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

REF **445003-01**

For In Vitro Diagnostic Use
For use with the BD MAX™ System

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English

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 SARS-CoV-2 in nasopharyngeal, anterior nasal, mid-turbinate, and oropharyngeal swab specimens as well as nasopharyngeal wash/aspirate or nasal aspirate specimens obtained from any individuals, including individuals without symptoms or other reasons to suspect COVID-19.

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.

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 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.

EXPLANATION OF THE TEST

Total nucleic acid (TNA) is isolated and purified using BD SARS-CoV-2 Reagents for BD MAX™ System from nasal, nasopharyngeal, or oropharyngeal swabs collected in BD Universal Viral Transport System (UVT) or Copan Universal Transport Media System (UTM) and nasal swabs collected in 0.85% saline. Patient sample is transferred to the Sample Buffer Tube provided with the BD SARS-CoV-2 Reagents for BD MAX™ System 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 SARS-CoV-2 primers and probes and to the BD MAX™ TNA MMK master mix. 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
445003-01	**BD MAX™ ExK™ TNA-3 Sample Buffer Tube** (with 25 septum caps)	24
	BD MAX™ TNA Unitized Reagent Strip (TNA) Unitized Reagent Strip containing all liquid reagents and disposable pipette tips necessary for specimen processing and TNA extraction.	
	BD MAX™ ExK™ TNA Extraction Tube (B4) Dried extraction reagent containing magnetic affinity beads and Proteinase K.	24 (2 x 12 tubes)
	BD SARS-CoV-2 Reagents for BD MAX™ System Primers and Probes Dried primers and probes for SARS-CoV-2.	
	BD MAX™ TNA MMK (C3) Dried PCR Master Mix containing dNTPs and RT-polymerase.	

EQUIPMENT AND MATERIALS REQUIRED BUT NOT PROVIDED

- BD MAX™ System (BD Catalog Number 441916)
- BD MAX™ Sample Rack (BD Catalog Number 441935, 443550, 443551, 444807, or 444808)
- BD PCR Cartridges (BD Catalog Number 437519)
- SARS CoV-2 and RNase P Controls
- Copan UTM Collection Kit
- BD UVT Collection Kit
- 0.85% Saline
- Vortex Genie 2 (VWR Catalog Number 58815-235 or equivalent)
- Multi-Tube Vortex Mixer (VWR Catalog Number 58816-115 or equivalent)
- Rack compatible with a multi-tube vortexer (e.g., Cryogenic Vial Holder or equivalent)
- Variable Volume Calibrated Pipettor (1 mL volume capable)
- Aerosol resistant micropipette tips
- Disposable gloves, powderless
- Sterile, polypropylene plastic, preservative-free collection container (VWR Catalog Number 21008-951 or equivalent)

WARNINGS AND PRECAUTIONS

Master Mix contains: N, N-dimethylformamide; dimethyl formamide; CAS Number 68-12-2.

Extraction Tube contains: Proteinase, Tritirachium album serine; CAS Number 39450-01-6. PAMAM dendrimer, ethylenediamine core, generation 0.0 solution; CAS Number 155773-72-1. Triton; CAS Number 9002-93-1

Neutralization Buffer and Wash Buffer contain: CMIT/MIT mixture (3:1) - a mixture of: 5-chloro-2-methyl-4-isothiazolin-3-one [EC No. 247-500-7] and 2-methyl-4-isothiazolin-3-one [EC No. 220-239-6] (3:1); CAS Number 55965-84-9.

Sample Tube contains: Triton; CAS Number 9002-93-1. 3-[bis(2-carboxyethyl)phosphanyl] propanoic acid hydrochloride; CAS Number 51805-45-9.

Danger

H311 Toxic 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.
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.
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.
P361+P362 Take off contaminated clothing
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.
- Positive results are indicative of the presence of SARS-CoV-2 RNA.
- 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 PCR Cartridge after use. The seals of the BD 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.
- Collect and dispose of all used and unused reagents and any other contaminated disposable materials following procedures for biohazardous or potentially biohazardous waste. It is the responsibility of each laboratory to handle solid and liquid waste according to their nature and degree of hazardousness and to adequately treat and dispose of them (or have them treated and disposed of) in accordance with any applicable regulations. Do not discharge liquid waste down the drain where prohibited.
- 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 kit ships at ambient temperature and is stable at 2–25 °C through the stated expiration date. Do not use if expired.
  NOTE: The reagents are considered unusable by the BD MAX™ System on the expiration date printed on the product label.
- The BD MAX™ TNA Extraction Tubes (B4), BD MAX™ TNA MMK (C3), and BD SARS-CoV-2 Reagents for BD MAX™ System Primers and Probes are provided in sealed pouches. To protect from humidity, immediately re-seal after opening.
- The Extraction Tubes, MMK Master Mix, and Primers and Probes are stable for up to 8 days at 2–25 °C after initial opening and re-sealing of the pouch. Unreconstituted Extraction Tubes, MMK Master Mix, and Primers and Probes are stable for up to 4 hours at 2–25 °C after being removed from their protective pouches.

INSTRUCTIONS FOR USE

Swab Specimen Collection/Transport in Universal Viral Transport (UVT) or Universal Transport Media (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. 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.
3. If a delay in testing or shipping is expected, store specimens at -70 °C or below. Frozen storage for up to 30 days was evaluated. Frozen specimens should not exceed two (2) freeze thaw cycles.

Swab Specimen Collection/Transport in 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. Nasal swab specimens should be collected and expressed directly into the saline tube.
2. Store specimens at 2–8 °C for up to 72 hours after collection. If a delay in testing or shipping is expected, store specimens at -70 °C or below.

   Sample stability when using BD SARS-CoV-2 Reagents for BD MAX™ System has not been established for suggested temperatures and time, but is based on CDC guidelines.[4]

Saliva Specimen Collection/Transport and Processing

Note: Ensure the patient does not eat, drink, smoke, chew gum, brush their teeth, or use mouthwash for 30 minutes prior to collection. Wear gloves when handling specimens. If gloves come in contact with the specimen, immediately change them to prevent contamination of other specimens.

1. Affix a patient label to the sterile, polypropylene plastic, preservative-free collection container. Performance with other collection methods and collection devices has not been established.
2. Direct the patient to generate a pool of saliva in their mouth. This may take several minutes. The production of saliva can be stimulated by gently massaging the outside of one's cheek.
3. Using the sterile collection container, collect 2–3 mL of saliva. Do not include any bubbles in this measurement.
4. Recap the sterile specimen container. Avoid touching the opening of the container.
5. After collection, saliva specimens can be transported and stored at 2–25 °C for up to 120 hours. Ensure specimens are protected from leakage during shipment and storage.
6. Dilute 1 mL of saliva into 3 mL of UVT/UTM (4 mL total volume). The resulting diluted specimen may be stored at 2–25 °C for up to 72 hours.

BD MAX™ Sample Buffer Tube Preparation for use with nasal, nasopharyngeal, oropharyngeal swab, or saliva specimens in Universal Viral Transport (UVT) or Universal Transport Media (UTM) or nasal swab specimens 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) 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 or saline 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 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 TNA Unitized Reagent Strips from the BD SARS-CoV-2 Reagents 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. 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:

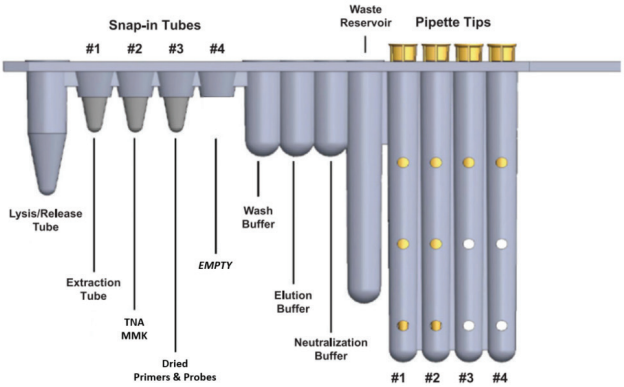


Figure 1: Snap Extraction Tubes and Master Mix Tube into Unitized Reagent Strips

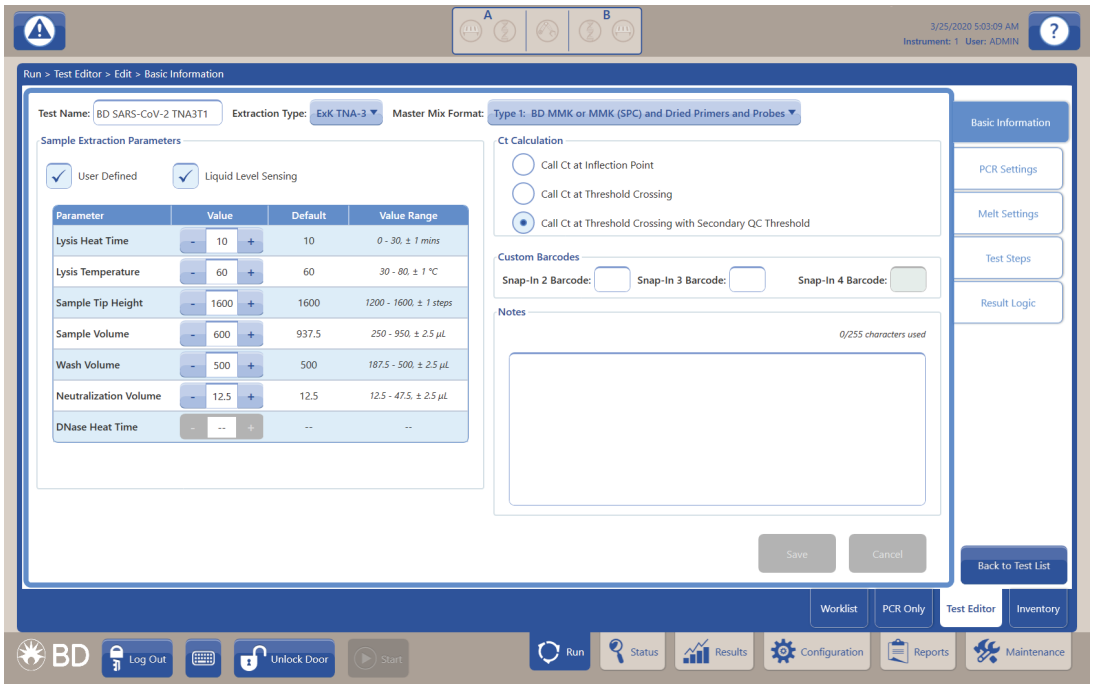
Note: Failure to add extraction tube or master mix tubes may result in instrument contamination.

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

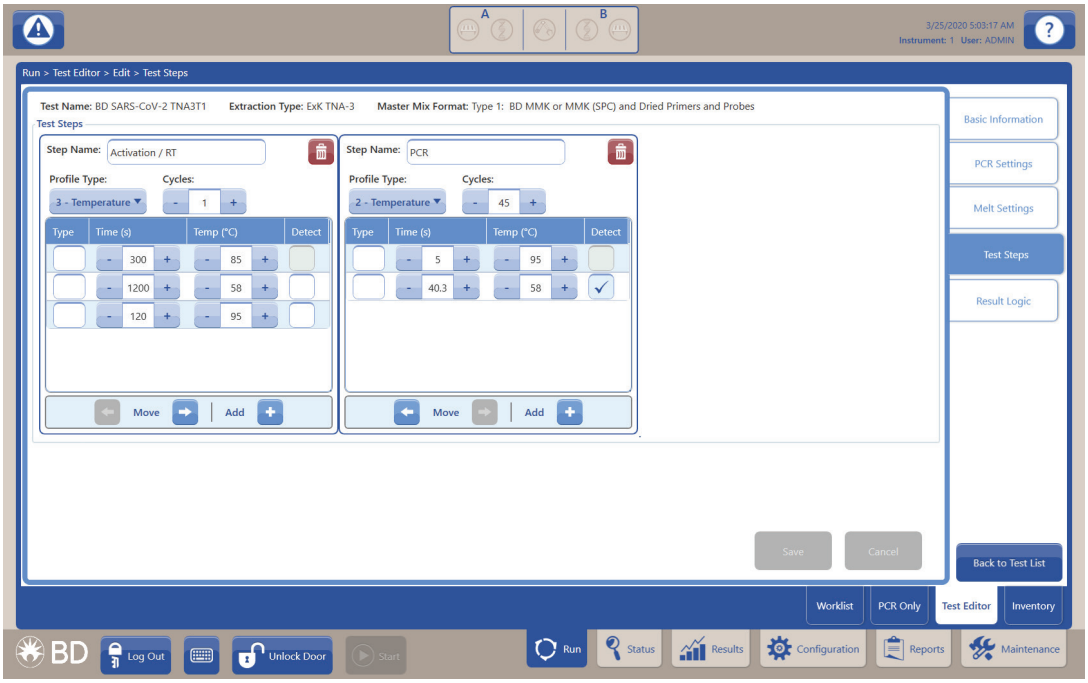
Basic Information Section



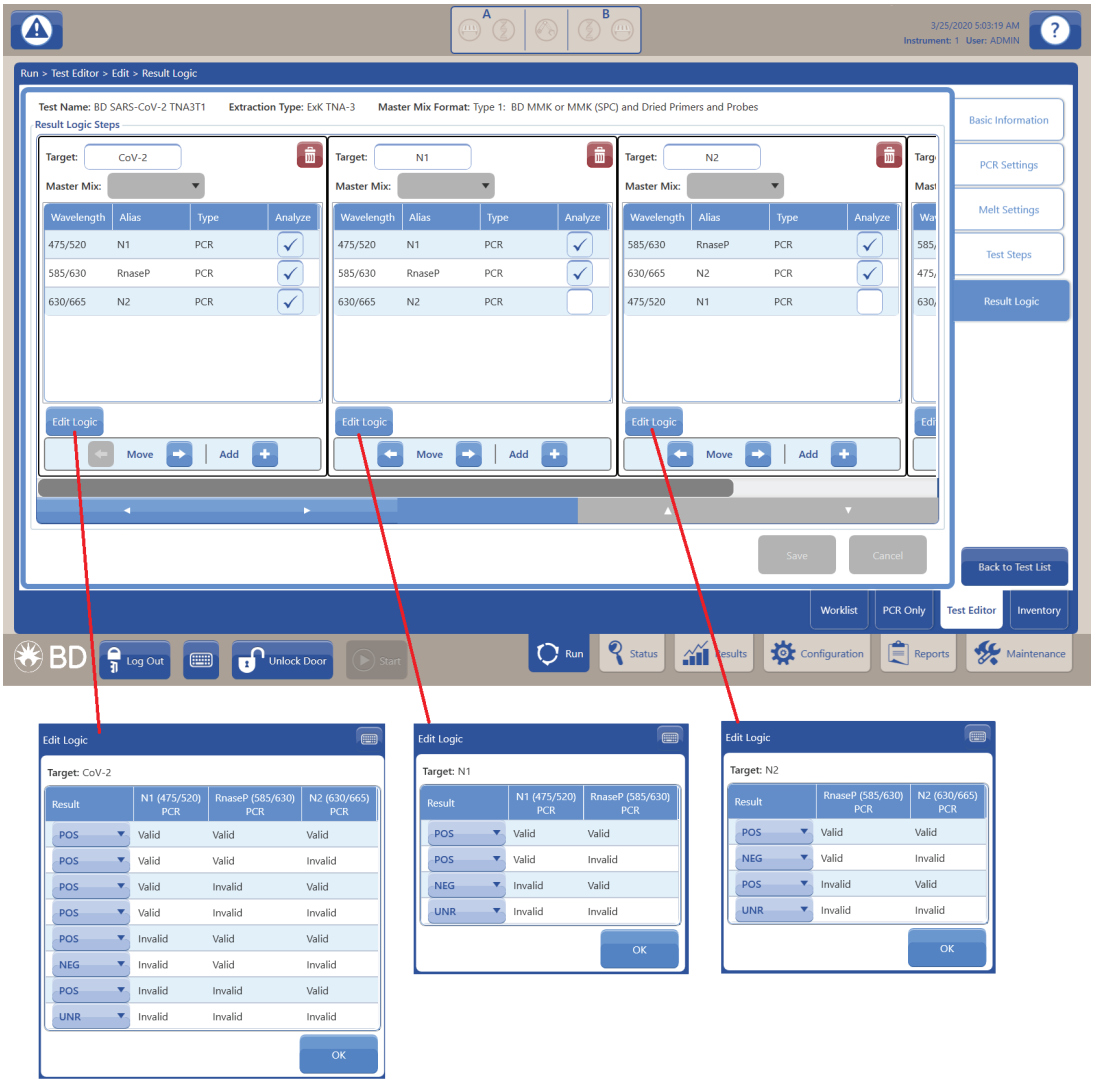
PCR Setting Section

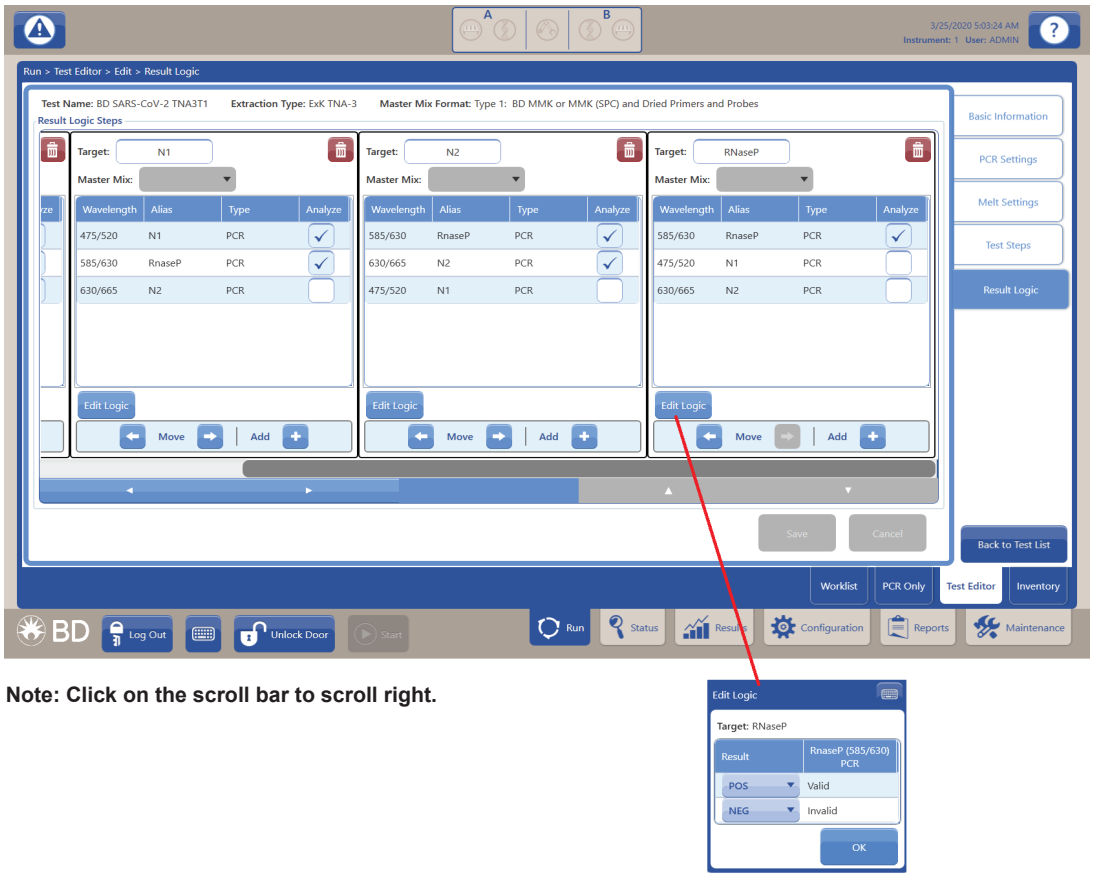
Melt Settings Section

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 SARS-CoV-2 Reagents for BD MAX™ System kit by either scanning the barcode with the scanner or by manual entry and then save.

   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.

14. Place the required number of BD 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).

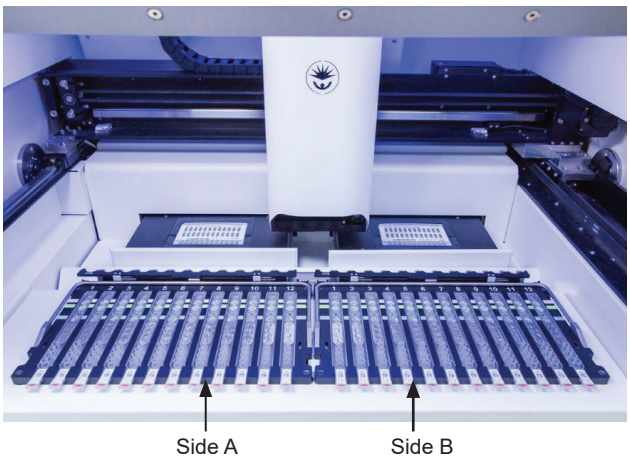


Figure 3: Load Rack(s) onto the BD MAX™ System

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. All test controls should be examined prior to interpretation of patient results. If the controls are not valid, the patient results cannot be interpreted. 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 RNase P positive control 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, 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.

External Negative and Positive Controls

If the positive or negative controls are processed in the run and do 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
External Negative Control	Known Negative Sample	Reagent and/or environmental contamination and reagent failure including primer and probe integrity	NEG	NEG	POS	NEG
	RNase P Positive Control		NEG	NEG	POS	NEG
External Positive Control	N1 and N2 Positive Control	Substantial reagent failure including primer and probe integrity	POS	POS	N/A	POS

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/UNR	POS/NEG	POS	Positive	Report as Positive
NEG/UNR	POS	POS/NEG	POS	Positive	Report as Positive
NEG	NEG	POS	NEG	Negative	Report as Not Detected
UNR	UNR	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/saline 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/saline 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/saline 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 on the 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, oropharyngeal, and nasal swab samples collected in BD Universal Viral Transport System (UVT) or Copan Universal Transport Media System (UTM) nasal swabs collected in 0.85% saline (self-collected under supervision of a healthcare provider or healthcare provider-collected). Use of BD SARS-CoV-2 Reagents for BD MAX™ System with other sample types, including nasopharyngeal wash/aspirate or nasal aspirates and mid-turbinate nasal swabs (self-collected under supervision of or collected by a healthcare provider), has not been assessed and performance characteristics are unknown.
- 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.
- Human blood, Flonase, Zicam, Zanamivir, and purified mucin were found to interfere with the BD SARS-CoV-2 Reagents for BD MAX™ System at concentrations greater than 0.02% v/v, 1.7% v/v, 0.5% v/v, 0.33 mg/mL, and 6.0 µg/mL in UVT, respectively.
- The effect of homeopathic medications for respiratory symptoms on the assay performance was not tested.
- BD SARS-CoV-2 Reagents have 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.
- Clinical performance has not been established with all the 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.

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 (Catalog Number NR-52285), or quantified heat-inactivated virus, obtained from ATCC® (Catalog Number VR-1986HK), was serially diluted into pooled negative nasopharyngeal clinical matrix, a total of 5 concentrations levels, with 2 serial dilutions between each level.

Confirmation of the estimated LoD was performed with one reagent lot in replicates of 20 prepared in each specified clinical matrix. The LoD is the lowest concentration (reported as genomic equivalents/mL, GE/mL, or genomic copies/mL, GC/mL) of SARS-CoV-2 that can be reproducibly distinguished from negative samples ≥95%. The LoD for the assay with genomic RNA and heat-inactivated virus in pooled nasopharyngeal swab matrix is 40 GE/mL and 640 GC/mL, respectively. The LoD for the assay with heat-inactivated virus is 5,120 GE/mL in saliva. The LoD difference observed between heat-inactivated virus and genomic RNA is due to the testing material.

Table 3: LoD determination from SARS-CoV-2 USA-WA1/2020 strain

Strain	Matrix	Concentration	Total Valid Results	Positives			Mean Ct		
				CoV-2	N1	N2	N1	N2	RNase P
USA-WA1/2020 Genomic RNA	Nasopharyngeal	40 GE/mL	20	20	20	20	33.4	33.7	21.4
USA-WA1/2020 Heat-Inactivated Virus	Nasopharyngeal	640 GC/mL	20	20	20	20	33.2	33.2	21.0
USA-WA1/2020 Heat-Inactivated Virus	Saliva	5,120 GC/mL	20	20	20	20	31.6	31.6	21.7

Reactivity/Inclusivity

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 by December 11, 2021 (n=4,349,356). Alignments against the N gene showed that both N1 and N2 primer/probe sets are a perfect match to 90.3% of sequences in the database, 97.6% of the sequences were a perfect match to the N1 primer set region, and 92.8% were a perfect match to the N2 primer set region. In total, 99.8% are a perfect match to either the N1 or the N2 region primer set.

All variants have a perfect match to either the N1 region or the N2 region primer set.

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.

Additionally, 35 organisms were evaluated for cross-reactivity with the BD SARS-CoV-2 Reagents for BD MAX™ System in the detection of SARS-CoV-2 viral RNA. All organisms tested produced negative results when tested at the following concentrations.

Table 4: Organisms evaluated for cross-reactivity

Organism	Concentration Tested
Adenovirus 1	1.02E+08 $TCID_{50}$/mL
Adenovirus 4	1.26E+06 $TCID_{50}$/mL
Adenovirus 7	9.55E+06 $TCID_{50}$/mL
Bordetella pertussis	1.13E+10 CFU/mL
Candida albicans	2.40E+07 CFU/mL
Chlamydia pneumoniae	1.40E+08 IFU/mL
Human coronavirus 229E	1.17E+05 $TCID_{50}$/mL
Human coronavirus NL63	1.41E+05 $TCID_{50}$/mL
Human coronavirus OC43	1.51E+06 $TCID_{50}$/mL
Enterovirus B	3.80E+06 U/mL
Enterovirus C	1.58E+06 $TCID_{50}$/mL
Enterovirus D	9.55E+06 IFU/mL
Haemophilus influenzae	5.00E+04 CFU/mL
Influenza A (H1N1)	1.41E+05 $TCID_{50}$/mL
Influenza A (H3N2)	1.26E+06 $TCID_{50}$/mL
Influenza B	1.70E+05 $TCID_{50}$/mL
Legionella pneumophila	5.00E+04 CFU/mL
MERS Coronavirus	7.20E+05 Genome copies/µL
Human Metapneumovirus (hMPV)	3.80E+06 $TCID_{50}$/mL
Mycoplasma pneumoniae	1.00E+09 CFU/mL
Mycobacterium tuberculosis	1.00E+06 copies/µL
Parainfluenza 1	3.39E+07 $TCID_{50}$/mL
Parainfluenza 2	2.19E+06 $TCID_{50}$/mL
Parainfluenza 3	8.51E+07 $TCID_{50}$/mL
Parainfluenza 4	1.15E+07 $TCID_{50}$/mL
Pneumocystis jirovecii (PJP)	1.00E+08 nuclei/mL/vial
Pseudomonas aeruginosa	6.00E+07 CFU/mL
Respiratory syncytial virus (RSV)	5.01E+05 $TCID_{50}$/mL

Organism	Concentration Tested
Rhinovirus	4.17E+05 $TCID_{50}$/mL
SARS 1 Coronavirus	3.40E+05 cps/µL
Staphylococcus epidermidis	6.00E+07 CFU/mL
Streptococcus pneumoniae	6.00E+07 CFU/mL
Streptococcus pyogenes	1.20E+09 CFU/mL
Streptococcus salivarius	5.00E+04 CFU/mL
Pooled human nasal matrix to represent diverse microbial flora in human respiratory tract	N/A

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 Reagents for BD MAX™ System in the absence and presence of assay analytes. Mucin was found to interfere at levels above 6.0 µg/mL. Whole human blood was found to interfere at levels above 0.02% volume/volume. Flonase was found to interfere at levels above 1.7% volume/volume. Zicam was found to interfere at levels above 0.5% volume/volume. Zanamivir was found to interfere at levels above 0.33 mg/mL. Results demonstrated no reportable interference with any other substance tested (refer to Table 5).

Table 5: Endogenous and Commercial Exogenous Substances Tested with BD SARS-CoV-2 Reagents for BD MAX™ System

Brand Name or Description	Active Ingredient	Concentration Tested	Positive Testing (Positive/Total)			Negative Testing (Negative/Total)	Result
			SARS-CoV-2	N1	N2		
Mucin	Purified Mucin	60 µg/mL	3/3	3/3	2/3	3/3	I
		6.0 µg/mL	3/3	3/3	3/3	3/3	NI
Whole Blood	N/A	2% v/v	3/3	3/3	2/3	3/3	I
		0.2% v/v	3/3	3/3	2/3	3/3	I
		0.02% v/v	3/3	3/3	3/3	3/3	NI
Nasal corticosteroids (Flonase)	Fluticasone	17% v/v	3/3	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	3/3	0/3	2/3	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	Benzocaine, Methanol	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	2/3	3/3	I
		0.33 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	3/3	NI

I: Reportable Interference with the BD SARS-CoV-2 Reagents for BD MAX™ System at high concentrations. NI: No reportable interference with the BD SARS-CoV-2 Reagents for BD MAX™ System.

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 6: 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]	34.8[b]	20.9
~3-5x LoD	10	100% (10/10)	10/10	32.6	10/10	33.0	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.

The performance of BD SARS-CoV-2 Reagents for BD MAX™ System with nasal swab clinical samples collected in UVT or saline were evaluated using 10 individual negative clinical samples and 30 contrived positive clinical samples collected from asymptomatic donors for each workflow.

Nasal swabs were collected per IRB approved protocol. In brief, nasal swabs were self-collected by inserting the swab ~1 inch into one nostril and rolling the swab around 5 times to ensure both mucus and cells were collected. The same swab was then inserted into the second nostril and the collection method was repeated. Samples were 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 (20 samples) and ~3-5x LoD (10 samples), respectively.

The low positive and moderate positive samples showed 100% agreement with the expected results. All negative samples were negative in the background of individual clinical sample matrix.

Table 7: Clinical evaluation with contrived nasal swab samples collected in UVT

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	20	100% (20/20)	20/20	34.1	20/20	33.7	23.9
~3-5x LoD	10	100% (10/10)	10/10	33.7	10/10	33.5	24.5
Negative	10	N/A (0/10)	10/10	N/A	10/10	N/A	24.3

Table 8: Clinical evaluation with contrived nasal swab samples collected in 0.85% saline (3 mL)

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	20	100% (20/20)	20/20	34.4	20/20	34.4	28.7
~3-5x LoD	10	100% (10/10)	10/10	32.5	10/10	32.5	27.8
Negative	10	N/A (0/10)	10/10	N/A	10/10	N/A	29.1

The performance of BD SARS-CoV-2 Reagents for BD MAX™ System with retrospective collected nasopharyngeal swab clinical samples was evaluated using 100 individual negative clinical samples and 30 positive clinical samples as determined by an alternative NAAT. Clinical samples were collected from patients with signs and symptoms of an upper respiratory infection.

The positive samples showed 100% agreement with the expected results. The negative samples showed 97% agreement with the expected results.

The performance of BD SARS-CoV-2 Reagents for BD MAX™ System with saliva clinical samples was evaluated using 30 individual negative clinical samples and 50 contrived positive clinical samples collected from asymptomatic donors for each workflow. Saliva samples were collected in a sterile container per IRB approved protocol. Samples were stored frozen until use.

Low positive and moderate positive contrived clinical samples were prepared by spiking quantified heat-inactivated virus (SARS-CoV-2 USA-WA1/2020 strain) into individual negative clinical matrix to approximately ~1-2x LoD (30 samples), ~3-5x LoD (20 samples), and ~10x LoD (10 samples), respectively. The low positive, moderate positive, and high positive samples showed 100% agreement with the expected results. All negative samples were negative in the background of individual clinical sample matrix.

Table 9: Clinical evaluation with contrived saliva 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	30	100% (30/30)	30/30	30.9	30/30	31.5	21.9
~3-5x LoD	20	100% (20/20)	20/20	29.8	20/20	30.3	21.9
~10x LoD	10	100% (10/10)	10/10	29.5	9/10[a]	29.4[a]	21.8
Negative	30	N/A (0/30)	30/30	N/A	30/30	N/A	21.3

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

Table 10: Clinical comparison with an alternative NAAT

		Alternative NAAT	
		Positive	Negative
BD SARS-CoV-2 Reagents	Positive	30	3
	Negative	0	97
	Total	30	100
Positive Percent Agreement		100%	
Negative Percent Agreement		97%	

Post Market Clinical Evaluation Study

A prospective clinical study was conducted from September 2020 – January 2021 to evaluate the clinical performance of the BD SARS-CoV-2 Reagents for BD MAX™ System compared to an FDA authorized SARS-CoV-2 molecular assay. Nasopharyngeal specimens were collected from subjects suspected of COVID-19 or subjects suspected of COVID-19 presenting with one or more symptoms of COVID-19, at four geographically diverse clinical sites in the United States. The specimens were stored in viral transport media and tested at one of two clinical centers using the BD SARS-CoV-2 Reagents for BD MAX™ System and the FDA authorized SARS-CoV-2 molecular assay. Samples with initial BD MAX™ non-reportable results (unresolved, indeterminate, or incomplete) were repeated with a new aliquot of viral transport media.

One site enrolled specimens from subjects 1 month and older; three sites enrolled subjects 18 years and older. The population consisted of 40% males and 60% females. Of the 709 specimens tested on the BD MAX™ System, one specimen had a final result of unresolved and is not included in the data analysis. There were 708 compliant specimens with a paired BD MAX™ SARS-CoV-2 result and an FDA authorized molecular assay result for analysis. Discrepant specimens were tested with up to two additional FDA authorized SARS-CoV-2 nucleic acid amplification assays.

The positive and negative percent agreement with 95% confidence intervals of the BD SARS-CoV-2 Reagents for BD MAX™ System compared to an FDA EUA SARS-CoV-2 nucleic acid amplification assay are shown in Table 11.

Table 11: Percent Agreement of BD SARS-CoV-2 Reagents for BD MAX™ System vs. FDA Authorized Molecular Assay

	FDA Authorized Molecular Assay		
BD SARS-CoV-2 Reagents for BD MAX™ System Result	**Positive**	**Negative**	**Total**
Positive	138	19[a]	157
Negative	0	551	551
Total	138	570	708
Positive Percent Agreement	100% (95% CI: 97.3%–100.0%)		
Negative Percent Agreement	96.7% (95% CI: 94.9%–97.9%)		

[a] Five (5) of the 19 BD SARS-CoV-2 Reagents for BD MAX™ System positive/EUA comparator negative specimens were positive by at least one additional FDA authorized SARS-CoV-2 nucleic acid amplification assay. Two additional specimens were considered SARS-CoV-2 presumptive positive by one method.

Non-Reportable Results

In the clinical evaluation study, the initial total non-reportable rate representing unresolved, indeterminate, and incomplete results was 1.4% (10/709; 95% CI: 0.8%–2.6%). Following a valid repeat test, 0.1% (1/709; 95% CI: 0.0%–0.8%) specimens remained non-reportable.

Table 12: Non-reportable Rates[a]

Unresolved Rate		Indeterminate Rate		Incomplete Rate		Total Non-reportable Rate	
Initial (95% CI)	**Final (95% CI)**	**Initial (95% CI)**	**Final (95% CI)**	**Initial (95% CI)**	**Final (95% CI)**	**Initial (95% CI)**	**Final (95% CI)**
1.4% (10/709) (0.8%, 2.6%)	0.1% (1/709) (0.0%, 0.8%)	0.0% (0/709) (0.0%, 0.5%)	0.0% (0/709) (0.0%, 0.5%)	0.0% (0/709) (0.0%, 0.5%)	0.0% (0/709) (0.0%, 0.5%)	1.4% (10/709) (0.8%, 2.6%)	0.1% (1/709) (0.0%, 0.8%)

[a] Note that samples associated with BD MAX™ System runs with an external control failure are designated as invalid (INV). Of the 709 total samples tested, there were 64 initial INV results due to external control failures. The samples were successfully repeated with either a positive or negative result.

Clinical Performance in Asymptomatic Individuals

The clinical performance of the BD SARS-CoV-2 Reagents for the BD MAX™ System in subjects without signs and symptoms of respiratory infection (asymptomatic individuals) was evaluated in comparison to a FDA cleared RT-PCR assay. Nasopharyngeal specimens were collected from subjects without signs and symptoms of respiratory infection and without known exposure to COVID-19 at four (4) geographically diverse clinical sites in the United States. Retrospective specimens from pre-surgery patients were also included. The specimens were stored in viral transport media and tested at one testing center using the BD SARS-CoV-2 Reagents for BD MAX™ System and an FDA cleared SARS-CoV-2 RT-PCR assay.

Four (4) sites enrolled subjects 18 years and older. The population consisted of 36.8% males and 63.2% females. There were 223 compliant specimens with a paired BD SARS-CoV-2 for BD MAX™ System and FDA cleared molecular assay results for analysis. One (1) specimen did not contain sufficient volume for testing with the BD MAX™ SARS-CoV-2 reagents and the FDA cleared molecular assay. Discrepant specimens were tested with an additional FDA authorized SARS-CoV-2 nucleic acid amplification assay.

The positive and negative percent agreement and the 95% confidence intervals of the BD SARS-CoV-2 Reagents for BD MAX™ System compared to a FDA cleared SARS-CoV-2 nucleic acid amplification assay are shown in Table 13.

Table 13: Percent Agreement of BD SARS-CoV-2 Reagents for BD MAX™ System vs. FDA Cleared Molecular Assay

	FDA De Novo granted Molecular Assay		
BD SARS-CoV-2 Reagents for BD MAX™ System Result	**Positive**	**Negative**	**Total**
Positive	21	2[a]	23
Negative	0	200	200
Total	21	202	223
Positive Percent Agreement:	100.0% (95.0% CI: 84.5%–100.0%)		
Negative Percent Agreement:	99.0% (95.0% CI: 96.5%–99.7%)		

[a] One (1) of the 2 BD SARS-CoV-2 Reagents for BD MAX™ System positive/ FDA cleared comparator negative specimens were positive by an additional FDA authorized SARS-CoV-2 nucleic acid amplification assay.

Within-Lab Precision and Lot-to-Lot

Within-laboratory precision was evaluated for the BD SARS-CoV-2 Reagents for BD MAX™ System at one site with three reagent lots. Testing was performed over twelve (12) days, two (2) users, two (2) runs per day each (one BD MAX™ instrument), three (3) replicates per panel/run, for a total of 144 replicates per target and level. Test samples were contrived in simulated nasopharyngeal matrix spiked with heat-inactivated virus at three target levels. The following target concentrations were used for spiking levels of the target organisms contained in each panel member:

- Moderate Positive (MP): 3x LoD
- Low Positive (LP): 2x LoD
- True negative (TN): no target

Precision study results for the BD SARS-CoV-2 Reagents for BD MAX™ System are described in Table 14. The qualitative and quantitative reproducibility is presented below in Table 15. Ct, internal criterion used to determine a final assay result, was selected as an additional means of assessing assay reproducibility. Overall mean Ct. values with variance components (SD and %CV) are shown in Table 15.

Table 14: Overall Precision Study Results Using Three Lots of the BD SARS-CoV-2 Reagents for BD MAX™ System (Percent Agreement with Expected Results)

Sample Concentration	SARS-CoV-2	N1	N2	RNase P
Moderate Positive (3x LoD)	100% (144/144) 97.4–100	100% (144/144) 97.4–100	100% (144/144) 97.4–100	100% (144/144) 97.4–100
Low Positive (2x LoD)	100% (144/144) 97.4–100	100% (144/144) 97.4–100	100% (144/144) 97.4–100	100% (144/144) 97.4–100
True Negative[a]	100% (144/144) 97.4–100	100% (144/144) 97.4–100	100% (144/144) 97.4–100	100% (144/144) 97.4–100

[a] For the True Negative category, the reported agreement indicates percent of negative results.

Table 15: Lot-to-Lot Quantitative Reproducibility Study Results Using Three Lots of the BD SARS-CoV-2 Reagents for BD MAX™ System.

Target	Level	N	Mean Ct	Between Lot		Between Day		Between Operator		Between Run		Within Run (Repeatability)		Total	
				SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
N1	MP	144	31.45	0.00	0.00	0.00	0.00	0.30	0.96	0.00	0.00	0.33	1.04	0.45	1.42
N1	LP	144	32.05	0.09	0.28	0.00	0.00	0.26	0.80	0.00	0.00	0.41	1.28	0.49	1.54
N2	MP	144	31.43	0.00	0.00	0.00	0.00	0.02	0.07	0.12	0.38	0.42	1.34	0.44	1.39
N2	LP	144	31.98	0.17	0.53	0.01	0.05	0.00	0.00	0.10	0.30	0.56	1.74	0.59	1.85
RNase P	MP	144	23.34	0.04	0.18	0.00	0.00	0.00	0.00	0.12	0.52	0.30	1.30	0.33	1.41
RNase P	LP	144	23.29	0.06	0.28	0.00	0.00	0.03	0.14	0.11	0.47	0.32	1.39	0.35	1.50
RNase P	TN	144	22.79	0.00	0.00	0.00	0.00	0.00	0.00	0.14	0.63	0.76	3.33	0.77	3.38

Instrument-to-Instrument Reproducibility

For the Instrument Reproducibility Study, the data were collected over a period of five (5) days, two (2) users, two (2) runs per day each, three (3) replicates per panel/run, on each of three (3) BD MAX™ instruments, for a total of 60 replicates per instrument per target and level, 180 overall.

The qualitative and quantitative reproducibility is presented below by target. Ct, internal criterion used to determine a final assay result, was selected as an additional means of assessing assay reproducibility. Overall mean Ct. values with variance components (SD and %CV) are shown in Table 17.

Table 16: Overall Reproducibility Study Results Using One Lot of the BD SARS-CoV-2 Reagents for BD MAX™ System (Percent Agreement with Expected Results)

Sample Concentration	SARS-CoV-2	N1	N2	RNase P
Moderate Positive (3x LoD)	99.4% (179/180) 96.9–99.9	99.4% (179/180) 96.9–99.9	99.4% (179/180) 96.9–99.9	99.4% (180/180) 97.9–100
Low Positive (2x LoD)	100% (180/180) 97.9–100	100% (180/180) 97.9–100	100% (180/180) 97.9–100	100% (180/180) 97.9–100
True Negative[a]	99.4% (179/180) 96.9–99.9	99.4% (179/180) 96.9–99.9	99.4% (179/180) 96.9–99.9	99.4% (180/180) 97.9–100

[a] For the True Negative category, the reported agreement indicates percent of negative results.

Table 17: Instrument-to-Instrument Quantitative Reproducibility Study Results Using One Lot of the BD SARS-CoV-2 Reagents for BD MAX™ System.

Target	Level	N	Mean Ct	Between Lot		Between Day		Between Operator		Between Run		Within Run (Repeatability)		Total	
				SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
N1	MP	179	31.73	0.37	1.16	0.07	0.22	0.18	0.58	0.08	0.25	0.39	1.23	0.58	1.82
N1	LP	180	32.29	0.32	0.99	0.00	0.00	0.05	0.17	0.00	0.00	0.42	1.31	0.53	1.65
N2	MP	179	31.41	0.05	0.15	0.00	0.00	0.00	0.00	0.20	0.63	0.44	1.40	0.48	1.54
N2	LP	180	31.93	0.00	0.00	0.00	0.00	0.00	0.00	0.19	0.59	0.56	1.77	0.59	1.86
RNase P	MP	180	23.53	0.23	0.96	0.03	0.12	0.00	0.00	0.08	0.33	0.32	1.34	0.40	1.69
RNase P	LP	180	23.42	0.09	0.40	0.05	0.22	0.00	0.00	0.05	0.20	0.34	1.46	0.36	1.55
RNase P	TN	180	22.96	0.12	0.54	0.00	0.00	0.00	0.00	0.00	0.00	0.70	3.03	0.71	3.08

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.
4. Centers for Disease Control and Prevention. Interim guidelines for collecting, handling, and testing clinical specimens from persons for Coronavirus Disease 2019 (COVID-19).

Change History

Revision	Date	Change Summary
(04)	2021-03	Added limitation regarding performance in a vaccinated population. Made typographical and formatting updates.
(05)	2021-06	Added intended use, procedure, and data as needed to include testing from saliva and asymptomatic individuals. Updated Warnings and Precautions section. Updated storage information of swabs in UVT/UTM. Updated *in silico* comparison in the Reactivity/Inclusivity section and added post market clinical evaluation, precision, and reproducibility studies. Made typographical and formatting updates.
(06)	2022-03	Updated intended use. Updated name of catalog number 437519. Updated waste disposal statement. Added clarification for expected system behavior in regard to expired reagents. Updated open pouch stability information. Updated Figure 2. Added additional limitations. Removed limitation regarding Tobramycin. Added interfering substances. Updated *in silico* comparison in the Reactivity/Inclusivity section. Updated asymptomatic data. Updated symbols glossary. Made typographical and formatting updates.

SYMBOLS GLOSSARY [L006715(06) 2021-08]

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
EC REP	Authorized representative in the European Community
CH REP	Authorised representative in Switzerland
	Date of manufacture
	Use-by date
LOT	Batch code
REF	Catalogue number
SN	Serial number
STERILE	Sterile
STERILE A	Sterilized using aseptic processing techniques
STERILE EO	Sterilized using ethylene oxide
STERILE R	Sterilized using irradiation
STERILE	Sterilized using steam or dry heat
STERILIZE	Do not resterilize
NON STERILE	Non-sterile
	Do not use if package is damaged and consult *instructions for use*
STERILE	Sterile fluid path
STERILE EO	Sterile fluid path (ethylene oxide)
STERILE R	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* or consult electronic *instructions for use*
	Caution
LATEX	Contains or presence of natural rubber latex
IVD	In vitro diagnostic medical device
CONTROL –	Negative control
CONTROL +	Positive control
Σ	Contains sufficient for <*n*> tests
	For IVD performance evaluation only
	Non-pyrogenic

Symbol	Meaning
#	Patient number
	This way up
	Do not stack
	Single sterile barrier system
PHT DEHP BBP	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	CE marking; Signifies European technical conformity
	Device for near-patient testing
	Device for self-testing
Rx Only	This only applies to US: "Caution: Federal Law restricts this device to sale by or on the order of a licensed practitioner."
CC	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
H_2	Hydrogen gas is generated
	Perforation
	Start panel sequence number
	End panel sequence number
	Internal sequence number
MD	Medical device
	Contains hazardous substances
	Ukrainian conformity mark
FC	Meets FCC requirements per 21 CFR Part 15
c UL us	UL product certification for US and Canada
UDI	Unique device identifier

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