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BD Veritor™ SARS-CoV-2 Assay, development and performance of a rapid antigen test

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Vice-President R&D
BD, Integrated Diagnostic Solutions

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- Global position: One of the top 5 medical technology companies in the world with ~\$16 billion annual revenues
- Founded in 1897: A legacy of health impact
- Global reach: Serving 190+ countries
- Employees: 65,000
- Annual investment in innovation: \$1+ billion



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Life Sciences Medical Interventional

Discovery

Diagnostics

Medication management

Therapy management

Informatics: integrated workflow management and data analytics

Enabling research inside and outside the cell





Improving diagnostic accuracy and efficiency







Integrating medication management across the care continuum















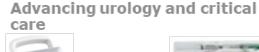


Integrating diabetes management



Maximizing outcomes for surgical processes

















The role of antigen testing in COVID-19

Molecular Diagnostic (PCR) Test

Highly sensitive, detects genetic sequences specific to SARS-CoV-2

Ability to

Rapid Antigen Test

Fast, point-of-care test, detects protein specific to SARS-CoV-2
Results in 15 minutes



Serology Test

Blood sample detects presence of antibodies produced in response to infection



Quickly diagnose to guide possible quarantine, reduce exposure and inform initial care

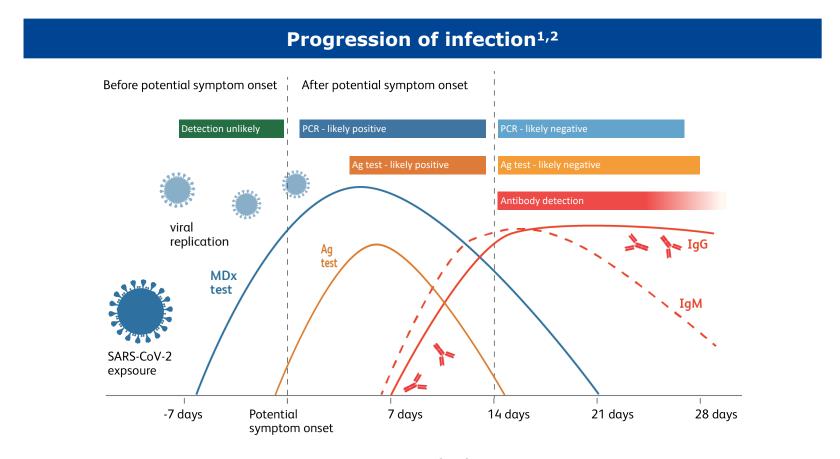
- Test outside of an acute care setting due to limited patient mobility, high risk susceptibility
- Test symptomatic patient, resident or staff member with high risk of exposure



When to test for SARS-CoV-2

Different tests are appropriate at different times and for different objectives. Which test is appropriate depends on a variety of criteria, including:

- What's the testing objective (e.g. inform diagnosis, confirm diagnosis, guide quarantine, clear for return to work)?
- What's the patient's condition and potential exposure (e.g. highly symptomatic, mildly symptomatic, asymptomatic)?
- What's the patient care setting and access to a lab?
- How quickly do you need an answer?



Progression of infection

References:

- Sethuraman N, Jeremiah SS, Ryo A. Interpreting Diagnostic Tests for SARS-CoV-2. JAMA. 2020;323(22):2249–2251
- 2. Long, Q., Liu, B., Deng, H. et al. Antibody responses to SARS-CoV-2 in patients with COVID-19. Nat Med 26, 845–848 (2020)
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WHO COVID antigen test performance requirements

Key Feature	Acceptable	Desirable
Sensitivity	≥ 80%	≥90%
Specificity	≥ 97%	>99%

Type of analysis	Qualitative (yes/no), semi-quantitative or quantitative	Not applicable	
Interpretation	Visual manual and/or hardware reader (proprietary or smart phone application)	Visual manual read or digital readout via smartphone application reader with connectivity	
Sample type	Nasopharyngeal, oropharyngeal swab (or wash) nasal swab (anterior nares or mid-turbinate), nasal wash, sputum	Anterior nares, saliva/oral fluid, sputum	Specimens that are easier to collect and associated with lower risk of aerosols are preferred i.e., saliva/oral fluid. Ideally the test can meet LOD requirements in an upper and a lower respiratory tract specimen.

 $\frac{https://www.who.int/publications/m/item/covid-19-target-product-profiles-for-priority-diagnostics-to-support-response-to-the-covid-19-pandemic-v.0.1$



BD Veritor™ System

- Digitally read, lateral-flow-based rapid antigen detection system
 - Instrument analyzes and corrects for nonspecific binding and detects positives not recognized by the unaided eye to provide an objective digital result.
- Provides objective, lab-quality immunoassay test results for healthcare providers and laboratorians in physician offices, clinics, and hospitals within minutes.
- The system streamlines the point-of-care (POC) diagnostic workflow and allows providers to quickly review patient results and determine the appropriate treatment in a single consultation.
- CLIA Complexity WAIVED & FDA 510(k) approved for the detection of influenza A and B, respiratory syncytial virus (RSV) and group A strep.
 - Used for the direct and qualitative detection of influenza A and B viral nucleoprotein antigens from samples collected from symptomatic patients.
 - Nasal swabs, throat swabs or Nasopharyngeal swabs.
- 5 Globally, 66,000 Veritor™ Instruments Placements, with >63,000 in the US.





The BD Veritor™ System for Rapid Detection of SARS-CoV-2

- Easy-to-use mid-nasal collection, simple workflow
- Easy-to-read, fast, and reliable results
- Reporting options from simple manual to automated connectivity
- BD Support





Simple sample collection, processing, and testing

BD Veritor™ System for Rapid Detection of SARS-CoV-2

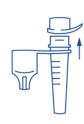
Detection of SARS-CoV-2 antigen in samples processed from nasal swab

Assay time of 15 minutes, with 1 minute of hands on-time*





STEP 1
Collect patient sample (mid-nasal)



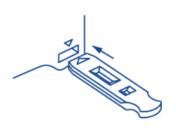
STEP 2 Remove cap & insert swab into tube



STEP 3
Mix sample for 15 sec with reagent, then remove swab



STEP 4
Close dispensing cap,
then dispense sample
into test device



STEP 5
Insert test device into the analyzer
For Walk Away mode, insert immediately
For Analyze Now mode, insert after timing the assay development

*BD Veritor System for Rapid Detection of SARS-CoV-2 [package insert 500050809]. Franklin Lakes, NJ: Becton, Dickinson and Company.



BD Veritor Plus Analyzer workflow allows batching using Analyze Now mode of the instrument



^{*5} minute incubation for Group A Strep, as per package insert

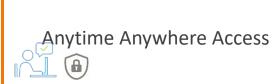


^{*10} minute incubation for Flu A+B or RSV, as per package insert

^{*15} minute incubation for SARS-CoV-2, as per package insert

BD Synapsys™ informatics solution for the BD Veritor™ Plus System







Cybersecurity



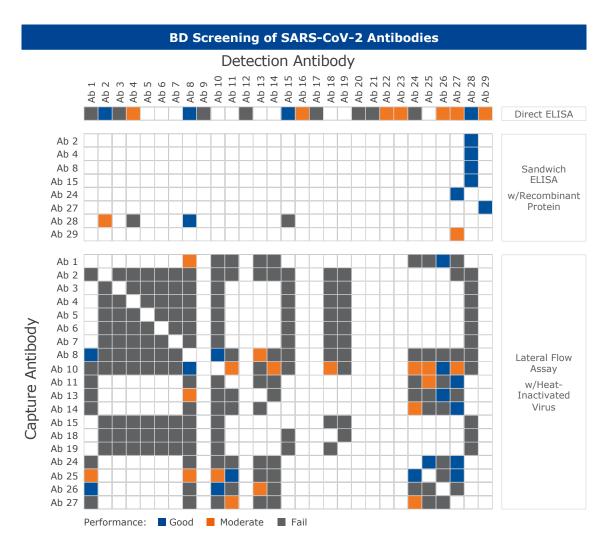
Remote Service and Support

Available

- Access BD Synapsys informatics from anywhere to securely review your patient test results
- BD Synapsys informatics offers strong security and data privacy capabilities and helps facilitate compliance
- Connectivity to send patient test result to LIS/EMR
- Remote installation and post go live support for standard maintenance and product update/upgrade



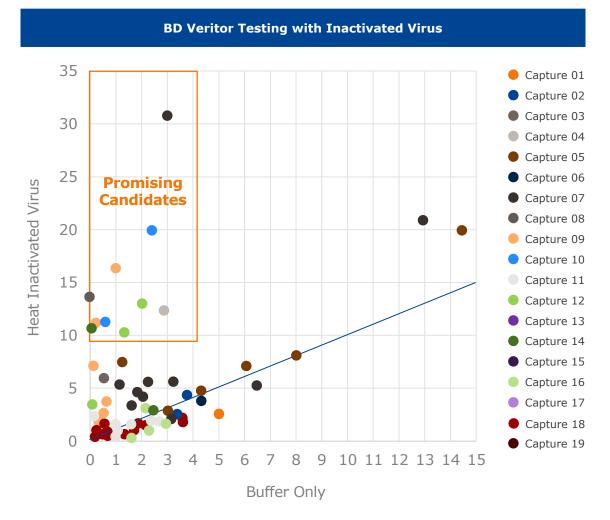
BD Veritor™ - SARS-CoV-2 Development approach



- BD has identified 100+ antibodies that recognize either the SARS-CoV-2 Spike (S) or Nucleocapsid Protein (NP).
- We have focused on developing an assay that recognizes Nucleocapsid protein:
 - Nucleocapsid protein is higher abundant per virus than Spike protein
 - Spike protein is more susceptible to mutation than Nucleocapsid protein
- BD has tested these 100+ Abs, either in direct ELISA or paired in Sandwich ELISA, dipstick or full lateral flow assay devices with either recombinant protein, heat or gamma-inactivated virus and clinical samples.
- Several promising antibody pairings have been identified and went under further evaluation and assay optimization.



BD Veritor™ - SARS-CoV-2 Development approach



- 19 antibodies were striped onto nitrocellulose membranes and tested in combination with each other as capture antibodies conjugated to BD Veritor™ detector particles sprayed onto conjugation pads and assembled into full BD Veritor™ lateral flow devices.
- Multiple Buffer with different salt, detergents concentration and pH were used to determine the background signal (x-axis) and **heat-inactivated virus** was used as the sample to create the assay signal (y-axis).
- Most promising pairs that were identified are highlighted in the orange box.







Limit of Detection

Limiting dilutions of a viral sample inactivated by gamma irradiation diluted into human nasal matrix. The last dilution demonstrating 100% positivity was then tested in an additional 20 replicates.



High dose Hook effect

No high dose hook effect was observed up to $2.8 \times 10E5$ TCID50/mL of gamma-inactivated virus.



Cross-reactivity

Cross-reactivity was evaluated by testing a panel of high prevalence respiratory pathogens that could potentially cross-react. Each organism and virus was tested in triplicate.

Starting Material Concentration	Estimated LOD	No. Positive/Total	% Positive	
2.8 x 10 ⁵ TCID ₅₀ /mL	1.4 x 10 ² TCID ₅₀ /mL	19/20	95%	

Potential Cross-Reactant	Concentration Tested	Cross-Reactivity (Yes/No)
Human coronavirus 229E (heat inactivated)	1.0 x 10 ⁵ U/mL	No
Human coronavirus OC43	$1.0 \times 10^5 \text{ TCID}_{50}/\text{mL}$	No
Human coronavirus NL63	$1.0 \times 10^5 \text{ TCID}_{50}/\text{mL}$	No
Adenovirus	$1.0 \times 10^5 \text{ TCID}_{50}/\text{mL}$	No
Human Metapneumovirus	$1.0 \times 10^{5} \text{ TCID}_{50}/\text{mL}$	No
Parainfluenza virus 1	$1.0 \times 10^{5} \text{ TCID}_{50}/\text{mL}$	No
Parainfluenza virus 2	$1.0 \times 10^5 \text{ TCID}_{50}/\text{mL}$	No
Parainfluenza virus 3	$5.2 \times 10^5 \text{ TCID}_{50}/\text{mL}$	No
Parainfluenza virus 4	$1.6 \times 10^{4} \text{ TCID}_{50}/\text{mL}$	No
Influenza A	$2.5 \times 10^{5} \text{ TCID}_{50}/\text{mL}$	No
Influenza B	$2.9 \times 10^5 \text{ TCID}_{50}/\text{mL}$	No
Enterovirus	$4.0 \times 10^5 \text{ TCID}_{50}/\text{mL}$	No
Respiratory syncytial virus	$4.0 \times 10^5 \text{ TCID}_{50}/\text{mL}$	No
Rhinovirus	$1.1 \times 10^5 \text{ PFU/mL}$	No
SARS-coronavirus	$4.5 \times 10^5 \text{ PFU/mL}$	No
MERS-coronavirus	$1.5 \times 10^5 \text{ TCID}_{50}/\text{mL}$	No
Haemophilus influenza	1.4 x 10 ⁶ CFU/mL	No
Streptococcus pneumoniae	1.0×10^6 CFU/mL	No
Streptococcus pyogenes	1.6×10^6 CFU/mL	No
Candida albicans	1.8 x 10 ⁶ CFU/mL	No
Pooled human nasal wash	100%	No
Bordetella pertussis	1.4×10^6 CFU/mL	No
Mycoplasma pneumoniae	1.0×10^6 CFU/mL	No
Chlamydia pneumoniae	1.0×10^6 IFU/mL	No
Legionella pneumophila	1.0 x 10 ⁶ CFU/mL	No





Interfering substances

21 potentially interfering endogenous substances were tested to determine whether they would cause false positive or false negative results in the BD Veritor System for Rapid Detection of SARS-CoV-2 assay. There was no evidence of interference at the concentrations tested.

Substance	Concentration Tested	Interference (Yes/No)
Afrin Nasal Spray (Oxymetazoline)	5% v/v	No
Flonase (Fluticasone)	5% v/v	No
Nasacort (Triamcinolone)	5% v/v	No
Neo-Synephrine (Phenylephrine hydrochloride)	5% v/v	No
Oseltamivir	2.2 μg/mL	No
Mucin protein	2.5 mg/mL	No
Rhinocort (Budesonide)	5% v/v	No
Saline nasal spray	15% v/v	No
Zanamivir	282 ng/mL	No
Zicam Cold Remedy (Galphimia glauca, Luffa operculate, Sabadilla)	5% v/v	No
Whole blood	4% v/v	No
Cepacol (Menthol/Benzocaine)	1.5 mg/mL	No
Ricola (menthol)	1.5 mg/mL	No
Tobramycin	4 μg/mL	No
Sucrets(Dyclonin/Menthol)	1.5 mg/mL	No
NeiMed Naso Gel	5% v/v	No
Zicam nasal spray (Oxymetazoline)	10% v/v	No
Alkalol nasal wash	10% v/v	No
Fisherman's Friend (menthol)	1.5 mg/mL	No
Chloraseptic (Phenol Spray)	15% v/v	No
Mupirocin	10 mg/mL	No



Microbial interference

The BD Veritor System for Rapid Detection of SARS-CoV-2 assay was evaluated with various organisms. The testing demonstrated no evidence that any of the tested organisms induced false negative results when present in the same sample with SARS-CoV-2 at the tested concentrations.

Potential Microbial Interferent	Concentration Tested	Interference (Yes/No)
Human coronavirus 229E	1.0 x 10 ⁵ U/mL	No
Human coronavirus OC43	1.0 x 10 ⁵ TCID ₅₀ /mL	No
Human coronavirus NL63	1.0 x 10 ⁵ TCID ₅₀ /mL	No
Adenovirus	1.0 x 10 ⁵ TCID ₅₀ /mL	No
Human Metapneumovirus	1.0 x 10 ⁵ TCID ₅₀ /mL	No
Parainfluenza virus 1	1.0 x 10 ⁵ TCID ₅₀ /mL	No
Parainfluenza virus 2	1.0 x 10 ⁵ TCID ₅₀ /mL	No
Parainfluenza virus 3	5.2 x 10 ⁵ TCID ₅₀ /mL	No
Parainfluenza virus 4	1.6 x Chloroacetic 10 ⁴ TCID ₅₀ /mL	No
Influenza A	2.5 x 10 ⁵ TCID ₅₀ /mL	No
Influenza B	2.9 x 10 ⁵ TCID ₅₀ /mL	No
Enterovirus D68	4.0 x 10 ⁵ TCID ₅₀ /mL	No

Potential Microbial Interferent	Concentration Tested	Interference (Yes/No)
Respiratory syncytial virus	4.0 x 10 ⁵ TCID ₅₀ /mL	No
Rhinovirus	1.1 x 10 ⁵ PFU/mL	No
SARS-coronavirus	4.5 x 10 ⁵ PFU/mL	No
MERS-coronavirus	1.5 x 10 ⁵ TCID ₅₀ /mL	No
Haemophilus influenza	1.4 x 10 ⁶ CFU/mL	No
Streptococcus pneumoniae	1.0 x 10 ⁶ CFU/mL	No
Streptococcus pyogenes	1.6 x 10 ⁶ CFU/mL	No
Bordetella pertussis	1.4 x 10 ⁶ CFU/mL	No
Mycoplasma pneumoniae	1.0 x 10 ⁶ CFU/mL	No
Chlamydia pneumoniae	1.0 x 10 ⁶ IFU/mL	No
Legionella pneumophila	1.0 x 10 ⁶ CFU/mL	No
Pooled human nasal wash	N/A	No
Candida albicans	1.8 x 10 ⁶ CFU/mL	No



Reproducibility

The reproducibility of the BD Veritor System for Rapid Detection of Sars-CoV-2 was evaluated by 3 operators, using 3 BD Veritor Plus Analyzer instruments and 3 different kit lots, over 3 days. The reproducibility sample panel was composed of simulated Sars-CoV-2 samples seeded at concentrations across the range of the assay.

Sample	Oper	ator #1	Oper	ator #2	Oper	ator #3	To	otal
	% Positive	95% CI						
Negative	0% (0/27)	(0.0%,12.5%)	0% (0/27)	(0.0%,12.5%)	0% (0/27)	(0.0%,12.5%)	0% (0/81)	(0.0%,4.5%)
Low Positive (3x LoD)	100% (27/27)	(87.5%,100.0%)	100% (27/27)	(87.5%,100.0%)	100% (27/27)	(87.5%,100.0%)	100% (81/81)	(95.5%,100.0%)
Low Positive (5x LoD)	100% (27/27)	(87.5%,100.0%)	100% (27/27)	(87.5%,100.0%)	100% (27/27)	(87.5%,100.0%)	100% (81/81)	(95.5%,100.0%)
Moderate Positive (10x LoD)	100% (27/27)	(87.5%,100.0%)	100% (27/27)	(87.5%,100.0%)	100% (27/27)	(87.5%,100.0%)	100% (81/81)	(95.5%,100.0%)
High Positive (40x LoD)	100% (27/27)	(87.5%,100.0%)	100% (27/27)	(87.5%,100.0%)	100% (27/27)	(87.5%,100.0%)	100% (81/81)	(95.5%,100.0%)



BD Veritor™ FDA-Emergency Use Authorization (EUA) study and Head-to-Head Quidel® Sofia® study

- The performance of the BD Veritor™ System for Rapid Detection of SARS-CoV-2 (Veritor¹)
 versus the Quidel® Lyra® Real-Time PCR SARS-CoV-2 Assay (Lyra®) was determined from a
 population (N=254) of individuals displaying symptoms consistent with COVID-19
- This FDA-EUA study involved acceptance criteria including a PPA for Veritor™ and Lyra®
 (reference method) of ≥80% with at least 30 positive specimens by Lyra®
- A post-EUA study was conducted in order to understand the relative performance of Veritor™
 to another antigen test Quidel[®] Sofia[®] 2 SARS Antigen FIA test (Sofia[®] 2)
- The population included in both studies reflects the intended use population for POC antigen testing (i.e., outpatient settings, walk-in clinics, drive-through testing facilities etc.)

¹Young *et al.* Clinical evaluation of BD Veritor™ SARS-CoV-2 point-of-care test performance compared to PCR-based testing and versus the Sofia® 2 SARS Antigen point-of-care test. J Clin Microbiology (2020).

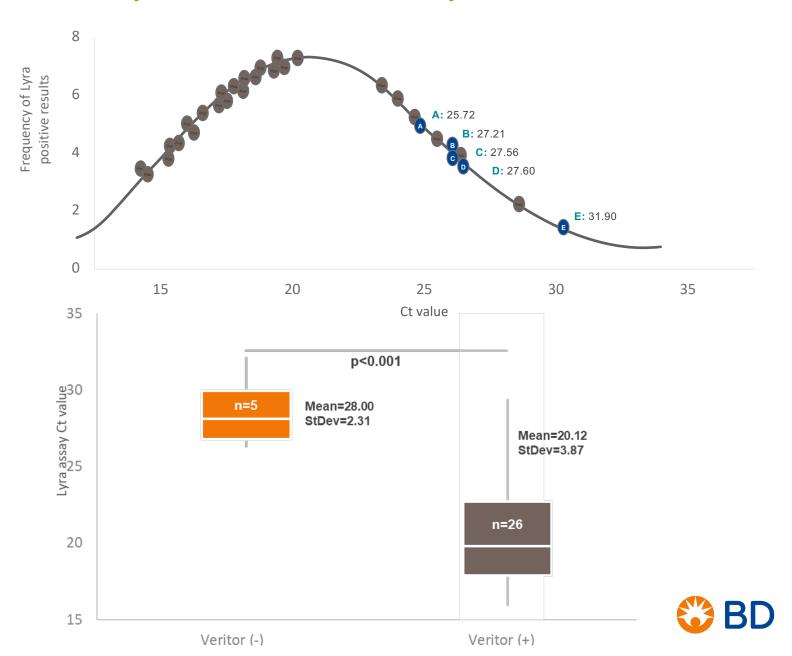
EUA and BD Veritor™/Sofia® 2 H2H studies

EUA study (N=254)	Veritor/Sofia H2H (N=373)
Collection sites	
5 drive-through sites (n=42)	1 drive-through sites (n=9)
11 outpatient centers (n=74)	1 outpatient centers (n=50)
4 research clinics (n=72)	2 research clinics (n=307)
1 skilled nursing facility (n=66)	1 Urgent care site (n=7)
Collection procedure and order	
Standard of care collection 1st	Standard of care collection 1 st
Nasal swab collection 2 nd	Nasal swab collection 2 nd and 3 rd (randomized)
One swab: BD Veritor™ SARS-CoV-2 antigen	One swab for BD Veritor™ SARS-CoV-2 antigen
and BD MAX SARS-CoV-2 PCR (remnant)	One swab for Quidel® Sofia® 2 SARS-CoV-2 antigen
NP or OP swab 3 rd	NP swab 4 th
Quidel [®] Lyra [®] SARS-CoV-2 PCR	Quidel [®] Lyra [®] SARS-CoV-2 PCR



BD Veritor™ performance vs. Lyra® in EUA study

Performance	5 Days from Symptom Onset
PPA %, [95% CI]	83.9 [67.4, 92.9]
NPA %, [95% CI]	100 [98.1, 100]
OPA %, [95% CI]	97.8 [94.9, 99.1]
True positives	26
False negatives	5
True negatives	195
False positives	0
Total	226



H2H performance for Veritor™ versus Sofia® 2

		Veritor vs. Sofia 2	
Performance	Overall	Veritor collected 1st	Sofia 2 collected 1st
PPA %, [95% CI]	97.4 (86.5, 99.5)	100 (81.6, 100)	95.2 (77.3, 99.2)
NPA %, [95% CI]	98.1 (96.0, 99.1)	98.8 (95.6, 99.7)	97.5 (93.7, 99.0)
OPA %, [95% CI]	98.1 (96.1, 99.1)	98.9 (96.0, 99.7)	97.2 (93.7, 98.8)
Veritor (+)/Sofia 2(+)	37	17	20
Veritor (-)/Sofia 2(+)	1 ^a	0	1
Veritor (+)/Sofia 2(-)	6 ^b	2	4
Veritor (-)/Sofia 2(-)	317	161	156
Total	361	180	181

- Veritor returned 43 positive results and Sofia® 2 returned 38 positive results
- Veritor had a PPA, NPA, and OPA of 97.4%, 98.1%, and 98.1%, respectively, with Sofia[®]
- Discordant testing in the H2H study showed
 - One PCR positive missed by Veritor
 - Five PCR positives missed by Sofia®
 - One Veritor positive result was negative by PCR



a) Represents 1 Veritor (-)/Sofia[®] 2 (+) result that was positive by the Lyra[®] SARS-CoV-2 PCR assay

b) Represents 5 Veritor (+)/Sofia[®] 2 (-) results that were positive by the Lyra[®] SARS-CoV-2 PCR assay, and 1 Veritor (+)/Sofia[®] 2 (-) result that was negative by the Lyra[®] SARS-CoV-2 PCR assay

Additional clinical evidence

Performance	5 Days from Symptom Onset
PPA %, [95% CI]	93.5 [79.3, 98.2]
NPA %, [95% CI]	99.3 [96.4, 99.9]
OPA %, [95% CI]	98.4 [95.3, 99.4]
True positives	29
False negatives	2
True negatives	152
False positives	1
Total	184

- The performance of the BD Veritor™ System for Rapid Detection of SARS-CoV-2 versus the Quidel® Lyra® Real-Time PCR SARS-CoV-2
 Assay was determined from a population (N=184) of individuals displaying two or more self-reported symptoms consistent with COVID-19
- The population included in this study reflects the intended use population for POC antigen testing, (i.e., outpatient settings, walk-in clinics, drive-through testing facilities etc.)
- Samples were collected at 16 geographically diverse outpatients clinics.



Antigen-based testing but not real-time PCR correlates with SARS-CoV-2 virus culture²

- OBJECTIVE: determine whether BD Veritor™ System for Rapid Detection of SARS-CoV-2 differentiates SARS-CoV-2-contagious individuals (e.g., those still shedding infectious virus) from non-contagious individuals compared to RT-PCR methodology.
 - Quidel[®] Lyra[®] SARS-CoV-2 Assay positive and negative specimens obtained from a diverse set of collection sites across the USA
 - The RT-PCR assay and the BD Veritor™ System for Rapid Detection of SARS-CoV-2 were compared to SARS-CoV-2
 TMPRSS2 culture (a sensitive virus culture test utilizing the VeroE6TMPRSS2 cell line), which served as the reference
 method for determining infectiousness.



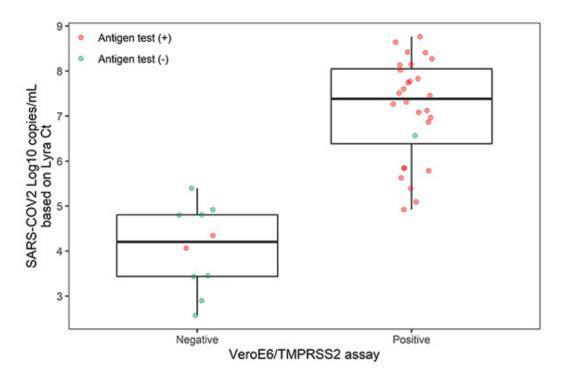
Positive BD Veritor™ test correlates with presence of infectious virus²

Performance Values	Antigen Test Performance	rt-PCR Performance
PPA	96.4 (82.3–99.4)	100 (87.7–100)
NPA	98.7 (96.1–99.7)	95.5 (91.1–97.8)
PPV	90.0 (76.3–97.6)	73.7 (60.8–85.3)
NPV	99.5 (97.7–100)	100 (98.4–100)
OPA	98.4 (96.0–99.4)	96.0 (92.8–97.8)
Culture (+)/test (+)	27	28
Culture (-)/test (+)	3	10
Culture (+)/test (-)	1	0
Culture (–)/test (–)ª	220	213

Prevalence was 11.2%.

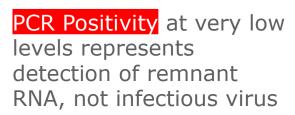
Abbreviations: NPA, negative percentage agreement; NPV, negative predictive value; OPA, overall percentage agreement; PPA, positive percentage agreement; PPV, positive predictive value; rt-PCR, real-time polymerase chain reaction.

^aIncludes 176 specimen sets that were rt-PCR and antigen negative, with unavailable culture results.

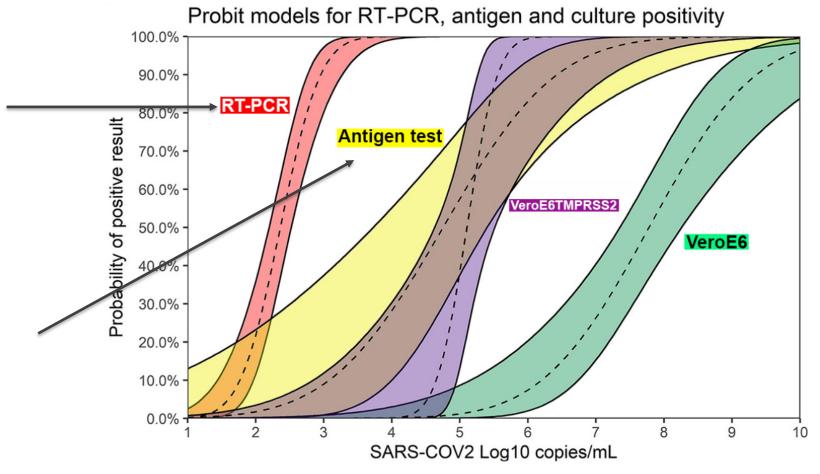


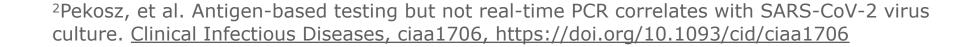


Positive BD Veritor™ test correlates with presence of infectious virus²



Veritor closely matches High Sensitivity Virus Culture







Regulatory approval

Africa CDC recommends use of Tests that have been assessed through a national Emergency Use Authorization (EUA) and/or the WHO Emergency use list¹

The BD Veritor[™] has received the following approvals:

FDA EUA, CE Mark, Health Canada, TGA

VERITOR Cat #	RA STATUS	COUNTRY
#082 (FDA)	Under Prep.	Ethiopia
	Under review MOH	Kenya, Ghana, Tanzania, Nigeria, Egypt, Algeria
	Approved	Ukraine, UAE, South Africa
#089 (CE)	Under review MOH	Morocco, Georgia, Ghana, Iran, Egypt
	Approved	Kuwait, UAE, Oman, Saudi Arabia, Turkey, Ukraine, South Africa



Conclusion

- BD Veritor™ System and Assay have demonstrated high accuracy against RT-PCR assay within 5 to 7 days since symptoms onset in symptomatic population.
- Antigen test demonstrated high correlation with viral culture compared to RT-PCR, which supports the differentiation between SARS-CoV-2-contagious individuals (e.g., those still shedding infectious virus) from non-contagious individuals
- This is an assay that diagnoses infectious individuals rather than COVID at all stages of illness.
- This is more than just a diagnostic tool, this is a public healthoriented tool
- To learn more about BD Veritor, please visit https://lp.bd.com/pocrapiddiagnostic.html





Thank you