Compliance 2019-2020 Edition



Lab Compliance Essentials **covers:**

- Latest Fraud and Abuse Laws
- Rules and Regulations
- False Claims Act
- Anti-Kickback Laws
- Stark Laws
- "*Qui tam*" provisions
- Anti-retaliation provisions
- FCA enforcement actions
- Billing Practices
- Contract Sales Agreements
- Registry Payments
- Lab/Physician Relationships
- Gifts
- **And Much More!**

A Practical, Plain-Language Guide to Protecting Your Lab against Costly False-Claims, Anti-Kickback, and Stark Law Violations

For over two decades, clinical labs have been the target of a relentless stream of **investigations, audits, reviews, lawsuits**—and even **criminal prosecutions**—by the Centers for Medicare and Medicaid Services, and other Federal and State agencies.

Without a doubt, enforcement actions for **False-Claims violations** top the list. But the government has also systematically and aggressively grown the number of investigations into **Anti-Kickback** and **Stark Law violations.**

And that's just the tip of the iceberg. Investigations and **enforcement actions by state governments** have become increasingly aggressive... **whistleblower lawsuits** continue to grow sharply... and the ACA has earmarked **over $350 Million in funds for stepped up enforcement though 2020**, so you can be sure that labs like yours will come under increasing legal scrutiny.

Lab Compliance Essentials gives you the **practical, plain-language help** you need to understand the laws, and take **proven steps to protect your lab** from costly False-Claims, Anti-Kickback, Stark Law, and other legal and compliance violations.

For more information, please visit our website at **G2Intelligence.com/shop**

Or contact Andrea: **888-729-2315**, **Andrea@plainlanguagemedia.com**