BD SARS-CoV-2/Flu for BD MAX™ System

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

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English

2 °C 25 °C IVD bd.com/e-labeling R_x Only

INTENDED USE

BD SARS-CoV-2/Flu for BD MAX™ System is an automated multiplexed real-time RT-PCR test intended for the simultaneous qualitative detection and differentiation of nucleic acid from SARS-CoV-2, influenza A and/or influenza B in nasopharyngeal and anterior nasal swabs collected from individuals suspected of respiratory viral infection consistent with COVID-19 by their healthcare provider. Clinical signs and symptoms of respiratory viral infection due to SARS-CoV-2 and influenza can be similar. Testing is limited to laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, that meet the requirements to perform moderate or high complexity tests.

BD SARS-CoV-2/Flu for BD MAX™ System is intended for use in simultaneous detection and differentiation of SARS-CoV-2, influenza A, and/or influenza B nucleic acid in clinical specimens, and is not intended to detect influenza C. The SARS-CoV-2, influenza A, and/or influenza B RNA is generally detectable in upper respiratory samples during the acute phase of infection.

Positive results are indicative of active infection but do not rule out bacterial infection or co-infection with other pathogens not detected by the test. Clinical correlation with patient history and other diagnostic information is necessary to determine patient infection status. The agent detected may not be the definite cause of disease.

Laboratories within the United States and its territories are required to report all SARS-CoV-2 results to the appropriate public health authorities.

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

BD SARS-CoV-2/Flu for BD MAX™ System is intended for use by qualified clinical laboratory personnel specifically instructed and trained on the use of the BD MAX™ System and in vitro diagnostic procedures. BD SARS-CoV-2/Flu 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 SARS-CoV-2/Flu for BD MAX™ System from nasopharyngeal or anterior nasal swabs collected in BD Universal Viral Transport System (UVT) or Copan Universal Transport Media System (UTM) and anterior nasal swabs collected in 0.85% saline. Patient sample is transferred to the BD Molecular Respiratory Sample Buffer Tube provided with the BD SARS-CoV-2/Flu for BD MAX™ System and placed in the BD MAX™ System. The BD Respiratory Unitized Reagent Strip contains a combination of lytic and extraction reagents designed to perform cell lysis and TNA extraction. Eluted TNA is transferred to the SARS-CoV-2/Flu master mix. The final rehydrated master mix is transferred to a PCR cartridge for rRT-PCR.

The BD SARS-CoV-2/Flu 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, a conserved region of the matrix protein M1 gene for influenza A, conserved regions of the matrix protein M1 gene and hemagglutinin (HA) gene for influenza B, and the human RNase P gene. The primer and probe sets for SARS-CoV-2 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). SARS-CoV-2 targets, N1 and N2, are indistinguishable as they are detected in the same optical channel. Influenza B targets, M1 and HA, are also indistinguishable and are detected in the same optical channel.

An internal control targeting the human RNase P gene will be co-amplified along with SARS-CoV-2, influenza A, and influenza B 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 TNA 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. Eluted TNA is added to neutralization buffer, mixed, and transferred to BD SARS-CoV-2/Flu master mix for rehydration. After reconstitution, the BD MAX™ System dispenses a fixed volume of rRT-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 targets 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
445011	**BD SARS-CoV-2/Flu for BD MAX™ System Master Mix (D9)** *Dried PCR Master Mix containing nucleotides and specific molecular probes (0.005% w/v) and primers (0.009% w/v) along with PCR enzyme (0.004% w/v).*	24 (2 x 12 tubes)
	BD Respiratory for BD MAX™ System Extraction Tube (D4) *Dried extraction reagent containing DNA/RNA magnetic affinity beads (6.41% w/v) and Proteinase K (6.7% w/v).*	24 (2 x 12 tubes)
	BD Respiratory for BD MAX™ System Unitized Reagent Strip *Unitized Reagent Strip containing wash buffer with 0.004% v/v Tween® 20 (0.75 mL), elution buffer with 0.004% v/v Tween 20 (0.75 mL), and neutralization buffer with 0.004% v/v Tween 20 (0.75 mL) reagents and disposable pipette tips necessary for sample processing and TNA extraction.*	24 tests
	BD Molecular Respiratory Sample Buffer Tubes *(with 2% v/v of Triton® X-100)*	24 (2 x 12 tubes)
	Septum Caps	25

EQUIPMENT AND MATERIALS REQUIRED BUT NOT PROVIDED

- BD MAX™ System (BD Catalog No. 441916)
- BD MAX™ Sample Rack (BD Catalog No. 441935, 443550, 443551, 444807, or 444808)
- BD MAX™ PCR Cartridges (BD Catalog No. 437519)
- Copan UTM Collection Kit
- BD UVT Collection Kit
- 0.85% Saline
- Vortex Genie 2 (VWR Catalog No. 58815-235 or equivalent)
- Multi-Tube Vortex Mixer (VWR Catalog 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

Danger

H312 Harmful in contact with skin.
H315 Causes skin irritation.
H317 May cause an allergic skin reaction.
H319 Causes serious eye irritation.
H334 May cause allergy or asthma symptoms or breathing difficulties if inhaled.
H335 May cause respiratory irritation.
H350 May cause cancer.
H360 May damage fertility or the unborn child.
H402 Harmful to aquatic life.
H411 Toxic to aquatic life with long lasting effects.
P201 Obtain special instructions before use.
P202 Do not handle until all safety precautions have been read and understood.
P233 Keep container tightly closed.
P261 Avoid breathing dust/fume/gas/mist/vapors/spray.
P264 Wash thoroughly after handling.
P271 Use only outdoors or in a well-ventilated area.
P272 Contaminated work clothing should not be allowed out of the work place.
P273 Avoid release to the environment.
P280 Wear protective gloves/protective clothing/eye protection/face protection.
P281 Use personal protective equipment as required.
P284 [In case of inadequate ventilation] wear respiratory protection.
P308+P313 IF exposed or concerned: Get medical advice/attention.
P332+P313 IF skin irritation occurs: Get medical advice/attention.
P333+P313 IF skin irritation or rash occurs: Get medical advice/attention.
P342+P311 If experiencing respiratory symptoms: Call a POISON CENTER/doctor.
P337+P313 IF eye irritation persists: Get medical advice/attention.
P305+P351+P338 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P302+P352 IF ON SKIN: Wash with plenty of water.
P312 Call a POISON CENTER/doctor if you feel unwell.
P321 Specific treatment.
P342+P311 If experiencing respiratory symptoms: Call a POISON CENTER/doctor/...
P304+P340 IF INHALED: Remove person to fresh air and keep comfortable for breathing.
P362+P364 Take off contaminated clothing and wash it before reuse.
P363 Wash contaminated clothing before reuse.
P391 Collect spillage.
P403 Store in a well-ventilated place.
P405 Store locked up.
P501 Dispose of contents/container to an appropriate treatment and disposal facility in accordance with applicable laws and regulations, and product characteristics at time of disposal.

- For *in vitro* diagnostic use under Emergency Use Authorization only.
- For Prescription Use only.
- This product has not been FDA cleared or approved, but has been authorized for emergency use by FDA under an EUA for use by authorized laboratories.
- This product has been authorized for use by laboratories certified under the Clinical Laboratory Improvement Amendments (CLIA) of 1988, 42 U.S.C. 263a, that meet requirements to perform moderate or high complexity tests.
- This product has been authorized only for the detection of nucleic acid from SARS-CoV-2, influenza A, and influenza B, not for any other viruses or pathogens.
- The emergency use of this product is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of *in vitro* diagnostics for detection and/or diagnosis of COVID-19 under Section 564(b)(1) of the Federal Food, Drug and Cosmetic Act, 21 U.S.C.§360bbb-3(b)(1), unless the declaration is terminated or authorization is revoked sooner.
- Positive results are indicative of the presence of SARS-CoV-2, influenza A, and/or influenza B RNA.
- Laboratories within the United States and its territories are required to report all SARS-CoV-2 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/Flu 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/Flu 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/Flu for BD MAX™ System components are stable at 2–25 °C through the stated expiration date. Do not use expired components.
- The BD SARS-CoV-2/Flu Master Mix and Extraction Tubes are provided in sealed pouches. To protect from humidity, immediately re-seal after opening.
- Reagent tubes are stable for up to 14 days at 2–25 °C after initial opening and re-sealing of the pouch.

INSTRUCTIONS FOR USE

Swab Specimen Collection/Transport in Universal Viral Transport (UVT) or Universal Transport Medium (UTM)

Note: Wear gloves when handling specimens. If gloves come in contact with the specimen, immediately change them to prevent contamination of other specimens.

1. Nasopharyngeal or anterior nasal 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. After collection, specimens can be stored for up to 24 hours at 2–25 °C.
3. If delivery and processing of samples exceeds specified time period, specimens should be transported in dry ice and once in laboratory frozen at -70 °C or colder.

Swab Specimen Collection/Transport in 0.85% Saline

Note: Wear gloves when handling specimens. If gloves come in contact with the specimen, immediately change them to prevent contamination of other specimens.

1. Anterior nasal swab specimens should be collected and expressed directly into the saline tube.
2. After collection, specimens can be stored for up to 24 hours at 2–25 °C.
3. If delivery and processing of samples exceeds specified time period, specimens should be transported in dry ice and once in laboratory frozen at -70 °C or colder.

BD Molecular Respiratory Sample Buffer Tube Preparation for use with nasopharyngeal or anterior nasal swab specimens in Universal Viral Transport (UVT) or Universal Transport Media (UTM) or anterior nasal swabs collected in 0.85% saline

Note: Wear gloves when handling 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), Universal Transport Media (UTM), or saline specimen to come to room temperature before proceeding.

1. Uncap the BD Molecular Respiratory Sample Buffer Tube and transfer (using a calibrated, variable pipette) 750 µL from the UVT/UTM or saline specimen directly into the BD Molecular Respiratory Sample Buffer Tube.
2. Recap the tube with a blue septum cap and vortex or mix by inversion 8–10 times.
3. Label the BD Molecular Respiratory 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 or saline 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 SARS-CoV-2/Flu for BD MAX™ System kit. Gently tap each Unitized Reagent Strip onto a hard surface to ensure that all the liquids are at the bottom of the tubes.
4. Remove from the protective pouches the required number of Extraction Tube(s) and Master Mix Tube(s) from the BD SARS-CoV-2/Flu kit.
5. Remove excess air, and close pouches with the zip seal.
6. For each sample to be tested, place one (1) Unitized Reagent Strip on the BD MAX™ System Rack, starting with Position 1 of Rack A.
7. Snap one (1) Extraction Tube (D4) (white foil) into each Unitized Reagent Strip in Position 1 as shown in Figure 1.
8. Snap one (1) BD SARS-CoV-2/Flu Master Mix tube (D9) (green foil) into each Unitized Reagent Strip in Position 2 as shown in Figure 1.

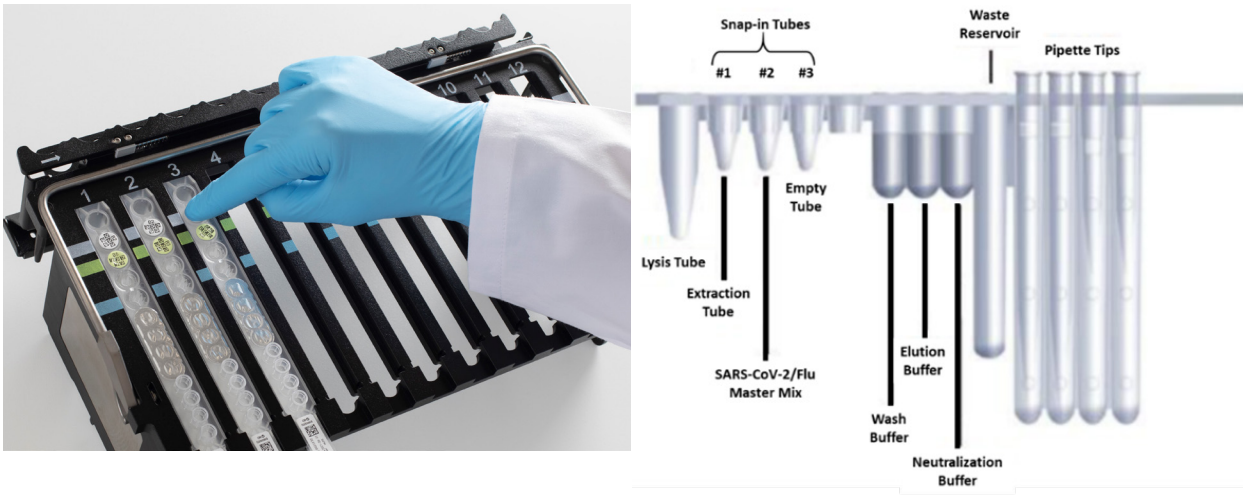

Figure 1: Snap Extraction Tubes and Master Mix Tubes into Unitized Reagent Strips

9. Click on the Run Tab and then the Inventory subtab. Enter the kit lot number for the BD SARS-CoV-2/Flu kit (for lot traceability) by either scanning the barcode with the scanner or by manual entry.

   NOTE: Repeat step 9 each time a new kit lot is used.

10. Navigate to the Worklist. Using the pull down menu select **<BD SARS CoV2 Flu 74>**.
11. Select the appropriate kit lot number (found on the outer box of the BD SARS-CoV-2/Flu kit) from the pull down menu.
12. Enter the BD Molecular Respiratory 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.
13. Repeat step 12 for all remaining Sample Buffer Tubes.
14. Place the Sample Buffer Tubes in the BD MAX™ System Rack(s) corresponding to the Unitized Reagent Strips assembled in steps 6 to 8.
15. Place the required number of BD MAX™ PCR Cartridge(s) into the BD MAX™ System (refer to Figure 2).
    - Each BD MAX™ PCR Cartridge accommodates 1 run of up to 12 samples for a total of 12 samples.
    - The BD MAX™ System will automatically select the position and row on the BD MAX™ PCR Cartridge for each run.
    - BD MAX™ PCR Cartridges are used on a per-run AND rack basis (1 run per cartridge and 1 cartridge per rack).
    - To maximize use of BD MAX™ PCR Cartridges, using 2000 Sample Mode, select Run Wizard under the Worklist tab for lane assignments.
    - Consult the BD MAX™ System User's Manual[3] for more details.

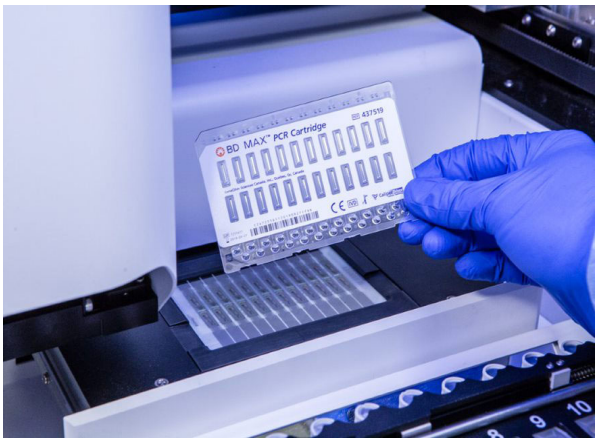

Figure 2: Load BD MAX™ PCR Cartridges

16. Load rack(s) into the BD MAX™ System (refer to Figure 3).

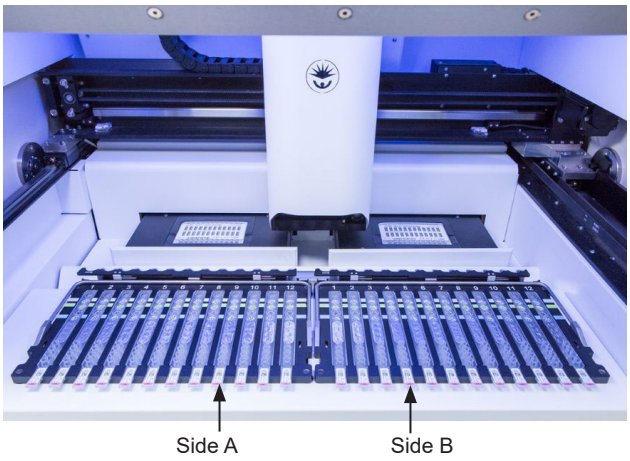

Figure 3: Load Rack(s) onto the BD MAX™ System

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

NOTE: When an Indeterminate (IND), Unresolved (UNR), or Incomplete (INC) result is obtained, or when an External Control failure occurs, repeat test from the primary sample (refer to Repeat Test Procedure section).

QUALITY CONTROL

Quality control procedures monitor the performance of the assay. Laboratories must establish the number, type and frequency of testing control materials according to guidelines or requirements of local, provincial, state, 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 Clinical Laboratory Standards Institute documents MM3[4] and EP12.[5]

1. 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 Table 2 for the interpretation of External Control assay results.)
2. One (1) External Positive Control and one (1) External Negative Control should 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.
3. 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.
4. Various types of External Controls are recommended to allow the user to select the most appropriate for their laboratory quality control program.
   a. External Negative Control (ENC): Commercially available control material, such as Microbiologics® Helix Elite™ Inactivated Standard Negative Cellularity Control (refer to Table 1), or a previously characterized sample known to be negative. 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.
   b. External Positive Control (EPC): Commercially available control materials, such as the Microbiologics® Helix Elite™ standards listed below (refer to Table 1), or previously characterized samples known to be positive.

Table 1: Commercially Available Standards for External Controls

Commercially Available Standards	Part Number
Microbiologics® Helix Elite™ Synthetic Standard SARS-CoV-2 Synthetic RNA (N gene Targets)	HE0060S
Microbiologics® Helix Elite™ Inactivated Standard Inactivated Influenza A/B and Respiratory Syncytial Virus	HE0044N
Microbiologics® Helix Elite™ Inactivated Standard Negative Cellularity Control	HE0058N

5. Suggested procedure for preparing an EPC or ENC using Microbiologics® Helix Elite™ Standards (see below) has been verified by BD. However, the choice of EPC and ENC for the BD SARS-CoV-2/Flu 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.
6. Preparation of Microbiologics® Helix Elite™ Inactivated Standard Negative Cellularity Control as an External Negative Control:
   a. Add 750 µL of nuclease-free water into a BD Molecular Respiratory Sample Buffer Tube.
   b. Rehydrate the Microbiologics® Negative Cellularity Control Standard with 100 µL of nuclease free water.
   c. Dilute the rehydrated standard 1:10 in nuclease free water (10 µL standard to 90 µL nuclease free water).
   d. Spike 75 µL of the diluted standard into the Sample Buffer Tube.
   e. Cap the External Negative Control Sample Buffer Tube and vortex for 10–30 seconds or invert 8–10 times. Process on the BD MAX™ System.
7. Preparation of Microbiologics® Helix Elite™ Standards as an External Positive Control:
   a. Add 750 µL of nuclease-free water into a BD Molecular Respiratory Sample Buffer Tube.
   b. Rehydrate the Microbiologics® Negative Cellularity Control Standard, Microbiologics® SARS-CoV-2 Synthetic RNA Standard, and Microbiologics® Inactivated Influenza A/B and Respiratory Syncytial Virus Standard each with 100 µL of nuclease free water.
   c. Dilute the Microbiologics® Negative Cellularity Control Standard and Microbiologics® Inactivated Influenza A/B and Respiratory Syncytial Virus Standard 1:10 in nuclease free water (10 µL standard to 90 µL nuclease free water).
   d. Dilute the Microbiologics® SARS-CoV-2 Synthetic RNA Standard 1:100 in nuclease free water (10 µL standard to 990 µL nuclease free water).
   e. Spike 75 µL of the diluted Microbiologics® Negative Cellularity Control Standard, 50 µL of the diluted Microbiologics® SARS-CoV-2 Synthetic RNA Standard, and 50 µL of the diluted Microbiologics® Inactivated Influenza A/B and Respiratory Syncytial Virus Standard into the Sample Buffer Tube.
   f. Cap the External Positive Control Sample Buffer Tube and vortex for 10–30 seconds or invert 8–10 times. Process on the BD MAX™ System.
8. Preparation of previously characterized nasopharyngeal specimen in UVT/UTM as an External Positive or Negative Control:
   a. Transfer 750 µL of the specimen to a BD Molecular Respiratory Sample Buffer Tube.
   b. Cap the External Control Sample Buffer Tube and vortex for 10–30 seconds or invert 8–10 times. Process on the BD MAX™ System.
9. All External Controls should yield the expected results (Table 2) with no failed external controls (Unresolved, Indeterminate, Incomplete results).

Table 2: BD SARS-CoV-2/Flu for BD MAX™ System External Control Expected Results

Control Type	Control	Used to Monitor	Expected Result		
			CoV-2 (SARS-CoV-2)	Flu A	Flu B
Negative External Control	Known Negative Specimen	Reagent and/or environmental contamination	NEG	NEG	NEG
	Microbiologics Negative External Control				
Positive External Control	Known Positive Specimen[a]	Substantial reagent failure including primer and probe integrity	POS/NEG	POS/NEG	POS/NEG
	Microbiologics Positive External Control		POS	POS	POS

[a] Known Positive Specimens are expected to be positive only for the virus(es) present in the specimen

10. An External Negative Control that yields a positive test result is indicative of a specimen handling and/or contamination event. Review the specimen handling technique to avoid mix-up 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.
11. 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 Troubleshooting 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 BD SARS-CoV-2/Flu for BD MAX™ System kit.
12. The RNase P gene serves as both an Extraction and Internal Amplification Control. In the event that SARS-CoV-2, influenza A, and influenza B are negative, an RNase P result must be positive for the SARS-CoV-2, influenza A, and influenza B results to be valid negative results. When either SARS-CoV-2, influenza A, and/or influenza B target results are positive, the RNase P result is ignored. An Unresolved (UNR) result is indicative of specimen-associated inhibition or reagent failure. Repeat any sample reported as Unresolved according to the "Repeat Test Procedure" section below.

RESULT INTERPRETATION

Results are available on the **<Results>** tab in the **<Results>** window on the BD MAX™ System monitor. The BD MAX™ System software automatically interprets test results. Results are reported for each of the analytes. A test result may be called as NEG (negative), POS (positive) or UNR (unresolved) based on the amplification status of the target and the Extraction and Internal Amplification Control, RNase P. IND (Indeterminate) or INC (Incomplete) results are due to BD MAX™ System failure. BD SARS-CoV-2/Flu for BD MAX™ System results interpretation is described below in Table 3.

Table 3: BD SARS-CoV-2/Flu for BD MAX™ System Result Interpretation

CoV2 (SARS-CoV-2)	Flu A	Flu B	Result Displayed[a]	Actions
POS	NEG	NEG	CoV2 POS FluA NEG FluB NEG	Report as: SARS-CoV-2 Detected Influenza A Not Detected Influenza B Not Detected
NEG	POS	NEG	CoV2 NEG FluA POS FluB NEG	Report as: SARS-CoV-2 Not Detected Influenza A Detected Influenza B Not Detected
NEG	NEG	POS	CoV2 NEG FluA NEG FluB POS	Report as: SARS-Cov-2 Not Detected Influenza A Not Detected Influenza B Detected
POS	POS	NEG	CoV2 POS FluA POS FluB NEG	Report as: SARS-CoV-2 Detected Influenza A Detected Influenza B Not Detected
POS	NEG	POS	CoV2 POS FluA NEG FluB POS	Report as: SARS-CoV-2 Detected Influenza A Not Detected Influenza B Detected
NEG	POS	POS	CoV2 NEG FluA POS FluB POS	Report as: SARS-CoV-2 Not Detected Influenza A Detected Influenza B Detected

SARS-CoV-2	Flu A	Flu B	Result Displayed[a]	Actions
POS	POS	POS	CoV2 POS FluA POS FluB POS	Report as: SARS-CoV-2 Detected Influenza A Detected Influenza B Detected
NEG	NEG	NEG	CoV2 NEG FluA NEG FluB NEG	Report as: SARS-CoV-2 Not Detected Influenza A Not Detected Influenza B Not Detected
			UNR[b]	Repeat Test[c]
			IND[d] (with Warning or Error Codes[e])	Repeat Test[c]
			INC[f] (with Warning or Error Codes[e])	Repeat Test[c]

[a] Laboratories should report their diagnostic result as appropriate and in compliance with their specific reporting system. Laboratories within the United States and its territories are required to report all SARS-CoV-2 results to the appropriate public health authorities.

[b] Unresolved

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

[d] Indeterminate

[e] Refer to Troubleshooting section of the BD MAX™ System User's Manual[3] for interpretation of warning and error codes.

[f] Incomplete

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 a new BD Molecular Respiratory Sample Buffer Tube and transfer (using a calibrated, variable pipette) 750 µL from the UVT/UTM/saline specimen directly into the BD Molecular Respiratory 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 a new BD Molecular Respiratory Sample Buffer Tube and transfer (using a calibrated, variable pipette) 750 µL from the UVT/UTM/saline specimen directly into the BD Molecular Respiratory 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 a new BD Molecular Respiratory Sample Buffer Tube and transfer (using a calibrated, variable pipette) 750 µL from the UVT/UTM/saline specimen directly into the BD Molecular Respiratory 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/Flu for BD MAX™ System has been evaluated only for use on the BD MAX™ System.
- Reliable results depend on proper sample collection, storage, and handling procedures.
- Performance of BD SARS-CoV-2/Flu for BD MAX™ System has only been established in nasopharyngeal swab specimens. Anterior nasal swabs are considered an acceptable specimen type for use with the BD SARS-CoV-2/Flu for BD MAX™ System, but performance with this specimen type has not been established.
- Use of BD SARS-CoV-2/Flu for BD MAX™ System with other specimen types has not been assessed and performance characteristics are unknown.
- The clinical performance has not been established in all circulating variants but is anticipated to be reflective of the prevalent variants in circulation at the time and location of the clinical evaluation. Performance at the time of testing may vary depending on the variants circulating, including newly emerging strains of SARS-CoV-2 and their prevalence, which change over time.

- Detection of SARS-CoV-2, influenza A, and/or influenza B 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 the BD SARS-CoV-2/Flu for BD MAX™ System test 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.
- The effect of interfering substances has only been evaluated for those listed in this labeling. Potential interference has not been evaluated for substances other than those described in the Interfering Substances section below. Interference by substances other than those described in the Interfering Substances section below could lead to erroneous results.
- Human blood, Flonase, Zicam and tobramycin were found to interfere with BD SARS-CoV-2/Flu for BD MAX™ System at concentrations greater than 0.2% v/v, 1.7% v/v, 0.5% v/v and 0.4 µg/mL in UVT, respectively.
- BD SARS-CoV-2/Flu for BD MAX™ System has not been evaluated for patients receiving intranasally administered influenza vaccine.
- The performance of this device has not been assessed in a population vaccinated against COVID-19.
- Enterovirus C (Coxsackievirus A17) was shown to interfere with BD SARS-CoV-2/Flu for BD MAX™ System at a concentration above 1.00E+04 $TCID_{50}$/mL in UVT.
- Results from analytical studies with contrived co-infected samples showed potential for competitive interference of influenza B at low concentrations (~2x LoD) when SARS-CoV-2 concentration is ≥1.00E+06 genomic copies/mL.
- The test is not intended to differentiate influenza A subtypes or influenza B lineages. If differentiation of specific influenza subtypes and lineages is needed, additional testing, in consultation with state or local public health departments, is required.

CONDITIONS OF AUTHORIZATION FOR THE LABORATORY

The BD SARS-CoV-2/Flu 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/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/vitro-diagnostics-euas. However, to assist clinical laboratories using the BD SARS-CoV-2/Flu for BD MAX™ System the relevant Conditions of Authorization are listed below.

- Authorized laboratories[a] using the BD SARS-CoV-2/Flu for BD MAX™ System must include with result reports, 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 BD SARS-CoV-2/Flu for BD MAX™ System must perform BD SARS-CoV-2/Flu for BD MAX™ System as outlined in the authorized labeling. 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/Flu for BD MAX™ System test are not permitted.
- Authorized laboratories that receive the BD SARS-CoV-2/Flu for BD MAX™ System test must notify the relevant public health authorities of their intent to run the test prior to initiating testing.
- Authorized laboratories using the BD SARS-CoV-2/Flu for BD MAX™ System test must have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.
- Authorized laboratories must collect information on the performance of the 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/Flu for BD MAX™ System test of which they become aware.
- All laboratory personnel using the BD SARS-CoV-2/Flu 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.
- Becton, Dickinson and Company, its authorized distributors, and authorized laboratories using the BD SARS-CoV-2/Flu for BD MAX™ System must 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.

[a]The letter of authorization refers to, “Laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, that meet requirements to perform moderate or high complexity tests” as “authorized laboratories”.

NON-CLINICAL PERFORMANCE EVALUATION

Limit of Detection (LoD)

The analytical sensitivity of the BD SARS-CoV-2/Flu for BD MAX™ System was assessed with limiting dilution for seven respiratory viruses (SARS-CoV-2, two strains of influenza A H1N1, two strains of influenza A H3N2, and two strains of influenza B). To confirm co-spiking of analytes does not impact analytical sensitivity, LoD was determined with co-spiked analytes, one strain per analyte. LoD studies determine the lowest detectable concentration of virus at which at least 95% of all (true positive) replicates test positive.

To determine the LoD, quantified inactivated SARS-CoV-2 or quantified influenza culture fluids were serially diluted into simulated nasopharyngeal matrix for 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 simulated nasopharyngeal matrix. The LoD is defined as the lowest concentration at which ≥95% of all replicates are expected to test positive. The verified LoD values for each virus tested are summarized in Table 4.

Table 4. BD SARS-CoV-2/Flu for BD MAX™ System Limit of Detection

Strain ID	LoD Concentration (in UVT)
SARS-CoV-2/USA-WA1/2020[a]	700 GC/mL
Influenza A H1N1 Brisbane/59/07[b]	0.025 $TCID_{50}$/mL
Influenza A H1N1 Idaho/07/2018[b]	0.20 $TCID_{50}$/mL
Influenza A H3N2 Switzerland/9715293/13[b]	0.10 $TCID_{50}$/mL
Influenza A H3N2 Kansas/14/2017[a]	4.8 $TCID_{50}$/mL
Influenza B Colorado/06/17[a]	0.05 $TCID_{50}$/mL
Influenza B Phuket/3073/13[b]	0.06 $TCID_{50}$/mL

[a] Co-spiked analyte LoD

[b] Individual analyte LoD

Reactivity/Inclusivity

The N1 and N2 primers and probes utilized for SARS-CoV-2 detection within the BD SARS-CoV-2/Flu 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. An *in silico* comparison of the N1 and N2 primer sets was performed using all available high quality SARS-CoV-2 sequences submitted to the GISAID EpiCoV database[6] by January 13, 2021 (n=329,434). Alignments against the N gene showed that both N1 and N2 primer/probe sets are a perfect match to 93.8% of sequences in the database, 96.8% of the sequences were a perfect match to the N1 primer set region, and 97.0% were a perfect match to the N2 primer set region. In total, 99.9% are a perfect match to either the N1 or the N2 region primer sets.

An *in silico* comparison of the influenza A primer set was performed using all available high quality Influenza A M1 (matrix protein) gene sequences submitted to the GISAID EpiCoV database[6] between May 1, 2008 and October 21, 2020 (n=87,051). Multiple alignment of the matrix gene showed that 90.2% of sequences are a perfect match to the primer/probe set while an additional 7.8% of sequences have a single base mismatch in the 5' end of a single primer. Multiple mismatches to the primers and probe occurred in only 0.25% of sequences.

An *in silico* comparison of the influenza B primer sets was performed using all available high quality Influenza B M1 gene and HA gene sequences submitted to the GISAID EpiCoV database[6] between May 1, 2008 and October 21, 2020. A total of 23,972 matrix and 49,852 HA sequences were used in this analysis. Multiple alignment of the M1 gene showed that 97.2% of sequences are a perfect match to the primer/probe set and 74.8% of HA sequences had one or fewer base pair mismatches.

BD SARS-CoV-2/Flu for BD MAX™ System was evaluated against multiple strains of influenza A H1N1 and H3N2 and influenza B strains including both the Yamagata and Victoria lineages. A total of 20 influenza A and 5 influenza B strains were evaluated at levels near the analytical LoD. Three replicates were tested for each strain. All strains were detected at 3x LoD except for one influenza A H1N1 strain (A/Wisconsin/505/2018 pdm09) and one influenza A H3N2 strain (A/Texas/71/2017), which were detected at 6x LoD.

Table 5. Analytical Reactivity/Inclusivity for BD SARS-CoV-2/Flu for BD MAX™ System

Virus	Strain	Type	Virus Concentration in UVT	Virus Concentration Relative to LoD	SARS-CoV-2 Result	Flu A Result	Flu B Result
Influenza A	H1N1	A/Maryland/08/2013 (H1N1) pdm09 Antiviral Resistance	1158.93 $TCID_{50}$/mL	3x LoD	NEG	POS	NEG
		A/Bangladesh/3002/2015 (H1N1) pdm09	2313.38 $CEID_{50}$/mL	3x LoD	NEG	POS	NEG
		A/Iowa/53/2015 (H1N1) pdm09	71.33 $TCID_{50}$/mL	3x LoD	NEG	POS	NEG
		A/Michigan/272/2017 (H1N1) pdm09	39.7 $TCID_{50}$/mL	3x LoD	NEG	POS	NEG
		A/Wisconsin/505/2018 (H1N1) pdm09	42.5 $TCID_{50}$/mL	6x LoD	NEG	POS	NEG
		A/St. Petersburg/61/2015 (H1N1pdm09)	2600.9 $CEID_{50}$/mL	3x LoD	NEG	POS	NEG
		A/Michigan/45/2015 (H1N1) pdm09	5748.7 $CEID_{50}$/mL	3x LoD	NEG	POS	NEG
		A/Louisiana/08/2013 (H1N1) pdm09 Antiviral Resistance	220.0 $TCID_{50}$/mL	3x LoD	NEG	POS	NEG
		A/North Carolina/4/2014 (H1N1) pdm09 Antiviral Resistance	2002.3 $CEID_{50}$/mL	3x LoD	NEG	POS	NEG
		A/New York/18/2009 (H1N1) pdm09 Antiviral Resistance	14.5 $TCID_{50}$/mL	3x LoD	NEG	POS	NEG
	H3N2	A/California/02/2014 (H3N2)	3.1 $TCID_{50}$/mL	3x LoD	NEG	POS	NEG
		A/Alaska/232/2015 (H3N2)	1650.9 $CEID_{50}$/mL	3x LoD	NEG	POS	NEG
		A/Singapore/ INFIMH-16-0019/2016 (H3N2)	42.2 FFU_{50}/mL	3x LoD	NEG	POS	NEG
		A/Texas/71/2017 (H3N2)	60.9 FFU_{50}/mL	6x LoD	NEG	POS	NEG
		A/Arizona/45/2018 (H3N2)	173.5 FFU_{50}/mL	3x LoD	NEG	POS	NEG
		A/Hong Kong/4801/14 (H3N2)	0.8 $TCID_{50}$/mL	3x LoD	NEG	POS	NEG
		A/Norway/466/14 (H3N2)	0.1 U/mL	3x LoD	NEG	POS	NEG
		A/South Australia/55/14 (H3N2)	0.2 U/mL	3x LoD	NEG	POS	NEG
		A/Stockholm/6/14 (H3N2)	0.1 U/mL	3x LoD	NEG	POS	NEG
		A/Wisconsin/04/2018 (H3N2)	2793.9 $CEID_{50}$/mL	3x LoD	NEG	POS	NEG
	Victoria	B/Maryland/15/2016	1.34 $TCID_{50}$/mL	3x LoD	NEG	NEG	POS
		B/Hong Kong/286/2017	0.63 $TCID_{50}$/mL	3x LoD	NEG	NEG	POS
		B/Hawaii/01/2018 (NA D197N)	236.1 $TCID_{50}$/mL	3x LoD	NEG	NEG	POS
Influenza B	Yamagata	B/Guangdong-Liwan/1133/2014	1208.8 $CEID_{50}$/mL	3x LoD	NEG	NEG	POS
		B/Oklahoma/10/2018 (NA D197N)	491.5 $TCID_{50}$/mL	3x LoD	NEG	NEG	POS

In addition, the BD SARS-CoV-2/Flu was shown to be inclusive for the CDC Human Influenza Virus Panel (2020). The lowest concentration in Sample Buffer Tube where at least one out of five replicates are positive is reported as the minimum reactive concentration.

Table 6. CDC Human Influenza Virus Panel (2020) Results

Influenza Virus (Type/Subtype)	Virus strain name	Minimum Reactive Concentration (EID_{50}/mL in Sample Buffer Tube)
Influenza A/H3N2	A/Perth/16/2009	3.41E+01
	A/Hong Kong 2671 2019	1.35E+01
Influenza A/H1N1	A/Christ Church/16/2010	2.70E+02
	A/Guangdongmaonan/1536/2019	2.15E+01
Influenza B/Victoria lineage	B/Michigan/09/2011	2.71E-02
	B/Washington/02/2019	5.41E+00
Influenza B/Yamagata lineage	B/Texas/81/2016	3.41E+00
	B/Phuket 3073/2013	2.71E+01

Cross-Reactivity

An *in silico* analysis was performed to evaluate the potential for all primers and probes contained within the BD SARS-CoV-2/Flu for BD MAX™ System master mix to amplify and detect unintended organisms. Each primer was 'BLAST' against the full nt database and alignments were kept if there were no more than three (3) base pair mismatches across the length of the primer, the 3' end of the primer matched the subject sequence, and no gaps were introduced to "force" an alignment. The plus/minus orientation between the primer (query) and the subject (database sequence) was determined, and all two-primer combinations (including each primer with itself) were identified where one primer matched the plus strand and the other matched the minus, representing potential amplicons. Amplicons were kept if the minus strand primer was downstream of the plus strand primer and the resulting amplicons were less than or equal to 3,000 base pairs long.

Influenza A: No relevant cross-reactivity was discovered.

Influenza B: No relevant cross-reactivity was discovered.

SARS-CoV-2: All identified hits are either SARS-CoV-2 or a closely related coronavirus from non-human species. No relevant cross-reactivity was discovered.

Additionally, 46 organisms and 1 nasopharyngeal pool were evaluated for cross-reactivity with the BD SARS-CoV-2/Flu for BD MAX™ System. The bacterial cells, yeasts, and viruses were tested in the BD Molecular Respiratory Sample Buffer Tube. All organisms tested produced negative results when tested at the concentrations in Table 7.

Table 7. Cross-Reactivity Testing Results

Organism	Concentration of Organism in Sample Buffer Tube	Negative Results (Negative/Total)
Adenovirus - type 1	1.00E+05 $TCID_{50}$/mL	3/3
Adenovirus - type 4	1.00E+05 $TCID_{50}$/mL	3/3
Adenovirus - type 7	1.00E+05 $TCID_{50}$/mL	3/3
Bordetella pertussis	1.00E+06 CFU/mL	3/3
Candida albicans	1.00E+06 CFU/mL	3/3
Chlamydia pneumonia	1.00E+06 IFU/mL	3/3
Corynebacterium diphtheriae	1.00E+06 CFU/mL	3/3
Cytomegalovirus	4.17E+04 U/mL	3/3
Enterovirus B (Echovirus 6)	1.00E+05 U/mL	3/3
Enterovirus C (Coxsackievirus A17)	1.00E+05 $TCID_{50}$/mL	3/3
Enterovirus D	1.00E+05 U/mL	3/3
Epstein Barr virus	1.00E+05 copies/mL	3/3
Escherichia coli	1.00E+06 CFU/mL	3/3
Haemophilus influenzae	1.00E+06 CFU/mL	3/3
Herpes simplex virus Type 1	1.41E+04 U/mL	3/3
Herpes simplex virus Type 2	1.41E+04 U/mL	3/3
Human coronavirus 229E	1.00E+05 U/mL	3/3
Human coronavirus HKU1[a]	1.00E+05 GC/mL	3/3
Human coronavirus NL63	1.41E+04 $TCID_{50}$/mL	3/3
Human coronavirus OC43	1.00E+05 $TCID_{50}$/mL	3/3
Human Metapneumovirus (hMPV)	1.00E+05 $TCID_{50}$/mL	3/3
Lactobacillus acidophilus	1.00E+06 CFU/mL	3/3
Legionella pneumophila	1.00E+06 CFU/mL	3/3
Measles	1.00E+05 U/mL	3/3
MERS-coronavirus[a]	1.00E+05 copies/mL	3/3
Moraxella catarrhalis	1.00E+06 CFU/mL	3/3
Mumps	1.00E+05 U/mL	3/3
Mycobacterium tuberculosis[a]	1.00E+06 copies/mL	3/3

Organism	Concentration of Organism in Sample Buffer Tube	Negative Results (Negative/Total)
Mycoplasma pneumoniae	1.00E+06 CFU/mL	3/3
Neisseria meningitidis	5.00E+03 CFU/mL	3/3
Neisseria gonnorrhoeae	1.00E+06 CFU/mL	3/3
Parainfluenza virus 1	1.00E+05 $TCID_{50}$/mL	3/3
Parainfluenza virus 2	1.00E+05 U/mL	3/3
Parainfluenza virus 3	1.00E+05 $TCID_{50}$/mL	3/3
Parainfluenza virus 4	1.00E+05 $TCID_{50}$/mL	3/3
Pneumocystis jirovecii (PJP)	1.00E+05 nuclei/mL	3/3
Pooled human expressed nasopharyngeal swab matrix	N/A	3/3
Pseudomonas aeruginosa	1.00E+06 CFU/mL	3/3
Respiratory syncytial virus	1.00E+05 U/mL	3/3
Rhinovirus	1.00E+05 $TCID_{50}$/mL	3/3
SARS-coronavirus[a]	1.00E+05 GE/mL	3/3
Staphylococcus aureus	1.00E+06 CFU/mL	3/3
Staphylococcus epidermis	1.00E+06 CFU/mL	3/3
Streptococcus pneumoniae	1.00+06 CFU/mL	3/3
Streptococcus pyogenes	1.00E+06 CFU/mL	3/3
Streptococcus salivarius	5.00E+03 CFU/mL	3/3
Varicella-zoster virus	1.00E+04 U/mL	3/3

[a] Genomic DNA or RNA tested

Microbial Interference

Forty-six (46) organisms and one nasopharyngeal pool were evaluated for potential interference with the BD SARS-CoV-2/Flu for BD MAX™ System. Organisms were tested at high concentration (≥10^6 CFU/mL, cells or genome equivalents/mL, ≥10^5 IFU/mL or $TCID_{50}$/mL, or highest concentration available) in the presence of assay analytes (SARS-CoV-2, influenza A and influenza B) co-spiked at 3x LoD. Enterovirus C (Coxsackievirus A17) was shown to interfere in the detection of influenza A and influenza B at concentrations above 1.00E+04 $TCID_{50}$/mL.

Table 8. Microbial Interference Testing Results

Organism	Concentration of Organism in Sample Buffer Tube	CoV2 (SARS-CoV-2)	Flu A	Flu B
		Positive/Total		
Adenovirus - type 1	1.00E+05 $TCID_{50}$/mL	3/3	3/3	3/3
Adenovirus - type 4	1.00E+05 $TCID_{50}$/mL	3/3	3/3	3/3
Adenovirus - type 7	1.00E+05 $TCID_{50}$/mL	3/3	3/3	3/3

Organism	Concentration of Organism in Sample Buffer Tube	CoV2 (SARS-CoV-2)	Flu A	Flu B
		Positive/Total		
Bordetella pertussis	1.00E+06 CFU/mL	3/3	3/3	3/3
Candida albicans	1.00E+06 CFU/mL	3/3	3/3	3/3
Chlamydia pneumonia	1.00E+06 IFU/mL	3/3	3/3	3/3
Corynebacterium diphtheriae	1.00E+06 CFU/mL	3/3	3/3	3/3
Cytomegalovirus	4.17E+04 U/mL	3/3	3/3	3/3
Enterovirus B (Echovirus 6)	1.00E+05 U/mL	3/3	3/3	3/3
Enterovirus C (Coxsackievirus A17)	1.00E+05 $TCID_{50}$/mL	3/3	1/3	0/3
	1.00E+04 $TCID_{50}$/mL	3/3	3/3	3/3
Enterovirus D	1.00E+05 U/mL	3/3	3/3	3/3
Epstein Barr virus	1.00E+05 copies/mL	3/3	3/3	3/3
Escherichia coli	1.00E+06 CFU/mL	3/3	3/3	3/3
Haemophilus influenzae	1.00E+06 CFU/mL	3/3	3/3	3/3
Herpes simplex virus Type 1	1.41E+04 U/mL	3/3	3/3	3/3
Herpes simplex virus Type 2	1.41E+04 U/mL	3/3	3/3	3/3
Human coronavirus 229E	1.00E+05 U/mL	3/3	3/3	3/3
Human coronavirus HKU1[a]	1.00E+05 GC/mL	3/3	3/3	3/3
Human coronavirus NL63	1.41E+04 $TCID_{50}$/mL	3/3	3/3	3/3
Human coronavirus OC43	1.00E+05 $TCID_{50}$/mL	3/3	3/3	3/3
Human Metapneumovirus (hMPV)	1.00E+05 $TCID_{50}$/mL	3/3	3/3	3/3
Lactobacillus acidophilus	1.00E+06 CFU/mL	3/3	3/3	3/3
Legionella pneumophila	1.00E+06 CFU/mL	3/3	3/3	3/3
Measles	1.00E+05 U/mL	3/3	3/3	3/3
MERS-coronavirus[a]	1.00E+05 copies/mL	3/3	3/3	3/3
Moraxella catarrhalis	1.00E+06 CFU/mL	3/3	3/3	3/3
Mumps	1.00E+05 U/mL	3/3	3/3	3/3
Mycobacterium tuberculosis[a]	1.00E+06 copies/mL	3/3	3/3	3/3
Mycoplasma pneumoniae	1.00E+06 CFU/mL	3/3	3/3	3/3
Neisseria meningitidis	5.00E+03 CFU/mL	3/3	3/3	3/3

Organism	Concentration of Organism in Sample Buffer Tube	CoV2 (SARS-CoV-2)	Flu A	Flu B
		Positive/Total		
Neisseria gonnorrhoeae	1.00E+06 CFU/mL	3/3	3/3	3/3
Parainfluenza virus 1	1.00E+05 $TCID_{50}$/mL	3/3	3/3	3/3
Parainfluenza virus 2	1.00E+05 U/mL	3/3	3/3	3/3
Parainfluenza virus 3	1.00E+05 $TCID_{50}$/mL	3/3	3/3	3/3
Parainfluenza virus 4	1.00E+05 $TCID_{50}$/mL	3/3	3/3	3/3
Pneumocystis jirovecii (PJP)	1.00E+05 nuclei/mL	3/3	3/3	3/3
Pooled human expressed nasopharyngeal swab matrix	N/A	3/3	3/3	3/3
Pseudomonas aeruginosa	1.00E+06 CFU/mL	3/3	3/3	3/3
Respiratory syncytial virus	1.00E+05 U/mL	3/3	3/3	3/3
Rhinovirus	1.00E+05 $TCID_{50}$/mL	3/3	3/3	3/3
SARS-coronavirus[a]	1.00E+05 GE/mL	3/3	3/3	3/3
Staphylococcus aureus	1.00E+06 CFU/mL	3/3	3/3	3/3
Staphylococcus epidermis	1.00E+06 CFU/mL	3/3	3/3	3/3
Streptococcus pneumoniae	1.00+06 CFU/mL	3/3	3/3	3/3
Streptococcus pyogenes	1.00E+06 CFU/mL	3/3	3/3	3/3
Streptococcus salivarius	5.00E+03 CFU/mL	3/3	3/3	3/3
Varicella-zoster virus	1.00E+04 U/mL	3/3	3/3	3/3

[a] Genomic DNA or RNA tested

Mixed Infection / Competitive Interference

To access potential competitive interference between SARS-CoV-2, influenza A, and influenza B, samples were tested in replicates of five (5) where low (approximately 2x their respective LoD) concentration of two analytes were mixed with high (approximately 1.00E+06 $TCID_{50}$/mL in UVT or 1.00E+06 GC/mL in UVT) concentration of the other analyte in simulated nasopharyngeal matrix.

Results of the study demonstrated that SARS-CoV-2 at 1.00E+06 GC/mL in UVT inhibits influenza B detection when present at low concentration (~2x LoD) in a sample. Inhibition was not observed when SARS-CoV-2 concentration was diluted to 1E+05 GC/mL in UVT.

Table 9. Mixed Infection / Competitive Interference Results

Co-Infection Condition	Virus 1 (High)		Virus 2		Virus 3		Positive Results		
	Description	Concentration	Description	Concentration	Description	Concentration	CoV2 (SARS-CoV-2)	Flu A	Flu B
1	SARS-CoV-2 (USA-WA1/2020)	1.00E+06 GC/mL	Influenza A (Kansas/14/17)	9.6 $TCID_{50}$/mL	Influenza B (Colorado/06/17)	0.10 $TCID_{50}$/mL	5/5	5/5	4/5
2	Influenza A (Michigan/45/2015 (H1N1) pdm09)	1.00E+06 $TCID_{50}$/mL	SARS-CoV-2 (USA-WA1/2020)	1400 GC/mL	Influenza B (Colorado/06/17)	0.10 $TCID_{50}$/mL	5/5	5/5	5/5
3	Influenza B (Guangdong-Liwan/1133/2014)	1.00E+06 $TCID_{50}$/mL	SARS-CoV-2 (USA-WA1/2020)	1400 GC/mL	Influenza A (Kansas/14/17)	9.6 $TCID_{50}$/mL	5/5	5/5	5/5
4	SARS-CoV-2 (USA-WA1/2020)	1.00E+05 GC/mL	Influenza B (Colorado/06/17)	0.10 $TCID_{50}$/mL	N/A		5/5	N/A	5/5

Interfering Substances

Nine (9) biological and chemical substances that may be present in nasopharyngeal swab specimens were evaluated for potential interference with the BD SARS-CoV-2/Flu for BD MAX™ System in the absence and presence of assay analytes (SARS-CoV-2, influenza A and influenza B). Whole human blood was found to interfere at levels above 0.2% volume/volume. Flonase was found to interfere at levels above 1.7% volume/volume. Tobramycin was found to interfere at levels above 0.4 µg/mL. Zicam was found to interfere at levels above 0.5% volume/volume. Results demonstrated no reportable interference with any other substance tested (refer to Table 10).

Table 10: Endogenous and Commercial Exogenous Substances Tested with BD SARS-CoV-2/Flu for BD MAX™ System

Brand Name or Description	Active Ingredient	Concentration Tested	Positive Testing (Positive/Total)			Negative Testing (Negative/ Total)	Result
			CoV2 (SARS-CoV-2)	Flu A	Flu B		
Mucin	Purified Mucin	60 µg/mL	3/3	3/3	3/3	3/3	NI
Whole Human Blood	N/A	2% v/v	2/3[a]	2/3[a]	2/3[a]	3/3	I
		0.2% v/v	3/3	3/3	3/3	3/3	NI
Nasal corticosteroids - Flonase	Fluticasone	17% v/v	1/3	0/3	1/3	3/3	I
		1.7% v/v	3/3	3/3	3/3	3/3	NI
Nasal gel – Zicam	Galphimia glauca, luffa operculata, sabadilla	5% v/v	2/3[b]	2/3[b]	2/3[b]	3/3	I
		0.5% v/v	3/3	3/3	3/3	3/3	NI
Homeopathic allergy relief medicine – Afrin	Oxymetazoline hydrochloride	8% v/v	3/3	3/3	3/3	3/3	NI
Throat lozenges, oral anesthetic and analgesic - Cepacol	Benzocaine, Menthol	0.8 mg/mL	3/3	3/3	3/3	3/3	NI
Anti-viral drugs (Relenza)	Zanamivir	3.3 mg/mL	3/3	3/3	3/3	3/3	NI
Antibiotic, nasal ointment (Mupirocin)	Mupirocin	10 mg/mL	3/3	3/3	3/3	3/3	NI
Antibacterial, systemic (Tobramycin)	Tobramycin	4 µg/mL	3/3	3/3	3/3	2/3[b]	I
		0.4 µg/mL	3/3	3/3	3/3	3/3	NI

[a]: Indeterminate (IND) result

[b]: Unresolved (UNR) result

I: Reportable Interference with the BD SARS-CoV-2/Flu for BD MAX™ System at high concentrations.

NI: No reportable interference with the BD SARS-CoV-2/Flu for BD MAX™ System.

CLINICAL EVALUATION

Clinical performance characteristics of the BD SARS-CoV-2/Flu for BD MAX™ System were determined from a total of 232 frozen retrospective nasopharyngeal swabs in UVT/UTM obtained from two external sources with historical positive or negative results for either SARS-CoV-2, influenza A, or influenza B. The specimens were collected as part of routine patient care between 30 November 2019 and 3 September 2020 from 116 males and 116 females ranging in age from 5 months to over 89 years old. All the specimens were tested in a blinded and randomized fashion with the BD SARS-CoV-2/Flu for BD MAX™ System and reference methods (RM). The RM for SARS-CoV-2 was an EUA authorized high sensitivity RT-PCR assay. The RM for influenza A and influenza B was an FDA-cleared RT-PCR assay.

Tables 11 through 13 describe the performance characteristics of the BD SARS-CoV-2/Flu for BD MAX™ System that were observed during the clinical evaluation.

Table 11: SARS-CoV-2 Clinical Performance

	Reference Method			
	SARS-CoV-2	**POSITIVE**	**NEGATIVE**	**Total**
BD SARS-CoV-2/Flu for BD MAX™ System	POSITIVE	50	0	50
	NEGATIVE	2[a]	30[b]	32
	Total	52	30	82
SARS-CoV-2 PPA: 96.2% (50/52) (95% CI: 87.0%–98.9%) **SARS-CoV-2 NPA:** 100% (30/30) (95% CI: 88.7%–100%)				

[a] 2/2 specimens were tested with discrepant method and yielded negative results for SARS-CoV-2. One (1) historical result was positive and the other negative.

[b] One unresolved (UNR) result was obtained during initial testing with BD SARS-CoV-2/Flu for BD MAX™ System and was excluded from analysis.

Table 12: Influenza A Clinical Performance

	Reference Method			
	Influenza A	**POSITIVE**	**NEGATIVE**	**Total**
BD SARS-CoV-2/Flu for BD MAX™ System	POSITIVE	59[a]	1[b]	60
	NEGATIVE	0	90	90
	Total	59	91	150
Influenza A PPA: 100% (59/59) (95% CI: 93.9%–100%) **Influenza A NPA:** 98.9% (90/91) (95% CI: 94.0%–99.8%)				

[a] One indeterminate (IND) result was obtained during initial testing with BD SARS-CoV-2/Flu for BD MAX™ System and was excluded from analysis.

[b] The specimen was tested with the discrepant method and yielded a positive result for influenza A. Historical result was positive.

Table 13: Influenza B Clinical Performance

	Reference Method			
	Influenza B	**POSITIVE**	**NEGATIVE**	**Total**
BD SARS-CoV-2/Flu for BD MAX™ System	**POSITIVE**	59	0	59
	NEGATIVE	1[a]	90[b]	91
	Total	60	90	150
Influenza B PPA: 98.3% (59/60) (95% CI: 91.1%–99.7%) **Influenza B NPA:** 100% (90/90) (95% CI: 95.9%–100%)				

[a] The specimen was tested with the discrepant method and yielded a positive result for influenza B. Historical result was positive.

[b] One indeterminate (IND) result was obtained during initial testing with BD SARS-CoV-2/Flu for BD MAX™ System and was excluded from analysis.

FDA SARS-CoV-2 REFERENCE PANEL TESTING

The evaluation of sensitivity and MERS-CoV cross-reactivity was performed using reference material (T1), blinded samples, and a standard protocol provided by the FDA. The study included a range-finding study and a confirmatory study for LoD. Blinded sample testing was used to establish specificity and to corroborate the LoD. The samples were tested using the BD MAX™ System. The results are summarized in Table 14.

Table 14: Summary of LoD Confirmation Result using the FDA SARS-CoV-2 Reference Panel

Reference Materials Provided by FDA	Specimen Type	Product LoD	Cross-Reactivity
SARS-CoV-2	Nasopharyngeal matrix	5,400 NDU/mL	N/A
MERS-CoV		N/A	ND

NDU/mL = RNA NAAT detectable units/mL

N/A = Not Applicable

ND = Not Detected

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Change History

Revision	Date	Change Summary
(01)	2021-02	Initial release.
(02)	2021-04	Addition of anterior nasal swabs collected in 0.85% saline as a specimen type and FDA SARS-CoV-2 Reference Panel Testing section. Corrected values in Table 6. Made typographical and formatting updates.

SYMBOLS GLOSSARY [L006715(05) 2021-04]

Some symbols listed below may not apply to this product.

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

Symbol	Meaning
	Manufacturer
	Authorized representative in the European Community
	Date of manufacture
	Use-by date
	Batch code
	Catalogue number
	Serial number
	Sterile
	Sterilized using aseptic processing techniques
	Sterilized using ethylene oxide
	Sterilized using irradiation
	Sterilized using steam or dry heat
	Do not resterilize
	Non-sterile
	Do not use if package is damaged
	Sterile fluid path
	Sterile fluid path (ethylene oxide)
	Sterile fluid path (irradiation)
	Fragile, handle with care
	Keep away from sunlight
	Keep dry
	Lower limit of temperature
	Upper limit of temperature
	Temperature limit
	Humidity limitation
	Biological risks
	Do not re-use
	Consult instructions for use For electronic instructions for use, the url accompanies the symbol.
	Caution
	Contains or presence of natural rubber latex
	*In vitro* diagnostic medical device
	Negative control
	Positive control
	Contains sufficient for <*n*> tests
	For IVD performance evaluation only
	Non-pyrogenic
	Patient number

Symbol	Meaning
	This way up
	Do not stack
	Single sterile barrier system
	Contains or presence of phthalate: combination of bis(2-ethylhexyl) phthalate (DEHP) and benzyl butyl phthalate (BBP)
	Collect separately Indicates separate collection for waste of electrical and electronic equipment required.
	CE marking; Signifies European technical conformity
	Device for near-patient testing
	Device for self-testing
	This only applies to US: "Caution: Federal Law restricts this device to sale by or on the order of a licensed practitioner."
	Country of manufacture "CC" shall be replaced by either the two letter or the three letter country code.
	Collection time
	Cut
	Peel here
	Collection date
	Keep away from light
	Hydrogen gas is generated
	Perforation
	Start panel sequence number
	End panel sequence number
	Medical device
	Contains hazardous substances
	Ukrainian conformity mark
	Meets FCC requirements per 21 CFR Part 15
	UL product certification for US and Canada
	Unique device identifier

BD

Technical Information: In the United States contact BD Technical Service and Support at 1.800.638.8663 or bd.com.

Becton, Dickinson and Company
7 Loveton Circle
Sparks, Maryland 21152 USA

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

REF 445003-01 REF 445011
P0259(02)

CE IVD bd.com/e-labeling **Rx Only**

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- BD SARS-CoV-2/Flu for BD MAX™ System has been authorized only for the detection of nucleic acid of SARS-CoV-2, influenza A, and influenza B, not for any other viruses or pathogens; and
- The emergency use of these products is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of in vitro diagnostics for detection and/or diagnosis of COVID-19 under Section 564(b)(1) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb- 3(b)(1), unless the declaration is terminated or authorization is revoked sooner.

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