COVID-19 test challenges and future predictions

By Brenda Silva

With demands for COVID-19 tests showing little sign of decline, many diagnostics companies have increased their efforts to develop and launch tests that offer quick turnaround times and reliable results. As of May 3, confirmed case statistics from the Johns Hopkins online dashboard report that over 7 million people in the U.S. have been tested for SARS-CoV-2 – the virus strain that causes coronavirus disease 19 (COVID-19) – with that number expected to reach 8 million test results by the end of May.

In an attempt to meet requests for more tests, several diagnostics companies have reprioritized in-house developments – opting to focus on creating in-lab/hospital, as well as at-home, testing options.

Current tests in progress

Considering the overwhelming effect that COVID-19 has had on 187 countries of the world – a total of over 3.5 million confirmed cases since it made its presence known four months ago – it seems only logical for diagnostics companies to develop and distribute as many tests as possible that have been approved for human use.

Beginning in March, Abbott announced the development of COVID-19 molecular tests for its m2000 instrument and ID NOW platform, and a serology test for its ARCHITECT system. Norman Moore, PhD, Director of Scientific Affairs for Infectious Diseases, Rapid Diagnostics, commented on Abbott's current approach to the pandemic.

"Given the global and widespread impact of this pandemic, we all have to bring everything we can to the fight. For Abbott, that means developing multiple tests across all of our diagnostic testing platforms – from portable, fast testing to large-scale testing for hospitals."

Todd Kelley, MD, Medical Director at Beckman Coulter, added, "Our team is laser-focused on developing and commercializing Access SARS-CoV-2 IgG and IgM serologic assays for the Access family of immunoassay systems, including Access 2 and DxI series, with testing on the DxC platform to be available shortly thereafter. We will launch the Access SARS CoV-2 IgG assay in May, followed by the Access SARS CoV-2 IgM assay."

At DiaSorin Molecular, Chief Scientific Officer Michelle Tabb, PhD, pointed out, "DiaSorin Molecular has been working to ensure our Simplexa COVID-19 Direct meets the expectations and demands of our customers while improving the workflow. We recently received Emergency Use Authorization (EUA) for additional specimen types and transport media including nasal swabs and bronchoalveolar lavages (BALs). We are also working on adding others including nasal aspirates, tracheal aspirates, sputum, and we are looking into saliva."

She added, "We are assessing how our COVID-19 test can better complement other clinical tools to help our customers diagnose and manage respiratory infections. Lastly, we are also exploring a higher throughput option for up to 96 test results at one time. This would also be a sample to answer to test without the need for nucleic acid extraction providing results in a little over an hour."

Reporting for Roche Diagnostics, John Osiecki, PhD, Director of Medical and Scientific Affairs, Molecular Diagnostics, said, "When Roche received EUA from the FDA (U.S. Food & Drug Administration) for the cobas SARS-CoV-2 test on March 12, we committed to shipping at least 400,000 tests per week to a network of about 30 labs across the U.S. Since we began shipping tests on March 13, we have been ramping up production to meet the increasing demand and have shipped many more tests than we committed to, across a network of U.S. labs that now includes more than 70 sites. As of April 13, we have shipped several million tests globally."

He continued, "We expect to have a high-volume immunoassay test available in early May and for monthly production levels to reach the high double-digit millions by June. We are also exploring the potential for SARS-CoV-2 tests for use at the point of care (POC), including an antigen test and a molecular test."

Accuracy of test results

In looking at factors that may cause interference with COVID-19 test result accuracy, some of the top comorbidities considered are diabetes, cardiovascular disease (CVD) and other respiratory diseases. However, available data has shown no evidence of these health issues affecting test results.

Beckman's Kelley said, "We haven't seen definitive evidence that patient comorbidities consistently affect result quality. There has been a fair amount of discussion related to sample acquisition problems for the various COVID-19 PCR tests. These are usually nasal swabs, and specimen acquisition is invasive and can be technically challenging to perform adequately."

Tabb at DiaSorin concurred and added, "One thing to consider is the overall testing and then positivity of the entire population versus the positivity in certain high-risk patient groups. The percentage positive may be skewed as we are not factoring in everyone that might be infected including those with mild illness or who are asymptomatic who have not sought testing. The data we have so far is limited and is a result of the initial limited testing."

Roche's Osiecki commented, "There is no known interference with nucleic acid tests like our cobas SARS-CoV-2 test from patient conditions like diabetes, cardiovascular disease or other respiratory infections. However, these factors may have an influence on the clinical interpretation of a patient's symptoms and the determination of the need for COVID-19 testing."

He suggested there are several factors that can lead to inaccurate results, in particular false positives or false negatives with any test, including PCR-based tests. Some of these include if the sample is collected too early, the sample is collected too late, the sample is contaminated or the sample is stored too long.

Challenges of developing COVID-19 tests

One of the biggest challenges affecting COVID-19 test development lies not in technology, but rather, in time – the most critical factor when lives can be saved and deaths can be avoided.

Kathryn Becker, PhD, Director of Global Scientific Affairs, Innovation and Companion Diagnostic Development, Molecular, at Abbott said, "One of the challenges is developing a test for a novel virus during a pandemic when speed is critical. Abbott brought together a team of experts that worked around the clock to develop quality tests that could be used in a variety of settings, including the point-of-care and hospital laboratories."

In agreement with Becker is DiaSorin's Tabb, whose teams also worked through various obstacles to get the tests into the hands of those who needed them ASAP.

"One of the most significant challenges was the speed of the

spreading pandemic and getting our kit in the hands of laboratories who urgently needed to perform testing. Our teams worked 24 hours a day, seven days a week in both Italy and California to develop the test, perform validations, and receive EUA in the U.S, CE marking in the EU and Health Canada Interim Order authorization."

She added, "Another challenge was the lack of reference material for development and validation. Inherently, there are not well-characterized reference materials available for novel organisms like SARS-CoV-2. Testing can be done in each individual organization, however, comparing assays on paper is impossible without a commutable reference material, and can only be accomplished with direct head-to-head comparisons."

Roche's Osiecki reiterated how the lack of reference materials can hamper test development.

"In the early stages of the COVID-19 outbreak, the primary challenge was developing an NA test to detect the genetic sequence of the SARS-CoV-2 virus without any actual samples from infected patients. It was also a challenge to match the approved specimen types with the reality of demand and supply in the market. Thanks in part to excellent collaboration from the FDA we were able to compress the process from the normal 18 months to about six weeks."

Pandemic 101 – industry lessons learned

As most of the clinical lab industry nods in exasperation that the COVID-19 pandemic appears to be a global concern expected to last much further into 2020, it's also important to consider what the industry has learned through this experience.

Abbott's Moore asserts, "The pandemic has reminded us of the complex nature of diagnosing and treating patients, and the importance of collaboration. In this situation, the industry is dealing with added constraints of testing for a virus that we are learning more about each every day. We need to work together to pool our knowledge in order to be able to adapt to the constraints and challenges of the pandemic."

Kelley from Beckman adds, "There has never been a time where the importance of the clinical laboratory and launching new, high-quality tests has been higher. The pandemic has also reinforced the value of connecting our innovation agenda to the latest needs in public health."

Also extolling the benefits of agency collaboration is DiaSorin's Tabb, who said, "In this time of crisis, we have learned to work even closer with governmental agencies like the FDA to be able to offer high-quality testing options. We have worked in close partnership to ensure testing is made available quickly backed with proper scientific validation and quality controls."

Roche's Osiecki summed up, "One thing the COVID-19 pandemic has brought into sharp relief is the critical role diagnostic testing plays in healthcare emergencies. The value of the clinical lab has become clear in enabling the healthcare industry to manage the crisis, while helping government leaders evaluate how and when the nation can return to normal life.

Influence of COVID-19 tests

After considering what the lab industry has learned thus far from the COVID-19 pandemic, many industry professionals can look to the future with a more-informed forecast about the potential influence that current COVID-19 tests could have on future test development and treatments (i.e. plasma-related therapies).

Becker from Abbott asserts, "Both molecular and serology testing are important for the next phase of battling this virus, including future tests and treatments. Testing can support enrollment of patients into therapeutic clinical studies and may help monitor treatment response. In studies focused on immune therapy, researchers are able to identify blood donors using serological tests."

Beckman's Kelley predicts, "Serologic assays will play an essential role in identifying patients who have been exposed to SARS-CoV-2 and have developed an immune response to the virus. These patients could act as donors of convalescent plasma, which can be used as a source of potentially protective or therapeutic antibodies. There has been a lot of publicity around this strategy, and there are clinical trials taking place right now to understand the clinical effectiveness better."

Tabb from DiaSorin suggests, "We have been working closely with our customers to prioritize next steps and look to future COVID-19 test developments. We will be working to get EUA on more sample types that make testing easier and safer for hospitals. This may also enable the screening of asymptomatic patients for pre-operation testing and population studies."

She continued, "The DiaSorin Group has also launched the LIAISON SARS-CoV-2 S1/S2 IgG assay that can help determine the immunity status of individuals. This may also help test plasma donations to determine eligibility in plasma-related therapies."

Osiedki from Roche summed up, "Intravenous immunoglobulin therapies hold great potential to transfer the antibodies one patient has developed to SARS-CoV-2 to another infected patient with the same blood type and a less robust immune system. High-quality COVID-19 antibody tests can play a significant role in this process by detecting true negative and true positive samples for the antibodies and thus enabling healthcare providers to identify the best candidates to donate blood plasma for the therapy regimen."