Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Analytic and Clinical Performance of Major Commercial Severe Acute Respiratory Syndrome Coronavirus 2 Molecular Assays in the United States

Michelle R. Campbell, MS, MLS(ASCP)CM,BMMa, Matthew J. Binnicker, PhD, D(ABMM)b,*

KEYWORDS
- COVID-19 • SARS-CoV-2 • Emergency use authorization • Molecular
- Analytical sensitivity • Analytical specificity • Clinical performance

KEY POINTS
- Molecular assays to detect SARS-CoV-2 have been rapidly developed in response to the COVID-19 pandemic.
- Comparing the analytical and clinical performance of major commercial SARS-CoV-2 molecular assays provides an objective means of evaluating accuracy before implementation.
- With rare exceptions, molecular assays for the detection of SARS-CoV-2 offer comparable analytical and clinical performance.
- The lessons learned from the COVID-19 pandemic can be applied to the development and implementation of laboratory diagnostics in future outbreaks of novel infectious diseases.

INTRODUCTION
The global coronavirus disease 2019 (COVID-19) pandemic, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has resulted in more than 276 million cases worldwide and greater than 51 million cases in the United States.
alone. With the rapid spread of the virus, the availability of clinical diagnostics to quickly and accurately detect SARS-CoV-2 has been essential to identify positive cases, manage patient care, and guide state and national response plans. To address the need for widespread testing, diagnostic test manufacturers and clinical laboratories have partnered to develop and implement molecular assays at an unprecedented pace. Increasing the testing capabilities in the United States has been facilitated by the issuance of emergency use authorizations (EUAs) by the U.S. Food and Drug Administration (FDA). Molecular diagnostic tests have been the primary means of diagnosing COVID-19, and at the time of preparing this article, greater than 200 SARS-CoV-2 molecular diagnostic tests have received EUA. However, as the number of commercially available SARS-CoV-2 molecular assays has increased, so has the need to understand the differences between these methods. This review compares the analytical and clinical performance of major SARS-CoV-2 molecular assays available in the United States and suggests future topics for consideration.

OVERVIEW OF SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUS 2 MOLECULAR ASSAYS

Selection of Assays

Commercially available SARS-CoV-2 molecular assays were included in this review if they were (1) listed in the 2021 College of American Pathologists’ (CAP) Quality Cross Check: SARS-CoV-2 Molecular Program COV2Q-A Participant Summary, and (2) ≥20 participating laboratories were listed as using the method in the CAP summary. The assays meeting these criteria are summarized in Table 1. The FDA maintains a complete list of individual EUAs for SARS-CoV-2 molecular diagnostic tests on its website. Multiplexed panels were out of scope for this review.

| Classification | Assay (Manufacturer) |
|----------------|----------------------|
| Rapid/POC²     | ID NOW COVID-19 (Abbott Diagnostics Scarborough, Inc., Scarborough, ME) |
|                | Xpert Omni SARS-CoV-2 (Cepheid, Sunnyvale, CA) |
|                | Xpert Xpress SARS-CoV-2 test (Cepheid) |
| Sample-to-answer² | BD SARS-CoV-2 Reagents for BD MAX System (Becton, Dickinson and Company [BD], Franklin Lakes, NJ) |
|                | BioGX SARS-CoV-2 Reagents for BD MAX System (BD) |
|                | BioFire COVID-19 Test (BioFire Defense, LLC, Salt Lake City, UT) |
|                | Simplexa COVID-19 Direct assay (DiaSorin Molecular LLC, Cypress, CA) |
|                | ePlex SARS-CoV-2 Test (GenMark Diagnostics, Inc., Carlsbad, CA) |
|                | ARIES SARS-CoV-2 Assay (Luminex Corporation, Austin, TX) |
|                | TaqPath COVID-19 Combo Kit (Thermo Fisher Scientific, Inc., Waltham, MA) |
| High-throughput² | Abbott RealTime SARS-CoV-2 assay (Abbott Molecular, Des Plaines, IL) |
|                | Aptima SARS-CoV-2 assay (Hologic, Inc., Marlborough, MA) |
|                | Panther Fusion SARS-CoV-2 Assay (Hologic) |
|                | cobas SARS-CoV-2 (Roche Molecular Systems, Inc., Pleasanton, CA) |
|                | Amplitude Solution with the TaqPath COVID-19 High-Throughput Combo Kit (Thermo Fisher Scientific) |

Abbreviations: POC, point-of-care; TAT, turnaround time.

² TAT of ≤1 h; often single-sample throughput.

² TAT of ~1 to 4 h; throughput of up to several dozen samples/run.

² TAT of >3 to 4 h; throughput of greater than 450 samples/run.
Once molecular SARS-CoV-2 assays were identified for inclusion, they were further divided into one of the following 3 categories, similar to those applied by Fung and colleagues: (1) rapid/point-of-care (POC), (2) sample-to-answer, and (3) high-throughput. Rapid/POC assays were those with a turnaround time (TAT) of \( \leq 1 \) hour, the capability to be performed in a setting with a Clinical Laboratory Improvement Amendments (CLIA) Certificate of Waiver, and having a typical throughput of 1 sample/run. Sample-to-answer platforms were those with a TAT of approximately 1 to 4 hours and a capacity to run several dozen samples/run. The final category consisted of assays performed using a high-throughput platform with the capacity to run more than 450 samples/day, but a typical TAT of greater than 3 to 4 hours (see Table 1).

**Molecular Technologies**

To date, most SARS-CoV-2 molecular assays have used real-time reverse transcription–polymerase chain reaction (RT-PCR) technology. However, additional molecular technologies including transcription-mediated amplification (TMA), nested PCR, reverse transcription loop-mediated isothermal amplification (RT-LAMP), or RT-PCR with electrochemical detection have also been developed (Table 2).

**Molecular Targets**

Molecular assays for the detection of SARS-CoV-2 often include greater than 1 gene target. Common targets include the RNA-dependent RNA polymerase (RdRp), nucleocapsid phosphoprotein (N), spike glycoprotein (S), small envelope protein (E), and open reading frame (ORF) genes. Of the assays included in this review, 6 target a single gene, whereas the remainder target \( \geq 2 \) genes (see Table 2).

**Acceptable Specimen Types**

Nasopharyngeal (NP) swabs in viral transport media or phosphate-buffered saline have been considered the gold-standard specimen type throughout the COVID-19 pandemic, and NP swabs are considered acceptable for all assays included in this review. In addition to NP swabs, many assays allow for other upper respiratory swab specimens to be tested, including oropharyngeal, nasal, and midturbinate swabs. A full list of acceptable specimen types are included in Table 2.

**ANALYTICAL PERFORMANCE**

**Analytical Sensitivity**

The analytical sensitivity (ie, limit of detection [LoD]) of a molecular assay is the lowest concentration of a target that can be detected in at least 19 (95%) of 20 replicates, as defined by the FDA Molecular Diagnostic Template for Commercial Manufacturers. The manufacturers’ established LoDs of major commercial SARS-CoV-2 molecular assays are summarized in Table 3. Although it is not possible to directly compare LoDs across all SARS-CoV-2 tests because of varying reporting units (eg, copies/mL vs genomic equivalents/mL), the analytical sensitivity varies across commercially available tests. Among assays with analytical sensitivity reported in copies/mL, the manufacturer’s established LoD ranges from \( \sim 30 \) copies/mL (cobas SARS-CoV-2) to 750–1000 copies/mL (ePlex SARS-CoV-2).

Several groups have evaluated these methods and performed independent studies to confirm the LoD against the manufacturers’ claims. In many studies, the LoDs were confirmed to be at or below the analytical sensitivity defined by the manufacturers. Exceptions included the ID NOW COVID-19 and the TaqPath COVID-19
| Assay                                      |Platforms                                      | Method                        | Gene Target(s) | Approved Specimen(s)                     |
|-------------------------------------------|-----------------------------------------------|-------------------------------|----------------|------------------------------------------|
| ID NOW COVID-19                           |ID NOW Instrument                             |RT, Isothermal amplification  |RdRp            |Nasal, NP, throat swabs                   |
| Abbott RealTime SARS-CoV-2 assay          |Abbott m2000 System                           |Real-time RT-PCR               |RdRp, N         |NP, OP, nasal swabs; BAL                  |
| BD SARS-CoV-2 Reagents for BD MAX System  |BD MAX System                                 |Real-time RT-PCR               |N1, N2          |NP, anterior nasal, MT, OP swabs; NP wash/aspirate, nasal aspirates |
| BioGX SARS-CoV-2 Reagents for BD MAX System|BD MAX System                                 |Real-time RT-PCR               |N1, N2          |NP, OP, OP swabs                         |
| BioFire COVID-19 Test                     |FilmArray 2.1 and FilmArray Torch Instrument Systems |RT, Nested multiplex PCR       |ORF1ab<sup>a</sup>, ORF8 |NP, OP, midturbinate, anterior nasal swabs; sputum, endotracheal aspirate, BAL or mini-BAL |
| Xpert Omni SARS-CoV-2                     |GeneXpert Omni System                         |Real-time RT-PCR               |E, N2           |NP, OP, anterior nasal, MT swabs; nasal wash/aspirate |
| Xpert Xpress SARS-CoV-2 test              |GeneXpert Dx and GeneXpert Infinity Systems  |Real-time RT-PCR               |E, N2           |NP, OP, anterior nasal, MT swabs; nasal wash/aspirate |
| Simplexa COVID-19 Direct assay            |LIAISON MDX                                   |Real-time RT-PCR               |ORF1ab, S       |NP, anterior nasal swabs; nasal wash/aspirate, BAL |
| ePlex SARS-CoV-2 Test                     |ePlex instrument                              |RT-PCR and electrochemical detection |N<sup>a</sup>    |NP swabs                                  |
| Aptima SARS-CoV-2 assay                   |Panther and Panther Fusion systems           |TMA, chemiluminescent         |ORF1ab<sup>a</sup> |NP, OP, anterior nasal, MT swabs; NP wash/aspirate, nasal aspirate |
| Panther Fusion SARS-CoV-2 Assay           |Panther Fusion System                         |Real-time RT-PCR               |ORF1ab<sup>a</sup> |NP, OP, MT, nasal swabs; NP wash/aspirate, nasal wash, BAL |
| ARIES SARS-CoV-2 Assay                    |ARIES instrument                              |RT-PCR                        |ORF1 a/b, E     |NP, OP, nasal swabs; self-collected anterior nasal (nasal) swabs |
| cobas SARS-CoV-2                          |cobas 6800 and 8800 Systems                   |Real-time RT-PCR               |ORF1 a/b, E     |NP, OP, nasal swabs; self-collected anterior nasal (nasal) swabs |
| Test                      | Amplification Method            | Sample Type                      |
|--------------------------|---------------------------------|----------------------------------|
| TaqPath COVID-19 Combo Kit | “Authorized real-time PCR instrument” | Real-time RT-PCR, Orf1ab, S, N NP and anterior nasal swabs |
| TaqPath COVID-19 Combo Kit | “Authorized real-time PCR instrument” | Real-time RT-PCR, Orf1ab, S, N NP, OP, MT, nasal swabs; NP aspirate, BAL, self-collected nasal swabs |

**Abbreviations:**
- BAL, bronchoalveolar lavage
- E, small envelope
- MT, midturbinate
- N, nucleocapsid phosphoprotein
- NP, nasopharyngeal
- OP, oropharyngeal
- Orf/ORF, open reading frame
- PCR, polymerase chain reaction
- RdRp, RNA-dependent RNA polymerase
- RT, reverse transcription
- S, spike glycoprotein
- TMA, transcription-mediated amplification

*a* Targets in 2 regions of a single gene.
Table 3
Analytical and clinical performance of major SARS-CoV-2 molecular assays

| Assay                              | Analytical Performance | Clinical Performance |
|------------------------------------|------------------------|----------------------|
|                                    | Analytical Sensitivity (LoD) | Analytical Specificity (Cross-Reactivity) (Observed, Y/N) | Positive Percent Agreement | Negative Percent Agreement |
|                                    | Claimed Observed        | Claimed Observed, Y/N | Claimed Observed            | Claimed Observed, Observed |
| ID NOW COVID-19                    | 125 GE/mL 262–20,000 copies/mL | N NA 48%–94% 100%     | 100% 98.4%–100%              |
|                                    |                        |                      | Abbott; Cradic et al,57 2020; Dinnes et al,58 2020; Fung et al,6 2020; Lee & Song,65 2021; Lephart, et al,41 2021; Mitchell & George,59 2020; Rhoads et al,60 2020; Zhen et al,42 2020 |
| Abbott RealTime SARS-CoV-2 assay   | 100 copies/mL 32–53 copies/mL | N N 93%–96% 100%     | 100% 100%                     |
| BD SARS-CoV-2 Reagents for BD MAX System | 640 GC/mL 251 copies/mL | N NA 100%            | Degli-Angeli et al,43 2020; Fung et al,6 2020; Lephart et al,41 2021 |
| BioGX SARS-CoV-2 Reagents for BD MAX System | 40 GE/mL NA          | N NA 90%–100%        | 100% 100%                     |
| BioFire COVID-19 Test              | 330 GC/mL 125–165 copies/mL 500 GE/mL | N NA 100% 98.7%–100% | 100% 100%                     |
|                                    |                        |                      | Eckbo et al,46 2021; Smith et al,45 2020 |
| Xpert Omni SARS-CoV-2              | 400 copies/mL NA       | Y<sup>b</sup> NA     | 100% 100%                     |
| Xpert Xpress SARS-CoV-2 test       | 0.0200 PFU/mL 0.01 PFU/mL 8.26–100 copies/mL | Y<sup>b</sup> Y<sup>c</sup> 97.8% 98.3%–100% | 95.6% 95.8%–100%               |
| Simplexa COVID-19 Direct assay     | 500 copies/mL<sup>d</sup> 39 ± 23–521 copies/mL | Y<sup>e</sup> N 96.7%–100% 88%–100% | 100% 95.5%–100%               |
| **Assay**                                      | **LoD**                  | **Range**                          | **PPA** | **LoD** | **Range** | **PPA** | **LoD** | **Range** | **PPA** | **References** |
|-----------------------------------------------|--------------------------|------------------------------------|---------|---------|-----------|---------|---------|-----------|---------|----------------|
| ePlex SARS-CoV-2 Test                         | 750–1000 copies/mL       | 100–1000 copies/ mL               | **Y**   | NA      | 94.4%     | 91.4%– 100% | 100%    | 100%     | Fung, et al. [5] 2020; Uhteg et al, [51] 2020; Zhen et al, [49] 2020; Zhen et al, [42] 2020 |
| Aptima SARS-CoV-2 assay                       | 0.01 TCID$_{50}$/ mL     | 0.01–0.003 TCID$_{50}$/ mL         | N       | N       | 100%      | 94.7%– 100% | 98.2%   | 98.7%– 100% | Pham et al, [62] 2020; Schneider et al, [53] 2021; Smith et al, [45] 2020; Yanson et al, [44] 2021 |
| Panther Fusion SARS-CoV-2 Assay               | 0.01 TCID$_{50}$/ mL     | 62.5–612 copies/ mL               | N       | NA      | 100%      | 98.7%– 100% | 100%    | 96%– 100% | Fung et al, [6] 2020; Smith et al, [45] 2020; Zhen et al, [49] 2020 |
| ARIES SARS-CoV-2 Assay                        | 180,000 NDU/ mL          | 1000–10,000 copies/ reaction range| N       | NA      | 100%      | 26.7%– 100% | 100%    | 100%     | Lee et al, [62] 2021; Tanida et al, [54] 2020 |
| cobas SARS-CoV-2                              | 25–46 copies/ mL         | ≤ 10–298 copies/ N mL             | NA      | **Y**   | 100%      | 94.2%– 100% | 100%    | 90%– 100% | Cradic et al, [57] 2020; Fung et al, [6]; Lee et al, [62] 2021; Pujadas et al, [64] 2020; Yanson et al, [44] 2021 |
| Amplitude Solution with the TaqPath COVID-19 High-Throughput Combo Kit | 250 GCE/mL               | NA                                 | **Y**   | NA      | 100%      | 85.3%– 100% | 100%    | 70%– 100% | Lee et al, [62] 2021; Matsumura et al, [55] 2021 |
| TaqPath COVID-19 Combo Kit                    | 10 GCE/ reaction          | 767 GC/mL                          | **Y**   | NA      | 100%      | 85.3%– 100% | 100%    | 70%– 100% | Lee et al, [62] 2021; Matsumura et al, [55] 2021 |

**Abbreviations:** GC, genomic copies; GCE, genome copy equivalents; GE, genomic equivalents; LoD, limit of detection; N, no; NA, information not available; NDU, nucleic acid amplification test-detectable units; PFU, plaque-forming unit; TCID$_{50}$, median tissue culture infectious dose; Y, yes.

- a Varies depending on the method of evaluation (eg, contrived vs clinical samples).
- b E primers and probes will detect human SARS-CoV.
- c E primers and probe detected SARS-CoV, resulting in a presumptive positive test result.
- d Specific to nasopharyngeal swabs.
- e Primer and/or probe sequence homology with SARS-CoV detected by *in silico* analysis, not observed during laboratory testing.
- f Varies depending on specimen type.
- g Varies depending on workflow used (with vs without sample delivery device).
- h Primer and/or probe sequence homology with SARS-CoV by *in silico* analysis, also observed in laboratory testing.
- i Overall PPA (PPA varies for individual gene targets).
- j Varies depending on the target and method of analysis.
- k Only confirmed through bridging study.
- l Primer and/or probe sequence homology for N gene with *Neisseria elongata*. Given low homology with N gene reverse primer and probe, the risk for nonspecific amplification was determined to be low. Primer and/or probe sequence homology was also identified for “different isolates of the same species” (eg, strains of *Bacillus anthracis*), but amplification was deemed unlikely to occur.
Combo Kit, both of which demonstrated higher LoDs (262–20,000 and 767 copies/mL, respectively) during independent evaluations. \(^6\, 41,\, 42,\, 55\) Of the rapid/POC assays, several studies have demonstrated that the Xpert Xpress SARS-CoV-2 test showed superior sensitivity (\(\sim 10–100\) copies/mL) compared with the ID NOW COVID-19 assay (262–20,000 copies/mL). \(^6\, 41,\, 42,\, 47,\, 55\) Independent studies generally confirmed the claimed analytical sensitivity of sample-to-answer assays, which range from approximately 40 to 1000 copies/mL. In contrast to several other sample-to-answer assays, the ePlex SARS-CoV-2 test has been shown to inconsistently detect samples with lower viral concentrations than the manufacturer’s claimed LoD of 750 to 1000 copies/mL. Zhen and colleagues demonstrated that at concentrations of 1000 and 500 copies/mL, a decrease was noted in percent detected from 100% to 70%. \(^49\) All high-throughput assays demonstrated excellent analytical sensitivity, with a study by Fung and colleagues determining the LoD for the cobas SARS-CoV-2 assay to be \(\leq 10\) copies/mL. \(^6\) Yanson and colleagues established a higher LoD for this assay at 298 copies/mL, although details for the lowest concentration tested were unavailable and the LoDs determined for other assays (eg, Aptima SARS-CoV-2 assay) were also significantly higher (\(\geq 4\) times) than observed in other studies. \(^44,\, 45,\, 52,\, 53\)

**Inclusivity**

Inclusivity studies can be performed by *in silico* analysis with the purpose of identifying the sequences that will be detected by the assay. Per FDA guidance, assays should detect 100% of SARS-CoV-2 strains, with a required risk assessment describing the potential impact on assay performance should sequences with less than 100% homology be identified during inclusivity studies. \(^38\) Of the reviewed assays, a small number of manufacturers evaluated inclusivity by performing laboratory testing in addition to *in silico* analysis. Manufacturers claimed 86.4% to 100% alignment of oligonucleotide primer and probe sequences with SARS-CoV-2 sequences available in public databases, such as NCBI and GenBank. No manufacturers predicted an impact on the ability of their assay to detect published SARS-CoV-2 strains, including those with less than 100% alignment with available SARS-CoV-2 sequences. \(^6\, 21,\, 39,\, 40\) It must be noted that reported coverage will vary based on the number of sequences available for comparison at the time the *in silico* analysis is performed. This is especially important as new variants of SARS-CoV-2 emerge.

**Analytical Specificity**

**Cross-reactivity**

The analytical specificity of molecular diagnostics can be evaluated through cross-reactivity studies. The purpose of these studies is to ensure that the molecular assay does not react with similar, potentially related pathogens or other organisms that may be present in clinical specimens. The FDA provides a list of recommended organisms to include in cross-reactivity studies by *in silico* analysis and laboratory testing. This includes other members of the family *Coronaviridae* (eg, human coronaviruses 229E, OC43, HKU1, NL63, SARS-CoV, and MERS-CoV) as well as organisms that are likely to be present in respiratory specimens. Recommendations are provided for follow-up studies should significant homology (\(>80\)%) with a potential cross-reactive sequence be identified. \(^38\)

Table 3 summarizes the results of cross-reactivity studies and *in silico* analyses performed by manufacturers to ensure analytical specificity. Multiple manufacturers reported the potential for cross-reactivity with coronaviruses known to infect animals (eg, bat and pangolin coronaviruses) as well as SARS-CoV, which is not unexpected because of high genetic homology with SARS-CoV-2. No manufacturers noted cross-
reactivity with MERS-CoV or other organisms likely to be present in respiratory samples. Independent evaluation of commercial assays has not revealed significant cross-reactivity that would raise concern for false-positive results because of the presence of nonspecific sequences.

**CLINICAL PERFORMANCE**

**Percent Agreement**

In addition to analytical studies, the clinical performance must also be evaluated when developing molecular assays for SARS-CoV-2. The FDA recommends calculating positive percent agreement (PPA) in comparison to a high sensitivity EUA RT-PCR test. Furthermore, it is recommended that the comparator assay uses an "internationally recognized standard" or the FDA’s SARS-CoV-2 Reference Panel to establish the sensitivity of the assay. Recommendations for assessing the agreement of negative results (ie, negative percent agreement [NPA]) are comparison with an EUA RT-PCR test using prospectively collected samples or "as agreement with expected results if samples were collected from individuals known to be negative for SARS-CoV-2 (eg, collected before December 2019)." The comparator EUA RT-PCR does not need to have identical targets to the assay being evaluated. The acceptance criteria for positive and negative agreement is ≥ 95%.

Table 3 summarizes available information on clinical performance, as demonstrated by PPA and NPA between methods. Manufacturer claims for overall PPA ranged from 90% to 100%. The ARIES SARS-CoV-2 assay demonstrated only 25% to 40% agreement for the ORF1ab target, but 100% agreement for the N target; however, only 1 of the 2 targets must be detected for the assay result to be interpreted as positive. During independent evaluations, the observed PPA for most commercial assays was similar to manufacturer claims with the exception of the ID NOW COVID-19 device and ARIES SARS-CoV-2 assay, which both claimed 100% PPA and demonstrated PPA ranging from 48% to 94% and 26.7% to 100% in published studies, respectively. Possible explanations for the differences observed with the ID NOW COVID-19 PPA may be variations in the comparator assays and the fact that the manufacturer evaluated PPA at 2 to 5 times the LoD, while the referenced studies may have included samples with lower viral loads. The study that determined the ARIES SARS-CoV-2 assay PPA to be 26.7% was based on comparison with the Xpert Xpress SARS-CoV-2 as the reference method and specifically evaluated weakly positive samples (ie, Ct > 34 in the Xpert Xpress SARS-CoV2 assay). When only strongly positive samples (ie, Ct < 34 for at least one target gene in the Xpert Xpress SARS-CoV2 assay) were included in the analysis, PPA increased to 100%. Manufacturer claims for NPA ranged from 95.6% to 100%. Most observed NPAs were similar to manufacturer claims, with the exception of the TaqPath COVID-19 Combo Kit, for which a single study observed 70% NPA based on consensus of 4 molecular assays.

Comparison with Clinical Evaluation

Although the "gold standard" for the diagnosis of SARS-CoV-2 infections is molecular testing, there is limited information on the clinical performance of these assays through comparison with clinical findings and radiologic evidence of COVID-19. In particular, chest computerized tomography (CT) has been suggested as a complementary diagnostic test for patients with suspected SARS-CoV-2 infection. Studies in which patients underwent both RT-PCR testing and chest CT imaging suggest that chest CT is highly sensitive for the diagnosis of SARS-CoV-2 infection and can identify
likely cases of SARS-CoV-2 that were missed by RT-PCR. Two studies of patients in Wuhan, China, demonstrated 97% sensitivity of chest CT using positive RT-PCR results as the reference standard. In another study, an in-depth evaluation of 5 patients with initial negative SARS-CoV-2 RT-PCR was performed and showed that chest CT findings were consistent with a SARS-CoV-2 infection before a positive RT-PCR result. Although studies directly evaluating SARS-CoV-2 RT-PCR results with imaging studies and other clinical/epidemiologic findings are few in number, there are now published data showing that in patients with COVID-19 (ie, as determined by clinical and/or radiology findings), SARS-CoV-2 molecular testing may need to be performed multiple times, or on alternate sample types (eg, bronchoalveolar lavage fluid) to yield a positive result.

It has also been demonstrated that the sensitivity of commercially available molecular assays may depend on when testing is performed during the course of disease. Theoretically, tests detecting SARS-CoV-2 RNA will have the lowest false-negative rate when the viral load is at its highest. He and colleagues proposed that peak viral loads occur around the time of symptom onset, which is typically 3 to 5 days post-exposure. This suggests that rapid/POC tests, such as the Xpert Xpress SARS-CoV-2 and ID NOW COVID-19 tests, are likely to provide the highest negative predictive value when performed in symptomatic patients who are early in their disease course. As the clinical course progresses and viral load decreases, the risk for false-negative results increases and using an assay with the lowest (ie, best) analytical sensitivity becomes increasingly important.

DISCUSSION

Although the rapid development and implementation of molecular assays to detect SARS-CoV-2 has addressed the acute need for diagnostic tools during the COVID-19 pandemic, there are remaining questions to consider. Of particular concern is whether currently available molecular assays will continue to detect emerging SARS-CoV-2 variants. The World Health Organization (WHO) continues to partner with leading institutions and experts to identify and classify emerging SARS-CoV-2 variants. These strains are classified as “variants of concern” (VOC) or “variants of interest” (VOI). According to WHO, VOCs are associated with increased transmissibility and/or virulence, a change in COVID-19 epidemiology or disease presentation or compromise the effectiveness of “public health and social measures or available diagnostics, vaccines, therapeutics.” As of December 2021, 5 VOCs have been identified and include lineages B.1.1.7 (alpha), B.1.351 (beta), P.1 (gamma), B.1.617.2 (delta), and B.1.1.529 (omicron) all of which have been reported in the United States. In early 2021, the FDA issued a letter to clinical laboratorians and health care providers warning that SARS-CoV-2 variants may not be detected by molecular tests, potentially resulting in false-negative results. Three EUA molecular tests—of which one was included in our review—were identified as potentially limited in their ability to detect variant strains. According to the FDA letter, the S gene target of the TaqPath COVID-19 Combo Kit may have compromised sensitivity in the presence of the B.1.1.7 (alpha) variant, although both the FDA and Thermo Fisher Scientific, Inc., noted that the overall sensitivity of the test is unlikely to be impacted because of the inclusion of multiple targets. Furthermore, the manufacturer theorizes that results suggesting S gene dropout (69–70del) may assist in the identification of samples infected with the alpha or omicron variant. Of note is the BA.2 descendant lineage of omicron, which does not display the 69-70del and would therefore not be identified by dropout of the S gene. In addition to mutations in the S gene, mutations in the N gene of the
omicron variant may impact detection in molecular tests employing this target. The molecular tests included in our review were not among those identified by the FDA as expected to fail to detect SARS-CoV-2 omicron. The inclusion of multiple gene targets is advantageous and may facilitate the identification of variant strains. The continued emergence of SARS-CoV-2 variants emphasizes the importance of assay design, and highlights the need for redundancy within the test, either by targeting multiple genes or at least 2 unique regions within the same gene.

It must also be noted that several features of COVID-19, such as the period of viral shedding and window of transmission, are not fully defined. With this in mind, a key aspect to consider when assessing the clinical performance of molecular SARS-CoV-2 assays is whether a positive result indicates an active infection or simply the presence of viral RNA from a resolved infection. A study evaluating hospitalized patients with COVID-19 noted that throat swabs and sputum samples remained positive for 2 and 3 weeks, respectively, despite the resolution of COVID-19 symptoms. Furthermore, replication-competent virus was not recovered from these patients beyond day 8 of symptoms, suggesting the period of active viral infection is likely shorter compared with detection of viral RNA. In the future, the development of new assays that can help to discriminate active from past infections should be a focus for test manufacturers. This will be important to ensure proper allocation of limited resources, avoid unnecessary medical costs for patients, and only isolate patients for the period that they represent a risk for ongoing viral transmission.

Lastly, the frequency of false-negative molecular SARS-CoV-2 results requires further study. A study by Green and colleagues evaluated a large cohort of 27,377 SARS-CoV-2 molecular assays from 22,338 patients with testing performed by New York-Presbyterian laboratories and included a review of patients with repeat testing (n = 3432 patients [2413 initial negative results, 802 initial positive results]). Most testing was performed using the Roche SARS-CoV-2 test performed on the cobas 6800, with a smaller proportion performed using the ID NOW, Xpert Xpress, Panther Fusion, and in-house developed assays. In patients with repeat testing, 60 oscillated between positive and negative results, emphasizing the need for judicious interpretation of single-test laboratory results in the context of clinical symptoms.

LIMITATIONS

This review is meant to provide an overview of the analytical and clinical performance of major commercial SARS-CoV-2 molecular assays in the United States. It is not intended to be an exhaustive summary of all available publications and relevant data. The observed analytical sensitivity (ie, LoD) data presented in Table 3 were not always evaluated and published in the same units and/or using the same specimen type(s) as studies outlined in manufacturers’ instructions for use, thereby limiting a direct comparison in many cases. In addition, information on observed analytical specificity (ie, cross-reactivity) was not available for several assays. Finally, the comparator assays used to determine clinical performance (ie, PPA/NPA) varied between studies, which further limits direct comparisons (see Table 3).

SUMMARY

Laboratory testing for SARS-CoV-2 has played a key role in the response to the COVID-19 pandemic. The rapid development of molecular assays has been crucial to identify positive cases, limit transmission of the virus, and manage patient care decisions. Overall, commercially available molecular assays for the detection of SARS-CoV-2 have demonstrated comparable performance. However, the sensitivity of these
assays has been shown to vary, especially when performed at different time points during the course of COVID-19 disease and on different specimen types (eg, NP swabs vs oropharyngeal swabs). Although rapid, POC molecular tests may assist in making a timely diagnosis of COVID-19, a negative result may not definitively rule out the disease and follow-up testing using a laboratory-based assay may be required.\textsuperscript{42,59,82,83} Future test development should focus on variant detection and discrimination, as well as differentiating active viral infection from persistent detection of viral RNA.

CLINICS CARE POINTS

- Greater than 200 SARS-CoV-2 molecular assays have received emergency use authorization by the U.S. Food and Drug Administration.
- In general, the analytic and clinical performance of commercially available molecular SARS-CoV-2 assays has been shown to be comparable by an independent evaluation of these methods.
- The selection of an appropriate commercial molecular SARS-CoV-2 assay is largely dependent on throughput, turnaround time, and cost considerations.
- The emergence of variant strains of SARS-CoV-2 may impact the performance characteristics of molecular assays, particularly those designed to target a single gene.
- Current SARS-CoV-2 molecular assays are unable to differentiate between active infection and persistent viral nucleic acid, which may lead to unnecessary isolation of non-infectious patients.

DISCLOSURE

M.J. Binnicker is a scientific advisory board member for DiaSorin Molecular and Mammoth Biosciences. M.R. Campbell has nothing to disclose.

REFERENCES

1. Coronavirus Resource Center. Johns Hopkins University & Medicine. Available at: https://coronavirus.jhu.edu/. Accessed December 21, 2021.
2. COVID Data Tracker. Centers for Disease Control and Prevention. Available at: https://covid.cdc.gov/covid-data-tracker/#variant-proportions. Accessed December 22, 2021.
3. In Vitro Diagnostics EUAs - Molecular Diagnostic Tests for SARS-CoV-2. U.S. Food & Drug Administration. Available at: https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas-molecular-diagnostic-tests-sars-cov-2#individual-molecular. Accessed June 13, 2021.
4. SARS-CoV-2 Proficiency Testing and Quality Improvement Programs. College of American Pathologists. SARS-CoV-2 Proficiency Testing and Quality Improvement Programs. Accessed June 13, 2021.
5. COV2Q-A 2021 Participant Summary; Quality Cross Check-SARS-CoV-2, Molecular. College of American Pathologists; 2021.
6. Fung B, Gopez A, Servellita V, et al. Direct comparison of SARS-CoV-2 analytical limits of detection across seven molecular assays. J Clin Microbiol 2020;58(9): e01535-20.
7. Guidance for SARS-CoV-2 Point-of-Care and Rapid Testing. Centers for Disease Control and Prevention. 2021. Available at: https://www.cdc.gov/coronavirus/2019-ncov/lab/point-of-care-testing.html. Accessed June 13, 2021.
8. ID NOW™ COVID-19 Product Insert [package insert]. Scarborough (ME): Abbott Diagnostics Scarborough, Inc.; 2020.
9. Abbott RealTime SARS-CoV-2 [package insert]. Des Plaines (IL): Abbott Molecular, Inc.; 2020.
10. ID NOW COVID-19 [package insert]. Scarborough (ME): Abbott Diagnostics Scarborough, Inc.; 2020.
11. BD SARS-CoV-2 Reagents for BD MAXTM System [package insert]. Sparks (MD): Becton, Dickinson and Company; 2021.
12. BD BioGX SARS-CoV-2 Reagents for BD MAXTM System [package insert]. Sparks (MD): Becton, Dickinson and Company; 2020.
13. BioFire® COVID-19 Test Instructions for Use [package insert]. Salt Lake City (UT): BioFire Defense, LLC; 2020/2021.
14. Xpert® Omni SARS-CoV-2 Instructions for Use [package insert]. Sunnyvale (CA): Cepheid; 2021.
15. Xpert® Xpress SARS-CoV-2 Instructions for Use [package insert]. Sunnyvale (CA): Cepheid; 2021.
16. Simplexa™ COVID-19 Direct [package insert]. Cypress (CA): DiaSorin Molecular, LLC; 2021.
17. ePlex®SARS-CoV-2 Test Assay Manual [package insert]. Carlsbad (CA): GenMark Diagnostics, Inc.; 2020.
18. ARIES®SARS-CoV-2 Assay [package insert]. Austin (TX): Luminex Corporation; 2020.
19. Aptima® SARS-CoV-2 Assay (Panther® System) [package insert]. San Diego (CA): Hologic, Inc.; 2020.
20. SARS-CoV-2 Assay (Panther Fusion® System). [package insert]. San Diego (CA): Hologic, Inc.; 2020.
21. TaqPath™ COVID-19 Combo Kit Instructions for Use [package insert]. Pleasanton (CA): Life Technologies Corporation; 2020.
22. TaqPath™ COVID-19 Combo Kit. Thermo Fisher Scientific. Available at: https://www.thermofisher.com/order/catalog/product/A47814#/A47814. Accessed June 23, 2021.
23. TaqPath™ COVID-19 High Throughput Combo Kit. Thermo Fisher Scientific. Available at: https://www.thermofisher.com/order/catalog/product/A49869#/A49869. Accessed June 25, 2021.
24. ID NOW COVID-19 EUA letter of authorization. U.S. Food & Drug Administration. 2020. Available at: https://www.fda.gov/media/136522/download. Accessed June 23, 2021.
25. Abbott RealTime SARS-CoV-2 assay EUA letter of authorization. U.S. Food & Drug Administration. 2020. Available at: https://www.fda.gov/media/136255/download. Accessed June 23, 2021.
26. BioGX SARS-CoV-2 Reagents for BD MAX System EUA letter of authorization. U.S. Food & Drug Administration. 2020. Available at: https://www.fda.gov/media/136650/download. Accessed June 23, 2021.
27. BD SARS-CoV-2 Reagents for BD MAX System EUA letter of authorization. U.S. Food & Drug Administration. 2021. Available at: https://www.fda.gov/media/136813/download. Accessed June 23, 2021.
28. BioFire COVID-19 Test EUA letter of authorization. U.S. Food & Drug Administration. 2021. Available at: https://www.fda.gov/media/136356/download. Accessed June 23, 2021.

29. Xpert Omni SARS-CoV-2 EUA letter of authorization. U.S. Food & Drug Administration. 2021. Available at: https://www.fda.gov/media/144029/download. Accessed June 23, 2021.

30. Xpert Xpress SARS-CoV-2 EUA letter of authorization. U.S. Food & Drug Administration. 2021. Available at: https://www.fda.gov/media/136316/download. Accessed June 23, 2021.

31. ePlex SARS-CoV-2 Test EUA letter of authorization. U.S. Food & Drug Administration. 2020. Available at: https://www.fda.gov/media/136283/download. Accessed June 23, 2021.

32. Panther Fusion SARS-CoV-2 assay EUA letter of authorization. U.S. Food & Drug Administration. 2020. Available at: https://www.fda.gov/media/136153/download. Accessed June 23, 2021.

33. ARIES SARS-CoV-2 Assay EUA letter of authorization. U.S. Food & Drug Administration. 2020. Available at: https://www.fda.gov/media/136694/download. Accessed June 23, 2021.

34. Aptima SARS-CoV-2 assay EUA letter of authorization. U.S. Food & Drug Administration. 2021. Available at: https://www.fda.gov/media/138097/download. Accessed June 23, 2021.

35. TaqPath COVID-19 Combo Kit EUA letter of authorization. U.S. Food & Drug Administration. 2020. Available at: https://www.fda.gov/media/136113/download. Accessed June 23, 2021.

36. Cobas SARS-CoV-2 EUA letter of authorization. U.S. Food & Drug Administration. 2021. Available at: https://www.fda.gov/media/136046/download. Accessed June 23, 2021.

37. Amplitude Solution with TaqPath COVID-19 High-Throughput Combo Kit EUA letter of authorization. U.S. Food and Drug Administration. 2021. Available at: https://www.fda.gov/media/147535/download. Accessed June 25, 2021.

38. Molecular Diagnostic Template for Commercial Manufacturers. U.S. Food & Drug Administration. Published 2020. Accessed June 23, 2021.

39. cobas® SARS-CoV-2 [package insert]. Indianapolis (IN): Roche Diagnostics; 2021.

40. Amplitude™ Solution with the TaqPath™ COVID-19 High-Throughput Combo Kit Instructions for Use [package insert]. Pleasanton (CA): Thermo Fisher Scientific; 2021.

41. Lephart PR, Bachman MA, LeBar W, et al. Comparative study of four SARS-CoV-2 Nucleic Acid Amplification Test (NAAT) platforms demonstrates that ID NOW performance is impaired substantially by patient and specimen type. Diagn Microbiol Infect Dis 2021;99(1):115200.

42. Zhen W, Smith E, Manji R, et al. Clinical evaluation of three sample-to-answer platforms for detection of SARS-CoV-2. J Clin Microbiol 2020;58(8).

43. Degli-Angeli E, Dragavon J, Huang ML, et al. Validation and verification of the Abbott RealTime SARS-CoV-2 assay analytical and clinical performance. J Clin Virol 2020;129:104474.

44. Yanson K, Lavier W, Neely L, et al. Performance evaluation of the BD SARS-CoV-2 reagents for the BD MAX™ system. medRxiv 2021;59(12):e0101921.

45. Smith E, Zhen W, Manji R, et al. Analytical and clinical comparison of three nucleic acid amplification tests for SARS-CoV-2 Detection. J Clin Microbiol 2020;58(9).
46. Eckbo EJ, Locher K, Caza M, et al. Evaluation of the BioFire(R) COVID-19 test and Respiratory Panel 2.1 for rapid identification of SARS-CoV-2 in nasopharyngeal swab samples. Diagn Microbiol Infect Dis 2021;99(3):115260.

47. Loeffelholz MJ, Alland D, Butler-Wu SM, et al. Multicenter Evaluation of the Cepheid Xpert Xpress SARS-CoV-2 Test. J Clin Microbiol 2020;58(8):e00926-20.

48. Wolters F, van de Bovenkamp J, van den Bosch B, et al. Multi-center evaluation of cepheid xpert(R) xpress SARS-CoV-2 point-of-care test during the SARS-CoV-2 pandemic. J Clin Virol 2020;128:104426.

49. Zhen W, Manji R, Smith E, et al. Comparison of four molecular in vitro diagnostic assays for the detection of SARS-CoV-2 in nasopharyngeal specimens. J Clin Microbiol 2020;58(8).

50. Bordi L, Piralla A, Lalle E, et al. Rapid and sensitive detection of SARS-CoV-2 RNA using the Simplexa COVID-19 direct assay. J Clin Virol 2020;128:104416.

51. Uhleg K, Jarrett J, Richards M, et al. Comparing the analytical performance of three SARS-CoV-2 molecular diagnostic assays. J Clin Virol 2020;127:104384.

52. Pham J, Meyer S, Nguyen C, et al. Performance characteristics of a High-throughput automated transcription-mediated amplification test for SARS-CoV-2 Detection. J Clin Microbiol 2020;58(10):e01669-20.

53. Schneider M, Iftner T, Ganzenmueller T. Evaluation of the analytical performance and specificity of a SARS-CoV-2 transcription-mediated amplification assay. J Virol Methods 2021;294:114182.

54. Tanida K, Koste L, Koenig C, et al. Evaluation of the automated cartridge-based ARIES SARS-CoV-2 Assay (RUO) against automated Cepheid Xpert Xpress SARS-CoV-2 PCR as gold standard. Eur J Microbiol Immunol (Bp) 2020;10(3):156–64.

55. Matsumura Y, Shimizu T, Noguchi T, et al. Comparison of 12 Molecular Detection Assays for Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). J Mol Diagn 2021;23(2):164–70.

56. Abbott RealTime SARS-CoV-2 Instructions for Use [package insert]. Des Plaines (IL): Abbott Molecular, Inc.; 2020.

57. Cradic K, Lockhart M, Ozbolt P, et al. Clinical evaluation and utilization of multiple molecular in vitro diagnostic assays for the detection of SARS-CoV-2. Am J Clin Pathol 2020;154(2):201–7.

58. Dinnes J, Deeks JJ, Adriano A, et al. Rapid, point-of-care antigen and molecular-based tests for diagnosis of SARS-CoV-2 infection. Cochrane Database Syst Rev 2020;8:CD013705.

59. Mitchell SL, George KS. Evaluation of the COVID19 ID NOW EUA assay. J Clin Virol 2020;128:104429.

60. Rhoads DD, Cherian SS, Roman K, et al. Comparison of Abbott ID Now, DiaSorin Simplexa, and CDC FDA Emergency Use Authorization Methods for the Detection of SARS-CoV-2 from Nasopharyngeal and Nasal Swabs from Individuals Diagnosed with COVID-19. J Clin Microbiol 2020;58(8):e00760-20.

61. ABBOTT RELEASES ID NOW™ COVID-19 INTERIM CLINICAL STUDY RESULTS FROM 1,003 PEOPLE TO PROVIDE THE FACTS ON CLINICAL PERFORMANCE AND TO SUPPORT PUBLIC HEALTH. 2020. Abbott Available at: https://abbott.mediaroom.com/2020-10-07-Abbott-Releases-ID-NOW-TM-COVID-19-Interim-Clinical-Study-Results-from-1-003-People-to-Provide-the-Facts-on-Clinical-Performance-and-to-Support-Public-Health. Accessed June 23, 2021.

62. Lee CK, Tham JWM, Png S, et al. Clinical performance of Roche cobas 6800, Luminex ARIES, MiRXES Fortitude Kit 2.1, Altona RealStar, and applied Biosystems
TaqPath for SARS-CoV-2 detection in nasopharyngeal swabs. J Med Virol 2021; 93(7):4603–7.

63. ePlex®Respiratory Pathogen Panel 2 [package insert]. Carlsbad (CA): GenMark Diagnostics, Inc.; 2020.

64. Pujadas E, Ibeh N, Hernandez MM, et al. Comparison of SARS-CoV-2 detection from nasopharyngeal swab samples by the Roche cobas 6800 SARS-CoV-2 test and a laboratory-developed real-time RT-PCR test. J Med Virol 2020;92(9):1695–8.

65. Lee J, Song JU. Diagnostic accuracy of the Cepheid Xpert Xpress and the Abbott ID NOW assay for rapid detection of SARS-CoV-2: a systematic review and meta-analysis. J Med Virol 2021;93(7):4523–31.

66. Green DA, Zucker J, Westblade LF, et al. Clinical performance of SARS-CoV-2 molecular tests. J Clin Microbiol 2020;58(8).

67. Younes N, Al-Sadeq DW, Al-Jighefee H, et al. Challenges in Laboratory Diagnosis of the Novel Coronavirus SARS-CoV-2. Viruses 2020;12(6):582.

68. Ai T, Yang Z, Hou H, et al. Correlation of Chest CT and RT-PCR Testing for Coronavirus Disease 2019 (COVID-19) in China: A Report of 1014 Cases. Radiology 2020;296(2):E32–40.

69. Song S, Wu F, Liu Y, et al. Correlation between chest CT findings and clinical features of 211 COVID-19 suspected patients in Wuhan, China. Open Forum Infect Dis 2020;7(6):ofaa171.

70. Xie X, Zhong Z, Zhao W, et al. Chest CT for Typical Coronavirus Disease 2019 (COVID-19) Pneumonia: Relationship to Negative RT-PCR Testing. Radiology 2020;296(2):E41–5.

71. He X, Lau EHY, Wu P, et al. Temporal dynamics in viral shedding and transmissibility of COVID-19. Nat Med 2020;26(5):672–5.

72. Tracking SARS-CoV-2 variants. World Health Organization. 2021. Available at: https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/. Accessed December 22, 2021.

73. US COVID-19 Cases Caused by Variants. Centers for Disease Control and Prevention. 2021. Available at: https://www.cdc.gov/coronavirus/2019-ncov/variants/variant-cases.html. Accessed December 22, 2021.

74. Genetic Variants of SARS-CoV-2 May Lead to False Negative Results with Molecular Tests for Detection of SARS-CoV-2 - Letter to Clinical Laboratory Staff and Health Care Providers. U.S. Food & Drug Administration. Genetic Variants of SARS-CoV-2 May Lead to False Negative Results with Molecular Tests for Detection of SARS-CoV-2 - Letter to Clinical Laboratory Staff and Health Care Providers. 2021. Accessed June 22, 2021.

75. Emerging SARS-CoV-2 Mutations and Variants. Thermo Fisher Scientific. 2021. Available at: https://www.thermofisher.com/us/en/home/clinical/clinical-genomics/pathogen-detection-solutions/covid-19-sars-cov-2/mutations-variants.html. Accessed December 22, 2021.

76. Threat Assessment Brief. Rapid increase of a SARS-CoV-2 variant with multiple spike protein mutations observed in the United Kingdom. European Centre for Disease Prevention and Control. 2020. Available at: https://www.ecdc.europa.eu/en/publications-data/threat-assessment-brief-rapid-increase-sars-cov-2-variant-united-kingdom. Accessed June 22, 2021.

77. Peter Horby CH, Davies Nick, Edmunds John, et al. NERVTAG: presented to SAGE on 21/1/21. 2021. Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/961037/NERVTAG_note_on_B.1.1.7_severity_for_SAGE_77_1_.pdf. Accessed June 26, 2021.
78. Enhancing readiness for Omicron (B.1.1.529): Technical Brief and Priority Actions for Member States. World Health Organization; 2021.
79. SARS-CoV-2 Viral Mutations: Impact on COVID-19 Tests. U.S. Food & Drug Administration. 2021. Available at: https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/sars-cov-2-viral-mutations-impact-covid-19-tests#omicron-reduced. Accessed December 22, 2021.
80. Wolfel R, Corman VM, Guggemos W, et al. Virological assessment of hospitalized patients with COVID-2019. Nature 2020;581(7809):465–9.
81. Sethuraman N, Jeremiah SS, Ryo A. Interpreting diagnostic tests for SARS-CoV-2. JAMA 2020;323(22):2249–51.
82. Coronavirus (COVID-19) Update: FDA Informs Public About Possible Accuracy Concerns with Abbott ID NOW Point-of-Care Test. U.S. Food & Drug Administration. 2020. Available at: https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-informs-public-about-possible-accuracy-concerns-abbott-id-now-point. Accessed July 17, 2021.
83. Thwe PM, Ren P. How many are we missing with ID NOW COVID-19 assay using direct nasopharyngeal swabs? Findings from a mid-sized academic hospital clinical microbiology laboratory. Diagn Microbiol Infect Dis 2020;98(2):115123.
84. Simplexa® COVID-19 Direct Kit. DiaSorin Molecular. Available at: https://molecular.diasorin.com/us/kit/simplexa-covid-19-direct-kit/. Accessed June 23, 2021.