

Xpert[®] Xpress CoV-2 *plus*

REF XP3SARS-COV2-10

Instructions for Use

For Use Under Emergency Use Authorization (EUA) Only

For Use with GeneXpert[®] Xpress System (point of care system)

IVD



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See Section 28, Revision History for a description of changes.

Xpert[®] Xpress CoV-2 *plus*

For use under Emergency Use Authorization (EUA) only.



1 Proprietary Name

Xpert[®] Xpress CoV-2 *plus*

2 Common or Usual Name

Xpert Xpress CoV-2 *plus*

3 Intended Use

The Xpert Xpress CoV-2 *plus* test is a rapid, real-time RT-PCR test intended for the qualitative detection of nucleic acid from SARS-CoV-2 in nasopharyngeal swab, anterior nasal swab, mid-turbinate nasal swab, oropharyngeal swab or nasal wash/aspirate specimens from individuals suspected of COVID-19 by their healthcare provider, as well as anterior nasal swab specimens from any individual, including from individuals without symptoms or other reasons to suspect COVID-19.

Testing of nasopharyngeal swab, anterior nasal swab, mid-turbinate nasal swab, oropharyngeal swab or nasal wash/aspirate specimens using the Xpert Xpress CoV-2 *plus* test run on the GeneXpert Dx and GeneXpert Infinity systems and is limited to laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. § 263a, that meet requirements to perform high or moderate complexity tests.

Testing of nasopharyngeal swab, anterior nasal swab or mid-turbinate nasal swab specimens using the Xpert Xpress CoV-2 *plus* test run on the GeneXpert Xpress System (Tablet and Hub Configurations) is limited to laboratories certified under CLIA that meet requirements to perform high, moderate, or waived complexity tests. Testing of these specimens is authorized for use at the Point of Care (POC), i.e., in patient care settings operating under a CLIA Certificate of Waiver, Certificate of Compliance, or Certificate of Accreditation.

Results are for the detection of SARS-CoV-2 RNA. The SARS-CoV-2 RNA is generally detectable in upper respiratory specimens during the acute phase of infection.

Positive results are indicative of active infection with SARS-CoV-2; clinical correlation with patient history and other diagnostic information is necessary to determine patient infection status. Positive results do not rule out bacterial infection or co-infection with other viruses. The agent detected may not be the definite cause of disease.

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

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

Testing with the Xpert Xpress CoV-2 *plus* test is intended for use by trained operators who are proficient in performing tests using either GeneXpert Dx, GeneXpert Infinity, and/or GeneXpert Xpress systems. The Xpert Xpress CoV-2 *plus* test is only for use under the Food and Drug Administration's Emergency Use Authorization.

4 Summary and Explanation

An outbreak of respiratory illness of unknown etiology in Wuhan City, Hubei Province, China was initially reported to the World Health Organization (WHO) on December 31, 2019.¹ Chinese authorities identified a novel coronavirus (2019-nCoV), which has resulted in thousands of confirmed human infections that have spread globally, resulting in a pandemic of coronavirus disease 2019 (COVID-19). Cases of severe illness and some deaths have been reported. The International Committee on Taxonomy of Viruses (ICTV) renamed the virus SARS-CoV-2.² COVID-19 is associated with a variety of clinical outcomes, including asymptomatic infection, mild upper respiratory infection, severe lower respiratory disease including pneumonia and respiratory failure, and in some cases, death.

The Xpert Xpress CoV-2 plus is a molecular in vitro diagnostic test that aids in the detection and diagnosis of SARS-CoV-2 and is based on widely used nucleic acid amplification technology. The Xpert Xpress CoV-2 plus test contains primers and probes and internal controls used in RT-PCR for the in vitro qualitative detection of SARS-CoV-2 RNA in nasopharyngeal swab, anterior nasal swab, mid-turbinate nasal swab specimens.

The term “qualified laboratories” refers to laboratories in which all users, analysts, and any person reporting results from use of this device are proficient in performing real-time RT-PCR assays.

5 Principle of the Procedure

The Xpert Xpress CoV-2 plus test is an automated in vitro diagnostic test for qualitative detection of nucleic acid from SARS-CoV-2. The Xpert Xpress CoV-2 plus test is performed on GeneXpert Xpress Systems. The primers and probes in the Xpert Xpress CoV-2 plus test are designed to amplify and detect unique sequences in the nucleocapsid (N), envelope (E) and RNA-dependent RNA polymerase (RdRP) genes of the SARS-CoV-2 virus genome.

The GeneXpert Xpress Systems automate and integrate sample preparation, nucleic acid extraction and amplification, and detection of the target sequences in simple or complex samples using real-time PCR assays. The systems consist of an instrument, computer, and preloaded software for running tests and viewing the results. The systems require the use of single-use disposable cartridges that hold the RT-PCR reagents and host the RT-PCR process. Because the cartridges are self-contained, cross-contamination between samples is minimized. For a full description of the systems, see the *GeneXpert Dx System Operator Manual* or the *GeneXpert Infinity System Operator Manual*.

The Xpert Xpress CoV-2 plus test includes reagents for the detection of RNA from SARS-CoV-2 in nasopharyngeal swab anterior nasal swabs, mid-turbinate nasal swabs. A Sample Processing Control (SPC) and a Probe Check Control (PCC) are also included in the cartridge utilized by the GeneXpert Xpress System. The SPC is present to control for adequate processing of the sample and to monitor for the presence of potential inhibitor(s) in the RT-PCR reaction. The SPC also ensures that the RT-PCR reaction conditions (temperature and time) are appropriate for the amplification reaction and that the RT-PCR reagents are functional. The PCC verifies reagent rehydration, PCR tube filling, and confirms that all reaction components are present in the cartridge including monitoring for probe integrity and dye stability.

The specimen is collected and placed into a viral transport tube containing 3 mL viral transport medium, 3 mL saline or 2 mL eNAT™. The specimen is briefly mixed by rapidly inverting the collection tube 5 times. Using the supplied transfer pipette, the sample is transferred to the sample chamber of the Xpert Xpress CoV-2 plus cartridge. The GeneXpert cartridge is loaded onto the GeneXpert Xpress System, which performs hands-off, automated sample processing, and real-time RT-PCR for detection of viral RNA.

6 Materials Provided

The Xpert Xpress CoV-2 plus kit contains sufficient reagents to process 10 specimens or quality control samples. The kit contains the following:

Xpert Xpress CoV-2 plus Cartridges with Integrated Reaction Tubes	10
Bead 1, Bead 2, and Bead 3 (freeze-dried)	1 of each per cartridge
Lysis Reagent (Guanidinium Thiocyanate)	1.0 mL per cartridge
Binding Reagent	1.0 mL per cartridge
Elution Reagent	2.0 mL per cartridge
Wash Reagent	0.5 mL per cartridge

Disposable Transfer Pipettes 10–12 per kit

Flyer 1 per kit

- Instructions to locate (and import) the ADF and documentation such as the Product Insert on www.cepheid.com.

Quick Reference Instructions 2 per kit

For use with the GeneXpert Xpress System (Tablet and Hub Configuration)

Note Safety Data Sheets (SDS) are available at www.cepheid.com or www.cepheidinternational.com under the **SUPPORT** tab.

Note The bovine serum albumin (BSA) in the beads within this product was produced and manufactured exclusively from bovine plasma sourced in the United States. No ruminant protein or other animal protein was fed to the animals; the animals passed ante- and post-mortem testing. During processing, there was no mixing of the material with other animal materials.

7 Storage and Handling

- Store the Xpert Xpress CoV-2 *plus* test cartridges at 2–28 °C.
- Do not open the cartridge lid until you are ready to perform testing.
- Do not use a cartridge that is wet or has leaked.

8 Materials Required but not Provided

- GeneXpert Xpress System (Tablet configuration): GeneXpert Xpress II and IV instruments with proprietary GeneXpert Xpress Software Version 5.0 and 5.1, tablet computer device with touchscreen, barcode scanner, external CD drive, wireless printer, Getting Started Guide, and *GeneXpert Xpress System User's Guide*
- GeneXpert Xpress System (Hub configuration): GeneXpert Xpress IV instrument, GeneXpert Hub with proprietary GeneXpert Xpress Software Version 6.1 or higher, GeneXpert Hub with integrated computer, touchscreen monitor and barcode scanner, external CD drive, Getting Started Guide, and *GeneXpert Xpress System User's Guide*

9 Materials Available but not Provided

ZeptoMetrix® External Controls

- SARS-Related Coronavirus 2 (SARS-CoV-2) Positive Control, Catalog# NATSARS(COV2)-ERC
- SARS Associated Coronavirus 2 (SARS-CoV-2) Negative Control, Catalog# NATSARS(COV2)-NEG

eNAT Molecular Collection and Preservation Medium from Copan Italia S.p.A (Brescia, IT)

- eNAT Molecular Collection and Preservation Medium, Copan Catalog # 6U073S01
- eNAT Molecular Collection and Preservation Medium, Copan Catalog # 6U074S01

10 Warnings and Precautions

10.1 General

- For *in vitro* diagnostic use.
- For use under emergency use authorization only.
- For prescription use only
- This product has not been FDA cleared or approved but has been authorized by FDA under an EUA for use by authorized laboratories.

- This product has been authorized only for the detection of nucleic acid from SARS-CoV-2, not for any other virus 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 presence of SARS-CoV-2-RNA.
- Laboratories within the United States and its territories are required to report all results to the appropriate public health authorities.
- Performance characteristics of this test have been established with the specimen types listed in the Intended Use Section only. The performance of this assay with other specimen types or samples has not been evaluated.
- Treat all biological specimens, including used cartridges, as if capable of transmitting infectious agents. Because it is often impossible to know which might be infectious, all biological specimens should be treated using standard precautions. Guidelines for specimen handling are available from the U.S. Centers for Disease Control and Prevention³ and the Clinical and Laboratory Standards Institute.⁴
- Follow safety procedures set by your institution for working with chemicals and handling biological specimens.
- Refer to Copan eNAT® Package Insert for safety and handling information.
- Avoid direct contact between guanidine thiocyanate and sodium hypochlorite (bleach) or other highly reactive reagents such as acids and bases. These mixtures could release noxious gas.
- Consult your institution's environmental waste personnel on proper disposal of used cartridges, which may contain amplified material. This material may exhibit characteristics of federal EPA Resource Conservation and Recovery Act (RCRA) hazardous waste requiring specific disposal requirements. Check state and local regulations as they may differ from federal disposal regulations. Institutions should check the hazardous waste disposal requirements within their respective countries.
- Testing of nasopharyngeal swab, anterior nasal swab, nasal wash/aspirate, mid-turbinate nasal swab or oropharyngeal swab specimens using the Xpert Xpress CoV-2 plus test run on the GeneXpert Dx and GeneXpert Infinity systems, is limited to laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. § 263a, that meet requirements to perform high or moderate complexity tests.
- Testing of nasopharyngeal swab, mid-turbinate nasal swab or anterior nasal swab specimens using the Xpert Xpress CoV-2 plus test run on the GeneXpert Xpress System (Tablet and Hub Configurations), is authorized for use at the Point of Care (POC), i.e., in patient care settings operating under a CLIA Certificate of Waiver, Certificate of Compliance, or Certificate of Accreditation.

10.2 Specimens

Maintain proper storage conditions during specimen transport to ensure the integrity of the specimen (see Section 12, Specimen Collection, Transport, and Storage). Specimen stability under shipping conditions other than those recommended has not been evaluated.

10.3 Assay/Reagent

- Do not open the Xpert Xpress CoV-2 plus cartridge lid except when adding specimen.
- Do not use a cartridge that has been dropped after removing it from the packaging.
- Do not shake the cartridge. Shaking or dropping the cartridge after opening the cartridge lid may yield non-determinate results.
- Do not place the sample ID label on the cartridge lid or on the barcode label on the cartridge.
- Do not use a cartridge with a damaged barcode label.
- Do not use a cartridge that has a damaged reaction tube.
- Do not use reagents beyond their expiry date.
- Each single-use Xpert Xpress CoV-2 plus cartridge is used to process one test. Do not reuse processed cartridges.
- Each single-use disposable pipette is used to transfer one specimen. Do not reuse disposable pipettes.
- Do not use a cartridge if it appears wet or if the lid seal appears to have been broken.
- Wear clean lab coats and gloves. Change gloves between the handling of each specimen.
- In the event of a spill of specimens or controls, wear gloves and absorb the spill with paper towels. Then, thoroughly clean the contaminated area with a 10% freshly prepared household chlorine bleach. Allow a minimum of two minutes of contact time. Ensure the work area is dry before using 70% denatured ethanol to remove bleach residue. Allow

surface to dry completely before proceeding. Or, follow your institution's standard procedures for a contamination or spill event. For equipment, follow the manufacturer's recommendations for decontamination of equipment.

- Biological specimens, transfer devices, and used cartridges should be considered capable of transmitting infectious agents requiring standard precautions. Follow your institution's environmental waste procedures for proper disposal of used cartridges and unused reagents. These materials may exhibit characteristics of chemical hazardous waste requiring specific disposal. If country or regional regulations do not provide clear direction on proper disposal, biological specimens and used cartridges should be disposed per WHO [World Health Organization] medical waste handling and disposal guidelines.

11 Chemical Hazards^{5,6}

- Signal Word: WARNING
- UN GHS Hazard Statements
 - Harmful if swallowed.
 - May be harmful in contact with skin.
 - Causes eye irritation.
- UN GHS Precautionary Statements
 - Prevention
 - Wash hands thoroughly after handling.
 - Response
 - Call a POISON CENTER or doctor/physician if you feel unwell.
 - If skin irritation occurs: Get medical advice/attention.
 - IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
 - If eye irritation persists: Get medical advice/attention.

12 Specimen Collection, Transport, and Storage

Proper specimen collection, storage, and transport are critical to the performance of this test. Inadequate specimen collection, improper specimen handling and/or transport may yield a false result. See Section 12.1 for nasopharyngeal swab collection procedure, Section 12.2 for anterior nasal swab collection procedure, and Section 12.3 for mid-turbinate nasal swab collection procedure.

Nasopharyngeal swab, anterior nasal swab, and mid-turbinate nasal swab specimens can be stored at room temperature (15–30 °C) for up to 48 hours in viral transport medium, saline or eNAT medium until testing is performed on the GeneXpert Xpress Systems. Alternatively, nasopharyngeal swab, and anterior nasal swab, and mid-nasal turbinate swab specimens can be stored refrigerated (2–8 °C) up to seven days in viral transport medium, saline or eNAT medium until testing is performed on the GeneXpert Xpress Systems.

12.1 Nasopharyngeal Swab Collection Procedure

1. Insert the swab into either nostril, passing it into the posterior nasopharynx (see Figure 1).



Figure 1. Nasopharyngeal Swab Collection

2. Rotate swab by firmly brushing against the nasopharynx several times.
3. Remove and place the swab into the tube containing 3 mL of viral transport medium, 3 mL saline or 2 mL eNAT.
4. Break swab at the indicated break line and cap the specimen collection tube tightly.

12.2 Anterior Nasal Swab Collection Procedure

1. Insert a nasal swab 1 to 1.5 cm into a nostril. Rotate the swab against the inside of the nostril for 3 seconds while applying pressure with a finger to the outside of the nostril (see Figure 2).



Figure 2. Anterior Nasal Swab Collection for First Nostril

2. Repeat on the other nostril with the same swab, using external pressure on the outside of the other nostril (see Figure 3). To avoid specimen contamination, do not touch the swab tip to anything other than the inside of the nostril.

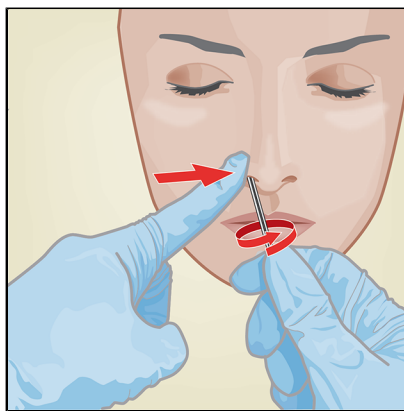


Figure 3. Anterior Nasal Swab Collection for Second Nostril

3. Remove and place the swab into the tube containing 3 mL of viral transport medium, 3 mL saline or 2mL eNAT. Break swab at the indicated break line and cap the specimen collection tube tightly.

12.3 Mid-Turbinate Nasal Swab Collection Procedure

1. Insert the mid-turbinate nasal swab into either nostril, passing it into the mid-turbinate area (see Figure 4).

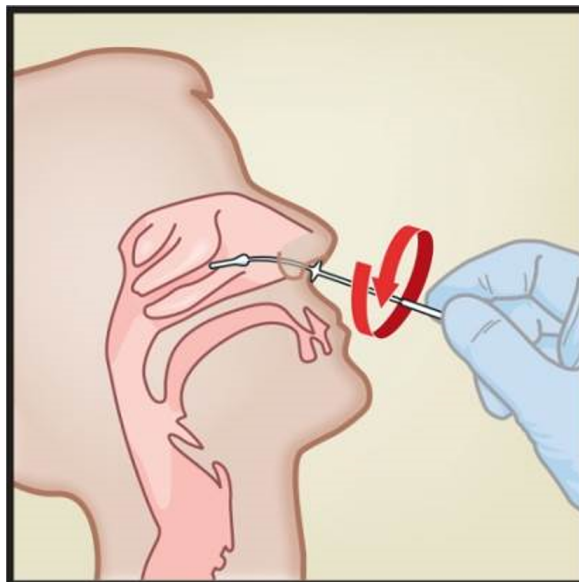


Figure 4. Mid-Turbinate Nasal Swab Specimen Collection

2. Rotate swab by firmly brushing against the mid-turbinate area several times.
3. Remove and place the swab into the tube containing 3 mL of viral transport medium, 3 mL saline or 2mL eNAT.
4. Break swab at the indicated break line and cap the specimen collection tube tightly.

13 Starting the System

The recommended environmental operating conditions for Xpert Xpress CoV-2 plus test are 15–30°C (59–86 °F), 20–80% relative humidity, noncondensing.

1. Put on a clean pair of gloves.
2. Determine which system configuration you have (Figure 5).

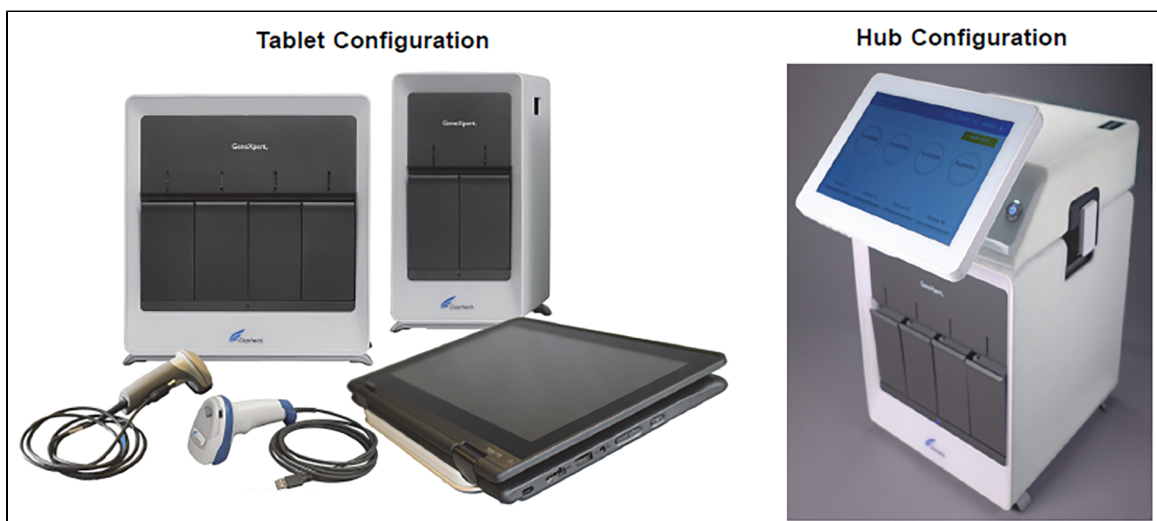


Figure 5. Tablet and Hub System Configurations

- For the *Tablet* configuration, see Section 13.1, Starting the Tablet Configuration.
- For the *Hub* configuration, see Section 13.2, Starting the Hub Configuration.

13.1 Starting the Tablet Configuration

1. Turn on the GeneXpert Xpress instrument (GeneXpert Xpress II or GeneXpert Xpress IV).
2. Turn on the tablet computer:
 - *Windows*® 7: The **Windows 7 account** screen appears. Touch the **Cepheid-Admin** icon to continue.
 - *Windows*® 10: The **Windows Lock** screen appears. Swipe up to continue. The **Windows Password** screen appears.
3. Touch **Password** to display the **keyboard**, then type your password.
4. Touch the **arrow** button at the right of the password entry area. The GeneXpert Xpress Software starts.

13.2 Starting the Hub Configuration

1. Turn on the GeneXpert Xpress IV instrument (in two or four modules configuration).
2. Turn on the Hub computer. The **Windows Lock** screen appears.
3. Swipe up to continue. The **Windows Password** screen appears.
4. Touch **Password** to display the **keyboard**, then type your Windows password.
5. Touch the **arrow** button at the right of the password entry area. The GeneXpert Xpress Software starts, and a **login** screen appears.
6. If enabled, you may log in by scanning a barcode on your institutional ID, using the barcode scanner (located behind the right side of the touchscreen). Then proceed to Step 9. Otherwise, follow the steps below to login manually.
7. Enter your User Name and Password (the virtual keyboard appears once you touch the entry fields).
8. Touch the **X** in the upper right of the virtual keyboard. The keyboard disappears, and the **LOGIN** button appears at the bottom of the screen. Touch the **LOGIN** button to continue.
9. The **Database Maintenance Reminder** screen and the **Archive Tests Reminder** dialog boxes may appear, depending on your system configuration. For more information, see the *GeneXpert Xpress System User's Guide*.

13.3 Determining Your Software Version

When your Xpress opening screen appears, you can determine your software version and the procedure to follow based on one of the following two screens (see Figure 6).



Figure 6. Xpress Opening Screens and Software Versions

- For Software Version 5.0 or Software Version 5.1, see Section 14.
- For Software Version 6.1 or higher, see Section 16.

14 GeneXpert Xpress Software Version 5.0 or Software Version 5.1

1. On the **Welcome** screen, touch the **TOUCH HERE TO BEGIN** button (see Figure 7).

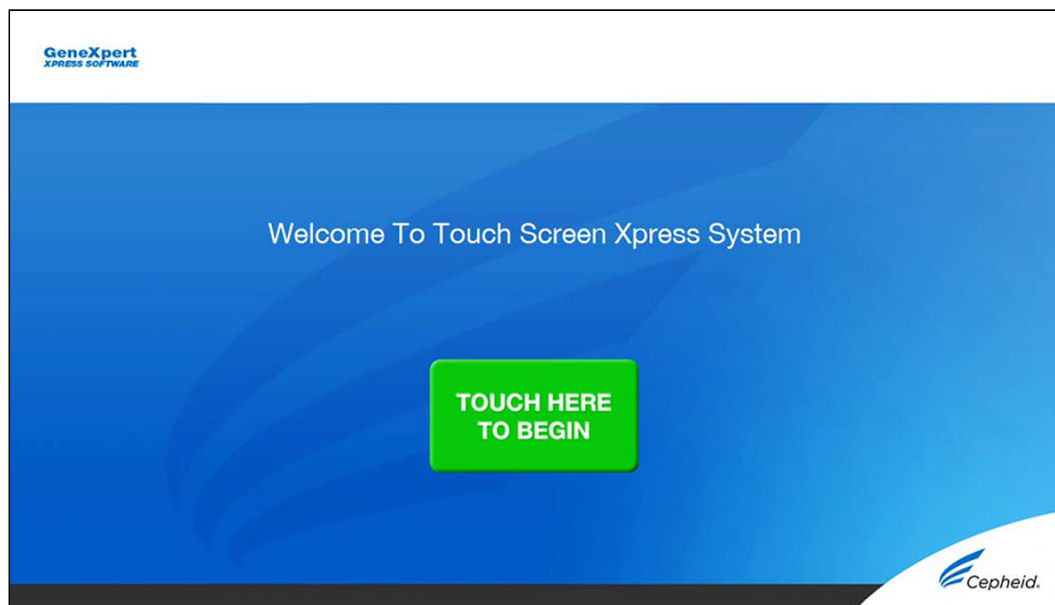


Figure 7. Welcome Screen

2. The **VIEW PREVIOUS TESTS** button appears. The **RUN NEW TEST** button will appear on the **Home** screen within 3 minutes.

Note If the **Home** screen does not display **RUN NEW TEST**, the instrument was not powered up or is no longer powered on. Exit the software using the **EXIT** button. The GeneXpert Xpress instrument must first be turned on then turn on the computer. Click on **software icon** to launch software and enter password.

14.1 Starting a Test

Note

Instructions showing how to prepare the sample and the cartridge are shown on-screen in a video and are also described in the *Quick Reference Instructions (QRI)*.

Important Start the test within 30 minutes of adding the sample to the cartridge.

1. Put on a new pair of gloves if performing a new test. Touch the **RUN NEW TEST** button on the **Home** screen (see Figure 8) to run a patient specimen or an external control.

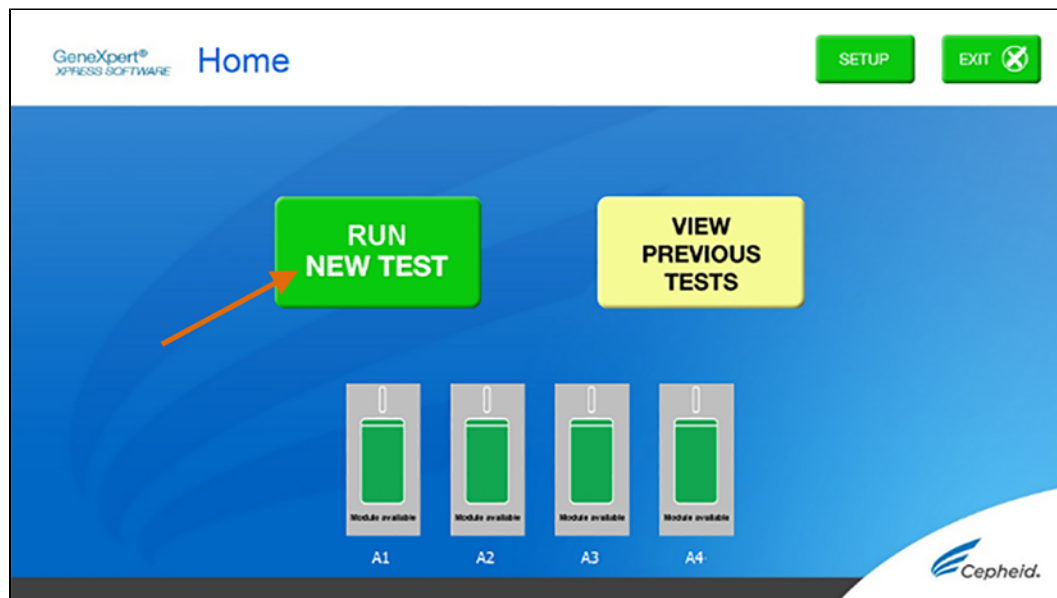


Figure 8. RUN NEW TEST button on Home Screen (GeneXpert Xpress IV screen shown)

2. Check that the specimen transport medium tube cap is closed.
3. If there is a Patient/Sample ID barcode, touch the **YES** button, then scan the Patient/Sample ID with the scanner. If there is no Patient/Sample ID barcode, touch the **NO** button, then manually enter the Patient/Sample ID and touch the **OK** button. For external control, type **Positive Control** or **Negative Control**.
4. Confirm the Patient/Sample ID. Touch **YES** if the Patient/Sample ID is correct.

14.2 Preparing the Specimen or External Control and Cartridge

It is recommended that external controls be tested following the manufacturer's instruction at the frequency noted below.

- Each time a new lot of Xpert Xpress CoV-2 plus kits is received.
 - Each time a new shipment of Xpert Xpress CoV-2 plus kits is received even if it is the same lot previously received.
 - Each time a new operator is performing the test (i.e., operator who has not performed the test recently).
 - When problems (storage, operator, instrument, or other) are suspected or identified.
 - If otherwise required by your institution's standard Quality Control (QC) procedures.
1. Remove a cartridge and a transfer pipette from the cartridge kit box.
 2. Scan the barcode on the cartridge with the scanner.

Note

If the barcode on the Xpert Xpress CoV-2 plus cartridge does not scan or scanning the barcode results in an error message stating the cartridge is expired, then repeat the test with a new cartridge. If you have scanned the cartridge barcode in the Xpress software and the assay definition file is not available, a screen will appear indicating the assay definition file is not loaded on the system. If this screen appears, contact Cepheid Technical Support.

3. Make the appropriate selection from the Select Assay menu, as shown in Figure 9.
 - Select **Xpert Xpress CoV-2 plus**.

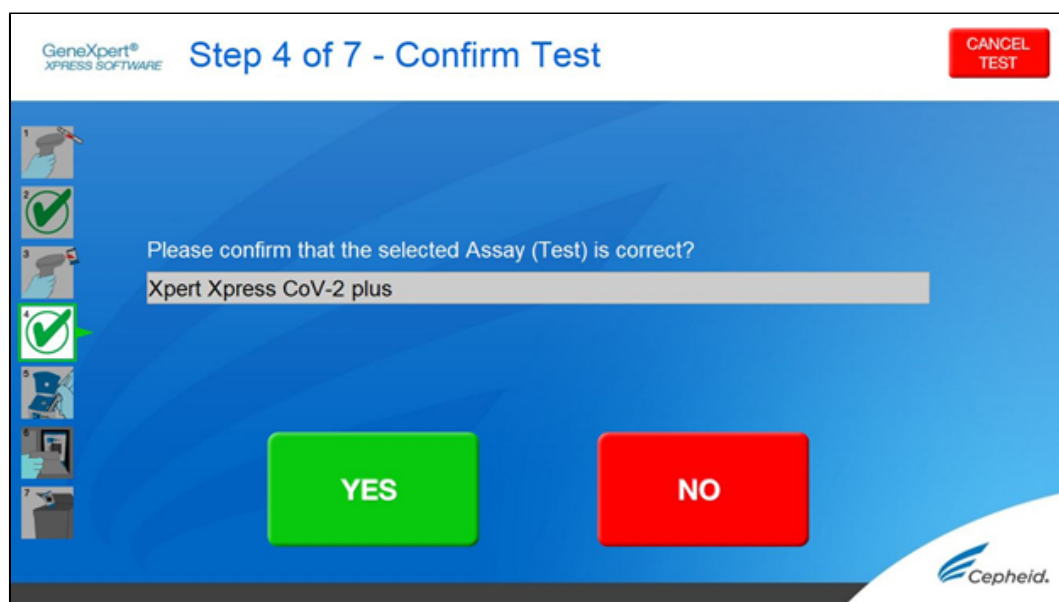


Figure 9. ConfirmTest Screen - Select Assay

4. Confirm the selected test from the **Select Assay** menu (shown in Figure 10 below) and touch **YES** if the displayed information is correct. Enter your user name and password if prompted.

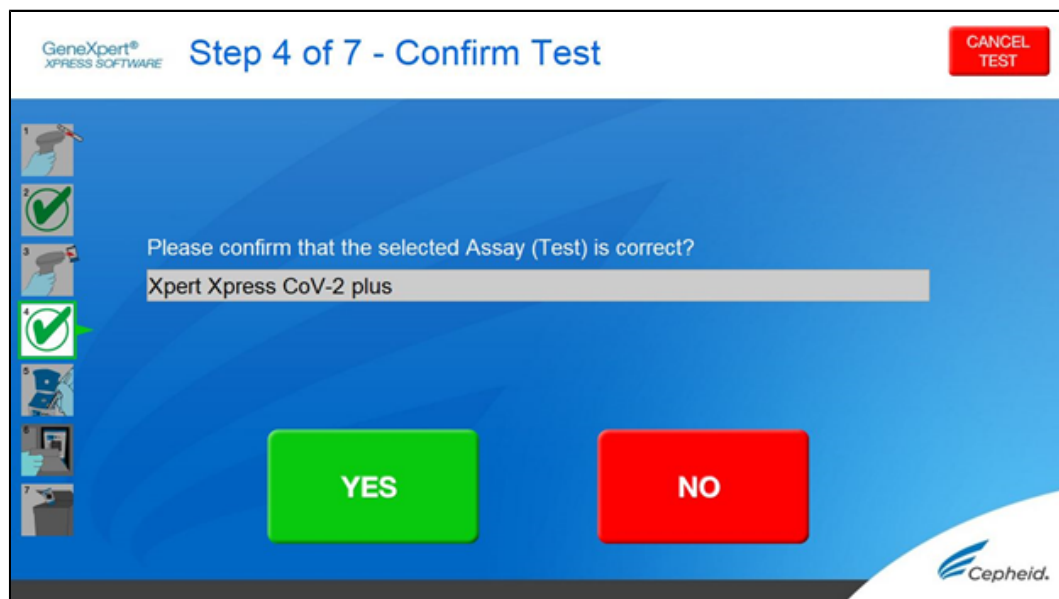


Figure 10. Confirm Test Screen

In the following steps, keep the cartridges upright when handling or scanning. Do not rotate or tip the cartridge, because damage to the contents or injury to personnel may occur.

5. Watch the video before continuing. The video will repeat. Touch the **SKIP VIDEO AND CONTINUE** button to exit video. The Load Cartridge screen appears.
6. Mix sample by rapidly inverting the specimen transport tube or external control tube 5 times. Open cap on the specimen transport tube or external control tube.
7. Open the cartridge lid by lifting the front of the cartridge lid.
8. Remove the transfer pipette from the wrapper.

Note Do not place unwrapped pipette on the workbench.

- Squeeze the top bulb of the transfer pipette completely until the top bulb is fully flat. While continuing to hold the bulb fully flat, place the pipette tip in the specimen transport tube. (see Figure 11).

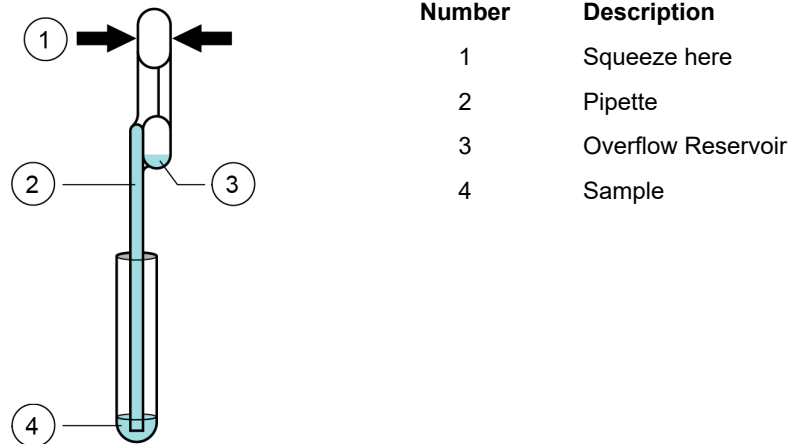


Figure 11. Transfer Pipette

- Keeping the pipette below the surface of the liquid, release the top bulb of the pipette slowly to fill the pipette with sample before removing from the tube. It is okay if liquid goes into the overflow reservoir (see Figure 10). Check that the pipette does not contain bubbles.
- To transfer the sample to the cartridge, squeeze the top bulb of the pipette completely again until it is fully flat to empty the contents of the pipette (300 µL) into the large opening (Sample Chamber) in the cartridge shown in Figure 12. Some liquid may remain in the overflow reservoir. Dispose of the used pipette.



Figure 12. Xpert Xpress CoV-2 plus Cartridge (Top View)

Note Take care to dispense the entire volume of liquid into the Sample Chamber. False negative results may occur if insufficient sample is added to the cartridge.

- Close the cartridge lid

14.3 Loading the Cartridge

1. Pull open the module door with the flashing green light.
2. Load the cartridge with the barcode facing the operator onto the cartridge bay platform. Do not try to insert the cartridge past the cartridge bay platform.
3. Close the door until it clicks.
The green light will stop flashing, and the test starts. The **Test in Progress** screen appears. When the test is completed (green light goes out), the door will automatically unlock and the **Remove Cartridge** screen appears.
4. Follow the on-screen instructions to remove the cartridge and to reset the module for a new test.
5. Touch **CONTINUE** to view the result of the test.
6. To print results, touch the **PRINT RESULT** button.
7. Remove cartridge. Dispose of the used cartridge and gloves according to your institution's standard practices.
8. To log out, touch the **SIGN OUT** button.

Note Do not turn off or unplug the instruments while a test is in progress. Turning off or unplugging the GeneXpert Xpress instrument or computer will stop the test.

Note If the barcode on the Xpert Xpress CoV-2 plus cartridge does not scan or scanning the barcode results in an error message stating that the cartridge is expired, then repeat the test with a new cartridge.

Note If you have scanned the cartridge barcode in the Xpress software and the assay definition file is not available, a screen will appear indicating that the assay definition file is not loaded or that the product code was not found on the system. If this screen appears, contact Cepheid Technical Support.

14.4 Starting a New Test While a Test is Running

1. Put on a clean pair of gloves if performing a new test.
2. Touch the **HOME** button to go to the **Home** Screen.
3. Touch the **SIGN OUT** button to log out the previous user, if applicable.
4. Start a new test following the steps in Section 14.1, Starting a Test.

15 View Status of Tests in Progress, Completed Tests, and View Results of Past Tests

15.1 Tests in Progress

1. Touch the **HOME** button to view the status of tests in progress.
2. To view a test in progress, touch the **Test in progress touch for status** button.
The time remaining to complete the testing will appear on the progress bar at the bottom of the **Test in Progress** screen.

15.2 Completed Tests

1. When a test is completed, touch the **Test complete, touch to continue** button.
The **Remove Cartridge** screen appears.
2. Follow the on-screen instructions to remove the cartridge. Touch the **CONTINUE** button to view the result of the test. To print results, touch the **PRINT RESULT** button.

15.3 Results of Past Tests

1. Touch the **VIEW PREVIOUS TESTS** button on the **Home** screen shown in Figure 13.

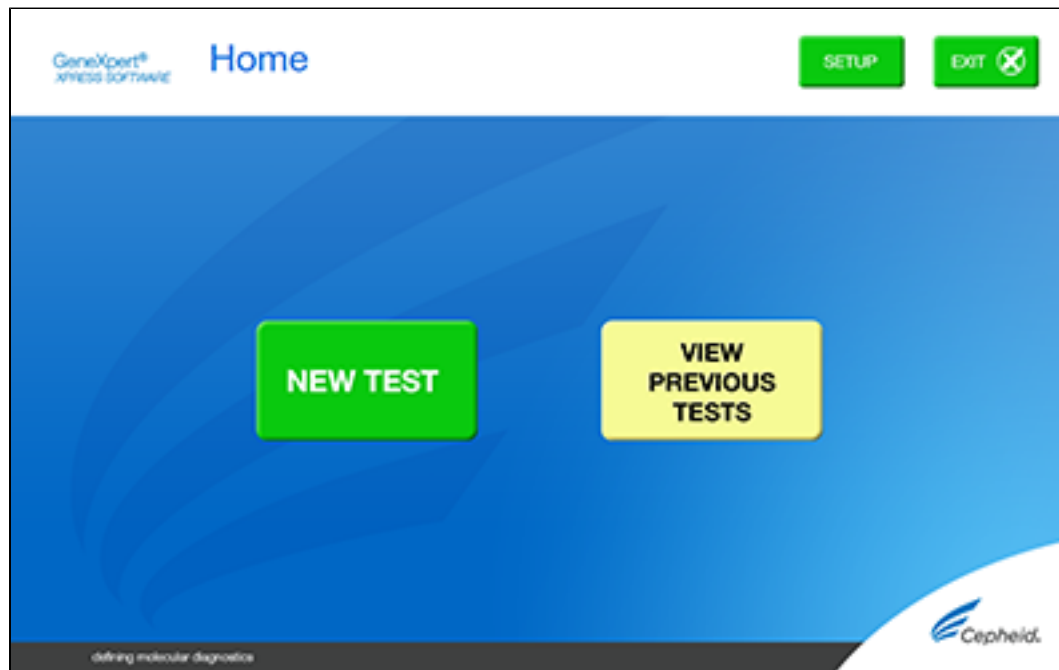


Figure 13. VIEW PREVIOUS TESTS button on Home Screen

2. Select the test by either touching the test name or using the **arrows** to select the test.
3. Touch the **SELECT** button shown in Figure 14 to view results.

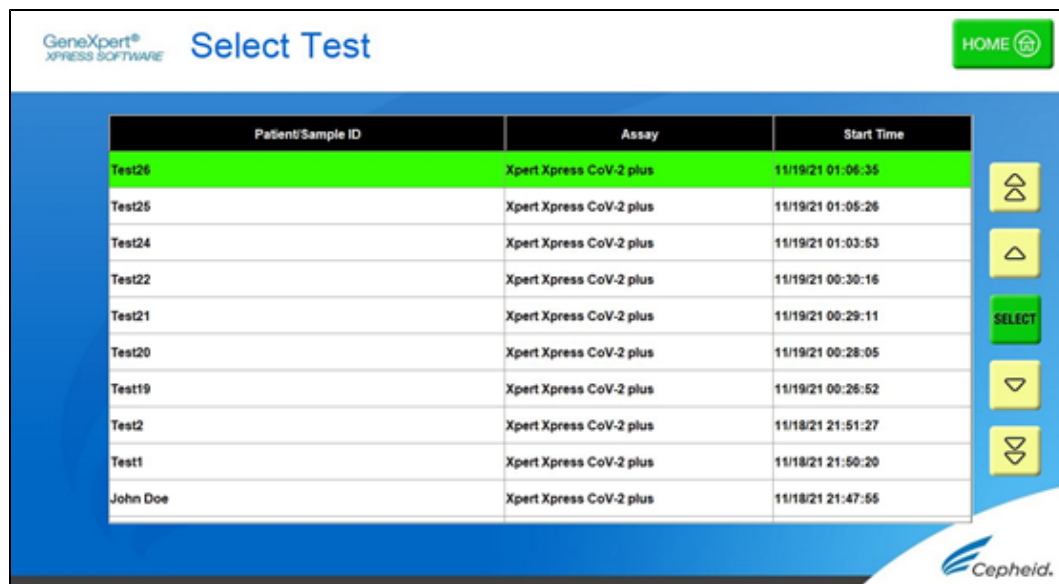


Figure 14. SELECT button

4. To print results, touch the **PRINT RESULT** button.

16 GeneXpert Xpress Software Version 6.1 or Higher

16.1 Starting a Test

Note Instructions showing how to prepare the sample and the cartridge are shown on-screen in videos and in the following procedure.

Important Start the test within 30 minutes of adding the sample to the cartridge.

1. Put on a new pair of gloves if performing a new test.
2. Touch the **NEW TEST** button on the **Home** screen (see Figure 15).

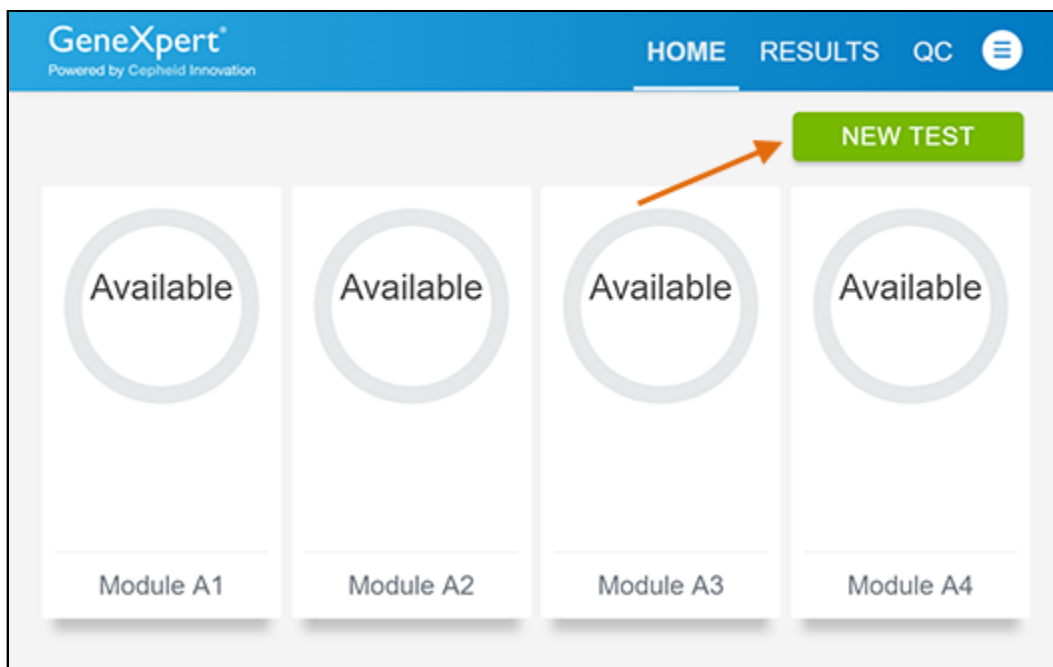


Figure 15. Home Screen

3. Check that the specimen transport medium tube cap is closed.
If Patient Information is configured by an administrator, then the **Patient Information** screen appears (see Figure 16).
If Patient Information is not configured, the **Sample ID** screen appears.
4. Skip to Section 16.2 if the **Sample ID** screen appears.

Patient Information

Enter a Patient ID by scanning the Patient ID barcode or tapping in the field below to type it in.

Patient ID

CLEAR CONTINUE

Figure 16. Patient Information Screen

5. Scan patient ID barcode or manually enter the Patient ID.
6. Touch **CONTINUE**. The Confirm **Patient Information** screen appears.
7. Verify the Patient ID and touch **CONFIRM**. The **Sample ID** screen appears.

16.2 Preparing the Specimen

1. Remove a cartridge and a transfer pipette from the cartridge kit box.
2. Check that the transport medium tube cap is closed. Scan Sample ID barcode or manually enter the Sample ID for patient specimen.
3. Touch **CONTINUE**. The Confirm Sample ID screen appears.
4. Verify the Sample ID and touch **CONFIRM**. The Scan Cartridge Barcode screen appears (see Figure 17).
In the following steps, keep the cartridges upright when handling or scanning. Do not rotate or tip the cartridge, because damage to the contents or injury to personnel may occur.

Note

If the barcode on the Xpert Xpress CoV-2 plus cartridge does not scan or scanning the barcode results in an error message stating that the cartridge is expired, then repeat the test with a new cartridge. If you have scanned the cartridge barcode in the Xpress software and the assay definition file is not available, a screen will appear indicating the assay definition file is not loaded on the system. If this screen appears, contact Cepheid Technical Support.

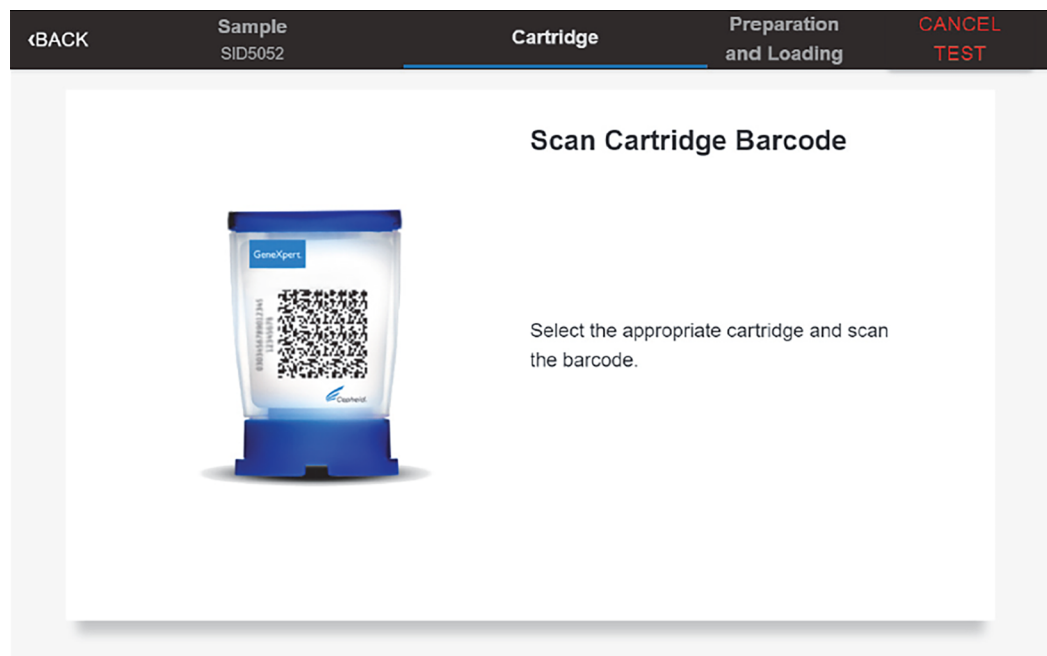


Figure 17. Scan Cartridge Barcode Screen

Select the appropriate cartridge with the sample and scan the cartridge barcode.

5. Verify that the correct cartridge has been scanned and that the assay name matches the name of the assay on the cartridge (see Figure 18).

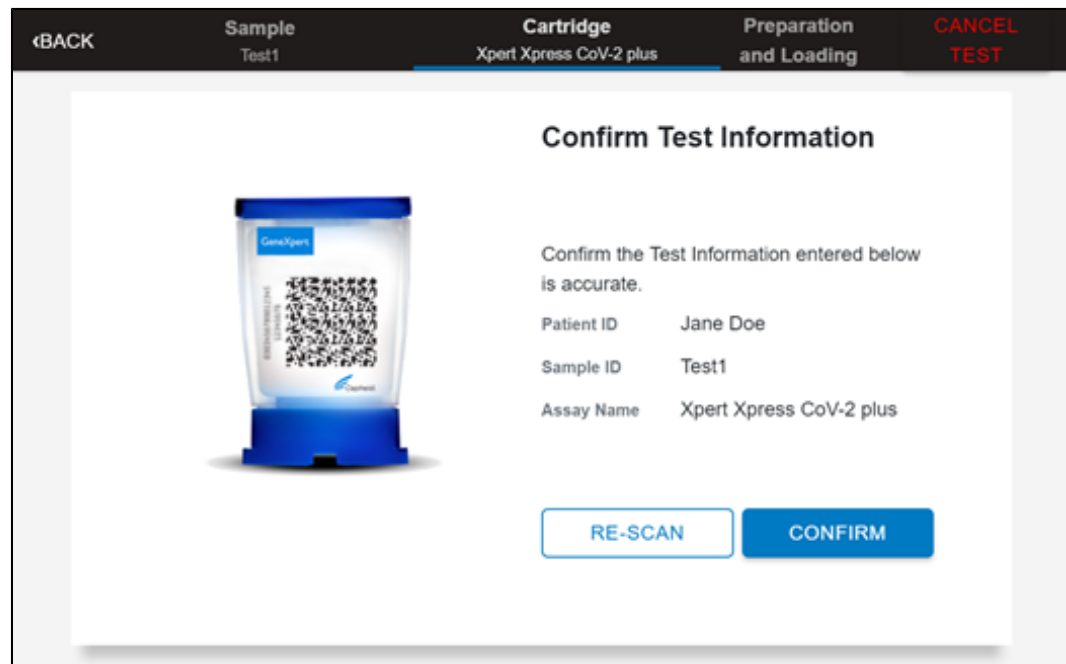


Figure 18. Confirm Test Information Screen

6. Touch **CONFIRM** if the displayed information is correct.
7. Depending on your configuration, the Enter Credentials to Continue screen may appear (see Figure 19). If enabled, you may log in by scanning your institutional ID. Otherwise, manually enter your User Name and Password and touch **LOGIN** to continue.

Enter Credentials to Continue

User Name

Password

LOGIN

[Scan Your ID Card](#)

Figure 19. Enter Credentials to Continue Screen

8. The Cartridge Preparation screen appears (see Figure 20).



Figure 20. Cartridge Preparation Screen

9. Watch the video before continuing. The video will repeat. Touch the **SKIP VIDEO AND CONTINUE** button to exit video.
10. Mix specimen by rapidly inverting the specimen transport tube 5 times. Open the lid on the specimen transport tube.
11. Open the cartridge lid by lifting the front of the cartridge lid.
12. Remove the transfer pipette from the wrapper.

Note Do not place unwrapped pipette on the workbench.

13. Squeeze the top bulb of the transfer pipette **completely until the top bulb is fully flat**. While continuing to hold the bulb fully flat, place the pipette tip in the specimen transport tube (see Figure 21).

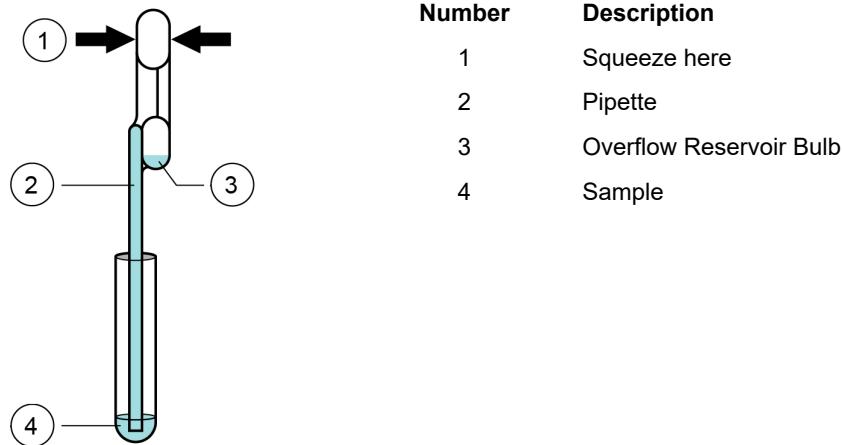


Figure 21. Transfer Pipette

14. Keeping the pipette below the surface of the liquid, release the top bulb of the pipette slowly to fill the pipette with sample before removing from the tube. It is okay if liquid goes into the overflow reservoir (see Figure 21). Check that the pipette does not contain bubbles.
15. To transfer the sample to the cartridge, squeeze the top bulb of the pipette completely again until it is fully flat to empty the contents of the pipette (300 μ L) into the large opening (Sample Chamber) of the cartridge shown in Figure 22. Some liquid may remain in the overflow reservoir. Dispose of the used pipette.

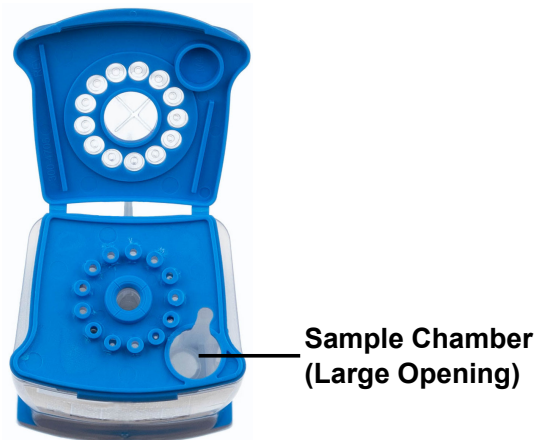


Figure 22. Xpert Xpress CoV-2 plus Cartridge (Top View)

Note Take care to dispense the entire volume of liquid into the Sample Chamber. False negative results may occur if insufficient sample is added to the cartridge.

16. Close the cartridge lid.
17. Go to Section 16.4, Loading the Cartridge.

16.3 Running External Controls

It is recommended that external controls be tested following the manufacturer's instruction at the frequency noted below.

- Each time a new lot of Xpert Xpress CoV-2 plus kits is received.
- Each time a new shipment of Xpert Xpress CoV-2 plus kits is received even if it is the same lot previously received.
- Each time a new operator is performing the test (i.e., operator who has not performed the test recently)
- When problems (storage, operator, instrument, or other) are suspected or identified

- If otherwise required by your institution’s standard Quality Control (QC) procedures
1. Put on a new pair of gloves if performing a new test. Touch the **QC** button on the Home screen (see Figure 23).

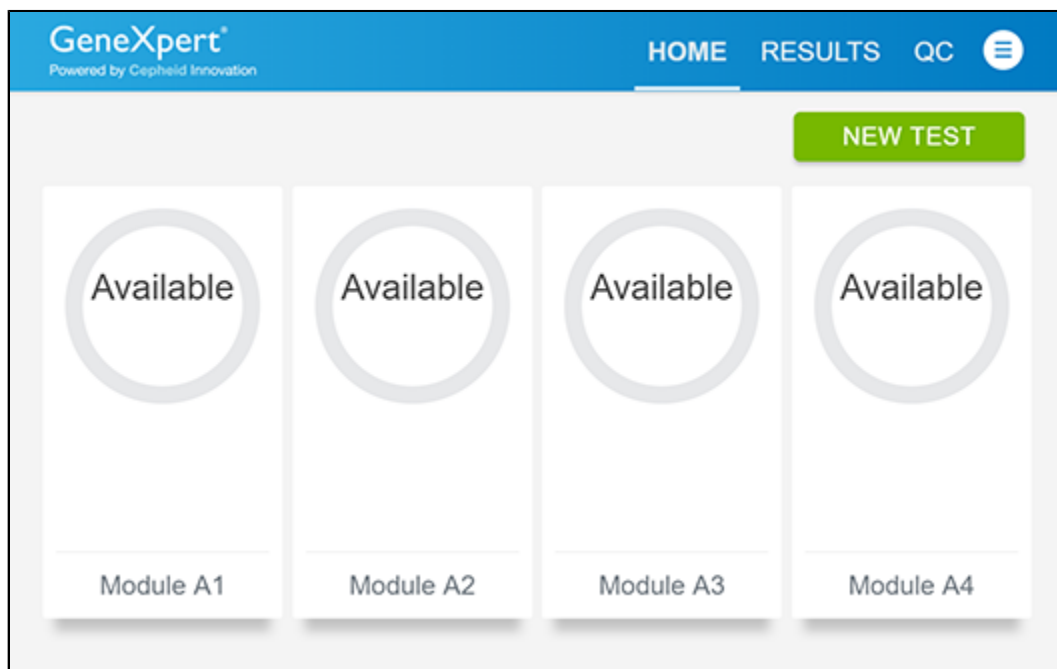


Figure 23. Home Screen

2. The Quality Control screen appears. Touch RUN QC POSITIVE Test, RUN QC NEGATIVE TEST or RUN PROFICIENCY TEST option (Figure 24).



Figure 24. Quality Control Screen

3. The Sample ID appears.
4. Enter the Sample ID, by typing Positive Control or Negative Control or scan the Sample ID barcode.
5. Touch CONTINUE. The Confirm Sample ID screen appears.
6. Verify the Sample ID and touch CONFIRM. The Scan Cartridge Barcode screen appears (see Figure 25).

Note In the following steps, keep the cartridges upright when handling or scanning. Do not rotate or tip the cartridge, because damage to the contents or injury to personnel may occur.

Note If the barcode on the Xpert Xpress CoV-2 plus cartridge does not scan or scanning the barcode results in an error message stating that the cartridge is expired, then repeat the test with a new cartridge. If you have scanned the cartridge barcode in the Xpress software and the assay definition file is not available, a screen will appear indicating the assay definition file is not loaded on the system. If this screen appears, contact Cepheid Technical Support.

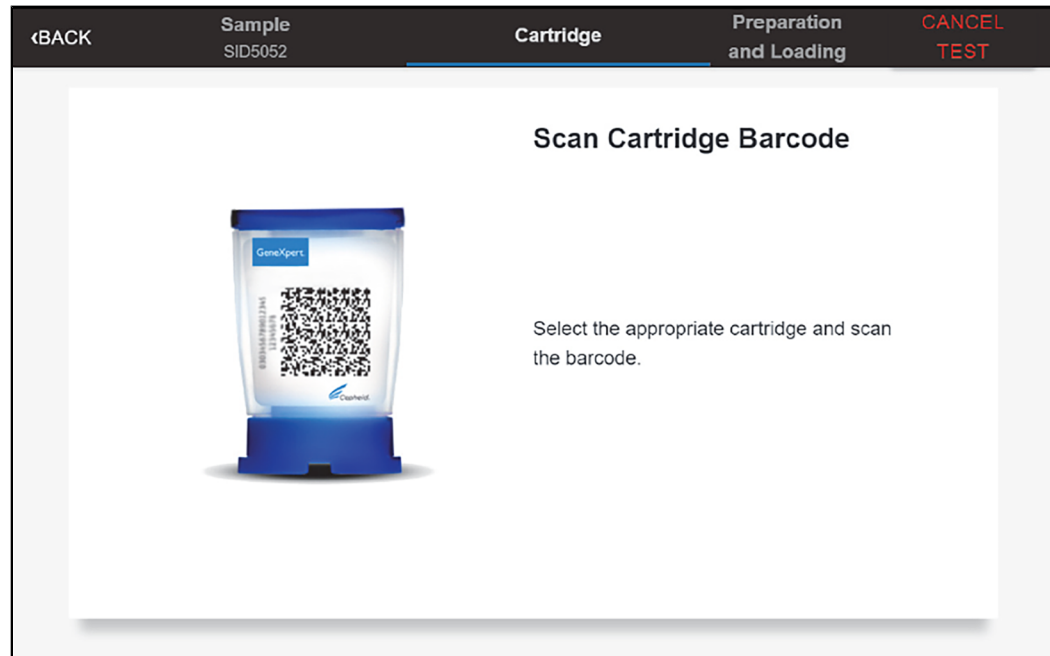


Figure 25. Scan Cartridge Barcode Screen

7. Select the appropriate cartridge with the sample and scan the cartridge barcode. After scanning, the Select Test screen appears.
8. Select Xpert Xpress_CoV-2-plus from the Select Assay menu.
9. Confirm the test information is correct then touch CONFIRM (see Figure 26).

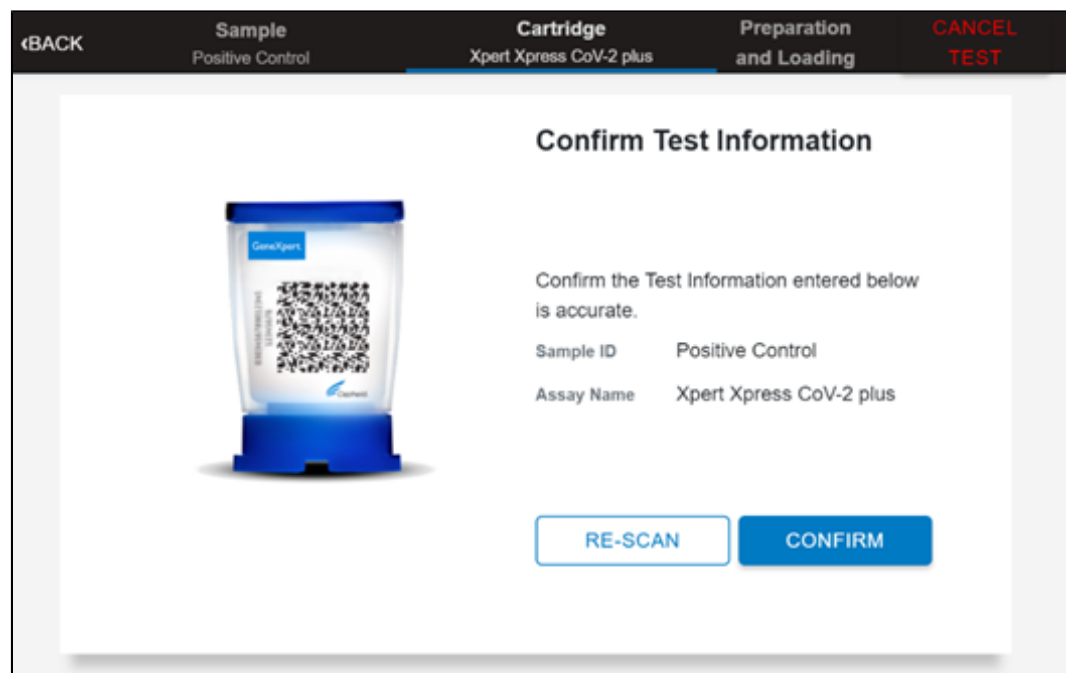


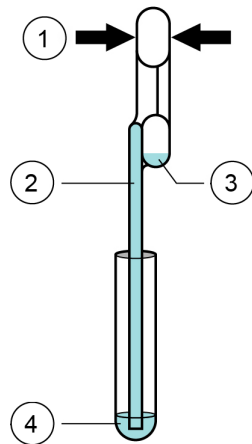
Figure 26. Confirm Test Information

10. Watch the video before continuing. The video will repeat. Touch the CONTINUE button to exit video.

11. Mix control by rapidly inverting the external control tube 5 times. Open the lid on the external control tube.
12. Open the cartridge lid by lifting the front of the cartridge lid.
13. Remove the transfer pipette from the wrapper.

Note Do not place unwrapped pipette on the workbench.

14. Squeeze the top bulb of the transfer pipette completely until the bulb is fully flat. While continuing to hold the bulb fully flat, place the pipette tip in the specimen transport tube (see Figure 27).



Number	Description
1	Squeeze here
2	Pipette
3	Overflow Reservoir Bulb
4	Sample

Figure 27. Transfer Pipette

15. Keeping the pipette below the surface of the liquid, release the top bulb of the pipette slowly to fill the pipette before removing from the tube. It is okay if liquid goes into the overflow reservoir (see Figure 27). Check that the pipette does not contain bubbles.
16. To transfer the external control to the cartridge, squeeze the top bulb of the pipette completely again until it is fully flat to empty the contents of the pipette into the large opening (Sample Chamber) of the cartridge shown in Figure 28. Dispose of the used pipette.

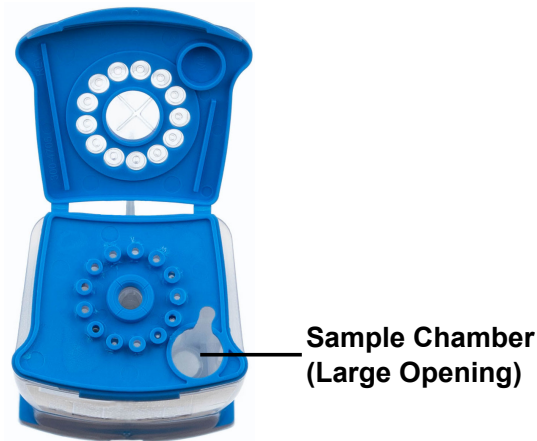


Figure 28. Xpert Xpress CoV-2 plus Cartridge (Top View)

Note Take care to dispense the entire volume of liquid into the Sample Chamber. False negative results may occur if insufficient sample is added to the cartridge.

17. Close the cartridge lid.
18. Go to Section 16.4, Loading the Cartridge.

16.4 Loading the Cartridge

1. Touch the **CONTINUE** button on the **Cartridge Preparation** screen. The **Load Cartridge into Module** screen appears (see Figure 29).
2. Open the module door with the flashing green light.



Figure 29. Load Cartridge into Module Screen

3. Load the cartridge with the barcode facing the operator on the cartridge bay platform. Do not try to insert the cartridge past the cartridge bay platform.
4. Close the door until it clicks. The green light will stop blinking and the test starts.
5. When the cartridge is loaded, the **Test Loading** screen appears, followed by the **Test Running** screen showing that the test is running. A circular graphic indicator at the right indicates the progress of the test and the time remaining until a test result is available.

Note While a test is running, you can start another test. See Section 16.5, Start a New Test While a Test is Running.

Note Do not turn off or unplug the instrument while a test is in progress. Turning off or unplugging the GeneXpert Xpress instrument or Hub stops the test. If necessary, touch the **STOP TEST** button to cancel a test while it is loading or running.

When the test is done, the green light goes out and the door automatically unlocks. The screen text changes to **Test Completed**. The **Test Completed** screen provides the results for the test just completed.

Note If an unexpected result occurs (e.g., Negative Quality Control result is positive or Positive Quality Control result is negative), test a new Quality Control sample using a new cartridge. If an unexpected result occurs upon retest, contact Cepheid Technical Support.

6. Open the module door, remove the used cartridge, and properly dispose of the cartridge according to your institution's policy.
7. Touch **HOME** to go back to the **Home** screen.
8. To log out, touch the **User Menu** icon, then select **Logout**.

16.5 Start a New Test While a Test is Running

You can start a new test while another test is in progress.

1. Touch the **HOME** button on the **Test Running** screen.
2. For a new user log in, touch the **User Menu** icon to log in.
3. Repeat the steps in Section 16.1, Preparing the Specimen, and Section 16.4.
4. After a second test has started, touch the **HOME** button.

The status of both tests appears. The **Home** screen displays the module(s) in use with a circular graphic indicator around each test and Patient Identification below the module graphic (see Figure 30).

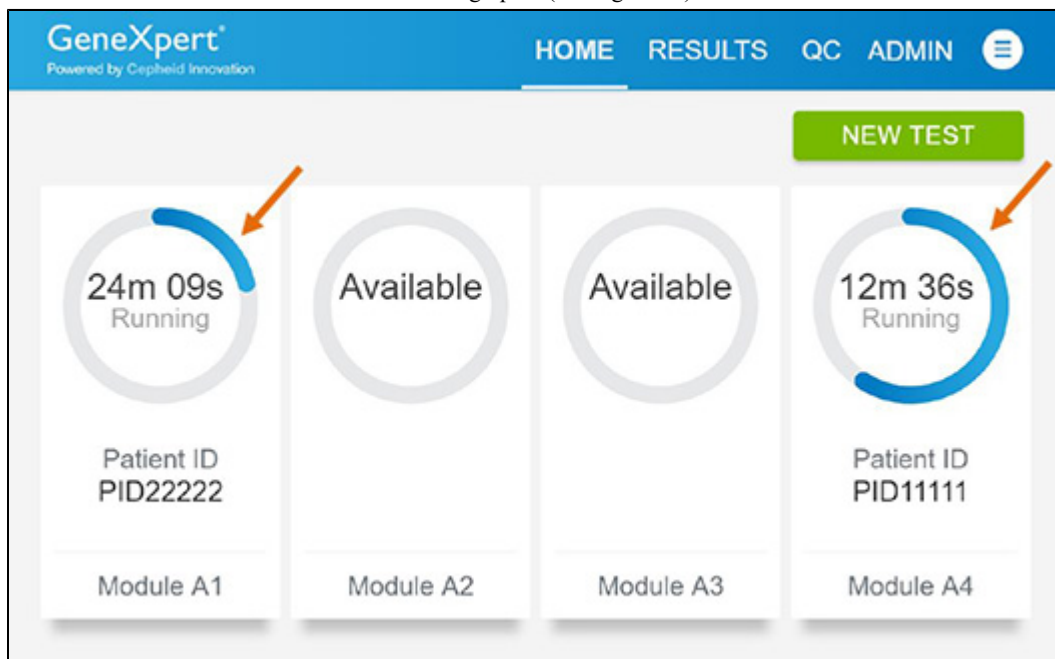


Figure 30. Home Screen showing Two Tests Running

- After a test has completed, the module icon text changes to **Complete** (see Figure 31). Touch **Complete View Results** to view test results.

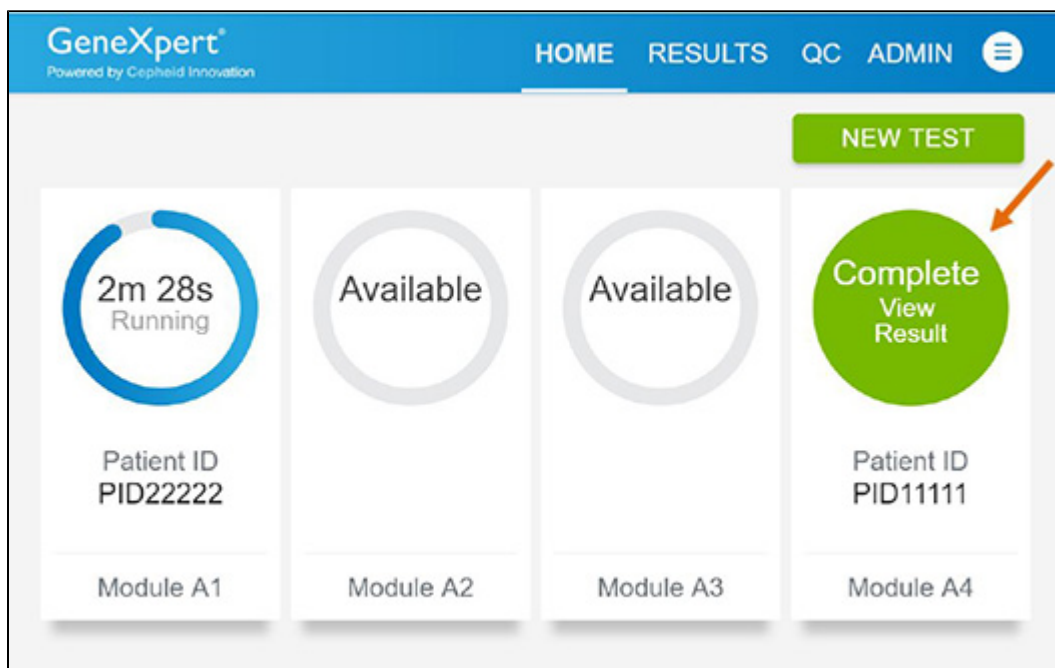


Figure 31. Home Screen with One of Two Tests Completed

16.6 Viewing Test Results

- Touch the **RESULTS** button located on the panel at the top of the screen (see Figure 32). The Results screen appears (see Figure 33). Test results are, by default, in order of the date and time that the test was run. Navigate through the test result pages by touching the numbered buttons or arrows at the bottom of the screen,

The screenshot shows the GeneXpert Results screen. At the top, there is a navigation bar with 'HOME', 'RESULTS', 'QC', and 'ADMIN' tabs. Below the navigation bar, there is a 'Results' section with a filter menu (Start Date, End Date, Assay Name, Test Type) and a search box for 'Search Patient/Sample ID'. An 'EXPORT' button is also present. The main content is a table with the following columns: Select All, Patient ID, Sample ID, Test Type, Assay Name, Start Date & Time, Reagent Lot, and Result. The table contains six rows of test results, all showing 'SARS-CoV-2 POSITIVE' results.

Select All	Patient ID *	Sample ID *	Test Type *	Assay Name *	Start Date & Time *	Reagent Lot *	Result *
<input type="checkbox"/>	Jane Doe	Test18	Specimen	Xpert Xpress CoV-2 plus	02/06/22 14:50:05	00100	SARS-CoV-2 POSITIVE
<input type="checkbox"/>	Jane Doe	Test17	Specimen	Xpert Xpress CoV-2 plus	02/06/22 14:49:41	00100	SARS-CoV-2 POSITIVE
<input type="checkbox"/>	John Doe	Test16	Specimen	Xpert Xpress CoV-2 plus	02/06/22 14:49:20	00100	SARS-CoV-2 POSITIVE
<input type="checkbox"/>	John Doe	Test15	Specimen	Xpert Xpress CoV-2 plus	02/06/22 14:48:54	00100	SARS-CoV-2 POSITIVE
<input type="checkbox"/>	Jane Doe	Test3	Specimen	Xpert Xpress CoV-2 plus	02/06/22 11:48:04	00100	SARS-CoV-2 POSITIVE
<input type="checkbox"/>	John Doe	Test2	Specimen	Xpert Xpress CoV-2 plus	02/06/22 11:47:37	00100	SARS-CoV-2 POSITIVE

Figure 32. Results Screen

2. Touch the desired result to open the Test Result screen (see Figure 33).
3. To view test report, touch the **REPORT** button then swipe across the screen from left to right to minimize screen and view report.

The screenshot shows the GeneXpert Test Result screen. At the top, there is a navigation bar with 'HOME', 'RESULTS', 'QC', and 'ADMIN' tabs. The main content is a 'Test Completed' screen for 'Module A3'. It displays the following information:

- Sample ID:** Test1
- Patient ID:** Jane Doe
- Test Type:** Specimen
- Assay Name:** Xpert Xpress CoV-2 plus
- User:** CLINICAL AFFAIRS DO NOT DELETE
- Start Date & Time:** 02/08/22 11:47:00

The result is displayed as **SARS-CoV-2 POSITIVE** in a red box. Below the result is a blue **REPORT** button. At the bottom, there is a 'Test Disclaimer' section with the text: 'Test Methodology: RT-PCR For In Vitro Diagnostic Use Only. For use under the Emergency Use Authorization (US).'

Figure 33. Test Result Screen (Example)

Note If an unexpected result occurs (e.g., Negative Quality Control result is positive or Positive Quality Control result is negative), test a new Quality Control sample using a new cartridge. If an unexpected result occurs upon retest, contact Cepheid Technical Support.

17 Quality Controls

17.1 Internal Controls

Each cartridge includes a Sample Processing Control (SPC) and Probe Check Control (PCC).

Sample Processing Control (SPC) – Ensures that the sample was processed correctly. The SPC verifies that sample processing is adequate. Additionally, this control detects sample-associated inhibition of the real-time PCR assay, ensures that the PCR reaction conditions (temperature and time) are appropriate for the amplification reaction, and that the PCR reagents are functional. The SPC should be positive in a negative sample and can be negative or positive in a positive sample. The SPC passes if it meets the validated acceptance criteria.

Probe Check Control (PCC) – Before the start of the PCR reaction, the GeneXpert System measures the fluorescence signal from the probes to monitor bead rehydration, reaction tube filling, probe integrity, and dye stability. The PCC passes if it meets the validated acceptance criteria.

17.2 External Controls

External controls should be used in accordance with local, state and federal accrediting organizations as applicable. If the expected results for the external control materials are not obtained, repeat the external controls, prior to releasing patient results. If the expected results for the external control material are not obtained upon repeat, contact Cepheid Technical Support.

18 Interpretation of Results

The results are interpreted automatically by the GeneXpert Xpress System and are clearly shown in the **View Results** window. Xpert Xpress CoV-2 plus test provides test results based on the detection of three gene targets according to the algorithms shown in Table 1.

Table 1. Xpert Xpress CoV-2 plus Possible Results

Result Text	N2	E	RdRP	SPC
SARS-CoV-2 POSITIVE	+	+	+	+/-
SARS-CoV-2 POSITIVE	+	+/-	+/-	+/-
SARS-CoV-2 POSITIVE	+/-	+	+/-	+/-
SARS-CoV-2 POSITIVE	+/-	+/-	+	+/-
SARS-CoV-2 NEGATIVE	-	-	-	+
INSTRUMENT ERROR or NO RESULT – REPEAT TEST	-	-	-	-

See Table 2 to interpret test result statements for the Xpert Xpress CoV-2 plus test.

Table 2. Xpert Xpress CoV-2 plus Test Results and Interpretation

Result	Interpretation
SARS-CoV-2 POSITIVE	<p>SARS-CoV-2 target RNA is detected.</p> <ul style="list-style-type: none"> The SARS-CoV-2 signal has a Ct within the valid range and endpoint above the minimum setting for one or more nucleic acid targets (N2, E, RdRP). SPC: NA; SPC is ignored because coronavirus target amplification occurred. Probe Check: PASS; all probe check results pass.
SARS-CoV-2 NEGATIVE	<p>SARS-CoV-2 target RNA is not detected.</p> <ul style="list-style-type: none"> The SARS-CoV-2 signals for nucleic acid targets (N2, E and RdRP) do not have a Ct within the valid range and endpoint above the minimum setting. SPC: PASS; SPC has a Ct within the valid range and endpoint above the minimum setting. Probe Check: PASS; all probe check results pass.
INSTRUMENT ERROR	<ul style="list-style-type: none"> If result is INSTRUMENT ERROR, touch CLEAR ERROR and follow the on-screen instructions. When the Home screen appears, repeat the test using a new cartridge according to the Retest Procedure in Section 19.2 of the IFU.
NO RESULT - REPEAT TEST	<ul style="list-style-type: none"> If result is NO RESULT - REPEAT TEST, retest with a new cartridge according to the Retest Procedure in Section 19.2 of the IFU. If retest is NO RESULT - REPEAT TEST, collect a new specimen for testing.

The Xpert Xpress CoV-2 plus test includes an Early Assay Termination (EAT) function which will provide earlier time to results in high titer specimens if the signal from the target nucleic acid reaches a predetermined threshold before the PCR cycles have been completed. When SARS CoV-2 titers are high enough to initiate the EAT function, the SPC and/or other target amplification curves may not be seen and their results may not be reported.

19 Retests

19.1 Reasons to Repeat the Assay

If any of the test results mentioned below occur, repeat the test once according to instructions in Section 19.2.

- An **INSTRUMENT ERROR** result could be due to, but not limited to, Probe Check Control failure, system component failure, or the maximum pressure limits were exceeded.
- A **NO RESULT-REPEAT TEST** indicates that insufficient data were collected. For example, cartridge failed integrity test, Probe Check Control failure, the operator stopped a test that was in progress, or a power failure occurred.

If an External Control fails to perform as expected, repeat external control test and/or contact Cepheid for assistance.

19.2 Retest Procedure

To retest a non-determinate result (**NO RESULT-REPEAT TEST**, or **INSTRUMENT ERROR**), use a new cartridge.

Use the leftover sample from the original specimen transport medium tube or new external control tube.

- Put on a clean pair of gloves. Obtain a new Xpert Xpress CoV-2 plus cartridge and a new transfer pipette.
- Check the specimen transport tube or external control tube is closed.
- Mix the sample by rapidly inverting the specimen transport medium tube or external control tube 5 times. Open the cap on the specimen transport tube or external control tube.
- Open the cartridge lid.

5. Using a clean transfer pipette (supplied), transfer sample (one draw) to the sample chamber with the large opening in the cartridge.
6. Close the cartridge lid.

20 Limitations

- Performance of the Xpert Xpress CoV-2 *plus* has only been established in nasopharyngeal swab and anterior nasal swab specimens. Specimen types other than nasopharyngeal swab and anterior nasal swab have not been assessed and performance characteristics are unknown.
- Nasopharyngeal swab, oropharyngeal swab and anterior nasal swab samples collected into saline should not be frozen.
- The performance of this test was established based on the evaluation of a limited number of clinical specimens. Clinical performance has not been established with 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.
- The performance of this device has not been assessed in a population vaccinated against COVID-19 or treated with COVID-19 therapies.
- Negative results do not preclude SARS-CoV-2 and should not be used as the sole basis for treatment or other patient management decisions.
- Results from the Xpert Xpress CoV-2 *plus* test should be correlated with the clinical history, epidemiological data, and other data available to the clinician evaluating the patient.
- As with any molecular test, mutations within the target regions of Xpert Xpress CoV-2 *plus* could affect primer and/or probe binding and result in failure to detect the presence of virus.
- This test cannot rule out diseases caused by other bacterial or viral pathogens.
- The performance of this test was validated using the procedures provided in this package insert only. Modifications to these procedures may alter the performance of the test.
- Erroneous test results might occur from improper specimen collection; failure to follow the recommended sample collection, handling, and storage procedures; technical error; or sample mix-up. Careful compliance with the instructions in this insert is necessary to avoid erroneous results.
- Viral nucleic acid may persist *in vivo*, independent of virus infectivity. Detection of analyte target(s) does not imply that the corresponding virus(es) are infectious or are the causative agents for clinical symptoms.
- This test has been evaluated for use with human specimen material only.
- This test is a qualitative test and does not provide the quantitative value of detected organism present.
- This test has not been evaluated for monitoring treatment of infection.
- This test has not been evaluated for screening of blood or blood products for the presence of SARS-CoV-2.
- The E gene targeted by the Xpert Xpress CoV-2 *plus* test can detect, in addition to SARS-CoV-2, other coronavirus species within the *Sarbecovirus* subgenus.
- The effect of interfering substances has only been evaluated for those listed within the labeling. Interference by substances other than those described can lead to erroneous results.
- Cross-reactivity with respiratory tract organisms other than those described herein can lead to erroneous results.

21 Conditions of Authorization for Laboratory and Patient Care Settings

The Cepheid Xpert Xpress CoV-2 *plus* 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/in-vitro-diagnostics-euas>

However, to assist clinical laboratories and/or Patient Care Settings using the Xpert Xpress CoV-2 *plus* (referred to in the Letter of Authorization as “Your Product”), the relevant Conditions of Authorization are listed below.

- Authorized laboratories^a using your product must include with test 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 your product must use your product 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 other ancillary reagents and authorized materials required to use your product are not permitted.
- Authorized laboratories that receive your product must notify the relevant public health authorities of their intent to run your product prior to initiating testing.
- Authorized laboratories using your product must have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.
- Authorized laboratories using your product must collect information on the performance of your product and report to DMD/OHT7-OIR/OPEQ/CDRH (via email: CDRH-EUARreporting@fda.hhs.gov) and Cepheid (+1 888 838 3222 or techsupport@cepheid.com) any suspected occurrence of false positive or false negative results and significant deviations from the established performance characteristics of the test of which they become aware.
- All operators using your product must be appropriately trained in performing and interpreting the results of your product, use appropriate personal protective equipment when handling this kit, and use your product in accordance with the authorized labeling.
- Cepheid, authorized distributors, and authorized laboratories using your product 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.

22 Clinical Evaluation

22.1 Clinical Evaluation—Performance of Xpert Xpress CoV-2 plus Test on NPS and NS Specimens Collected from Individuals Suspected of COVID-19

The performance of the Xpert Xpress CoV-2 plus test was evaluated using archived clinical nasopharyngeal (NPS) and anterior nasal swab (NS) specimens in viral transport medium or universal transport medium. Archived specimens were selected consecutively by date and previously known analyte result. A total of 164 NP swab and 111 NS specimens were tested with Xpert Xpress CoV-2 plus side by side with an FDA authorized SARS-CoV-2 RT-PCR test in a randomized and blinded fashion.

Positive Percent Agreement (PPA), Negative Percent Agreement (NPA), and non-determinate rate were determined by comparing the results of the Xpert Xpress CoV-2 plus test relative to the results of a SARS-CoV-2 FDA authorized RT-PCR test for the SARS-CoV-2 target.

For the NPS specimens, Xpert Xpress CoV-2 plus demonstrated a PPA and NPA of 100.0% and 96.5% for SARS-CoV-2, respectively (Table 3). The initial non-determinate rate for the Xpert Xpress CoV-2 plus test was 1.8% (3/164). On repeat testing, all three (3) specimens yielded valid results. The final non-determinate rate for the Xpert Xpress CoV-2 plus test was 0.0% (0/164).

Table 3. Xpert Xpress CoV-2 plus Performance Results Using NPS Specimens

Target	Number of Specimens	TP	FP	TN	FN	PPA (95% CI)	NPA (95% CI)
SARS-CoV-2	164	79	3	82	0	100.0% (95.4% - 100.0%)	96.5% (90.1% - 98.8%)

^a The letter of authorization refers to "authorized laboratories" as follows: "Testing of nasopharyngeal, oropharyngeal, nasal, or mid-turbinate swab or nasal wash/aspirate specimens using the Xpert Xpress CoV-2 plus test run on the GeneXpert Dx and GeneXpert Infinity Systems is limited to laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, that meet requirements to perform high or moderate complexity tests. Testing of nasopharyngeal, nasal, or mid-turbinate swab specimens using the Xpert Xpress CoV-2 plus test run on the GeneXpert Xpress System (Tablet and Hub Configurations) is limited to laboratories certified under CLIA that meet requirements to perform high, moderate, or waived complexity tests. Testing of these specimens is authorized for use at the Point of Care (POC), i.e., in patient care settings operating under a CLIA Certificate of Waiver, Certificate of Compliance, or Certificate of Accreditation."

TP: True Positive; FP: False Positive; TN: True Negative; FN: False Negative; CI: Confidence Interval

For the NS specimens, Xpert Xpress CoV-2 plus demonstrated a PPA and NPA of 100.0% and 100.0% for SARS-CoV-2, respectively (Table 4). On repeat testing, all three (3) specimens yielded valid results. The final non-determinate rate for the Xpert Xpress CoV-2 plus test was 0.0% (0/111).

Table 4. Xpert Xpress CoV-2 plus Performance Results Using NS Specimens

Target	Number of Specimens	TP	FP	TN	FN	PPA (95% CI)	NPA (95% CI)
SARS-CoV-2	111	46	0	65	0	100.0% (92.3% - 100.0%)	100.0% (94.4% - 100.0%)

TP: True Positive; FP: False Positive; TN: True Negative; FN: False Negative; CI: Confidence Interval

22.2 Clinical Evaluation—Performance of Xpert Xpress CoV-2 plus Test on Specimens Collected from Asymptomatic Screening Population

A total of 125 archived frozen de-identified clinical NS specimens from individuals without symptoms or other reasons to suspect COVID-19 were evaluated. These specimens were selected consecutively by date and previously known analyte result. The specimens from the asymptomatic screening individuals were tested with Xpert Xpress CoV-2 plus side by side with an FDA authorized SARS-CoV-2 RT-PCR test in a randomized and blinded fashion. The Xpert Xpress CoV-2 plus demonstrated a PPA and NPA of 100.0% and 99.0% for SARS-CoV-2, respectively (Section 22.2). The non-determinate rate for the Xpert Xpress CoV-2 plus test was 0% (0/125).

Table 5. Xpert Xpress CoV-2 plus Performance Results Using NS Specimens from Asymptomatic Screening Individuals

Target	Number of Specimens	TP	FP	TN	FN	PPA (95% CI)	NPA (95% CI)
SARS-CoV-2	125	20	1	104	0	100.0% (83.9% - 100.0%)	99.0% (94.8% - 99.8%)

TP: True Positive; FP: False Positive; TN: True Negative; FN: False Negative; CI: Confidence Interval

23 Analytical Performance

23.1 Analytical Sensitivity (Limit of Detection)

23.1.1 Analytical Sensitivity (Limit of Detection) for Nasopharyngeal Swab

The analytical sensitivity of the Xpert Xpress CoV-2 plus test was first estimated using two reagent lots by testing limiting dilutions of one strain of NATtrol SARS-CoV-2 virus diluted into pooled negative clinical NPS-UTM/VTM matrix, following the guidance in Clinical and Laboratory Standards Institute (CLSI) document EP17-A2. LoD was estimated by considering each target gene (E, N2, and RdRP) in addition to the overall positivity rate for the Xpert Xpress CoV-2 plus test. The estimated LoD value as determined by Probit regression analysis was based on the weakest target gene (N2) and verified using two lots of Xpert Xpress CoV-2 plus reagents in replicates of 20 for two clinical NPS matrices (UTM/VTM, saline, eNAT). The concentration level with observed hit rates greater than or equal to 95% in the estimated LoD determination study were 403, 200 and 70 copies/mL for the N2 target, RdRP target and E target, respectively. The claimed LoD is 403 copies/mL (Table 6).

Table 6. Xpert Xpress CoV-2 plus Limit of Detection in NPS-UTM/VTM Matrix

Concentration (copies/mL)	E gene			N2 gene			RdRP gene		
	# Positive	% Positive	Mean Ct	# Positive	% Positive	Mean Ct	# Positive	% Positive	Mean Ct
10	4	20	39.0	0	0	0.0	1	5	42.7
20 ^a	12	60	39.2	0	0	0.0	10	50	41.7
30	16	80	39.2	0	0	0.0	14	70	41.0
40	16	80	37.8	0	0	0.0	16	80	40.8
50	18	90	38.1	2	10	42.3	18	90	40.6
70	19	95	37.9	2	10	43.1	17	85	39.8
100	20	100	36.7	5	25	41.7	18	90	39.5
200	20	100	35.8	14	70	40.6	19	95	38.3
300	20	100	35.3	19	95	39.5	20	100	37.6
400	20	100	34.9	18	90	39.9	20	100	37.2
500	20	100	34.6	19	95	38.2	20	100	37.0
600 ^b	20	100	34.1	20	100	38.0	20	100	36.4
700 ^c	20	100	34.2	20	100	38.0	20	100	36.5
800 ^c	20	100	34.0	20	100	38.0	20	100	36.4

^a One of 20 replicates tested reported INVALID. The run was successfully repeated to obtain 20 valid replicates.

^b One of 20 replicates tested reported ERROR. The run was successfully repeated to obtain 20 valid replicates

^c One of 20 replicates tested reported NO RESULT. The run was successfully repeated to obtain 20 valid replicates

23.2 Analytical Reactivity (Inclusivity)

The inclusivity of Xpert Xpress CoV-2 plus primers was evaluated on June 30, 2022 using *in silico* analysis of the assay amplicons in relation to 11,650,640 SARS-CoV-2 sequences available in the GISAID gene database for three targets, E, N2 and RdRP. The 11,650,640 SARS-CoV-2 sequences were separated into the lineages of interest based on the Pango Lineage assigned to each genome by GISAID, and those with ambiguous nucleotides were removed. Thus, the following inclusivity analyses focuses on the combined, non-ambiguous sequences from the variants of interest and variants of concern as of June 30, 2022. These constituted 10,469,612 sequences for the E target, 10,587,381 sequences for the N2 target and 10,333,656 sequences for the RdRP target. Table 7 summarizes the effective predicted inclusivity for E, N2 and RdRP amplicons for the variants of interests and concern.

Table 7. Predicted Inclusivity for E, N2 and RdRP Amplicons for SARS-CoV-2 Variants of Interests and Concern

SARS-CoV-2 Target Amplicon	Exact Match	1 Mismatch ^a	2 or More Mismatches	Predicted Inclusivity

SARS-CoV-2 Target Amplicon	Exact Match	1 Mismatch ^a	2 or More Mismatches	Predicted Inclusivity
E	10,420,248 of 10,469,612 total (99.5%)	48,562 (0.5%)	802 (0.01%)	100%
N2	10,386,068 of 10,587,381 total (98.1%)	196,336 (1.9%)	4,977 (0.05%)	99.95%
RdRP	10,247,146 of 10,333,656 total (99.2%)	85,373 (0.8%)	1,137 (0.01%)	100%

^a Single-nucleotide mismatches are predicted to not impact the performance of the test.

The *in silico* inclusivity of the Xpert Xpress CoV-2 plus probe oligonucleotides for E, N2 and RdRP were also assessed against the top 20 most frequent matches in the GISAID EpiCoV sequence database as of June 15, 2022, which constituted 10,310,839 for the E target, 10,428,014 for the N2 target and 10,178,602 for the RdRP target. For each of the probe oligonucleotides used in the Xpert Xpress CoV-2 plus test, Table 8 summarizes the number sequences as well as the corresponding percentage of sequences from this dataset with exact match, 1 mismatch/insertion, and 2 or more mismatches/insertions in the alignment.

Table 8. Predicted Inclusivity for E, N2 and RdRP Probes for SARS-CoV-2 Variants of Interests and Concern

SARS-CoV-2 Target Probe	Exact Match	1 Mismatch/ Insertion ^a	2 or More Mismatches/ Insertions	Predicted Inclusivity
E	10,300,688 of 10,310,839 total (99.9%)	9,853 (0.1%)	22 (0.0002%)	100%
N2	10,351,581 of 10,428,014 total (99.3%)	72,957 (0.7%)	0 (0%)	100%
RdRP	0	10,140,254 of 10,178602 total (99.6%)	37,492 (0.4%)	99.6%

^a Single-nucleotide mismatches/insertions are predicted to not impact the performance of the test.

In addition to the *in silico* analysis of the SARS-CoV-2 primers and probes for inclusivity, the inclusivity of the Xpert Xpress CoV-2 plus test was evaluated by bench testing against multiple strains of SARS-CoV-2 at levels near the analytical LoD. A total of 25 strains comprised of 5 SARS-CoV-2 virus strains and 20 SARS-CoV-2 in vitro RNA transcripts representing variant strains were tested in this study with the Xpert Xpress CoV-2 plus test. Three (3) replicates were tested for each strain. All SARS-CoV-2 strains tested positive in all three replicates. Results are shown in Table 9.

Table 9. Analytical Reactivity (Inclusivity) of the Xpert Xpress CoV-2 plus Test

SARS-CoV-2 Strain	Tested Titer	Final SARS-CoV-2 Result Call-Out	Number of Positive Results Obtained out of the Total Number of Replicates Tested		
			E	N2	RdRP

SARS-CoV-2 Strain	Tested Titer	Final SARS-CoV-2 Result Call-Out	Number of Positive Results Obtained out of the Total Number of Replicates Tested		
			E	N2	RdRP
2019-nCoV/Italy-INMI1 ^a	5 TCID ₅₀ /mL	POS	3/3	3/3	3/3
England/204820464/2020 ^a	0.5 TCID ₅₀ /mL	POS ^b	3/4	3/4	3/4
Hong Kong/ VM20001061/2020 ^a	0.25 TCID ₅₀ /mL	POS	3/3	3/3	3/3
South Africa/KRISP- K005325/2020 ^a	0.25 TCID ₅₀ /mL	POS	3/3	3/3	3/3
USA/CA_CDC_5574/2020 ^a	0.25 TCID ₅₀ /mL	POS	3/3	3/3	3/3
Australia/VIC01/2020 ^c	1.2e3 copies/mL	POS	3/3	3/3	3/3
Wuhan-Hu-1 ^c	1.2e3 copies/mL	POS	3/3	3/3	3/3
Japan/ Hu_DP_Kng_19-020/2020 ^c	1.2e3 copies/mL	POS	3/3	3/3	3/3
USA/TX1/2020 ^c	1.2e3 copies/mL	POS	3/3	3/3	3/3
USA/MN2-MDH2/2020 ^c	1.2e3 copies/mL	POS	3/3	3/3	3/3
USA/CA9/2020 ^c	1.2e3 copies/ml	POS	3/3	3/3	3/3
France/HF2393/2020 ^c	1.2e3 copies/ml	POS	3/3	3/3	3/3
Taiwan/NTU02/2020 ^c	1.2e3 copies/ml	POS	3/3	3/3	3/3
USA/WA2/2020 ^c	1.2e3 copies/ml	POS	3/3	3/3	3/3
USA/CA-PC101P/2020 ^c	1.2e3 copies/ml	POS	3/3	3/3	3/3
Iceland/5/2020 ^c	1.2e3 copies/ml	POS	3/3	3/3	3/3
England/SHEF- C05B2/2020 ^c	1.2e3 copies/ml	POS	3/3	3/3	3/3
Belgium/ULG/10004/2020 ^c	1.2e3 copies/ml	POS	3/3	3/3	3/3
England/205041766/2020 ^c	1.2e3 copies/ml	POS	3/3	3/3	3/3
England/ MILK-9E05B3/2020 ^c	1.2e3 copies/ml	POS	3/3	3/3	3/3
South Africa/KRISP- EC-K005299/2020 ^c	1.2e3 copies/ml	POS	3/3	3/3	3/3
Japan/IC-0564/2021 ^c	1.2e3 copies/ml	POS	3/3	3/3	3/3
India/CT-ILSGS00361/2021 ^c	1.2e3 copies/ml	POS	3/3	3/3	3/3
India/MH-NCCS- P1162000182735/2021 ^c	1.2e3 copies/ml	POS	3/3	3/3	3/3
India/MH- SEQ-221_S66_R1_001/2021 ^c	1.2e3 copies/ml	POS	3/3	3/3	3/3

^a Heat-inactivated viral culture fluid (intact viral particles)

- ^b One of 3 replicates reported ERROR. The run was successfully repeated to obtain 3 valid replicates.
- ^c Synthetic, *in vitro* RNA transcript, TWIST controls

23.3 Analytical Specificity (Exclusivity)

The analytical specificity/cross-reactivity of the Xpert Xpress CoV-2 plus included evaluation of the SARS-CoV-2 test primer and probes with potentially cross-reactive microorganisms by *in silico* analysis. The analysis was conducted by mapping the primers and probes of Xpert Xpress CoV-2 plus individually to the microorganism sequences downloaded from the GISAID database. The E primers and probes are not specific for SARS-CoV-2 and will detect Human and Bat SARS-coronavirus. Other than that, no potential unintended cross reactivity with other organisms listed in Table 10 is expected based on the *in silico* analysis.

Table 10. Microorganisms Analyzed in the *in silico* Analysis for the SARS-CoV-2 Target

Microorganisms from the Same Genetic Family	High Priority Organisms
Human coronavirus 229E	Adenovirus (e.g., C1 Ad. 71)
Human coronavirus OC43	Cytomegalovirus
Human coronavirus HKU1	Enterovirus (e.g., EV68)
Human coronavirus NL63	Epstein-Barr virus
SARS-coronavirus	Human Metapneumovirus (hMPV)
MERS-coronavirus	Influenza A
Bat coronavirus	Influenza B
	Measles
	Mumps
	Parainfluenza virus 1-4
	Parechovirus
	Respiratory syncytial virus
	Rhinovirus
	<i>Bacillus anthracis</i> (Anthrax)
	<i>Bordetella pertussis</i>
	<i>Bordetella parapertussis</i>
	<i>Chlamydia pneumoniae</i>
	<i>Chlamydia psittaci</i>
	<i>Corynebacterium diphtheriae</i>
	<i>Coxiella burnetii</i> (Q-Fever)
	<i>Escherichia coli</i>
	<i>Fusobacterium necrophorum</i>
	<i>Haemophilus influenzae</i>
	<i>Lactobacillus</i> sp.
	<i>Legionella non-pneumophila</i>
	<i>Legionella pneumophila</i>
	<i>Leptospira</i>
	<i>Moraxella catarrhalis</i>

Microorganisms from the Same Genetic Family	High Priority Organisms
	<i>Mycobacterium tuberculosis</i>
	<i>Mycoplasma genitalium</i>
	<i>Mycoplasma pneumoniae</i>
	<i>Neisseria elongata</i>
	<i>Neisseria meningitidis</i>
	<i>Pneumocystis jirovecii</i> (PJP)
	<i>Pseudomonas aeruginosa</i>
	<i>Staphylococcus aureus</i>
	<i>Staphylococcus epidermidis</i>
	<i>Streptococcus salivarius</i>
	<i>Streptococcus pneumoniae</i>
	<i>Streptococcus pyogenes</i>
	<i>Aspergillus sp</i>
	<i>Candida albicans</i>

In addition to the *in silico* analysis of the SARS-CoV-2 primers and probes for cross-reactivity, the analytical specificity of the Xpert Xpress CoV-2 plus test was evaluated by bench-testing a panel of 55 microorganisms comprising 4 human coronaviruses, 1 MERS-Coronavirus, 1 SARS-Coronavirus, 19 other respiratory viruses, 26 respiratory bacteria, 2 yeast strains, 1 fungal strain, and 1 human nasal wash fluid representing a diverse microbial flora in the human respiratory tract. The panel was tested in different pools of microorganisms; if a pool produced a positive result, then each member of the pool would have been tested individually. Three replicates of each pool were tested. A sample was considered negative if all three replicates were negative. The bacterial and yeast strains were tested at concentrations of $\geq 1 \times 10^6$ CFU/mL with the exception of *Chlamydia pneumoniae* which was tested at 1.1×10^6 IFU/mL and *Lactobacillus reuteri* which was tested at 1.1×10^6 copies/mL of genomic DNA. Viruses were tested at concentrations of $\geq 1 \times 10^5$ TCID₅₀/mL. The results of the analytical specificity/exclusivity study demonstrate that the primer/probe sets included in the Xpert Xpress CoV-2 plus does not cross-react with the nucleic acids from non-intended respiratory microorganisms and phylogenetically related human coronavirus species. The one exception was the SARS-coronavirus, Urbani which yielded the expected test result of SARS-CoV-2 POSITIVE. We expected cross-reactivity for the E gene target with the SARS-coronavirus Urbani strain which has the highly conserved E gene target shared among coronaviruses in the B lineage *Betacoronavirus*. Results are shown in Table 11

Table 11. Analytical Specificity (Exclusivity) of the Xpert Xpress CoV-2 plus Test

Respiratory Microorganisms	Test Group	Tested Concentration	Final SARS-CoV-2 Result Call-Out	Number of Positive Results Obtained out of the Total Number of Replicates Tested		
				E	N2	RdRP
Human coronavirus, 229E	1	1.1e5 TCID ₅₀ /mL	NEG	0/3	0/3	0/3
Human coronavirus, OC43		1.1e5 TCID ₅₀ /mL				
MERS-coronavirus		1.1e5 TCID ₅₀ /mL				
Human coronavirus, NL63	2	1.1e5 TCID ₅₀ /mL	NEG	0/3	0/3	0/3

Respiratory Microorganisms	Test Group	Tested Concentration	Final SARS-CoV-2 Result Call-Out	Number of Positive Results Obtained out of the Total Number of Replicates Tested		
				E	N2	RdRP
Human coronavirus, HKU1 ^a	3	1.1e6 genome copies/mL	NEG	0/3	0/3	0/3
SARS-coronavirus, Urbani ^a	4	1.1e6 genome copies/mL	POS	3/3	0/3	0/3
Influenza A H1N1 (pdm2009), Michigan/272/2017	5	1.1e5 TCID ₅₀ /mL	NEG	0/3	0/3	0/3
Influenza B (Victoria Lineage), Hawaii/01/2018 (NA D197N)		1.1e5 TCID ₅₀ /mL				
RSV-A, Strain: 4/2015 Isolate #1		1.1e5 TCID ₅₀ /mL				
Adenovirus Type 1	6	1.1e5 TCID ₅₀ /mL	NEG	0/3	0/3	0/3
Adenovirus Type 7A		1.1e5 TCID ₅₀ /mL				
Cytomegalovirus		1.1e5 TCID ₅₀ /mL				
Echovirus	7	1.1e5 TCID ₅₀ /mL	NEG	0/3	0/3	0/3
Enterovirus, D68 strain US/KY/14-18953		1.1e5 TCID ₅₀ /mL				
Epstein Barr Virus (Human Herpes Virus 4 [Hhv-4])		1.1e5 TCID ₅₀ /mL				
Herpes Simplex Virus (HSV) type 1		1.1e5 TCID ₅₀ /mL				
Human metapneumovirus (hMPV-5, type B1)		1.1e5 TCID ₅₀ /mL				
Measles		1.1e5 TCID ₅₀ /mL				
Mumps virus		1.1e5 TCID ₅₀ /mL				
Human parainfluenza Type 1	8	1.1e5 TCID ₅₀ /mL	NEG	0/3	0/3	0/3
Human parainfluenza Type 2		1.1e5 TCID ₅₀ /mL				
Human parainfluenza Type 3		1.1e5 TCID ₅₀ /mL				
Human parainfluenza Type 4		1.1e5 TCID ₅₀ /mL				

Respiratory Microorganisms	Test Group	Tested Concentration	Final SARS-CoV-2 Result Call-Out	Number of Positive Results Obtained out of the Total Number of Replicates Tested		
				E	N2	RdRP
Rhinovirus, Type 1A		1.1e5 TCID ₅₀ /mL				
Acinetobacter baumannii	9	1.1e6 CFU/mL	NEG	0/3	0/3	0/3
<i>Burkholderia cepacia</i>		1.1e6 CFU/mL				
<i>Candida albicans</i>		1.1e6 CFU/mL				
<i>Candida parapsilosis</i>		1.1e6 CFU/mL				
<i>Bordetella pertussis</i>		1.1e6 CFU/mL				
<i>Chlamydia pneumoniae</i>		1.1e6 IFU/mL				
<i>Citrobacter freundii</i>		1.1e6 CFU/mL				
<i>Corynebacterium xerosis</i>		10				
<i>Escherichia coli</i>	1.1e6 CFU/mL					
<i>Enterococcus faecalis</i>	1.1e6 CFU/mL					
<i>Hemophilus influenzae</i>	1.1e6 CFU/mL					
<i>Legionella spp.</i>	1.1e6 CFU/mL					
<i>Moraxella catarrhalis</i>	1.1e6 CFU/mL					
<i>Mycobacterium tuberculosis (avirulent)</i>	11	1.1e6 CFU/mL	NEG	0/3	0/3	0/3
<i>Mycoplasma pneumoniae</i>		1.1e6 CFU/mL				
<i>Neisseria mucosa</i>		1.1e6 CFU/mL				
<i>Propionibacterium acnes (= Cutibacterium acnes) Z144</i>		1.1e6 CFU/mL				
<i>Pseudomonas aeruginosa, Z139</i>		1.1e6 CFU/mL				
<i>Staphylococcus aureus</i>		1.1e6 CFU/mL				
<i>Staphylococcus epidermidis</i>	12	1.1e6 CFU/mL	NEG	0/3	0/3	0/3

Respiratory Microorganisms	Test Group	Tested Concentration	Final SARS-CoV-2 Result Call-Out	Number of Positive Results Obtained out of the Total Number of Replicates Tested		
				E	N2	RdRP
<i>Staphylococcus haemolyticus</i>		1.1e6 CFU/mL				
<i>Streptococcus agalactiae</i>		1.1e6 CFU/mL				
<i>Streptococcus pneumoniae</i>		1.1e6 CFU/mL				
<i>Streptococcus pyogenes</i>		1.1e6 CFU/mL				
<i>Streptococcus salivarius</i>		1.1e6 CFU/mL				
<i>Streptococcus sanguinis</i>		1.1e6 CFU/mL				
Pneumocystis jirovecii (PJP)		1.1e6 CFU/mL				
<i>Lactobacillus reuteri</i> , F275 ^b	13	1.1e6 genome copies/mL	NEG	0/3	0/3	0/3
<i>Neisseria meningitides</i> ^b		1.1e6 genome copies/mL				
Pooled human nasal wash	14	n/a	NEG	0/3	0/3	0/3
Influenza C	15	1.1e5 TCID ₅₀ /mL	NEG	0/3	0/3	0/3

^a RNA specimens were tested in Tris-EDTA+((NH₄)₂)(SO₄) buffer using an ADF without sample preparation.

^b DNA specimens were tested in simulated NPS/NS background matrix using the full sample preparation ADF

23.4 Microbial Interference

Microbial interference of the Xpert Xpress CoV-2 plus test caused by the presence of bacterial or viral strains that might be encountered in human upper respiratory tract specimens was evaluated by testing a panel of 10 commensal microorganisms, consisting of 7 viral strains and 3 bacterial strains. Contrived samples consisted of SARS-CoV-2 virus seeded at 3x LoD into simulated nasopharyngeal swab (NPS)/ anterior nasal swab (NS) matrix in the presence of the seven (7) commensal virus strains (Adenovirus Type 1C, Human Coronavirus OC43, Rhinovirus Type 1A, Human metapneumovirus, Human parainfluenza Types 1, 2, and 3 spiked at 1x10⁵ units/mL) or three (3) commensal bacterial strains (*Haemophilus influenzae*, *Staphylococcus aureus*, *Staphylococcus epidermidis*) spiked at 1x10⁷ CFU/mL.

Replicates of 8 positive samples were tested with SARS-CoV-2 virus and each potential microbial interference strain combination. All 8 of 8 positive replicate samples were correctly identified as SARS-CoV-2 POSITIVE using the Xpert Xpress CoV-2 plus test. The one exception was Rhinovirus Type1A for which one of 8 replicates reported as ERROR. The run was successfully repeated to obtain 8 valid replicates. No interference by the listed above commensal viral or bacterial strains was reported at the concentrations tested.

23.5 Potentially Interfering Substances

Substances that could be present in the nasopharynx (or introduced during specimen collection and handling) and potentially interfere with accurate detection of SARS-CoV-2 were evaluated with direct testing on the Xpert Xpress CoV-2 plus. Potentially interfering substances in the nasal passage and nasopharynx may include, but are not limited to: blood, nasal secretions or mucus, and nasal and throat medications used to relieve congestion, nasal dryness, irritation, or asthma and allergy symptoms, as well as antibiotics and antivirals.

Positive and negative samples were prepared in simulated nasopharyngeal swab (NPS)/ anterior nasal swab (NS) matrix. Negative samples (N = 8) were tested in the presence of each substance to determine the effect on the performance of the sample processing control (SPC). Positive samples (N = 8) were tested per substance with SARS-CoV-2 virus spiked at 3x the LoD. The controls were samples with SARS-CoV-2 virus spiked at 3x LoD into simulated NPS/ NS matrix containing no potentially interfering substance. The substances, with active ingredients, that were evaluated are listed in Table 12. For substances that resulted in an INVALID test result, the concentration of the substance was reduced by half and re-tested. The results for the negative and positive samples are presented in Table 13 and Table 14 respectively.

Table 12. Potentially Interfering Substances Tested

Substance ID	Substance/Class	Substance/Active Ingredient	Concentrations Tested
No substance	Control	Simulated NPS/NS Matrix	100% (v/v)
Afrin	Nasal Spray	Oxymetazoline (0.05%)	15% (v/v)
Albuterol Sulfate	Beta-adrenergic bronchodilator	Albuterol Sulfate (5mg/mL)	0.83 mg/mL (equivalent to 1 dose per day)
BD Universal Transport Medium	Transport Media	BD Universal Transport Medium	100% (v/v)
Blood	Blood	Blood (Human)	2% (v/v)
Copan Swab M	Transport Media	Copan Swab M	100% (v/v)
FluMist	FluMist®	Live intranasal influenza virus vaccine	6.7% (v/v)
Fluticasone Propionate Nasal Spray	Nasal corticosteroid	Fluticasone Propionate	5 µg/mL; 2.5 µg/mL
Ibuprofen	Analgesic (nonsteroidal anti-inflammatory drugs (NSAID))	Ibuprofen	21.9 mg/dL
Menthol	Throat lozenges, oral anesthetic and analgesic	Benzocaine, Menthol	1.7 mg/mL
Mucin type II	Mucin	Purified Mucin protein (Porcine submaxillary gland, type II)	0.1% (w/v); 0.05% (w/v)
Mucin type I-S	Mucin	Purified Mucin protein (Bovine submaxillary gland, type I-S)	2.5 mg/mL; 1.25 mg/mL
Mupirocin	Antibiotic, nasal ointment	Mupirocin (2%)	10 mg/mL
Human peripheral blood mononuclear cells (PBMC)	Human peripheral blood mononuclear cells (PBMC)	Human peripheral blood mononuclear cells (PBMC)	1x10 ³ cells/µL
PHNY	Nasal Drops	Phenylephrine (1%)	15% (v/v)
Remel M4RT	Transport Media	Remel M4RT	100% (v/v)
Remel M5	Transport Media	Remel M5	100% (v/v)

Substance ID	Substance/Class	Substance/Active Ingredient	Concentrations Tested
Saline	Saline Nasal Spray	Sodium Chloride (0.65%)	15% (v/v)
Snuff	Tobacco	Nicotine	1% (w/v); 0.5% (w/v)
Tamiflu	Anti-viral drugs	Zanamivir	7.5 mg/mL
Tobramycin	Antibacterial, systemic	Tobramycin	4 µg/mL
Zicam	Nasal Gel	Luffa operculata, Galphimia glauca, Histaminum hydrochloricum Sulfur (0.05%)	15% (w/v)
Zinc	Zinc supplement	Zinc Gluconate	0.1 µg/mL

The results from the study (Table 13) show that all 22 of the potentially interfering substances at the concentrations tested showed no clinically significant interference on assay performance. For substances that reported an INVALID test result (fluticasone propionate (positive and negative), mucin type II (negative only), mucin type I-S (negative only), Snuff (negative only), the concentration of the substance was decreased by half and no interference was observed.

Table 13. SARS-CoV-2 Negative Samples Tested in the Presence of Potentially Interfering Substances

Substance	Concentration Tested	Number of Correct Results / Number Tested
Simulated NPS/NS Matrix (No substance)	100% (v/v)	8/8
Afrin	15% (v/v)	8/8
Albuterol Sulfate	0.83 mg/mL	8/8
BD Universal Transport Medium	N/A	8/8
Blood	2% (v/v)	8/8
Copan Swab M	N/A	8/8
FluMist®	6.7% (v/v)	8/8
Fluticasone Propionate Nasal Spray	5 µg/mL	7/8 ^a
	2.5 µg/mL	8/8 ^b
Ibuprofen	21.9 mg/dL	8/8
Menthol	1.7 mg/mL	8/8
Mucin (Type II)	0.1% (w/v)	7/8 ^a
	0.05% (w/v)	8/8 ^b
Mucin (Type I-S)	2.5 mg/mL	7/8 ^a
	1.25 mg/mL	8/8 ^a
Mupirocin	10 mg/mL	8/8
Human Peripheral Blood Mononuclear Cells (PBMC)	1x10 ³ cells/µL	8/8
PHNY	15% (v/v)	8/8

Remel M4RT	N/A	8/8
Remel M5	N/A	8/8
Saline	15% (v/v)	8/8
Snuff	1% (w/v)	7/8 ^a
	0.5% (w/v)	8/8 ^a
Tamiflu	7.5 mg/mL	8/8
Tobramycin	4 µg/mL	8/8
Zicam	15% (w/v)	8/8
Zinc	0.1 µg/mL	8/8

^a One of 8 replicates reported INVALID for fluticasone propionate nasal spray, mucin type II, mucin type I-S, and Snuff.

^b For each of the four substances that reported INVALID (fluticasone propionate nasal spray, mucin type II, mucin type I-S, and Snuff), the concentration of each substance was decreased by half and tested with n=8 cartridges such that 8/8 replicates reported valid test results of "SARS-CoV-2 NEGATIVE".

Table 14. SARS-CoV-2 Positive Samples Tested in the Presence of Potentially Interfering Substances

Substance	Concentration Tested	Number of Correct Results/Number Tested			
		SARS-CoV-2 (USA/WA/1/2020)	E	N2	RdRP
Control Simulated NPS/ NS Matrix (No substance)	100% (v/v)	8/8	8/8	8/8	8/8
Afrin	15% (v/v)	8/8	8/8	8/8	8/8
Albuterol Sulfate	0.83 mg/mL	8/8	8/8	8/8	8/8
BD Universal Transport Medium	N/A	8/8	8/8	8/8	8/8
Blood	2% (v/v)	8/8	8/8	8/8	8/8
Copan 3U045N.PH (Cepheid Swab/M)	N/A	8/8	8/8	8/8	8/8
FluMist	6.7% (v/v)	8/8	8/8	8/8	8/8
Fluticasone Propionate Nasal Spray	5 µg/mL	7/8 ^a	7/8 ^a	7/8 ^a	7/8 ^a
	2.5 µg/mL	8/8 ^b	8/8 ^b	8/8 ^b	8/8 ^b
Ibuprofen	21.9 mg/dL	8/8	8/8	8/8	8/8
Menthol	1.7 mg/mL	8/8	8/8	8/8	8/8
Mucin (Type II)	0.1 % (w/v)	8/8	8/8	8/8	8/8
Mucin (Type I-S)	2.5mg/mL	8/8	8/8	8/8	8/8
Mupirocin	10 mg/mL	8/8	8/8	8/8	8/8
Human peripheral blood mononuclear cells (PBMC)	1x10 ³ cells/µL	8/8	8/8	8/8	8/8
PHNY	15% (v/v)	8/8	8/8	8/8	8/8
Remel M4RT	N/A	8/8	8/8	8/8	8/8
Remel M5	N/A	8/8	8/8	8/8	8/8

Substance	Concentration Tested	Number of Correct Results/Number Tested			
		SARS-CoV-2 (USA/WA/1/2020)	E	N2	RdRP
Saline	15% (v/v)	8/8	8/8	8/8	8/8
Snuff	1% (w/v)	8/8	8/8	8/8	8/8
Tamiflu	7.5 mg/mL	8/8	8/8	8/8	8/8
Tobramycin	4 µg/mL	8/8	8/8	8/8	8/8
Zicam	15% (w/v)	8/8	8/8	8/8	8/8
Zinc	0.1 µg/mL	8/8	8/8	8/8	8/8

^a With 5 µg/mL of Fluticasone propionate nasal spray, one of 8 replicates reported **INVALID**. No clinically significant difference was observed between the control mean Ct for each target gene and the test mean Ct for each target gene.

^b For the substance that reported **INVALID** (fluticasone propionate nasal spray), the concentration was decreased by half and no interference was observed.

23.6 Carry-Over Contamination

A study was conducted to assess whether the single-use, self-contained Xpert Xpress CoV-2 plus cartridge prevents specimen and amplicon carryover by testing a negative sample immediately after testing of a very high positive sample in the same GeneXpert module. The negative sample used in this study consisted of simulated NPS/NS matrix and the positive sample consisted of high SARS-CoV-2 virus concentration (inactivated SARS-CoV-2 USA-WA1/2020 at 5e4 copies/mL) seeded into negative NPS/NS matrix. The negative sample was tested in a GeneXpert module at the start of the study. Following the initial testing of the negative sample, the high positive sample was processed in the same GeneXpert module immediately followed by another negative sample. This was repeated 20 times in the same module, resulting in 20 positives and 21 negatives for the module. The study was repeated using a second GeneXpert module for a total of 40 positive and 42 negative samples. All 40 positive samples were correctly reported as **SARS-CoV-2 POSITIVE** and all 42 negative samples were correctly reported as **SARS-CoV-2 NEGATIVE** with the Xpert Xpress CoV-2 plus test. No specimen or amplicon carry-over contamination was observed in this study.

24 References

- Centers for Disease Control and Prevention. <https://www.cdc.gov/coronavirus/2019-ncov/index.html>. Accessed February 9, 2020.
- bioRxiv. (<https://www.biorxiv.org/content/10.1101/2020.02.07.937862v1>). Accessed March 3, 2020.
- Centers for Disease Control and Prevention. Biosafety in Microbiological and Biomedical laboratories (refer to latest edition). <http://www.cdc.gov/biosafety/publications/>
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- REGULATION (EC) No 1272/2008 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 16 December 2008 on the classification labeling and packaging of substances and mixtures amending and repealing, List of Precautionary Statements, Directives 67/548/EEC and 1999/45/EC (amending Regulation (EC) No 1907/2007).
- Occupational Safety and Health Standards, Hazard Communication, Toxic and Hazard Substances (March 26, 2012) (29 C.F.R., pt. 1910, subpt. Z).

25 Cepheid Headquarters Locations

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26 Technical Assistance

Before Contacting Us

Collect the following information before contacting Cepheid Technical Support:

- Product name
- Lot number
- Serial number of the instrument
- Error messages (if any)
- Software version and, if applicable, Computer Service Tag Number

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Contact information for all Cepheid Technical Support offices is available on our website: www.cepheid.com/en_US/support/contact-us

27 Table of Symbols

Symbol	Meaning
	Catalog number
	<i>In vitro</i> diagnostic medical device
	Do not reuse
	Batch code
	Consult instructions for use
	Caution
	Manufacturer
	Country of manufacture
	Contains sufficient for <i>n</i> tests
	Control
	Expiration date
	Temperature limitation
	Biological risks
	For prescription use only



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For use under Emergency Use Authorization (EUA) Only

28 Revision History

Description of Changes: 302-7069, Rev. A to B

Purpose: Amendment to the Emergency Use Authorization of the Xpert Xpress CoV-2 plus

Section	Description of Change
Throughout	Updated format for Instructions for Use
18	Corrected Table 1 formatting error
23.2	Updated <i>in silico</i> inclusivity with data from analysis as of June 30, 2022
23.3	Updated Table 9 to include additional high priority microorganisms analyzed by <i>in silico</i> exclusivity analysis
23.5	Corrected the number of replicates reported for Zinc in Table 13