AVALON HEALTHCARE SOLUTIONS

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COVID-19 TESTING BRIEF

from Avalon Healthcare Solutions

CONTENTS

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Avalon is the expert in laboratory and medical specialty drug benefit management. Our solutions are driven by evidence-based medical science. Avalon's core program includes full delegation of Routine Testing Management, Genetic Testing Management, Independent Laboratory Network Management, and Medical Specialty Rx Management. Our comprehensive solutions manage all out-patient lab spend across all lab testing types. Avalon helps physicians, consumers, and payers maximize the cost-effective use of diagnostic laboratory tests. Avalon Healthcare Solutions is a registered d/b/a of Avalon Health Services, LLC.

AVALON LABORATORY NETWORK CAPABILITY & CAPACITY REPORT

- The current capacity of the Avalon network of COVID-19 testing laboratories is greater than 700,000 tests/day.
- The average turnaround time for COVID-19 PCR results is 2 days.
- Many of the labs in the network currently report unused capacity.

LAB	HEALTHPLAN	RT-PCR Y/N	MULTI PLAT-FORM	CAPA-CITY (PER DAY)	TAT	ANTI-BODY TESTING	FDA EUA	CAPACITY (PER DAY)	TURN-AROUND TIME
LabCorp	SC, NC	Y	Y	200,000	1 day	Y	Y	300,000	1-3 days
Quest	SC, NC, CBC, VT	Y	Y	200,000	1 day priority 2 days all	Y	Y	200,000	1-2 days
BioReference	SC, NC, CBC, VT	Y	Y	70,000	1 day	Y	Y	260,000	3 days
GenetWorx	SC, NC	Y	Y	40,000	2 days	Y	Y	1,000	1 day
Sonic CPL (Clinical Pathology Lab)	SC	Y	Y	20,000	1-3 days	Y	Y	100,000	1 day
Mako Medical Lab	SC, NC	Y	Y	35,000	1-2 days	Y	Y	20,000	1 day
Premier Medical Lab	SC	Y	Y	50,000	1-2 days	Y	Y	50,000	1-2 days
Eurofins-Diatherix**	SC, NC, CBC, VT	Y	N	30,000	1-2 days	Y	Y	15,000	2-4 days
Aegis	SC, NC, CBC, VT	Y	Y	10,000	2 days	Y	N	N/A	N/A
MDL (Medical Diagnostic Lab)	SC, NC, CBC, VT	Y	N	12,000	2-3 days	Y	Y	1,000	3 days
Neogenomics	SC, NC, CBC, VT	Y	Y	5,000	1-2 days	N	N/A	N/A	N/A
BAKO	SC, NC, CBC, VT	Y	N	2,500	1-2 days	N	N/A	N/A	N/A
Luxor	SC	Y	Y	5,000	1 day	Y	Y	1,000	1-2 days
AccuReference	CBC	Y	Y	5,000	2 days	Y	Y	1,700	1 day
Precision Genetics	SC, NC	Y	N	4,000	1-2 days	Y	Y	1,250	2-4 days
AIT	SC, NC, CBC	Y	Y	3,000	1-2 days	N	N/A	N/A	N/A
PathGroup	NC	Y	Y	8,000	2-3 days	Y	Y	1,000	1 day
Radeas	SC, NC	Y	Y	2,400	1-2 days	Y	Y	4,000	1 day
LabTech	SC, NC	Y	Y	10,000	2 days	Y	Y	3,000	1 day
Wake Medical Lab Consultants	NC	Y	Y	1,500	1 day	Y	Y	4,800	1 day
SMA	CBC	Y	Y	1,000	1 day	N	N/A	TBD	TBD
Inform Diagnostics	SC, NC, CBC, VT	Y	N	200	1-2 days	N	N/A	N/A	N/A

GROWING TREND: AT-HOME COVID-19 TESTING

Some companies announced that their test will be available at-home without involving healthcare professionals.

• Gauss, a computer vision startup, and Cellex, a biotech company that works on diagnostics, announced that they will seek EUA from the FDA for their rapid COVID-19 test that can be fully performed by people at home without involving a laboratory. The company claimed 90% sensitivity and 100% specificity for its antigen test. This test integrates an antigen test with Gauss's app where users will take a picture of the rapid test, and Gauss's app will use artificial intelligence to deliver back the results to the user within 15 minutes.[1] Currently, Cellex has FDA authorization for its COVID-19 antibody test as high or moderate complexity.[2]

• Visby test received FDA EUA for high or moderate complexity only. It is a portable PCR test with 100% sensitivity and 100% specificity. And, the company seems determined to get FDA EUA for home use.[3]

The progress on COVID-19 test development has been curious. It will be interesting to know if the FDA will ever grant at-home COVID-19 test EUAs.

AT-HOME TESTING: A TALE OF TWO LABS

As previously reported, both Quest Diagnostics and LabCorp offer an at-home diagnostic test (RT-PCR) for COVID-19. The following chart outlines the similarities and differences between the two tests.

QUEST AND LABCORP - SAME LOGISTICS	QUEST DIFFERENCE	LABCORP DIFFERENCE
Order Online, Test Can Be Received At Home	Will not charge health plan or federal government	Will charge health plan on behalf of consumer
Separate Physician Charge Is Applied	Test may be taken to Walmart for pharmacist supervision	
Samples May Be Returned Via FedEx		

RESPIRATORY PATHOGEN PANELS INCLUDING COVID-19

On September 8, 2020, LabCorp announced the introduction of a diagnostic (PCR) respiratory panel that includes COVID-19, Flu A/B and RSU. The company has also applied for EUA to offer the same panel as an at-home test. Quest Diagnostics has signaled that they intend to launch a similar product. As described by the Avalon Pathogen Panel Testing policy AHS G2149, this panel could be considered as a covered service. Current CPT code 87631 may describe the panel. However, this CPT code is not specific to COVID-19, and plans may struggle to clearly determine if the accurate rate has been applied.

These new diagnostic respiratory panels present more than one challenge to claims operations. First, under the CARES Act plans and issuers shall not impose any cost sharing requirements (including deductibles, copayments, and coinsurance), prior authorization requirements, or other medical management requirements for benefits that must be provided under the Act.

It is important to note that several in vitro diagnostic kit manufacturers are producing and marketing diagnostic multiplex test kits that exceed five respiratory pathogens. These are not testing laboratories, but these companies do sell these kits to the laboratory industry, including hospital laboratories. Some examples of these companies and the number of pathogens to be detected by their products are included in the following chart:

COMPANY OR PRODUCT	NUMBER OF PATHOGENS
Genmark	21
ThermoFisher	3
Qiagen	22
Luminex	20
BioFire	23
Cephid	4

HOW MUCH DO C19 LAB TESTS COST?

A new study in the Journal of General Internal Medicine examined approximately 182,000 claims for COVID diagnostic tests billed by independent labs and the outpatient hospital setting. The highest charge for COVID diagnostic testing was $14,750. However, the study revealed the following typical ranges for charges:

- Independent Labs: $67 to $100
- Hospital outpatient: $94 to $204

Independent labs performed 50% of COVID testing while hospitals performed about 35%.The range of charges for antibody testing was $42 to $55 with 97% of the testing billed by independent labs. The study noted that charges varied widely by state.

CORONAVIRUS TESTING IN THE OUTPATIENT SETTING POLICY UPDATES

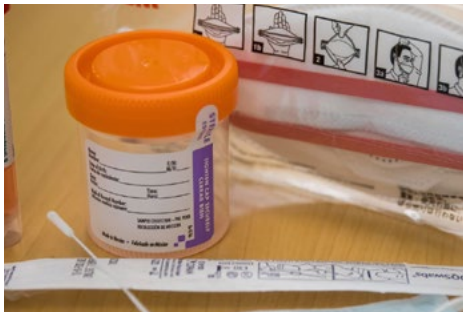
On September 8, 2020, Avalon's independent Clinical Advisory Board (CAB) met for its third-quarter policy review meeting. During this meeting, Avalon's policy on coronavirus testing titled "Coronavirus Testing in the Outpatient Setting" was updated.

This policy was initially written in May 2020 with the focus on all evidence-based scientific literature available at that time. Since then, most clinical professional guidelines such as those from the World Health Organization (WHO), the Centers for Disease Control and Prevention (CDC), the National Institutes of Health (NIH), the American Medical Association (AMA), the Infectious Diseases Society of America (IDSA), and others were updated as well.

CAB reaffirmed its previous position stating that current evidence supports the clinical utility of nucleic acid tests as diagnostic tests for COVID-19 for symptomatic patients, asymptomatic individuals with a known exposure, and those undergoing aerosol producing procedures. Large molecular panels remained as not recommended, and small pathogen panels remained recommended. CAB debated the utility and dangers of antigen testing and because it is a public emergency, and because these tests are becoming better than initially introduced. They concluded that diagnostic antigen testing should be recommended for symptomatic patients. The antibody testing recommendation remained the same as before. It is not recommended except for children with the multisystem inflammatory syndrome (MIS-C). Finally, CAB added their position about neutralizing antibody testing as not recommended since the clinical utility of this testing was not yet demonstrated in the literature.

Accordingly, two main changes were made in the policy. The first change is for diagnostic antigen tests as a recommended test. The second change is the addition of neutralizing antibody tests as not recommended.

For the coding updates, the AMA added one additional CPT code 86413 for quantitative antibody testing with the effective date of September 8th. Per the AMA Website, this service provides precise quantitative measurements and is intended to aid in detecting the "presence and temporal evolution of the adaptive immune response to SARS-CoV-2". It is not for the testing of convalescent plasma but assesses the quantitative levels of antibody response after COVID-19 infection.[4]



CDC TESTING FOR COVID-19 GUIDANCE UPDATE

The CDC issued a document titled "Overview of Testing for SARS-CoV-2 (COVID-19)" at the beginning of the pandemic in early spring. Since then, the document was updated several times.

The latest update was issued on September 18, 2020, to reinforce the need to test asymptomatic individuals.[5] The CDC now recommends viral testing that detects SARS-CoV-2 nucleic acid or antigen "to diagnose acute infection of both symptomatic and asymptomatic individuals, to guide contact tracing, treatment options, and isolation requirements". The CDC did not recommend antibody testing because it does not have the FDA authorization as a diagnostic test. However, the CDC suggested that antibody test may be used in certain situations such as "to support clinical assessment of persons who present late in their illnesses when used in conjunction with viral detection tests" and for individuals "suspected to have a post-infectious syndrome caused by SARS-CoV-2 infection (e.g., Multisystem Inflammatory Syndrome in Children; MIS-C)".

In general, the CDC encouraged or recommended testing in symptomatic and asymptomatic individuals with known or unknown COVID-19 contact history. According to the CDC, a positive test does not need to be repeated for 3 months. For self-isolation, the CDC recommended isolating "for at least 10 days after symptom onset and resolution of fever for at least 24 hours, without the use of fever-reducing medications, and with improvement of other symptoms". The CDC's complete guidance regarding COVID-19 testing can be found **here**.

CHANGES IN REGULATORY OVERSIGHT OF LABORATORY DEVELOPED TESTS

Two recent events affected the long-time debate about the regulatory oversight of laboratory developed tests (LDTs). The impact of these actions remains unclear at this time.

In August 2020, the U.S. Department of Health and Human Services announced that the FDA would no longer require premarket review of LDTs absent notice-and-comment rulemaking, as opposed to through guidance documents, compliance manuals, website statements, or other informal issuances.[6] The notice clarifies that clinical laboratories that develop LDTs may voluntarily seek approval,

clearance, or an Emergency Use Authorization (EUA) from FDA, but that laboratories are not required to do so. The notice further explains that that clinical laboratories remain subject to regulation under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), regardless of whether they elect to seek premarket review of their LDTs.

On September 15, 2020, HHS Secretary Azar issued an internal memorandum prohibiting the FDA from signing any new rules on its own -- reserving that power to the HHS Secretary, to whom the FDA Commissioner reports. The memo stated that any "prior delegation of rulemaking authority, including the authority to sign or issue a rule or a proposed rule, is rescinded." HHS's language regarding the requirement for notice and comment rulemaking is not limited to COVID-19 tests. As a result, it would appear that HHS intends for this announcement to apply to all tests offered as LDTs—not just tests for COVID-19.

On September 20, 2020, HHS posted a document to its website that clarified that the memo only applies to rulemaking, which follows different procedures and legal requirements than product approvals and authorizations. For example, EUAs will not need to be signed by the secretary.[7]

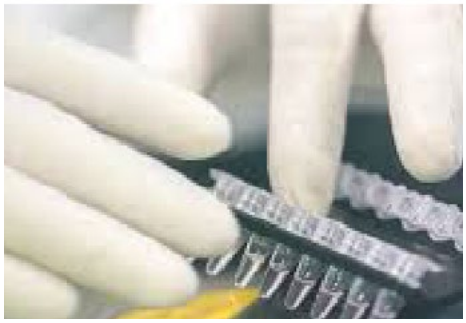
By way of background, the regulatory oversight of lab testing is shared by FDA and the Centers for Medicare & Medicaid Services (CMS). Clinical testing in the United States must be performed

in laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), a law that bestowed regulatory authority on CMS. The CLIA regulations establish quality standards for laboratory testing performed on specimens from humans, such as blood, body fluid and tissue, for the purpose of diagnosis, prevention, or treatment of disease, or assessment of health.

According to the FDA, a laboratory developed test (LDT) is "a type of in vitro diagnostic test that is designed, manufactured and used within a single laboratory". CLIA has a very specific set of rules, and under these rules, the laboratory must perform strict validations before offering a test to patients and physicians. If it is an FDA-approved test, the laboratory must follow a specific set of experiments to verify the test's performance. If it is an LDT or FDA-approved and modified test, the laboratory must establish test performance before reporting patient test results.[8]

No one in the laboratory is allowed to start testing without performing clinical test validations. Violation can result in the imposition of serious consequences for both the laboratory and its personnel. Even if the FDA is not overseeing LDTs, they are still being regulated under CLIA.

This is a fluid situation, coming in the middle of a presidential election and when Congress is actively considering legislative proposals to reform the regulation of laboratory tests. Avalon will keep its customers apprised of the latest news on this issue.



COVID-19 FDA EUA TESTING OVERVIEW

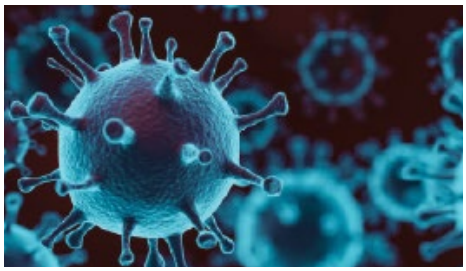
Avalon has developed a dashboard to keep track of all COVID-19 laboratory tests with the FDA Emergency Use Authorizations (EUAs) that can be found **here**.

As of the last FDA update on September 22, 2020, there are four antigen tests, forty-six antibody tests, two hundred nucleic acid tests, and one miscellaneous COVID-19 related-test received FDA EUAs.

At this time, there are only four antigen tests that received FDA EUA. Their performance improved since their introduction, and their validation protocols improved as well. The first antigen test Sofia from Quidel utilized only five frozen positive samples in their initial validation[9] and, LumiraDx utilized over eighty positive samples.[10]

There are 200 molecular tests available. They exist in different formats such as high-complexity, moderate-complexity, and waived or point-of-care (POC). The POC format tests are authorized for use in some type of healthcare setting requiring at minimum CLIA certificate of waiver, certificate of compliance, or certificate of accreditation. The Roche Liat system received FDA EUA for their combined COVID-19 and flu test[11]. So far, in addition to CDC's diagnostic multiplex assay for flu and COVID-19[12], this is the only test that received FDA EUA for testing flu and COVID-19, but many other manufacturers and labs announced their development. Soon, we should expect to see more of combined small panels for flu and COVID-19 receiving FDA authorizations.

Currently, forty-six antibody tests received FDA EUA. They are all moderate or high complexity and must be performed in the CLIA labs. For neutralizing antibody tests, some companies announced their development. On September 17th, AXIM Biotech has filed EUA with the FDA.[13] They claimed that this rapid diagnostic test will be useful for screening plasma, to verify vaccine efficacy, and for immunity passports. Today, according to current literature, their performance is still unknown, and clinical utility is unclear.



When a vaccine becomes available, the neutralizing antibody test's performance and clinical utility will be determined. Mayo Clinic has launched its neutralizing antibody test to support research.[14] Finally, there are at least fifteen home collection kits that received FDA EUAs, and this list keeps growing very fast. The home collection kits contain nasal swabs or saliva collection devices that patients can collect at home and mail the sample to the lab for testing.

REFERENCES

[1] Gauss and Cellex partner on first at-home COVID-19 rapid antigen test and computer vision mobile app. (9/16/2020). Press Release. Retrieved from https://covid19.gauss.com/press-release.html#

[2] Cellex. (2020). Cellex qSARS-CoV-2 IgG/IgM Rapid Test. Retrieved from https://www.fda.gov/media/136625/download

[3] Visby Medical. (2020). Visby Medical COVID-19 Test. Retrieved from https://www.fda.gov/media/142228/download

[4] American Medical Association CPT Category I Pathology and Laboratory and Proprietary Laboratory Analyses (PLA) Codes for Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) (Coronavirus disease [COVID-19]).

[5] CDC. (2020j, 09/18/2020). Overview of Testing for SARS-CoV-2. Retrieved from https://www.cdc.gov/coronavirus/2019-nCoV/hcp/clinical-criteria.html

[6] FDA (2020, 09/01/2020). Rescission of Guidances and Other Informal Issuances Concerning Premarket Review of Laboratory Developed Tests. https://www.hhs.gov/coronavirus/testing/recission-guidances-informal-issuances-premarket-review-lab-tests/index.html

[7] https://www.hhs.gov/about/news/2020/09/20/hhs-statement-on-regulatory-process.html

[8] Code of Federal Regulations. Title 42. Chapter IV. Subchapter G. Part 493. Laboratory Requirements. Subpart 1253 Standard: Establishment and verification of performance specifications. https://www.ecfr.gov/cgi-bin/text-idx?SID=1248e3189da5e5f936e55315402bc38b&node=pt42.5.493&rgn=div5#se42.5.493_11253

[9] Sofia Quidel_Corporation. (2020, 05/2020). Sofia 2 SARS Antigen FIA. Retrieved from https://www.fda.gov/media/137885/download

[10] LumiraDx. (2020). SARS-CoV-2 Ag Test. Retrieved from https://www.fda.gov/media/141304/download

[11] Roche Molecular Systems, Inc. (2020). Cobas SARS-CoV-2 & Influenza A/B Nucleic Acid Test for use on the Cobas Liat System. Retrieved from https://www.fda.gov/media/142190/download

[12] CDC. (2020e, 7/2/2020). Influenza SARS-CoV-2 (Flu SC2) Multiplex Assay. Retrieved from https://www.fda.gov/media/139744/download

[13] AXIM® Biotechnologies Files Emergency Use Authorization With the FDA for First–in-Class COVID-19 Rapid Diagnostic Test for Neutralizing Antibodies. IR Team. Sep 16, 2020. Press Release. Retrieved from https://aximbiotech.com/axim-biotechnologies-files-emergency-use-authorization-with-the-fda-for-first-in-class-covid-19-rapid-diagnostic-test-for-neutralizing-antibodies/

[14] Ginger Plumbo. Mayo Clinic launches neutralizing antibody test to advance COVID-19 therapies. June 11, 2020 News Network. Retrieved from https://newsnetwork.mayoclinic.org/discussion/mayo-clinic-launches-neutralizing-antibody-test-to-advance-covid-19-therapies/