With Sputum Test for SARS-CoV-2, MicroGen Dx Aims to Challenge Quest, LabCorp

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NEW YORK – Although hundreds of labs across the US have been providing testing for SARS-CoV-2, Quest Diagnostics and Laboratory Corporation of America are the industry's leaders and have provided hundreds of thousands of tests.

But MicroGenDx CEO Rick Martin thinks they've dropped the ball – and believes his lab can do better. "People assume that LabCorp or Quest … because they're the biggest labs, they would be the most proficient at setting up for large scale testing or molecular," Martin said. "They're simply not."

Citing statistics from the California Department of Public Health reporting more than 57,400 people in the state still have pending test results, Martin noted that the backlog could have serious consequences for patients, including potential false negatives. "If you do a nasopharyngeal swab and you think that RNA's going to last on that swab forever, it's not," Martin said. "So, you're going to get a lot of false negatives."

He added that MicroGenDx has talked to patients with "all the symptoms" of the SARS-CoV-2 virus who received a negative result from LabCorp, only to be found positive after they were retested at his lab.

In a recent statement, Quest acknowledged a backlog that resulted from "a sharp influx of test orders that continued to outpace our growing capacity." It noted that for several days after it launched its test, only its lab in San Juan Capistrano, California performed SARS-CoV-2 testing, and added that much of its testing was based on its laboratory-developed test, which was "less suited to high-throughput environments."

The Secaucus, New Jersey-based lab company added it has reduced its backlog 28 percent since March 25, from 160,000 tests to 115,000 tests as of Wednesday.

LabCorp didn't respond to requests for comment.

MicroGenDx's's secret to providing faster results is offering testing with another type of sampling: sputum or saliva. The Orlando, Florida-based company developed a SARS-CoV-2 test based on the protocols of the US Centers for Disease Control and Prevention test, which was issued Emergency Use Authorization from the US Food and Drug Administration in February. MicroGenDx then designed three primers for their laboratory-developed test, and submitted validation data to the FDA this week under the agency's EUA guidance. Martin said that he expects EUA to be issued for the test by next week.

The firm is also seeking FDA approval for the test. Although the company's MicroGenDx COVID-19 KEY test is a laboratory-developed test and doesn't technically need to be approved by the FDA, Martin said MicroGenDx still wants FDA authorization because healthcare professionals often want an FDA seal of approval.

Right now, MicroGenDx is the only commercial laboratory in the US offering sputum testing for SARS-CoV-2. Other firms and organizations, including the New England Biological Institute, are working on sputum tests for the virus, but Quest and LabCorp for the most part only accepting nasopharyngeal or oropharyngeal swabs. LabCorp has also been accepting nasopharyngeal or orpharyngeal aspirates or washes, and bronchoalveolar lavage.

MicroGenDx's PCR test works with nasopharyngeal swabs or sputum samples and runs on the Roche LightCycler instrument. Currently, MicroGenDx's CLIA-certified, CAP-accredited lab, which is located in Lubbock, Texas, has nine Roche instruments and can run 1,000 tests in one cycle for a total of up to 10,000 a day. Martin noted that the lab has moved to three shifts and may soon be able to perform 14,000-15,000 tests per day. Despite this capacity, however, Martin added that in the first few days of testing, the lab was only receiving enough samples to run 400 to 500 tests a day. Now they've topped 1,000 per day, but "we're sitting at capacity, and it's a shame," he said.

MicroGenDx was inspired to validate the test for sputum and saliva due to the nationwide shortage of nasopharyngeal swabs. Both validations had 100 percent sensitivity and 100 percent specificity, according to Nick Sanford, the company's laboratory section director. The company also validated sterile saline as a transfer media, due to the low supply of viral transport media.

The sputum samples have been performing much better than the swabs, Martin said, because the viral particle load on the nasopharyngeal swabs was 3.5 million particles of SARS-CoV-2, whereas the viral load on sputum was 21 million particles. MicroGenDx's test has a limit of detection of 283 particles, Sanford noted.

"If you think about it, it's logical," Sanford said. "It's an airborne droplet coming out of your nose and your mouth. The fact that anybody thinks a nasopharyngeal is required to get a diagnosis, I think is just because that's what the CDC validated first and everybody took that and ran with it."

The advantage of using sputum or saliva over a nasopharyngeal swab is the increased sample volume and the potential availability for more targets, said William Abrams, an adjunct professor

at New York University's School of Dentistry. "It depends on the quantity of viral particles present in the collected sample," Abrams said. "It's likely that if the virus is actively shedding, I think are you will see it’s footprint in saliva."

Part of the difficulty with sputum testing for SARS-CoV-2 is that patients with symptoms don't have productive coughs and forcing them to cough something up could spread viral particles in the air and endanger the healthcare professional taking the sample. MicroGenDx decided to try testing patients' saliva too, and noticed that saliva often had just as many, if not more, viral particles of the virus.

"If you're trying to extract RNA, if you're trying to get it out of mucus materials, it's more difficult," Martin said. "But saliva is a lot cleaner, so you're going to get a higher load of the viral RNA out of saliva than trying to get it out of the mucus material."

Another potential issue with sputum is its thickness due to mucins, said Abrams. The increased viscosity could cause difficulty preparing the sample for extraction, he added. There's also potential for higher variability in saliva samples due to a patient’s saliva inadequacy, so Abrams said it would be up to the company to address that variability.

The lab is conducting paired sample analysis to continue verifying the validity of saliva samples and having patients submit second samples of either a swab or sputum that they didn't submit before, Sanford said. MicroGenDx is also considering time course studies to see how far after symptom onset the virus can be detected, he added.

While MicroGenDx may be the only commercial lab offering sputum-based testing for the coronavirus, several companies have developed sputum- or saliva-based testing for SARS-CoV-2. PerkinElmer's New Coronavirus Nucleic Acid Detection Kit, which can detect SARS-CoV-2 in sputum, plasma, or serum samples as well as oropharyngeal and nasopharyngeal swabs and bronchoalveolar lavage, received EUA from the FDA last month. Meanwhile, Primer Design, a Novacyt subsidiary, has its Genesig real-time PCR Coronavirus (COVID-19) CE-IVD assay, which is validated for swabs and sputum as well, and Mologic is developing a saliva-based assay to detect coronavirus antigens.

Developing its own test has also helped the lab improve turnaround time for results, Martin said. "Because we're not using the standard kits, we've been able to stockpile our reagents and master mix and the things we need for our test," he noted. Right now, MicroGenDx is delivering a 24-hour turnaround time for SARS-CoV-2 testing, compared to Quest's 2 to 3-day turnaround.

The test is not covered by insurance and patients will have to pay $125 out of pocket for the SARS-CoV-2 test. MicroGenDx will provide an invoice for patients to consult with their health plans. "I would love to be able to take insurance and file a claim, but I'm not taking the risk to file a Humana claim and get it denied in six months," Martin added.

Besides its SARS-CoV-2 assay, the lab offers other tests, including a rapid test for mycobacterium launched in February. The Acid Fast Bacilli (AFB) panel is a two-step PCR and

next-generation sequencing assay for identifying four main mycobacteria species: *Mycobacterium avium*, *Mycobacterium intercellulare*, *Mycobacterium abscessus*, and *Mycobacterium masiliensis*.

The PCR-based panel for the four species is run on the Roche LightCycler and has same-day results. It can be followed up with comprehensive NGS, using the Illumina Miseq platform with results in three days. The NGS test can identify any other mycobacterium species, Martin said.

Later this year, depending on how long the current pandemic lasts, Martin said the company is looking to add biomarkers for white blood cell count and C-reactive protein in its NGS test, mainly for orthopedic samples.

The company also has a quantitative PCR-based panel and NGS assay based on targeted 16S sequencing that identifies common microbes. The PCR panel can determine 17 microbes and resistance factors that can determine resistance to eight classes of antibiotics, and the NGS panel is used to more comprehensively analyze present microbes.

While the company is still offering its complete suite of tests, SARS-CoV-2 is a primary focus for MicroGenDx, as it is for the rest of the world. "I just want the world to know the fact that we don't need to be in a search for nasopharyngeal swabs," Martin said. "We're going to have evidence to show that phlegm, saliva, mucus in your mouth is going to be loaded with the COVID-19 virus, therefore allowing for easier testing."

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