Department of Health & Social Care

Technical validation report for BD Veritor

August 2021 (Version 2.0)

Contents

Assay description and intended purpose

1. The BD Veritor™ System (256089 “BD Veritor system for Rapid Detection of SARS-CoV-2, 30 pack) for rapid detection of SARS-CoV-2 is a rapid (approximately 15 minutes) chromatographic digital immunoassay intended for the direct and qualitative detection of SARS-CoV-2 nucleocapsid antigens in nasal swabs from individuals with or without symptoms, who are suspected of infection with, or exposure to COVID-19, by their healthcare provider. The test is not intended to be interpreted visually but with the BD Veritor™ Plus Analyzer.

2. Results are for the identification of SARS-CoV-2 nucleocapsid antigen. This antigen is generally detectable in upper respiratory samples during the acute phase of infection. Positive results indicate the presence of viral antigens, but clinical correlation with patient history and other diagnostic information is necessary to determine infection status.

   The BD Veritor™ System for Rapid Detection of SARS-CoV-2 is intended for use in point of care settings by laboratory personnel and healthcare providers appropriately trained in the use of the BD Veritor™ System. In the United States, the BD Veritor™ System for Rapid Detection of SARS-CoV-2 is only for use under the Food and Drug Administration’s Emergency Use Authorization. The assay is a standalone test for use on the BD Veritor™ Plus Analyzer.

   There test requires no pipetting steps, but full PPE is required by a healthcare worker using the test. See a report on the viral inactivation of the buffer.

   - A one-minute treatment with BD Veritor Extraction Reagent reduced SARS-CoV-2 titre by ≥4.5 log10 TCID50/ml. ≥5.4 and ≥5.7 log10 TCID50/ml reduction could be demonstrated after five and ten minutes, respectively. All treatment times reduced virus titre to below the limit of detection of the tests.

Type of sample to be used in validation

1. Acceptable specimens for testing with this kit only include nasal swab specimens obtained by the dual nares collection method collected and tested directly (that is swabs that have not been placed in transport media). This kit is not intended for testing liquid samples such as wash or aspirate samples or swabs in transport media as results can be compromised by over dilution. The BD Veritor™ System for Rapid Detection of SARS-CoV-2 includes swabs for nasal specimen collection.

   The company state:

   Specimens obtained early during symptom onset will contain the highest viral titers; specimens obtained after 5 days of symptoms are more likely to produce negative results when compared to an RT-PCR assay. Inadequate specimen collection, improper specimen handling and/or transport may yield a falsely negative result; therefore, training in specimen collection is highly recommended due to the importance of specimen quality for generating accurate test results.

Equipment and reagents

1. List all the equipment required that is or is not supplied by the manufacturer

   Product components supplied:

   - BD Veritor™ System Test Devices: foil pouched test device containing one reactive strip. Each strip has one line of murine anti-SARS coronavirus monoclonal antibody on the test line, and one of biotin coupled to bovine protein on the positive control line.
   - Murine and Leporine anti-SARS coronavirus and anti-biotin monoclonal antibodies conjugated to detector reagents are bound in the sample delivery area.
   - Extraction Reagent: 3Detergent solution with less than 0.1% sodium azide (preservative).
   - Specimen sampling swabs: for sample collection and transfer.
   - SARS-CoV-2 (+) Control Swab: non-infectious, recombinant viral protein antigen with less than 0.1% sodium azide.
   - SARS-CoV-2 (-) Control Swab: buffer with less than 0.1% sodium azide.
   - Assay documentation
   - Instructions for use

   Product components required but not supplied:

   - BD Veritor™ Plus Analyzer (Catalog Number 256066)
   - BD Veritor™ System Barcode Scanning Module (Catalog Number 256068 or 445010)* – optional
   - Timer
   - Tube rack for specimens
   - Any necessary personal protective equipment

BD Optional equipment:

- USB Printer cable for BD Veritor™ Plus Analyzer (Catalog Number 443907)
- Epson Printer model TM-T20 II
- BD Veritor™ Plus Connect

Performance characteristics

Analytical Sensitivity and Linearity of SARS COV-2 targets

1. Dilution series: Ideally, this should be calculated using a validated standard dilution series. If not possible (as standard material not available), use 5 clinical positive replicates, with a 5 log dilution, plus 5 negatives. If feasible, repeat over several days, different users and machines (feasibility may be limited due to availability of positive material). Where dry swabs are to be used, known amounts of standard material should be added to the swab, and then tested as per IFU.

Table 1: results from dilution series of different standard materials obtained from NIBSC

Type of material	TCID50/ml	neat	1 in 2	1 in 4	1 in 8	1 in 16
Heat/acetic acid inactivated virus in UTM	100	positive	negative	negative	negative	negative
Recombinant protein in UTM	10	positive	negative	negative	negative	negative

2. Linearity and efficiency. The assay gives a qualitative result so this section is not applicable

3. Lowest limits of detection (LLOD). LLOD claimed by company is 1.4 x 102 TCID50/mL using gamma irradiated material. This has been confirmed by data in Table 1.

Precision and robustness

1. Intra-assay precision. The assay gives a qualitative result so this section is not applicable.

   Inter-assay precision. The assay gives a qualitative result so this section is not applicable.

2. Repeatability: Spike 30 negative samples with known amount of agent/positive material (suggested 3x the LLOD), all should be positive. This information given within the manufacturer IFU

Analytical specificity (Interferences and cross-reactions)

1. Cross-reactivity to non-target samples or organisms. A range of samples either direct clinical samples or spiked samples that are known positives for other diseases, both closely related to be tested.

Table 2: cross-reactivity check from the manufacturer IFU

Potential cross-reactant	Concentration tested	Cross-reactivity (Yes or No)
Human coronavirus 229E (heat inactivated)	1.0 x 10^5 U/mL	No
Human coronavirus OC43	1.0 x 10^5 TCID50/mL	No
Human coronavirus NL63	1.0 x 10^5 TCID50/mL	No
Adenovirus	1.0 x 10^5 TCID50/mL	No
Human Metapneumovirus	1.0 x 10^5 TCID50/mL	No
Parainfluenza virus 1	1.0 x 10^5 TCID50/mL	No
Parainfluenza virus 2	1.0 x 10^5 TCID50/mL	No
Parainfluenza virus 3	5.2 x 10^5 TCID50/mL	No
Parainfluenza virus 4	1.6 x 10^4 TCID50/mL	No
Influenza A	2.5 x 10^5 TCID50/mL	No
Influenza B	2.9 x 10^5 TCID50/mL	No
Enterovirus	4.0 x 10^5 TCID50/mL	No
Respiratory syncytial virus	4.0 x 10^5 TCID50/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 TCID50/mL	No
Haemophilus influenzae	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
Candida albicans	1.8 x 10^6 CFU/mL	No

Potential cross-reactant	Concentration tested	Cross-reactivity (Yes or No)
Pooled human nasal wash	100%	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

2. Cross-reactivity of the BD Veritor™ System for Rapid Detection of SARS-CoV-2 was evaluated by testing a panel of high prevalence respiratory pathogens that could potentially cross-react with the BD Veritor™ System for Rapid Detection of SARS-CoV-2. Each organism and virus was tested in triplicate. The final concentration of each organism is documented in the following table. TVG were unable to corroborate as we were unable to source full materials required.

Diagnostic sensitivity and specificity (clinical validation with confirmed positives and negatives)

1. Diagnostic sensitivity. Confirmed clinical samples from patients (positive PCR result) should be used. Preferably, depending on the availability of samples, ~150 samples should be included to align with MHRA TPP. Clinical sensitivity (95% CI) and positive predictive value (PPV) should be calculated in comparison with a CE reference method that itself has good sensitivity and specificity.

Table 3: comparison with reference method (note prevalence of 37.1%). Data have been included from 2 UK sites and 1 site in Belgium

(See SARS-CoV-2 Diagnostic Tests: Algorithm and Field Evaluation From the Near Patient Testing to the Automated Diagnostic Platform)

		Comparator		
		Positive	Negative	Total
BD Veritor	Positive	161	5	166
	Negative	28	315	343
Total		189	320	509

2. Sensitivity = 85.2% (95% CI 79.1 to 89.8) this meets the acceptable criteria for sensitivity of the POC TPP (desirable>97% = acceptable = >80%).

Table 4: performance of BD Veritor at different viral loads, as defined by CT value (available from 2 UK sites)

	Site 1			**Site 2**			**Total**	
CT	Genesig	Positive match on BD	Sens %	Cepheid / Altona	Positive match on BD	Sens %	Positive match on BD	Sens %
<25	6	6	100	8	8	100	14	100
25-30	10	9	90	10	10	100	19	95
30-35	6	4	66.7	11	10	90.9	14	82.3
>35	4	2	50	4	4	100	6	75
undefined	0	0	0	4	0	0	0	0

3. Diagnostic specificity. Confirmed clinical samples from patients (negative PCR result) should be used. Preferably, depending on the availability of samples, ~250 samples should be included to align with MHRA TPP. Clinical specificity (95% CI) and negative predictive value (PPV) should be calculated in comparison with a CE reference method that itself has good sensitivity and specificity.

   Specificity = 98.4% (95% CI 96.2 to 99.4) this meets the acceptable criteria for specificity of the POC TPP (desirable >99% = acceptable = >95%).

Summary

1. TVG uses a wide range of sites in order to validate new technologies/tests. These independent sites use a range of RT-qPCR assays against different genomic regions and it is recognised that for some assay comparisons the sensitivity of RT-qPCR assay(s) may subtly differ from the true sensitivity of the test if compared to the same genomic region.

   This assay meets the acceptable criteria for sensitivity and specificity of the MHRA TPP for POC assays, although we don’t have full CT data from all datasets.

Extra data tables

Table 5: failure rate of the BD Veritor assay

Total number of samples tested	Number of RC* failures	Percentage of IC failures (%)	Number of technical failures	Percentage of technical failures (%)	Total number of failures	Percentage of total failures (%)
510	1	0.2	0	0	1	0.2

*Run control

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