BD SARS-CoV-2 Reagents for BD MAX™ System

USA-For Emergency Use Authorization (EUA) only
For *In Vitro* Diagnostic Use
For use with the BD MAX™ System

REF **445003**
P0252(01)
2020-04
English

IVD R_x Only

INTENDED USE

The BD SARS-CoV-2 Reagents for BD MAX™ System is a real-time RT-PCR test intended for the qualitative detection of nucleic acid from the SARS-CoV-2 in nasal, nasopharyngeal and oropharyngeal swab samples from individuals suspected of COVID-19 by their healthcare provider. Testing is limited to U.S. laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, to perform moderate and high complexity tests.

Results are for the identification of SARS-CoV-2 RNA. The SARS-CoV-2 RNA is generally detectable in upper respiratory samples during the acute phase of infection. Positive results are indicative of the presence of SARS-CoV-2 RNA; clinical correlation with patient history and other diagnostic information is necessary to determine patient infection status. Positive results do not rule out bacterial infection or co-infection with other viruses. The agent detected may not be the definite cause of disease. Laboratories within the United States and its territories are required to report all positive results to the appropriate public health authorities.

Negative results do not preclude SARS-CoV-2 infection and should not be used as the sole basis for patient management decisions. Negative results must be combined with clinical observations, patient history, and epidemiological information.

The BD SARS-CoV-2 Reagents for BD MAX System is intended for use by qualified and trained clinical laboratory personnel specifically instructed and trained in the techniques of real-time PCR, *in vitro* diagnostic procedures, and use of the BD MAX System. The BD SARS-CoV-2 Reagents for BD MAX System is only for use under the Food and Drug Administration's Emergency Use Authorization.

EXPLANATION OF THE TEST

Total nucleic acid (TNA) is isolated and purified using BD MAX™ ExK™ TNA-3 kit from nasal, nasopharyngeal, or oropharyngeal swabs collected in BD Universal Viral Transport System (UVT) or Copan Universal Transport Media System (UTM). Patient sample is transferred to the Sample Buffer Tube (SBT) provided with the BD MAX ExK TNA-3 kit and placed in the BD MAX System. The BD MAX ExK TNA-3 unitized reagent strip contains a combination of lytic and extraction reagents designed to perform cell lysis and TNA extraction. Eluted TNA is transferred to BD MAX TNA MMK master mix and SARS-CoV-2 primers and probes. The final rehydrated master mix is transferred to a PCR cartridge for rRT-PCR.

The BD SARS-CoV-2 Reagents for BD MAX System utilizes multiplexed primers and probes targeting RNA from the nucleocapsid phosphoprotein gene (N1 and N2 regions) of the SARS-CoV-2 coronavirus, and the human RNase P gene. The primer and probe sets are based on the United States Centers for Disease Control and Prevention (US CDC) assay for specific detection of SARS-CoV-2 by amplifying two unique regions of the N gene (i.e., N1 and N2).

An internal control targeting the human RNase P gene will be co-amplified along with N1 and N2 gene targets (if present) and will serve as an endogenous nucleic acid extraction control present in all properly collected patient samples. This control serves as both an extraction control and an internal amplification control.

PRINCIPLES OF THE PROCEDURE

A combination of lytic and extraction reagents is used to perform cell lysis and DNA/RNA extraction. Nucleic acids released from the target organisms are captured on magnetic affinity beads. The beads, together with the bound nucleic acids, are washed and the nucleic acids are eluted by a combination of heat and pH variation. Neutralization buffer is used to rehydrate BD SARS-CoV-2 Reagents for BD MAX System Primers and Probes. Eluted TNA is added to the rehydrated primers and probes, mixed, and transferred to BD MAX TNA MMK master mix for rehydration. After reconstitution, the BD MAX System dispenses a fixed volume of RT-PCR-ready solution containing extracted nucleic acids into the PCR Cartridge. Microvalves on the cartridge are sealed by the system prior to initiating PCR in order to contain the amplification mixture and thus prevent evaporation and contamination.

The amplified cDNA targets are detected using hydrolysis (TaqMan®) probes, labeled at one end with a fluorescent reporter dye (fluorophore), and at the other end, with a quencher moiety. Probes labeled with different fluorophores are used to detect the target analytes in different optical channels of the BD MAX System. When the probes are in their native state, the fluorescence of the fluorophore is quenched due to its proximity to the quencher. However, in the presence of target cDNA, the probes hybridize to their complementary sequences and are hydrolyzed by the 5'–3' exonuclease activity of the DNA polymerase as it synthesizes the nascent strand along the cDNA template. As a result, the fluorophores are separated from the quencher molecules and fluorescence is emitted. The amount of fluorescence detected in the optical channels is directly proportional to the quantity of the corresponding probe that is hydrolyzed. The BD MAX System monitors these signals at each cycle of the PCR and interprets the data at the end of the reaction to provide qualitative test results for each analyte.

REAGENTS AND MATERIALS

REF	Contents	Quantity
445003	**BD SARS-CoV-2 Reagents for BD MAX System Primers and Probes** Dried primers and probes for SARS-CoV-2	24 (2 x 12 tubes)
	BD MAX TNA MMK Dried PCR Master Mix containing dNTPs and RT-polymerase	24 (2 x 12 tubes)

EQUIPMENT AND MATERIALS REQUIRED BUT NOT PROVIDED

- BD MAX System (BD Cat. No. 441916)
- BD MAX Sample Rack (BD Cat. No. 441935, 443550, 443551, 444807, or 444808)
- BD MAX ExK TNA-3 (BD Cat. No. 442827)
- BD MAX PCR Cartridges (BD Cat. No. 437519)
- SARS CoV-2 Controls
- Copan UTM Collection Kit
- BD UVT Collection Kit
- Vortex Genie 2 (VWR Cat. No. 58815-235 or equivalent)
- Multi-Tube Vortex Mixer (VWR Cat. No. 58816-115 or equivalent)
- Rack compatible with a multi-tube vortexer (e.g., Cryogenic Vial Holder or equivalent)
- Variable Volume Calibrated Pipettor (750 µL volume capable)
- Aerosol resistant micropipette tips
- Disposable gloves, powderless

WARNINGS AND PRECAUTIONS

- For *in vitro* diagnostic use under Emergency Use Authorization only.
- For Prescription Use only.
- Positive results are indicative of the presence of SARS-CoV-2 RNA.
- Laboratories within the United States and its territories are required to report all positive results to the appropriate public health authorities.
- All patient samples should be handled as if infectious, using good laboratory procedures as outlined in the CLSI Document M29-A4[1] and in Biosafety in Microbiological and Biomedical Laboratories.[2] Only personnel proficient in handling infectious materials and the use of BD SARS-CoV-2 and BD MAX System should perform this procedure.
- All human-sourced materials should be considered potentially infectious and should be handled with universal precautions. If spillage occurs, follow appropriate site procedures.
- Closely follow procedures and guidelines provided to ensure that the test is performed correctly. Any deviation from the procedures and guidelines may affect optimal test performance.

- Do not use expired reagents and/or materials.
- Do not use the kit if the label that seals the outer box is broken upon arrival.
- Do not use reagents if the protective pouches are open or broken upon arrival.
- Do not use reagents if desiccant is not present or broken inside reagent pouches.
- Do not remove desiccant from reagent pouches.
- Close protective pouches of reagents promptly with the zip seal after each use. Remove any excess air in the pouches prior to sealing.
- Protect reagents against heat and humidity. Prolonged exposure to humidity may affect product performance.
- Do not use reagents if the foil has been broken or damaged.
- Do not mix reagents from different pouches and/or kits and/or lots.
- Do not interchange or re-use caps, as contamination may occur and compromise test results.
- Check Unitized Reagent Strips for proper liquid fills (ensure that the liquids are at the bottom of the tubes).
- Check Unitized Reagent Strips to ensure that all pipette tips are present.
- Proceed with caution when using chemical solutions, as Extraction Tube barcode readability may be altered.
- Good laboratory technique is essential to the proper performance of this assay. Extreme care should be taken to preserve the purity of all materials and reagents.
- In cases where other PCR tests are conducted in the same general area of the laboratory, care must be taken to ensure that the BD SARS-CoV-2 components, any additional reagents required for testing, and the BD MAX System are not contaminated. Avoid microbial and ribonuclease (RNase)/deoxyribonuclease (DNase) contamination of reagents at all times. The use of sterile RNase/DNase-free disposable aerosol resistant or positive displacement pipette tips is recommended. Use a new tip for each specimen. Gloves must be changed before manipulating reagents and cartridges.
- To avoid contamination of the environment by amplicons, do not break apart the BD MAX PCR Cartridge after use. The seals of the BD MAX PCR Cartridges are designed to prevent contamination.
- The laboratory should routinely perform environmental monitoring to minimize the risk of cross-contamination.
- Wear protective clothing and disposable gloves while handling all reagents.
- Wash hands thoroughly after performing the test.
- Do not pipette by mouth.
- Do not smoke, drink, chew or eat in areas where specimens or kit reagents are being handled.
- Dispose of unused reagents and waste in accordance with local, state, provincial and/or federal regulations.
- Consult the BD MAX System User's Manual[3] for additional warnings, precautions and procedures.

STORAGE

BD SARS-CoV-2 Reagents for BD MAX System components are provided in sealed pouches and ships at ambient temperature. To protect the product from humidity, immediately re-seal after opening.

INSTRUCTIONS FOR USE

Swab Specimen Collection/Transport

Note: Wear gloves when handling Universal Viral Transport (UVT) or Universal Transport Media (UTM) specimens. If gloves come in contact with the specimen, immediately change them to prevent contamination of other specimens.

1. Nasal, nasopharyngeal, or oropharyngeal swab specimens should be collected and expressed directly into the BD Universal Viral Transport System or the Copan Universal Transport Media System according to their respective package insert instructions.
2. Transport the UVT/UTM specimen according to the manufacturer's instructions for use.

BD MAX Sample Buffer Tube Preparation

Note: Wear gloves when handling Universal Viral Transport (UVT) or Universal Transport Media (UTM) specimens. If gloves come in contact with the specimen, immediately change them to prevent contamination of other specimens.

Note: If frozen, allow Universal Viral Transport (UVT) or Universal Transport Media (UTM) specimen to come to room temperature before proceeding.

1. Uncap the BD MAX TNA-3 Sample Buffer Tube and transfer (using a calibrated, variable pipette) 750 µL from the UVT/UTM specimen directly into the BD MAX TNA-3 Sample Buffer Tube.
2. Recap the tube with a blue septum cap and vortex or mix by inversion 5 times.

3. Label the BD MAX TNA-3 Sample Buffer Tube with patient information.
   Note: Do not obscure the barcodes on the tube. Obscuring the barcode may result in BD MAX System catalog failure and inability to test the sample.
4. Repeat Steps 1 to 3 for each UVT/UTM sample that will be tested on the BD MAX System.
5. Proceed directly with the BD MAX System Operation.

BD MAX System Operation

Note: Refer to the BD MAX System User's Manual[3] for detailed instructions (Operation section).

1. Power on the BD MAX System (if not already done) and log in by entering **<user name>** and **<password>**.
2. Gloves must be changed before manipulating reagents and cartridges.
3. Remove the required number of Unitized Reagent Strips from the BD MAX ExK TNA-3 kit. Gently tap each Unitized Reagent Strip onto a hard surface to ensure that all the liquids are at the bottom of the tubes. Remove the required number of Extraction Tube(s) from the protective pouch. Remove excess air, and close pouches with the zip seal.
4. From the BD SARS-CoV-2 Reagents for BD MAX System kit, remove the required number of BD MAX TNA MMK Master Mix Tube(s) and BD SARS-CoV-2 Reagents for BD MAX System Primers and Probes Tube(s) from their protective pouches. Remove excess air, and close each pouch with the zip seal.
5. For each specimen to be tested, place one (1) Unitized Reagent Strip on the BD MAX System Rack. Assemble the strip as in Figure 1:

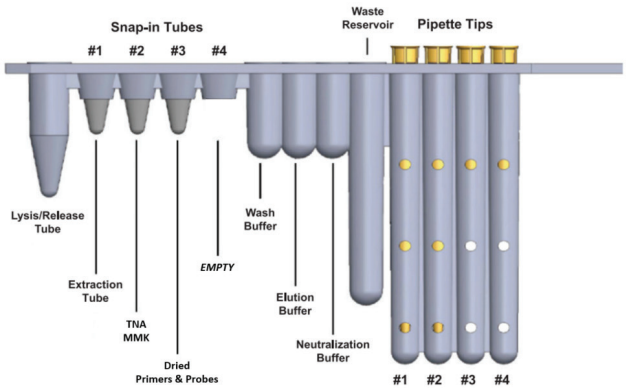


Figure 1: Snap Extraction Tubes and Master Mix Tube into Unitized Reagent Strips

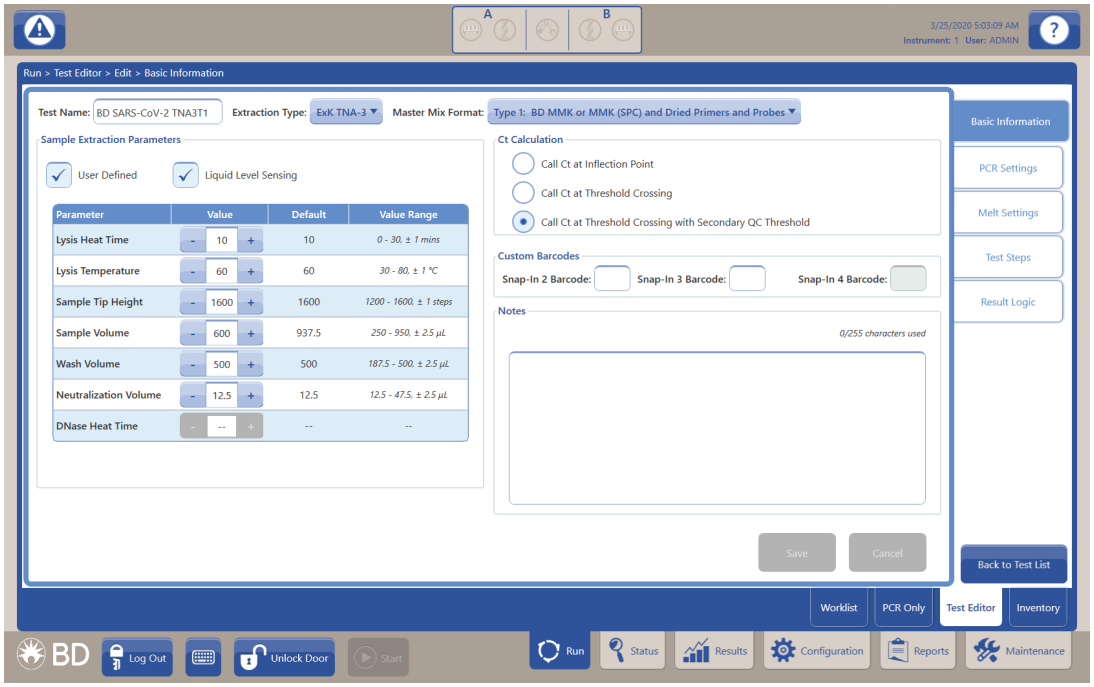
Note: Failure to add extraction tube or master mix tubes may result in instrument contamination.

Note: A conical snap-in tube is fully seated in the strip when a 'click' is heard. Refer to above for reagent placement in the Unitized Reagent Strip.

- Position 1= Snap the BD MAX ExK TNA-3 Extraction Tube into Position 1.
- Position 2= Snap the BD MAX TNA MMK Master Mix Tube into Position 2.
- Position 3= Snap the BD SARS-CoV-2 Reagents for BD MAX System Primers and Probes into Position 3.
- Position 4= Leave Position 4 empty (no conical snap-in tube).

6. Create the User Defined Protocol (UDP) as follows:
   - Navigate to Run > Test Editor tab.
   - Click "Create".
   - Complete each section of the user protocol as outlined in the screen shots below.

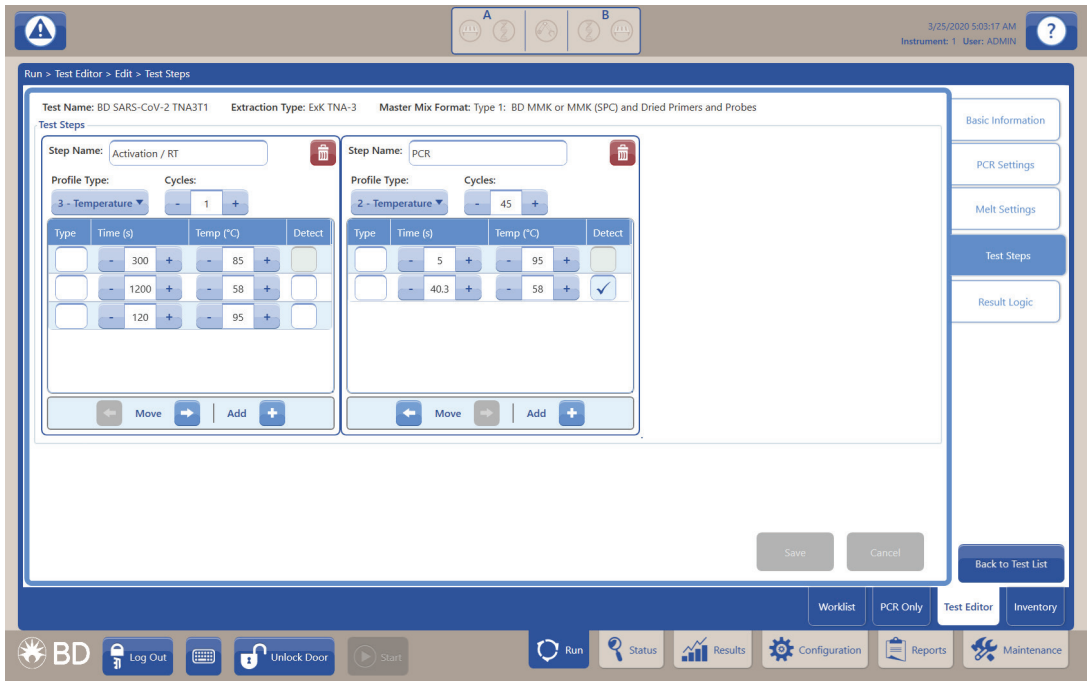
Basic Information Section



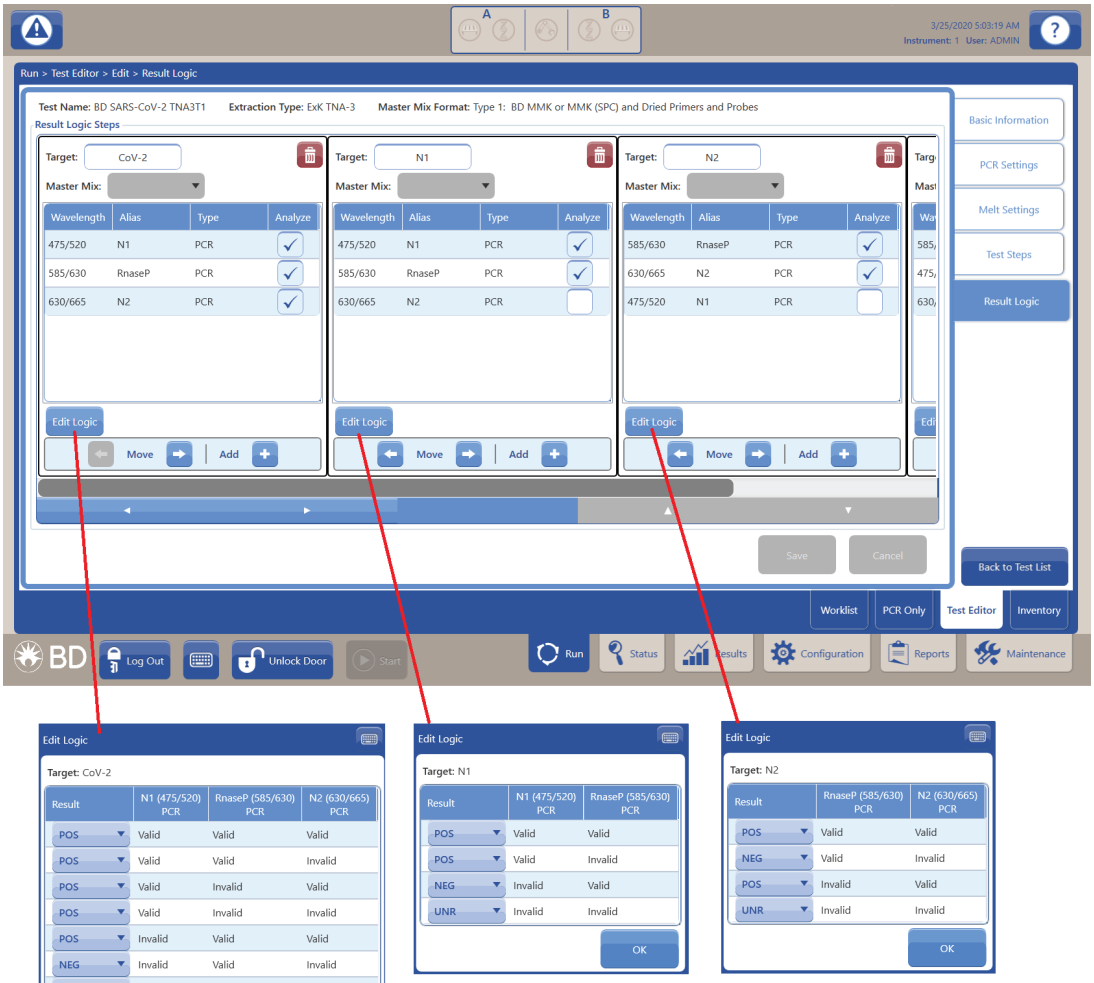
PCR Setting Section

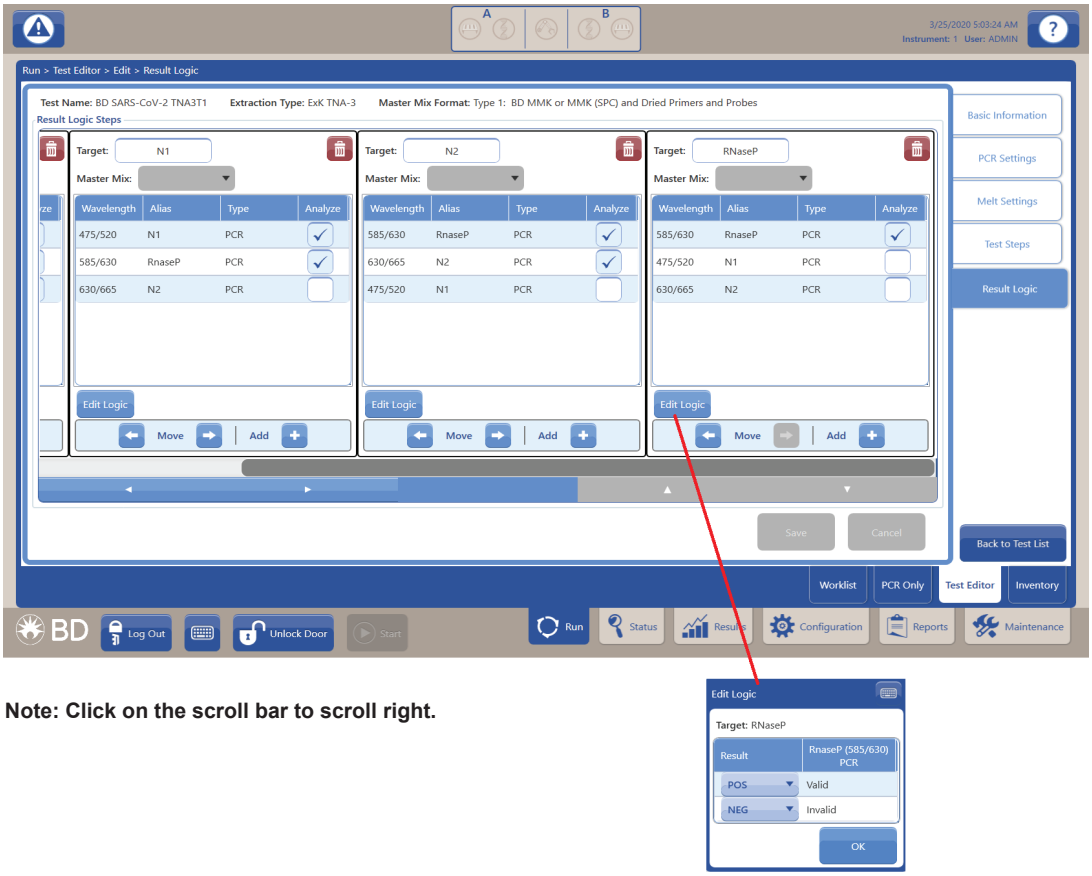
Melt Settings Section

Test Steps Section



Result Logic Section (enter result logic by clicking the “Edit Logic” button)





Note: Click on the scroll bar to scroll right.

7. Click **<SAVE>** after all information has been entered into the Test Editor. The UDP only needs to be created once, and steps 6 and 7 do not need to be repeated for subsequent runs.
8. Click on the Run tab, then Inventory. Enter the kit lot number for the BD MAX ExK TNA-3 kit in the Kit Lot Number field and BD SARS-CoV-2 Reagents for BD MAX System in the Master Mix Lot Number field (for lot traceability) by either scanning the barcode with the scanner or by manual entry.

   Note: Repeat step 8 each time a new kit lot is used.
9. Navigate to the Worklist (RUN > WORKLIST). Using the pull down menu select the UDP previously created in Step 6 (example: BD SARS-CoV-2 TNA3).
10. Enter the Sample Buffer Tube ID, Patient ID and Accession Number (if applicable) into the Worklist, either by scanning the barcode with the scanner or by manual entry.
11. Select the appropriate kit lot number (found on the outer box) from the pull down menu.
12. Repeat Steps 9 to 11 for all remaining Sample Buffer Tubes.
13. Place the Sample Buffer Tubes into the BD MAX System Rack(s) corresponding to the Unitized Reagent Strips previously assembled.

    Note: Place the Sample Buffer Tubes into the sample rack with 1D barcode labels facing outward (this makes scanning Sample Buffer Tubes easier during sample login).

14. Place the required number of BD MAX PCR Cartridge(s) into the BD MAX System (refer to Figure 2).

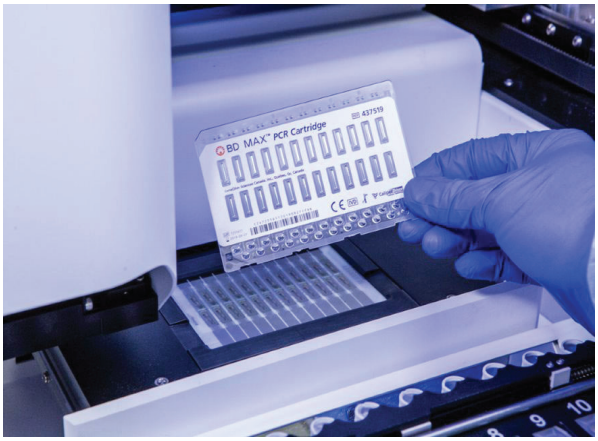


Figure 2: Load BD PCR Cartridges

15. Load rack(s) onto the BD MAX System (refer to Figure 3).

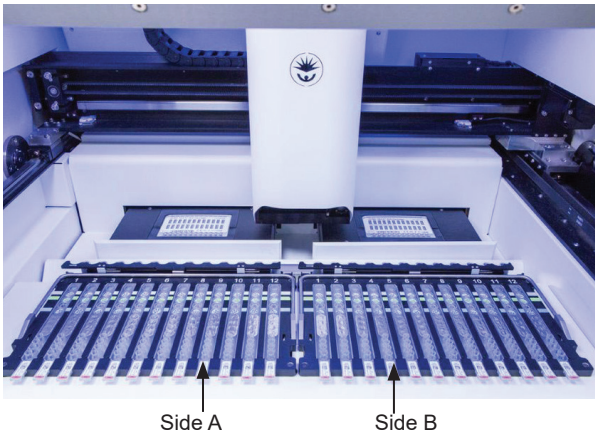


Figure 3: Load Rack(s) onto the BD MAX System

16. Close the BD MAX System lid and click **<Start>** to begin the processing.

QUALITY CONTROL

Quality control procedures monitor the performance of the assay. Laboratories must establish the number, type, and frequency of testing of control materials according to guidelines or requirements of local, provincial, state, and federal and/or country regulations or accreditation organizations in order to monitor the effectiveness of the entire analytical process. For general Quality Control guidance, the user may wish to refer to CLSI MM3 and EP12.[1,2]

External Control materials are not provided by BD. External Positive and Negative Controls are not used by the BD MAX System software for the purpose of sample test result interpretation. External Controls are treated as if they were patient samples. (Refer to the table in the Results Interpretation section for the interpretation of External Control assay results.)

It is recommended that one (1) External Positive Control and one (1) External Negative Control be run at least daily until adequate process validation is achieved on the BD MAX System in each laboratory setting. Reduced frequency of control testing should be in accordance with applicable regulations.

The External Positive Control is intended to monitor for substantial reagent failure. The External Negative Control is intended to detect reagent or environmental contamination (or carry-over) by target nucleic acids.

Various types of External Controls are recommended to allow the user to select the most appropriate for their laboratory quality control program.

External Negative Control: A previously characterized sample known to be negative or a Sample Buffer Tube with 750 µL water added. BD recommends that the External Negative Control be prepared prior to the External Positive Control in order to reduce the potential for contamination as a result of control preparation.

External Positive Control: Commercially available control material from Microbiologics, BioGX, CDC/IDT, or other authorized control material may be used.

For the preparation of External Control suspensions, it is recommended that RNA suspensions be prepared in the Sample Buffer Tube according to manufacturer's instructions.

All External Controls should yield the expected results (positive for External Positive Control, negative for External Negative Control).

An External Negative Control that yields a positive result is indicative of sample handling and/or contamination. An External Positive Control that yields a negative result is indicative of a specimen handling/preparation problem. Review the specimen handling/preparation technique.

An External Control that yields an Unresolved, Indeterminate or Incomplete test result is indicative of a reagent or a BD MAX System failure. Check the BD MAX System monitor for any error messages. Refer to the System Error Summary section of the BD MAX System User's Manual[3] for interpretation of warning and error codes. If the problem persists, use reagents from an unopened pouch or use a new assay kit.

RESULT INTERPRETATION

Results are available on the results tab in the Results window on the BD MAX System monitor. The BD MAX System automatically interprets the test result when the SARS-CoV-2 User Defined Protocol (UDP) is used. All test controls should be examined prior to interpretation of patient results. If the controls are not valid, the patient results cannot be interpreted.

External Negative and Positive Controls

If the positive or negative control does not exhibit the expected performance as described in the Control Interpretations table below, the assay may have been set up/or executed improperly, or reagent or equipment malfunction could have occurred. In this case, invalidate the run and re-test all samples in that run.

The RNase P gene serves as both a sample extraction control (EC) and an internal amplification control (IAC). In the event that both N1 and N2 region results are negative, an RNase P result must be positive for the BD SARS-CoV-2 result to be a valid negative result. When either N1 or N2 target result is positive, the RNase P result is ignored.

If any of the above controls do not exhibit the expected performance as described, the assay may have been set up/or executed improperly, or reagent or equipment malfunction could have occurred. Invalidate the run and re-test.

Table 1: External Control Interpretations

Control Type	Used to Monitor	Expected Results			
		N1	N2	RNase P	CoV-2
Negative Control – Sample Buffer Tube with 750 µL water	Reagent and/or environmental contamination	UNR*	UNR*	NEG	UNR*
Negative Control – Known Negative Sample		NEG	NEG	POS	NEG
Extraction Control and RNase P Positive Control	Substantial reagent failure including primer and probe integrity	NEG	NEG	POS	NEG
N1 and N2 Positive Control	Substantial reagent failure including primer and probe integrity	POS	POS	NEG	POS

*UNR is expected result and does not need to be repeated.

Examination and Interpretation of Patient Specimen Results

Assessment of clinical specimen test results should be performed after the external positive and negative controls have been examined and determined to be valid and acceptable. If the controls are not valid, the patient results cannot be interpreted.

The table below lists the expected results. If results are obtained that do not follow these guidelines, re-extract and re-test the sample. If repeat testing yields similar results, collect a fresh sample from the patient for testing.

Table 2: Interpretation of Patient Specimen Results

N1 Region	N2 Region	Extraction Control (RNase P)	CoV-2	Result Interpretation[a,b]	Actions
Pos	Pos	Pos/Neg	Pos	Positive	Report as Positive
Pos	Neg	Pos/Neg	Pos	Positive	Report as Positive
Neg	Pos	Pos/Neg	Pos	Positive	Report as Positive
Neg	Neg	Pos	Neg	Negative	Report as Not Detected
Neg	Neg	Neg	UNR	UNR	Repeat Test[c]

[a]UNR = Unresolved

[b]Laboratories should report their diagnostic result as appropriate and in compliance with their specific reporting system.

[c]Repeat Test by preparing a fresh sample buffer tube from the original primary UVT or UTM sample.

UNRESOLVED, INDETERMINATE, AND INCOMPLETE RESULTS

When an Indeterminate (IND), Unresolved (UNR), or Incomplete (INC) result is obtained a repeat test from the primary sample must be performed. If an External Control fails, repeat testing of all specimens conducted on the same day using freshly prepared External Controls (see Quality Control).

Unresolved Result

Unresolved results may be obtained in the event that specimen-associated inhibition or reagent failure prevents proper target or RNase P amplification. Sample(s) can be repeated from the primary sample. Uncap the BD MAX TNA-3 Sample Buffer Tube and transfer (using a calibrated, variable pipette) 750 µL from the UVT/UTM specimen directly into the BD MAX TNA-3 Sample Buffer Tube. Restart from the BD MAX System Operation section.

Indeterminate Result

Indeterminate results may be obtained in the event that a System failure occurs. Sample(s) can be repeated from the primary sample. Uncap the BD MAX TNA-3 Sample Buffer Tube and transfer (using a calibrated, variable pipette) 750 µL from the UVT/UTM specimen directly into the BD MAX TNA-3 Sample Buffer Tube. Restart from the BD MAX System Operation section.

Incomplete Result

Incomplete results may be obtained in the event that Specimen Preparation or the PCR did not reach its expected time points. Sample(s) can be repeated from the primary sample. Uncap the BD MAX TNA-3 Sample Buffer Tube and transfer (using a calibrated, variable pipette) 750 µL from the UVT/UTM specimen directly into the BD MAX TNA-3 Sample Buffer Tube. Restart from the BD MAX System Operation section.

External Control Failure

External Controls should yield expected results when tested. If samples have to be repeated due to an incorrect External Control result, the samples should be repeated from the primary sample along with freshly prepared External Controls. Restart from the BD MAX System Operation section.

LIMITATIONS OF THE PROCEDURE

- BD SARS-CoV-2 Reagents for BD MAX System has been evaluated only for use in combination with the BD MAX ExK TNA-3 kit and BD MAX System.
- Reliable results depend on proper sample collection, storage and handling procedures.
- This test has been designed for the detection of SARS-CoV-2 RNA in nasopharyngeal and oropharyngeal swab samples collected in BD Universal Viral Transport System (UVT) or Copan Universal Transport Media System (UTM). Use of BD SARS-CoV-2 Reagents for BD MAX System with other sample types has not been assessed and performance characteristics are unknown.
- Nasal swabs and mid-turbinate nasal swabs are considered acceptable specimen types for use with BD SARS-CoV-2 Reagents for BD MAX System, but performance with these specimen types has not been established. Testing of nasal and mid-turbinate nasal swabs (self-collected under supervision of or collected by a healthcare provider) is limited to patients with symptoms of COVID-19. Please refer to FDA's FAQs on Diagnostic Testing for SARS-CoV-2 for additional information.
- Detection of SARS-CoV-2 RNA may be affected by sample collection methods, patient factors (e.g., presence of symptoms), and/or stage of infection.
- As with any molecular test, mutations within the target regions of SARS-CoV-2 could affect primer and/or probe binding resulting in failure to detect the presence of virus.
- Due to inherent differences between technologies, it is recommended that, prior to switching from one technology to the next, users perform method correlation studies in their laboratory to qualify technology differences. One hundred percent agreement between the results should not be expected due to aforementioned differences between technologies. Users should follow their own specific policies/procedures.
- False negative or invalid results may occur due to interference. The RNase P endogenous control is included to help identify the specimens containing substances that may interfere with nucleic acid isolation and PCR amplification.
- Good laboratory practices and careful adherence to the procedures specified in this Instructions For Use document are necessary to avoid contamination of reagents.
- For BD MAX TNA extraction: Tobramycin at $1.1x10^{-3}$ g/Sample Buffer Tube interferes with the assay. Lower concentrations of Tobramycin have not been evaluated.
- The effect of homeopathic medications for respiratory symptoms on the assay performance was not tested.
- BD SARS-CoV-2 Reagent and BD MAX ExK TNA-3 extraction have not been evaluated for patients receiving intranasally administered influenza vaccine.

CONDITIONS OF AUTHORIZATION FOR THE LABORATORY

The BD SARS-CoV-2 Reagents for BD MAX System Letter of Authorization, along with the authorized Fact Sheet for Healthcare Providers, the authorized Fact Sheet for Patients, and authorized labeling are available on the FDA website: https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations

To assist clinical laboratories running the BD SARS-CoV-2 Reagents for BD MAX System, the relevant Conditions of Authorization are listed below, and are required to be met by laboratories performing the EUA test.

- Authorized laboratories* using the BD SARS-CoV-2 Reagents for BD MAX System will include with result reports of the BD SARS-CoV-2 for BD MAX System test, all authorized Fact Sheets. Under exigent circumstances, other appropriate methods for disseminating these Fact Sheets may be used, which may include mass media.
- Authorized laboratories using the BD SARS-CoV-2 Reagents for BD MAX System will perform the BD SARS-CoV-2 Reagents for use with the BD MAX System as outlined in the BD SARS-CoV-2 Reagents for BD MAX System Instructions for Use. Deviations from the authorized procedures, including the authorized instruments, authorized extraction methods, authorized clinical specimen types, authorized control materials, authorized ancillary reagents, and authorized material required to perform the BD SARS-CoV-2 Reagents for BD MAX System test are not permitted.
- Authorized laboratories that receive the BD SARS-CoV-2 Reagents for BD MAX System test must notify the relevant public health authorities of their intent to run the test prior to initiating testing.
- All laboratory personnel using the BD SARS-CoV-2 Reagents for BD MAX System test must be appropriately trained in RT-PCR techniques, use appropriate laboratory and personal protective equipment when handling this kit, and use the test in accordance with the authorized labeling.
- Authorized laboratories using the BD SARS-CoV-2 Reagents for BD MAX System test will have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.
- Becton, Dickinson and Company, authorized distributors, and authorized laboratories using the BD SARS-CoV-2 Reagents for BD MAX System will ensure that any records associated with this EUA are maintained until otherwise notified by FDA. Such records will be made available to FDA for inspection upon request.
- Authorized laboratories will collect information on the performance of the BD SARS-CoV-2 Reagents for BD MAX System test and report to DMD/OHT7-OIR/OPEQ/ CDRH (via email: CDRH-EUA-Reporting@fda.hhs.gov) and to Becton, Dickinson and Company Customer Technical Support 1.800.638.8663 any suspected occurrence of false positive or false negative results and significant deviations from the established performance characteristics of the BD SARS-CoV-2 Reagents for BD MAX System test of which they become aware.

*For ease of reference, the letter of authorization refers to, “Laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, to perform moderate and high complexity tests” as “authorized laboratories”.

NON-CLINICAL PERFORMANCE EVALUATION

Limit of Detection (LoD)

LoD studies determine the lowest detectable concentration of the SARS-CoV-2 at which approximately 95% of all (true positive) replicates test positive.

To determine the LoD, quantified genomic viral RNA from SARS-CoV-2, obtained from BEI Resources (Cat. No. NR-52285), was serially diluted into pooled negative nasopharyngeal clinical matrix, a total of 5 concentrations levels, with 2-fold serial dilutions between each level.

Confirmation of the estimated LoD was performed with one reagent lot in replicates of 20 prepared in pooled nasopharyngeal swab clinical matrix. The LoD is the lowest concentration (reported as genomic equivalents/mL, GE/mL) of genomic RNA from SARS-CoV-2 that can be reproducibly distinguished from negative samples ≥ 95%. The LoD for the assay is 40 GE/mL.

Table 3. LoD determination using genomic RNA from SARS-CoV-2 USA-WA1/2020 strain

Strain	Concentration (GE/mL)	Total Valid Results	Positives			Mean Ct.score		
			CoV-2	N1	N2	N1	N2	RNase P
USA-WA1/2020 (Stock 4.8e+07 GE/mL)	40	20	20	20	20	33.4	32.9	21.4

Reactivity/ Inclusivity

The nCoV N1 and nCoV N2 primers and probes utilized within the BD SARS-CoV-2 Reagents for BD MAX System are identical in sequence to those reported in the CDC 2019-Novel Coronavirus (2019-nCoV) Real-Time RT-PCR Diagnostic Panel. The CDC reported an *in silico* analysis of primer and probe sequences within their IFU (CDC-006-0019, Rev 02), and has been copied below for reference:

An alignment was performed with the oligonucleotide primer and probe sequences of the CDC 2019 nCoV Real-Time RT-PCR Diagnostic Panel with all publicly available nucleic acid sequences for 2019-nCoV in GenBank as of February 1, 2020 to demonstrate the predicted inclusivity of the CDC 2019 nCoV Real-Time RT-PCR Diagnostic panel. All the alignments show 100% identity of the CDC panel to the available 2019-nCoV sequences with the exception of one nucleotide mismatch with the N1 forward primer in one deposited sequence.

Cross-Reactivity

The nCoV N1 and nCoV N2 primers and probes utilized within the BD SARS-CoV-2 Reagents for BD MAX System are identical in sequence to those reported in the CDC 2019-Novel Coronavirus (2019-nCoV) Real-Time RT-PCR Diagnostic Panel. The CDC reported an *in silico* analysis of primer and probe sequences within their IFU (CDC-006-0019, Rev 02), and has been copied below for reference:

BLASTn analysis queries of the 2019-nCoV rRT-PCR assays primers and probes were performed against public domain nucleotide sequences. The database search parameters were as follows: 1) The nucleotide collection consists of GenBank+EMBL+DDBJ+PDB+RefSeq sequences, but excludes EST, STS, GSS, WGS, TSA, patent sequences as well as phase 0, 1, and 2 HTGS sequences and sequences longer than 100Mb; 2) The database is non-redundant. Identical sequences have been merged into one entry, while preserving the accession, GI, title and taxonomy information for each entry; 3) Database was updated on 10/03/2019; 4) The search parameters automatically adjust for short input sequences and the expect threshold is 1000; 5) The match and mismatch scores are 1 and -3, respectively; 6) The penalty to create and extend a gap in an alignment is 5 and 2, respectively.

2019-nCoV_N1 Assay:

Probe sequence of 2019-nCoV rRT-PCR assay N1 showed high sequence homology with SARS coronavirus and Bat SARS-like coronavirus genome. However, forward and reverse primers showed no sequence homology with SARS coronavirus and Bat SARS-like coronavirus genome. Combining primers and probe, there is no significant homologies with human genome, other coronaviruses or human microflora that would predict potential false positive rRT-PCR results.

2019-nCoV_N2 Assay:

The forward primer sequence of 2019-nCoV rRT-PCR assay N2 showed high sequence homology to Bat SARS-like coronaviruses. The reverse primer and probe sequences showed no significant homology with human genome, other coronaviruses or human microflora. Combining primers and probe, there is no prediction of potential false positive rRT-PCR results.

In summary, the 2019-nCoV rRT-PCR assay N1 and N2, designed for the specific detection of 2019-nCoV, showed no significant combined homologies with human genome, other coronaviruses, or human microflora that would predict potential false positive rRT-PCR results.

CLINICAL EVALUATION

The performance of BD SARS-CoV-2 Reagents for BD MAX System with retrospective collected nasopharyngeal swab clinical samples was evaluated using 30 individual negative clinical samples and 50 contrived positive clinical samples collected from patients with signs and symptoms of an upper respiratory infection.

Clinical samples were collected by qualified personnel according to the package insert of the collection device. Samples were handled as described in the package insert of the collection device and stored frozen until use.

Low positive and moderate positive contrived clinical samples were prepared by spiking quantified genomic RNA (SARS-CoV-2 USA-WA1/2020 strain) into individual negative clinical matrix to approximately ~1-2x LoD (40 samples) and ~3-5x LoD (10 samples), respectively.

The low positive samples showed 95% agreement with the expected results. All moderate positive samples (~3-5x LoD) were positive and all negative samples were negative in the background of individual clinical sample matrix.

Table 4. Clinical evaluation with contrived nasopharyngeal swab samples

Sample Concentration	Total Valid Results	% Positive Results	N1 Region		N2 Region		RNase P
			Agreement with Expected Results	Mean Ct	Agreement with Expected Results	Mean Ct	Mean Ct
~1-2x LoD	40	95% (38/40)	37/40[a]	33.9[a]	37/40[b]	33.9[b]	20.9
~3-5x LoD	10	100% (10/10)	10/10	32.6	10/10	32.3	20.1
Negative	29[c]	N/A (0/29)[c]	29/29[c]	N/A	29/29[c]	N/A	20.4

[a] One sample was positive for N1 detection but negative for N2 detection

[b] One sample was positive for N2 detection but negative for N1 detection

[c] During screening one retrospective nasopharyngeal swab clinical sample resulted in an UNR for N1 and N2 and as a result the sample was removed from data analysis.

REFERENCES

1. Clinical and Laboratory Standards Institute. Protection of laboratory workers from occupationally acquired infections; Approved Guideline. Document M29 (Refer to the latest edition).
2. Centers for Disease Control and Prevention, and National Institutes of Health. Biosafety in microbiological and biomedical laboratories. Chosewood L.C. and Wilson D.E. (eds) (2009). HHS Publication No. (CDC) 21–1112.
3. BD MAX System User's Manual (refer to the latest revision) BD Life Sciences, Sparks, MD 21152 USA.

Change History

Revision	Date	Change Summary
01	2020-04	Initial release.

US Customers only: For symbol glossary, refer to bd.com/symbols-glossary

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YYYY-MM-DD / YYYY-MM (MM = end of month)
ГГГГ-ММ-ДД / ГГГГ-ММ (ММ = края на месеца)
RRRR-MM-DD / RRRR-MM (MM = konec měsíce)
ÅÅÅÅ-MM-DD / ÅÅÅÅ-MM (MM = slutning af måned)
JJJJ-MM-TT / JJJJ-MM (MM = Monatsende)
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AAAA-MM-DD / AAAA-MM (MM = fin del mes)
AAAA-KK-PP / AAAA-KK (KK = kuu lõpp)
AAAA-MM-JJ / AAAA-MM (MM = fin du mois)
GGGG-MM-DD / GGGG-MM (MM = kraj mjeseca)
ÉÉÉÉ-HH-NN / ÉÉÉÉ-HH (HH = hónap utolsó napja)
AAAA-MM-GG / AAAA-MM (MM = fine mese)
ЖЖЖЖ-АА-КК / ЖЖЖЖ-АА / (АА = айдың соңы)
YYYY-MM-DD/YYYY-MM(MM = 월말)
MMMM-MM-DD / MMMM-MM (MM = mėnesio pabaiga)
GGGG-MM-DD/GGGG-MM (MM = mēneša beigas)
JJJJ-MM-DD / JJJJ-MM (MM = einde maand)
ÅÅÅÅ-MM-DD / ÅÅÅÅ-MM (MM = slutten av måneden)
RRRR-MM-DD / RRRR-MM (MM = koniec miesiąca)
AAAA-MM-DD / AAAA-MM (MM = fim do mês)
AAAA-LL-ZZ / AAAA-LL (LL = sfârşitul lunii)
ГГГГ-ММ-ДД / ГГГГ-ММ (ММ = конец месяца)
RRRR-MM-DD / RRRR-MM (MM = koniec mesiaca)
GGGG-MM-DD / GGGG-MM (MM = kraj meseca)
ÅÅÅÅ-MM-DD / ÅÅÅÅ-MM (MM = slutet av månaden)
YYYY-AA-GG / YYYY-AA (AA = ayın sonu)
РРРР-ММ-ДД / РРРР-ММ (ММ = кінець місяця)
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CONTROL — Control / Контролно / Kontrola / Kontrol / Kontrolle / Μάρτυρας / Kontroll / Contrôle / Controllo / Бақылау / 컨트롤 / Kontrolė / Kontrole / Controle / Controlo / Контроль / kontroll / Контроль / 对照

CONTROL + — Positive control / Положителен контрол / Pozitivní kontrola / Positiv kontrol / Positive Kontrolle / Θετικός μάρτυρας / Control positivo / Positiivne kontroll / Contrôle positif / Pozitivna kontrola / Pozitív kontroll / Controllo positivo / Оң бақылау / 양성 컨트롤 / Teigiama kontrolė / Pozitīvā kontrole / Positieve controle / Kontrola dodatnia / Controlo positivo / Control pozitiv / Положительный контроль / Pozitif kontrol / Позитивний контроль / 阳性对照试剂

CONTROL – — Negative control / Отрицателен контрол / Negativní kontrola / Negativ kontrol / Negative Kontrolle / Αρνητικός μάρτυρας / Control negativo / Negatiivne kontroll / Contrôle négatif / Negativna kontrola / Negatív kontroll / Controllo negativo / Теріс бақылау / 음성 컨트롤 / Neigiama kontrolė / Negatīvā kontrole / Negatieve controle / Kontrola ujemna / Controlo negativo / Control negativ / Отрицательный контроль / Negatif kontrol / Негативний контроль / 阴性对照试剂

STERILE EO — Method of sterilization: ethylene oxide / Метод на стерилизация: етиленов оксид / Způsob sterilizace: etylenoxid / Steriliseringsmetode: ethylenoxid / Sterilisationsmethode: Ethylenoxid / Μέθοδος αποστείρωσης: αιθυλενοξείδιο / Método de esterilización: óxido de etileno / Steriliseerimismeetod: etüleenoksiid / Méthode de stérilisation : oxyde d'éthylène / Metoda sterilizacije: etilen oksid / Sterilizálás módszere: etilén-oxid / Metodo di sterilizzazione: ossido di etilene / Стерилизация әдісі – этилен тотығы / 소독 방법: 에틸렌옥사이드 / Sterilizavimo būdas: etileno oksidas / Sterilizēšanas metode: etilēnoksīds / Gesteriliseerd met behulp van ethyleenoxide / Steriliseringsmetode: etylenoksid / Metoda sterylizacji: tlenek etylu / Método de esterilização: óxido de etileno / Metodă de sterilizare: oxid de etilenă / Метод стерилизации: этиленоксид / Metóda sterilizácie: etylénoxid / Metoda sterilizacije: etilen oksid / Steriliseringsmetod: etenoxid / Sterilizasyon yöntemi: etilen oksit / Метод стерилізації: етиленоксидом / 灭菌方法：环氧乙烷

STERILE R — Method of sterilization: irradiation / Метод на стерилизация: ирадиация / Způsob sterilizace: záření / Steriliseringsmetode: bestråling / Sterilisationsmethode: Bestrahlung / Μέθοδος αποστείρωσης: ακτινοβολία / Método de esterilización: irradiación / Steriliseerimismeetod: kiirgus / Méthode de stérilisation : irradiation / Metoda sterilizacije: zračenje / Sterilizálás módszere: besugárzás / Metodo di sterilizzazione: irradiazione / Стерилизация әдісі – сәуле түсіру / 소독 방법: 방사 / Sterilizavimo būdas: radiacija / Sterilizēšanas metode: apstarošana / Gesteriliseerd met behulp van bestraling / Steriliseringsmetode: bestråling / Metoda sterylizacji: napromienianie / Método de esterilização: irradiação / Metodă de sterilizare: iradiere / Метод стерилизации: облучение / Metóda sterilizácie: ožiarenie / Metoda sterilizacije: ozračavanje / Steriliseringsmetod: strålning / Sterilizasyon yöntemi: irradyasyon / Метод стерилізації: опроміненням / 灭菌方法：辐射

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Keep dry / Пазете сухо / Skladujte v suchém prostředí / Opbevares tørt / Trocklagern / Φυλάξτε το στεγνό / Mantener seco / Hoida kuivas / Conserver au sec / Držati na suhom / Száraz helyen tartandó / Tenere all'asciutto / Құрғақ күйінде ұста / 건조 상태 유지 / Laikykite sausai / Uzglabāt sausu / Droog houden / Holdes tørt / Przechowywać w stanie suchym / Manter seco / A se feri de umezeală / Не допускать попадания влаги / Uchovávajte v suchu / Držite na suvom mestu / Förvaras torrt / Kuru bir şekilde muhafaza edin / Берегти від вологи / 请保持干燥

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µL/test / µL/тест / µL/Test / µL/εξέταση / µL/prueba / µL/teszt / µL/테스트 / мкл/тест / µL/tyrimas / µL/pārbaude / µL/teste / мкл/аналіз / µL/检测

Keep away from light / Пазете от светлина / Nevystavujte světlu / Må ikke udsættes for lys / Vor Licht schützen / Κρατήστε το μακριά από το φως / Mantener alejado de la luz / Hoida eemal valgusest / Conserver à l'abri de la lumière / Držati dalje od svjetla / Fény nem érheti / Tenere al riparo dalla luce / Қараңғыланған жерде ұста / 빛을 피해야 함 / Laikyti atokiau nuo šilumos šaltinių / Sargāt no gaismas / Niet blootstellen aan zonlicht / Må ikke utsettes for lys / Przechowywać z dala od źródeł światła / Manter ao abrigo da luz / Feriţi de lumină / Хранить в темноте / Uchovávajte mimo dosahu svetla / Držite dalje od svetlosti / Får ej utsättas för ljus / Işıktan uzak tutun / Берегти від дії світла / 请远离光线

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Fragile, Handle with Care / Чупливо, Работете с необходимото внимание. / Křehké. Při manipulaci postupujte opatrně. / Forsigtig, kan gå i stykker. / Zerbrechlich, vorsichtig handhaben. / Εύθραυστο. Χειριστείτε το με προσοχή. / Frágil. Manipular con cuidado. / Õrn, käsitsege ettevaatlikult. / Fragile. Manipuler avec précaution. / Lomljivo, rukujte pažljivo. / Törékeny! Óvatosan kezelendő. / Fragile, maneggiare con cura. / Сынғыш, абайлап пайдаланыңыз. / 조심 깨지기 쉬운 처리 / Trapu, elkitės atsargiai. / Trausls; rīkoties uzmanīgi / Breekbaar, voorzichtig behandelen. / Ømtålig, håndter forsiktig. / Krucha zawartość, przenosić ostrożnie. / Frágil, Manuseie com Cuidado. / Fragil, manipulaţi cu atenţie. / Хрупкое! Обращаться с осторожностью. / Krehké, vyžaduje sa opatrná manipulácia. / Lomljivo - rukujte pažljivo. / Bräckligt. Hantera försiktigt. / Kolay Kırılır, Dikkatli Taşıyın. / Тендітна, звертатися з обережністю / 易碎，小心轻放

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Preparation of External Positive Controls for BD SARS-CoV-2 Reagents for BD MAX™ System

Intended Use

The BD SARS-CoV-2 Reagents for BD MAX™ System is a real-time RT-PCR test intended for the qualitative detection of nucleic acid from the SARS-CoV-2 in nasal, nasopharyngeal and oropharyngeal swab samples from individuals suspected of COVID-19 by their healthcare provider. Testing is limited to laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, to perform moderate and high complexity tests.[1]

Results are for the identification of SARS-CoV-2 RNA. The SARS-CoV-2 RNA is generally detectable in upper respiratory samples during the acute phase of infection. Positive results are indicative of the presence of SARS-CoV-2 RNA; clinical correlation with patient history and other diagnostic information is necessary to determine patient infection status. Positive results do not rule out bacterial infection or co-infection with other viruses. The agent detected may not be the definite cause of disease. Laboratories within the United States and its territories are required to report all positive results to the appropriate public health authorities.[1]

Negative results do not preclude SARS-CoV-2 infection and should not be used as the sole basis for patient management decisions. Negative results must be combined with clinical observations, patient history, and epidemiological information.[1]

The BD SARS-CoV-2 Reagents for BD MAX System is intended for use by qualified and trained clinical laboratory personnel specifically instructed and trained in the techniques of real-time PCR, *in vitro* diagnostic procedures, and use of the BD MAX System. The BD SARS-CoV-2 Reagents for BD MAX™ System is only for use under the Food and Drug Administration's Emergency Use Authorization.[1]

Purpose

According to the "Guidance for COVID-19 Testing for CAP-Accredited Laboratories" by the College of American Pathologists, clinical laboratories using EUA assays for COVID-19 testing must perform quality control each of day of patient testing.[2] External positive and negative controls are samples that act as surrogates for clinical specimens. They are processed like a clinical specimen to monitor the ongoing performance of the entire analytic process in every assay run.

The purpose of this document is to provide clinical laboratories with suggested procedures for preparing External Positive Controls (EPC) for the BD SARS-CoV-2 Reagents on the BD MAX System using commercially prepared positive controls and materials.

Table 1. Commercially Prepared Controls for SARS-CoV-2

Manufacturer	SARS-CoV-2 Control	Other Control
BioGX SARS-CoV-2 & RNase P Synthetic Single- Stranded RNA Control Templates[3]	SARS-CoV-2 Nucleocapsid Phosphoprotein gene N1 SARS-CoV-2 Nucleocapsid Phosphoprotein gene N2	RNase P
Microbiologics® Helix Elite™ Synthetic RNA Standard[4]	1044 nucleotide segment of SARS-CoV-2 N (nucleocapsid) gene (N1, N2 and N3)	N/A
Integrated DNA Technologies Positive Control Plasmids[5,6]	Complete 2019-nCoV Nucleocapsid gene (N1, N2 and N3)	Portion of the RPP30 single copy gene found in humans

Each suggested procedure for preparing an EPC has been verified by BD. However, the choice of EPC for the BD SARS-CoV-2 Reagents for BD MAX System is ultimately the decision of the laboratory, in accordance with applicable local, state, and/or federal regulations, accreditation requirements and the laboratory's standard Quality Control (QC) procedures. Preparation of External Negative Controls (ENC) for the BD SARS-CoV-2 Reagents for BD MAX System is outside the scope of this document and should be provided by the laboratory.

A) BioGX SARS-CoV-2 Nucleocapsid N1 and N2 genes and RNase P

The BioGX SARS-CoV-2 & RNase P Synthetic Single- Stranded RNA Control Templates kit contains lyophilized control template beads for the SARS-CoV-2 Nucleocapsid Phosphoprotein gene (N1), SARS-CoV-2 Nucleocapsid Phosphoprotein gene (N2), and RNase P.[3] The beads are formulated with quantified RNA (single stranded RNA) at 1 x 10^5 copies per tube in a lyophilized bead format. Each product package contains 1 pouch of 12 tubes with each tube containing 1 lyophilized control template bead.[3] The BioGX SARS-CoV-2 & RNase P Synthetic Single- Stranded RNA Control Templates should be stored at 2-8°C.[3]

Table 2. Materials Needed for the BioGX External Positive Controls

Material	Part #
BioGX SARS-CoV-2 & RNase P Synthetic Single- Stranded RNA Control Templates	BD # 444214
BD MAX ExK TNA-3 Sample Buffer Tubes	BD # 442827
Nuclease-free water*	Invitrogen # 4387936**

**Alternate diluents e.g., Universal Transport Media (UTM) may be used if validated by the laboratory*

***or Equivalent*

Preparation of External Positive Controls from BioGX Control Beads

1. To prepare the SARS-CoV-2 N1 and N2 EPC, pipet 650 µL of nuclease-free water into a BD MAX ExK TNA-3 Sample Buffer Tube (SBT).
2. Rehydrate the BioGX SARS-CoV-2 N1 and N2 positive control beads individually with 100 µL of nuclease-free water.
3. Pipette the entire volume of the rehydrated N1 and N2 positive controls into the **same** SBT. Close the SBT with a blue septum cap and vortex or mix by inversion 5 times. Label the SBT as the SARS-CoV-2 N1/N2 EPC.

4. To prepare the RNase P positive control bead, repeat steps 1-3 above with a **new** BD MAX ExK TNA-3 SBT and the BioGX RNase P positive control beads. The rehydrated RNase P positive control bead is added to the separate SBT.
5. Close the SBT with a blue septum cap and vortex or mix by inversion 5 times. Label the tube as the RNase P EPC.
6. Proceed with testing the prepared SARS-CoV-2 N1/N2 EPC SBT and the RNase P EPC SBT with the BD SARS-CoV-2 Reagents for BD MAX System according to instructions in the Package Insert.[1] Each run should include an ENC prepared by the laboratory.

Expected Results

Laboratories should refer to the BD SARS-CoV-2 Reagents for BD MAX System Package Insert for full interpretation of external control test results.[1] The expected results are below.

Table 3. Expected results for the SARS-CoV-2 N1/N1 and RNase P External Positive Controls

External Positive Control	N1	N2	RNase P	COV-2	Result Interpretation
SARS CoV-2 N1/N2 EPC	Pos	Pos	Neg	Pos	Positive
RNase P EPC	Neg	Neg	Pos	Neg	Positive

The SARS CoV-2 N1/N2 EPC and RNase P EPC should yield the expected positive results.

B) Microbiologics SARS-CoV-2 Synthetic RNA (N gene targets)

The Microbiologics® Helix Elite™ SARS-CoV-2 synthetic RNA standard is a 1044-nucleotide portion of the SARS-CoV-2 N (nucleocapsid) gene containing the three markers N1, N2 and N3. Each kit includes 1 vial of dried synthetic RNA (concentration: 1x 10^9 cps/µL), 1 vial of molecular standard water, and a certificate of analysis.[4] The Helix Elite™ SARS-CoV-2 synthetic RNA standard should be stored at 2-25°C according to the manufacturer's instructions.[4]

Table 4. Materials Needed for the Microbiologics External Positive Control

Material	Part #
Microbiologics® Helix Elite™ Synthetic Standard SARS-CoV-2 Synthetic RNA (N gene Targets)	Microbiologics # HE0060S
BD MAX ExK TNA-3 Sample Buffer Tubes	BD # 442827
Molecular standard or Nuclease-free water*	Invitrogen # 4387936**
1X TE buffer, pH 8.0	Thermo Fisher Scientific # AM9849**
2 mL Tubes	VWR # 10025-756**

**Alternate diluents e.g., Universal Transport Media (UTM) may be used if validated by the laboratory*

***or Equivalent*

Preparation of External Positive Control from Microbiologics Standard

1. To prepare the SARS-CoV-2 Synthetic RNA EPC, add 750 µL of nuclease-free water into a BD MAX ExK TNA-3 Sample Buffer Tube (SBT).
2. Rehydrate the lyophilized powder of the Helix Elite™ SARS-CoV-2 Synthetic RNA standard in 100 µL of nuclease-free water for a concentration stock of 1x 10^7 cps/µL.
3. Dilute the rehydrated SARS-CoV-2 Synthetic RNA by transferring the 100 µL to 900 µL of TE buffer for a stock concentration of 1 x 10^6 cps/µL.

4. Prepare serial dilutions of the 1 x 10^6 cps/µL stock in TE buffer to prepare a 100 cps/µL stock (See Table 5 for dilution scheme).
5. Pipette 50 µL of the 100 cps/µL diluted stock into the SBT.
6. Close the SBT with a blue septum cap and vortex or mix by inversion 5 times. Label the SBT as the SARS-CoV-2 Synthetic RNA EPC.
7. Proceed with testing the SARS-CoV-2 Synthetic RNA EPC SBT with the BD SARS-CoV-2 Reagents for BD MAX System according to instructions in the Package Insert.[1] Each run should include an ENC prepared by the laboratory.
8. Aliquot 10 µL of the remaining 1 x 10^6 cps/µL stock into 2 mL tubes; store the tubes -20°C or colder.

Table 5. Microbiologics Control Dilution Scheme from Master Stock

Stock (cps/µL)	Dilution Factor	Total Volume of Buffer (µL)	Volume of Stock to Spike (µL)	Volume of TE Buffer (µL)	Dilution Conc (cps/µL)
1,000,000	10	1,000	100	900	100,000
100,000	10	1,000	100	900	10,000
10,000	10	1,000	100	900	1,000
1000	10	1,000	100	900	100

Expected Results

Laboratories should refer to the BD SARS-CoV-2 Reagents for BD MAX System Package Insert for full interpretation of external control test results.[1] The expected results are below.

Table 6. Expected results for the SARS-CoV-2 Synthetic RNA External Positive Control

External Positive Control	N1	N2	RNase P	COV-2	Result Interpretation
SARS-CoV-2 Synthetic RNA EPC	Pos	Pos	Neg	Pos	Positive

The SARS-CoV-2 Synthetic RNA EPC should yield the expected positive results.

C) IDT 2019-nCoV_N and Hs_RPP30 Positive Control Plasmids

The Integrated DNA Technologies (IDT) 2019-nCoV_N Positive Control plasmid contains the complete nucleocapsid gene from 2019-nCoV (SARS-CoV-2). The Hs_RPP30 Positive Control plasmid contains a portion of the RPP30 gene, a single copy gene present in the human genome.[5,6] The IDT control plasmids are derived from the CDC nCoV EUA kit. Control Plasmids are delivered at 250 µL (200,000 copies/µL) in IDTE, pH 8.0. Store at -20°C or colder.

Table 7. Materials Needed for the IDT External Positive Controls

Material	Part #
IDT 2019-nCoV_N_Positive Control	IDT # 10006625
IDT Hs_RPP30 Positive Control	IDT # 10006626
ExK TNA-3 Sample Buffer Tubes	BD # 442827
Nuclease-free water*	Invitrogen # 4387936**
1X TE, buffer pH 8.0	Thermo Fisher Scientific # AM9849**
2 mL Tubes	VWR # 10025-756**

**Alternate diluents e.g., Universal Transport Media (UTM) may be used if validated by the laboratory*

***or Equivalent*

Preparation of External Positive Controls from IDT Control Plasmids

1. To prepare the 2019-nCOV_N EPC add 750 µL of nuclease-free water into a BD MAX ExK TNA-3 Sample Buffer Tube (SBT).
2. Prepare a dilution of the stock IDT 2019-nCoV_N Positive Control plasmid (200,000 copies/µL) in TE buffer (See Table 8 for dilution scheme).
3. Pipette 50 µL of the 200 copies/µL diluted stock into the SBT.
4. Close the SBT with a blue septum cap and vortex or mix by inversion 5 times. Label the SBT as the 2019-nCOV_N EPC.
5. To prepare the Hs_RPP30 EPC, repeat steps 1-3 above with a **new** BD MAX ExK TNA-3 SBT and the IDT Hs_RPP30 Positive Control Plasmid.
6. Close the SBT with a blue septum cap and vortex or mix by inversion 5 times. Label the SBT as the Hs_RPP30 EPC.
7. Proceed with testing the 2019-nCoV_N EPC SBT and the Hs_RPP30 EPC SBT with the BD SARS-CoV-2 Reagents for BD MAX System according to instructions in the Package Insert.[1] Each run should include an ENC prepared by the laboratory.

Table 8. IDT 2019-nCoV_N and Hs_RPP30 Plasmid Dilution Scheme

Stock (cps/µL)	Dilution Factor	Total Volume of Buffer (µL)	Volume of Stock to Spike (µL)	Volume of TE buffer (µL)	Dilution Conc (cps/µL)
200,000	10	50	5	45	20,000
20,000	10	100	10	90	2,000
2,000	10	500	50	450	200

Expected Results

Laboratories should refer to the BD SARS-CoV-2 Reagents for BD MAX System Package Insert for full interpretation of external control test results.[1] The expected results are below.

Table 9. Expected results for the 2019-nCoV_N and Hs_RPP30 External Positive Control

External Positive Control	N1	N2	RNase P	COV-2	Result Interpretation
2019-nCoV_N EPC	Pos	Pos	Neg	Pos	Positive
Hs_RPP30 EPC	Neg	Neg	Pos	Neg	Positive

The 2019-nCoV_N EPC and Hs_RPP30 EPC should yield the expected positive results.

Expanding the Protocols

The example protocols described above may be expanded at the laboratory's discretion by increasing the number of each EPC for each run of the BD SARS-CoV-2 Reagents for BD MAX System. Please follow the Storage and Stability instructions in the respective Package Inserts of all media and materials used.

IMPORTANT NOTE: Laboratories should follow Good Laboratory Practices and Universal Precautions at all times during preparation and use of external control materials. All materials should be disposed of properly as required by the institution.

Technical Service and Support

BD is committed to providing our customers timely and accurate support. If there are any questions or concerns about this document or the contents, please contact BD Life Sciences – Integrated Diagnostic Solutions Technical Service and Support by dialing 1-800-638-8663 (U.S.).

References

(1) BD SARS-CoV-2 Reagents for BD MAX™ System Package Insert. Becton Dickinson and Company, Sparks, MD. (Latest version).
(2) College of American Pathologists "Guidance for COVID-19 Testing for CAP-Accredited Laboratories" https://www.cap.org/laboratory-improvement/news-and-updates/guidance-for-covid-19-testing-for-cap-accredited-laboratories Accessed March 21, 2020.
(3) BioGX SARS-CoV-2 & RNase P Synthetic Single- Stranded RNA Control Templates. Package Insert (Latest version)
(4) Microbiologics® Helix Elite™ Synthetic Standard SARS-CoV-2 Synthetic RNA (N Gene Targets). Package Insert (Latest version)
(5) Integrated DNA Technologies 2019-nCoV_N_Positive Control Plasmid. Product Description (Latest version)
(6) Integrated DNA Technologies Hs_RPP30 Positive Control Plasmid. Product Description (Latest version)

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