

Xpert[®] Xpress CoV-2 *plus* For Australia

REF XP3SARS-COV2-10

Instructions for Use

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

IVD

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See Section 27, Revision History for a description of changes.

Xpert[®] Xpress CoV-2 *plus* For Australia

IVD

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 or anterior nasal swab specimens from individuals suspected of COVID-19 by their healthcare provider.

Testing of nasopharyngeal 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 for use at the Point of Care (POC), i.e., in patient care settings.

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.

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.

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 or anterior 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 Xpress System User's Guide*.

The Xpert Xpress CoV-2 *plus* test includes reagents for the detection of RNA from SARS-CoV-2 in nasopharyngeal swab or anterior nasal swab. 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 <i>plus</i> 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 protein stabilizer of bovine origin 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.
- Positive results are indicative of presence of SARS-CoV-2-RNA.
- 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.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.

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^{3,4}

- 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 and Section 12.2 for anterior nasal swab collection procedure.

Nasopharyngeal swab and anterior 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 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.

Refer to the WHO Laboratory Biosafety Guidance Related to the Coronavirus Disease 2019 (COVID-19).

[https://www.who.int/publications-detail/laboratory-biosafety-guidance-related-to-coronavirus-disease-2019-\(covid-19\)](https://www.who.int/publications-detail/laboratory-biosafety-guidance-related-to-coronavirus-disease-2019-(covid-19))

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.

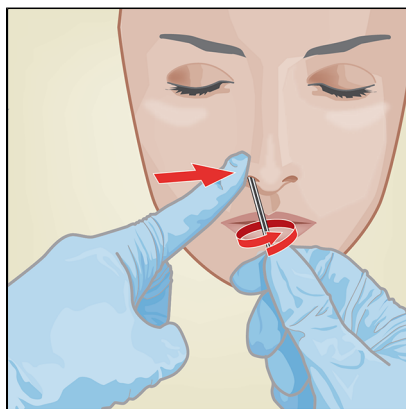


Figure 3. Anterior Nasal Swab Collection for Second Nostril

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.

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 4).

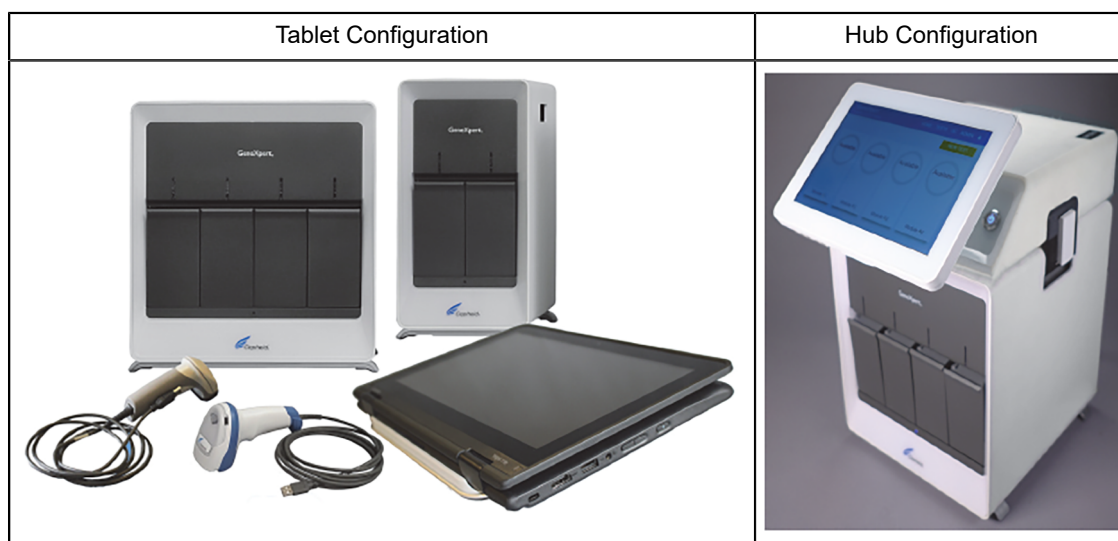


Figure 4. Tablet and Hub System Configurations

- 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 5).



Figure 5. 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 6).

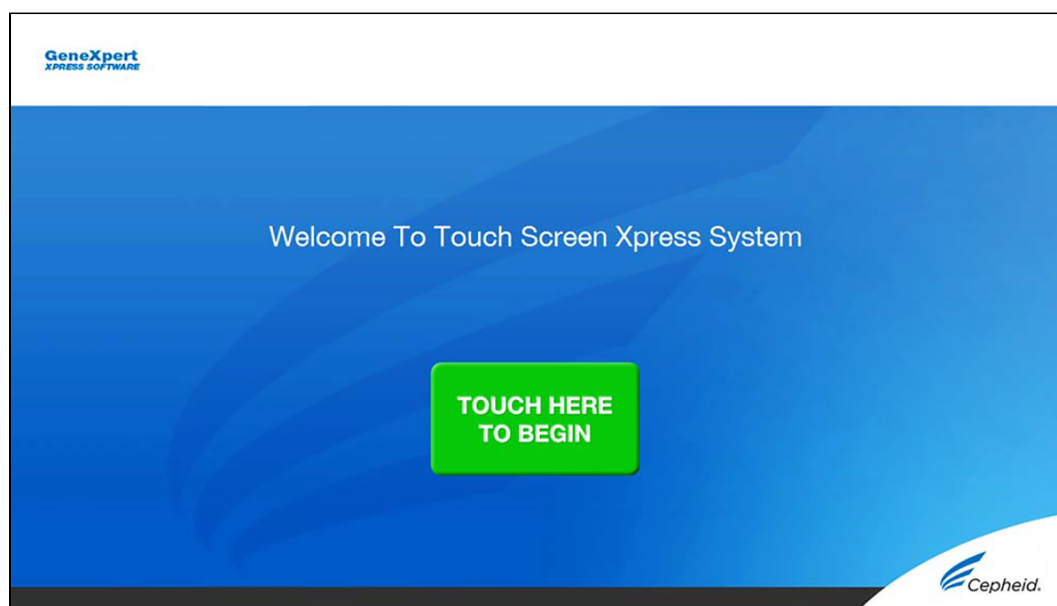


Figure 6. Welcome Screen

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 7) to run a patient specimen or an external control.

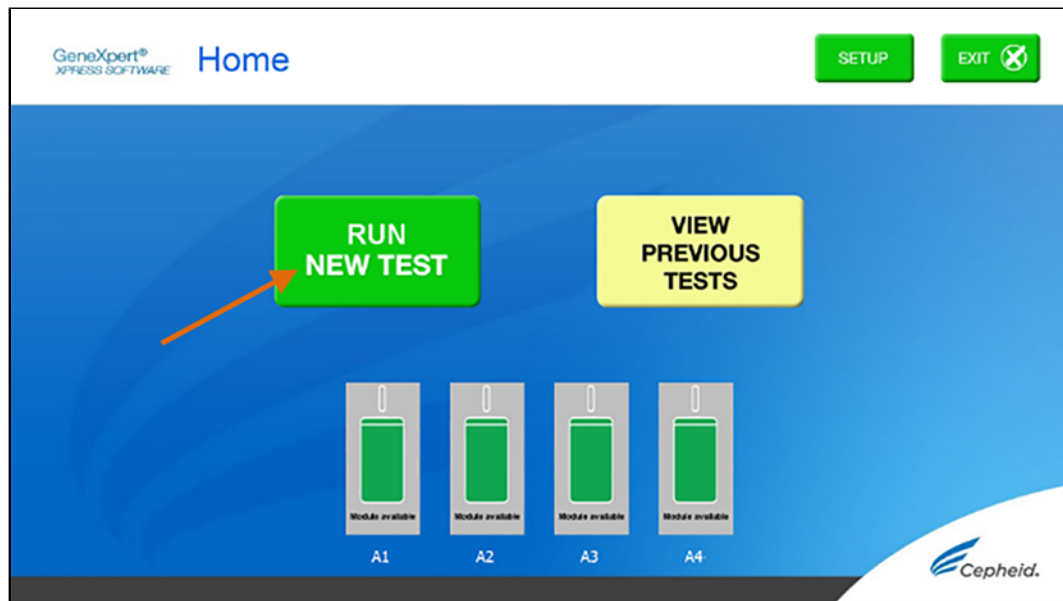


Figure 7. RUN NEW TEST button on Home Screen (GeneXpert Xpress IV screen shown)

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 8.
 - Select **Xpert Xpress CoV-2 plus**.

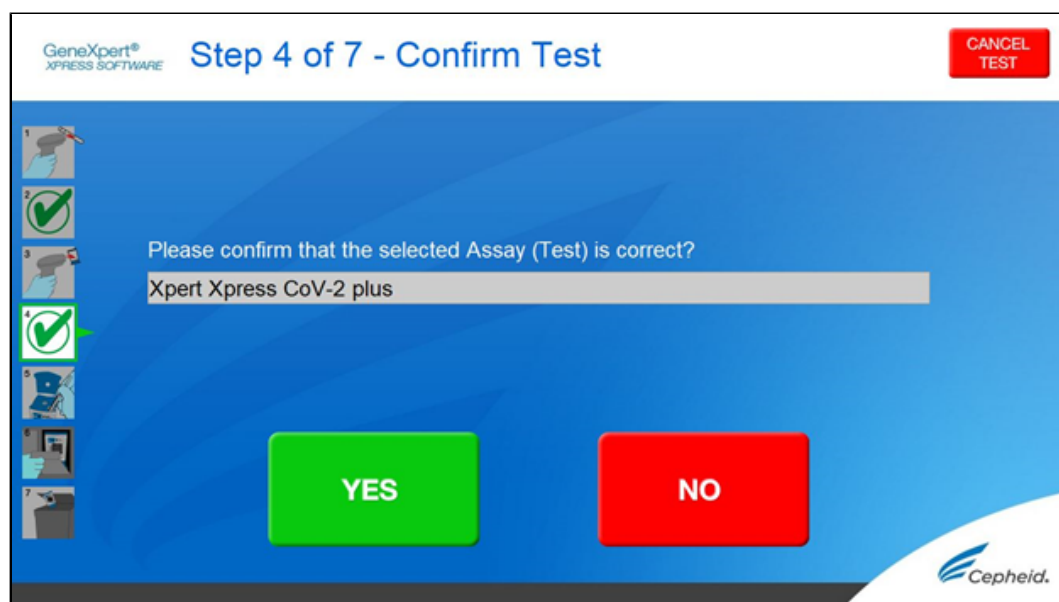


Figure 8. ConfirmTest Screen - Select Assay

4. Confirm the selected test from the **Select Assay** menu (shown in Figure 9 below) and touch **YES** if the displayed information is correct. Enter your user name and password if prompted.

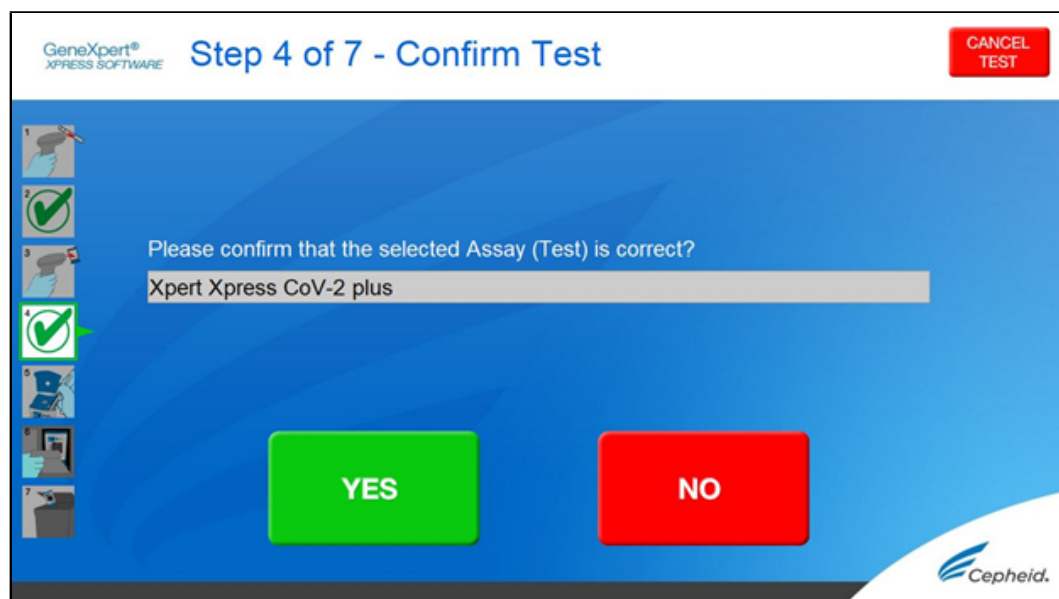


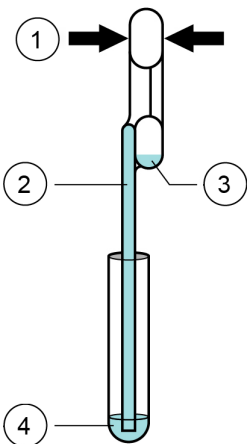
Figure 9. Confirm Test Screen

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.

9. 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 10).



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

Figure 10. Transfer Pipette

10. 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.
11. 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 11. Some liquid may remain in the overflow reservoir. Dispose of the used pipette.

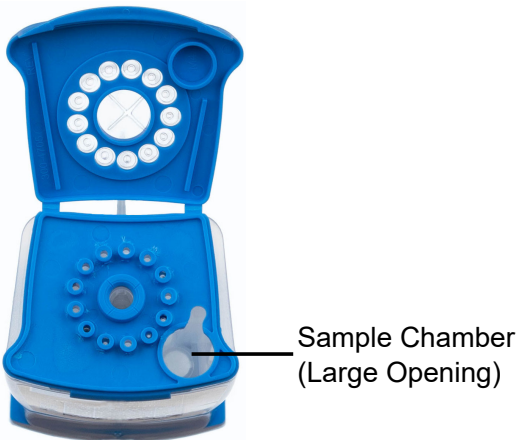


Figure 11. Xpert Xpress CoV-2 *plus* Cartridge (Top View)

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.

12. 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 12.

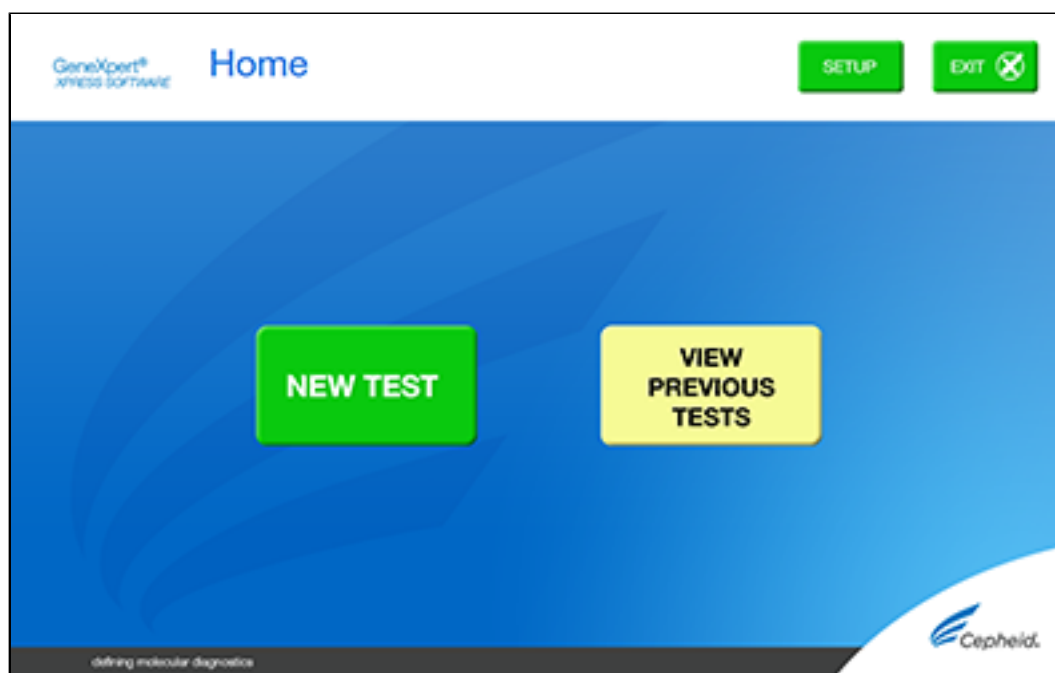


Figure 12. VIEW PREVIOUS TESTS button on Home Screen

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 13 to view results.

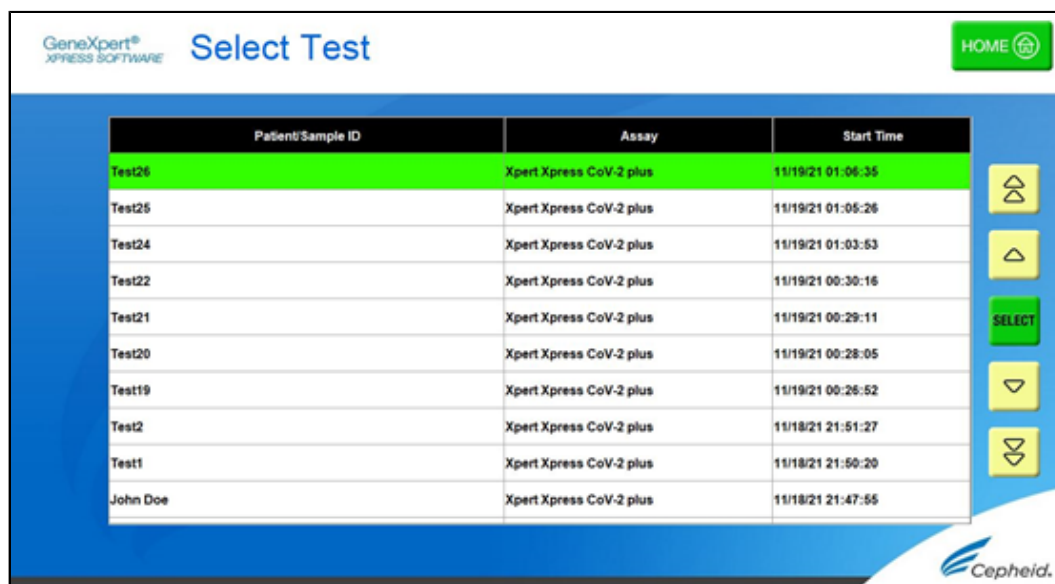


Figure 13. SELECT button

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 14).

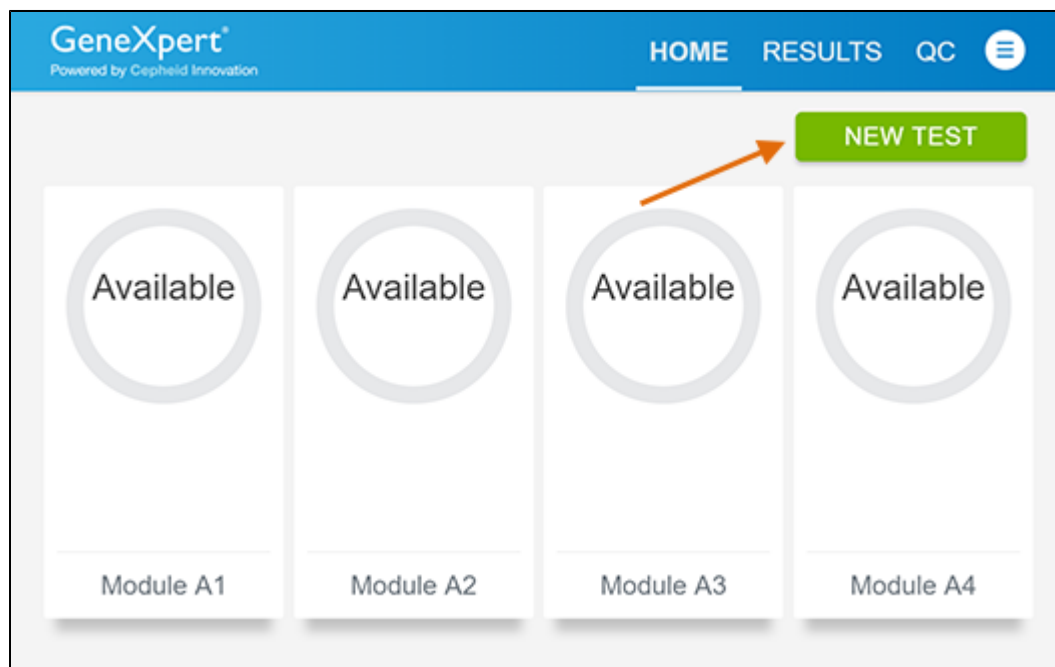


Figure 14. Home Screen

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 15).
If Patient Information is not configured, the **Sample ID** screen appears.
4. Skip to Section 16.2 if the **Sample ID** screen appears.

Figure 15. 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 16).
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.

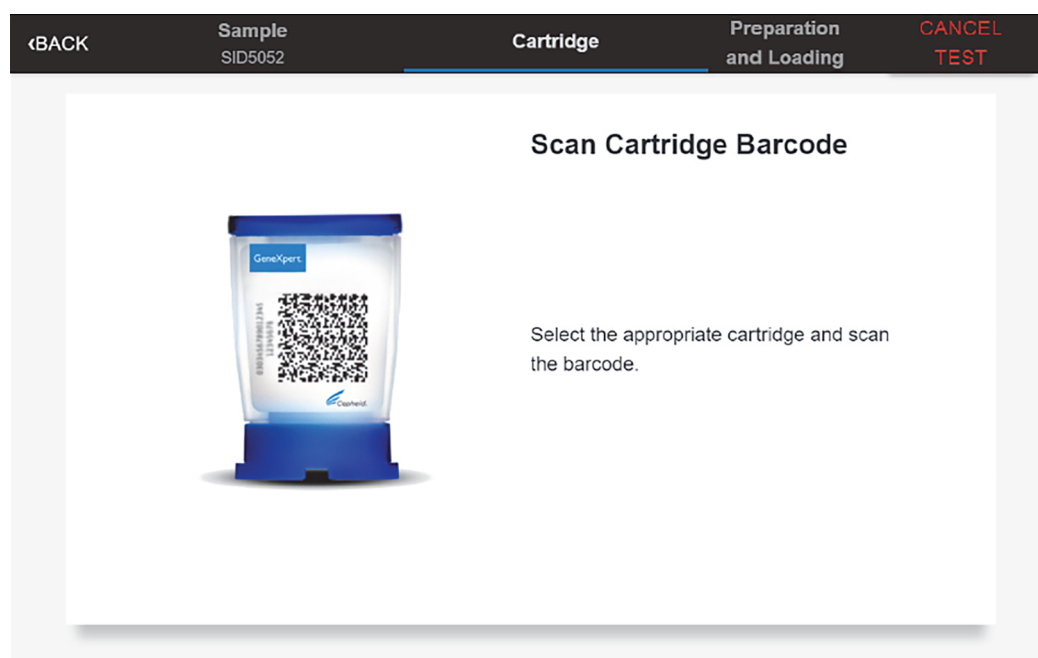


Figure 16. Scan Cartridge Barcode Screen

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 17).

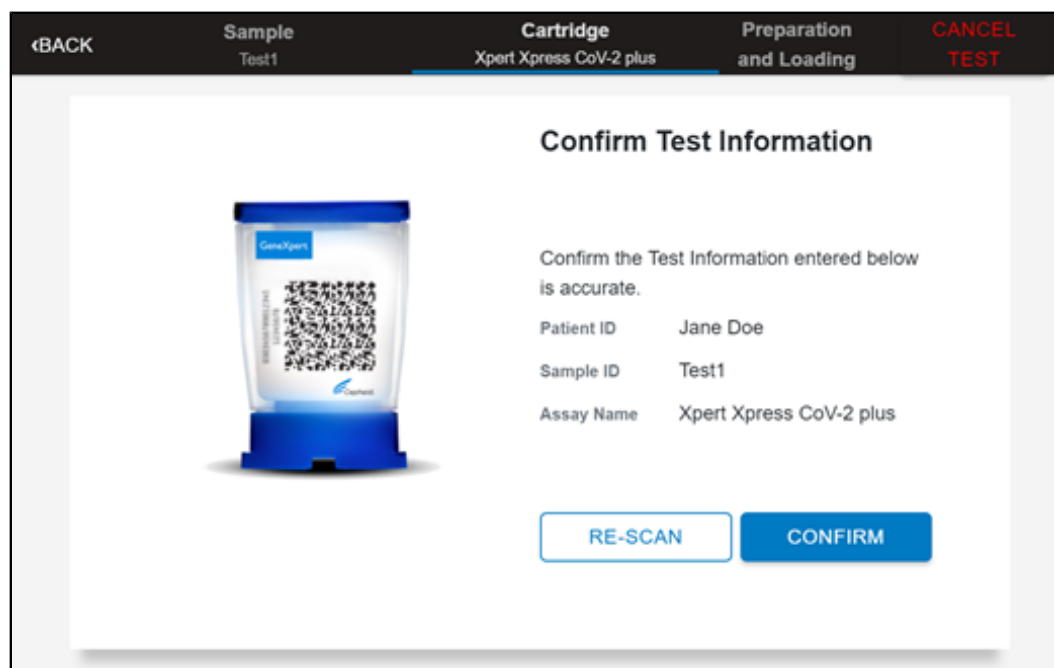
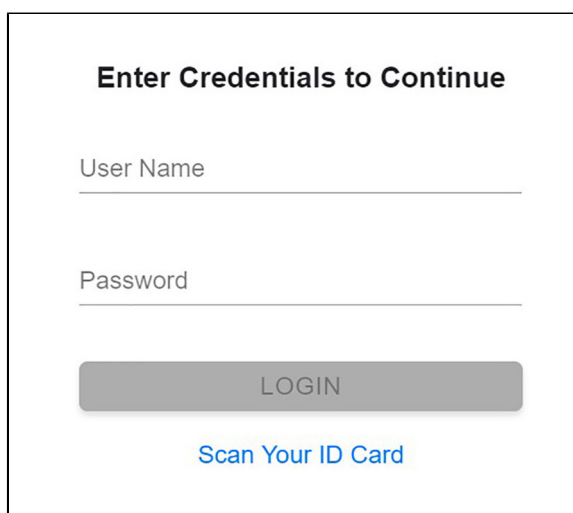


Figure 17. Confirm Test Information Screen

6. Touch **CONFIRM** if the displayed information is correct.
7. Depending on your configuration, the Enter Credentials to Continue screen may appear (see Figure 18). If enabled, you may log in by scanning your institutional ID. Otherwise, manually enter your User Name and Password and touch **LOGIN** to continue.

The screen displays the title "Enter Credentials to Continue" at the top. Below the title are two input fields: "User Name" and "Password". Under the "Password" field is a grey button labeled "LOGIN". At the bottom of the screen is a blue link that says "Scan Your ID Card".

Enter Credentials to Continue

User Name

Password

LOGIN

Scan Your ID Card

Figure 18. Enter Credentials to Continue Screen

8. The Cartridge Preparation screen appears (see Figure 19).

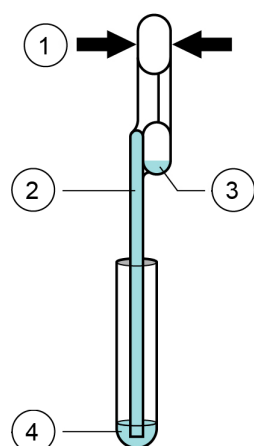


Figure 19. Cartridge Preparation Screen

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 20).



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

Figure 20. 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 20). 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 µL) into the large opening (Sample Chamber) of the cartridge shown in Figure 21. Some liquid may remain in the overflow reservoir. Dispose of the used pipette.



Figure 21. 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 22).

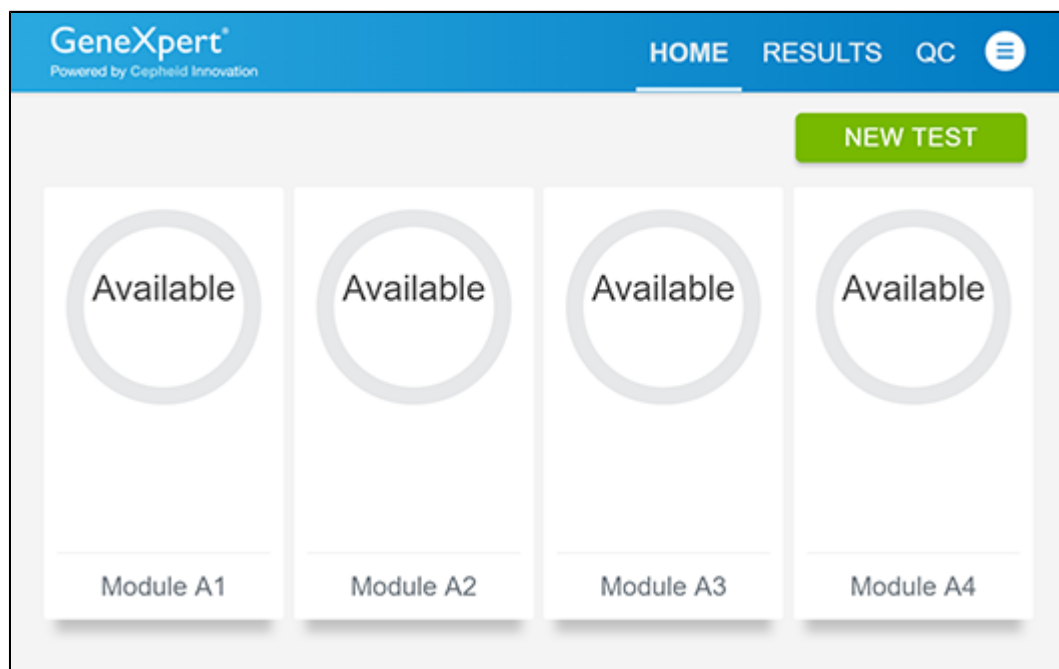


Figure 22. Home Screen

2. The Quality Control screen appears. Touch RUN QC POSITIVE Test, RUN QC NEGATIVE TEST or RUN PROFICIENCY TEST option (Figure 23).



Figure 23. 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 24).

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.

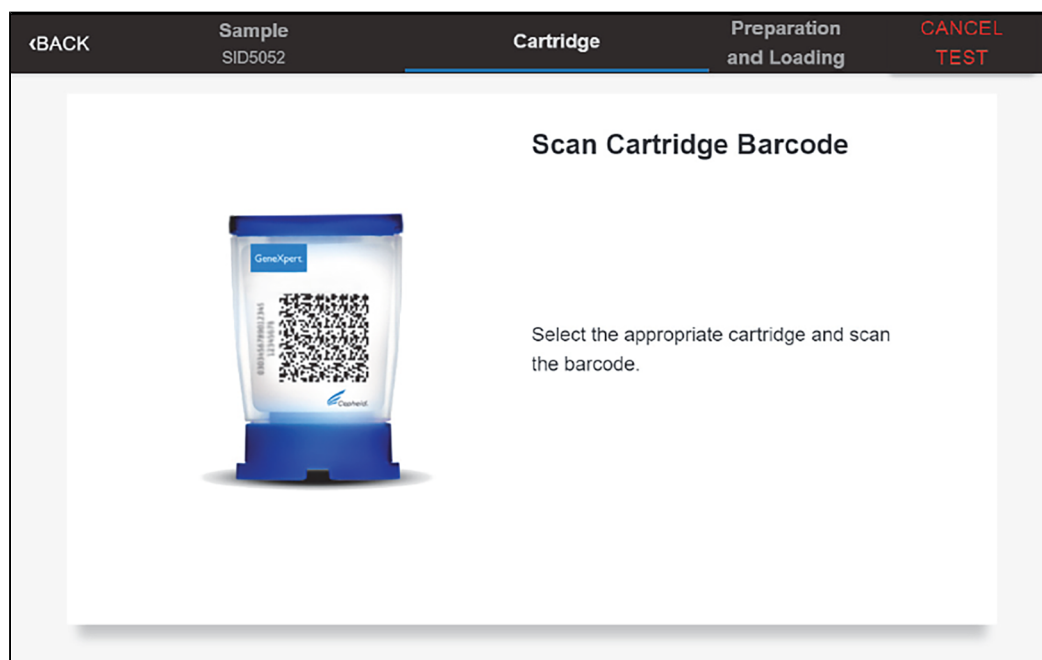


Figure 24. Scan Cartridge Barcode Screen

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 25).

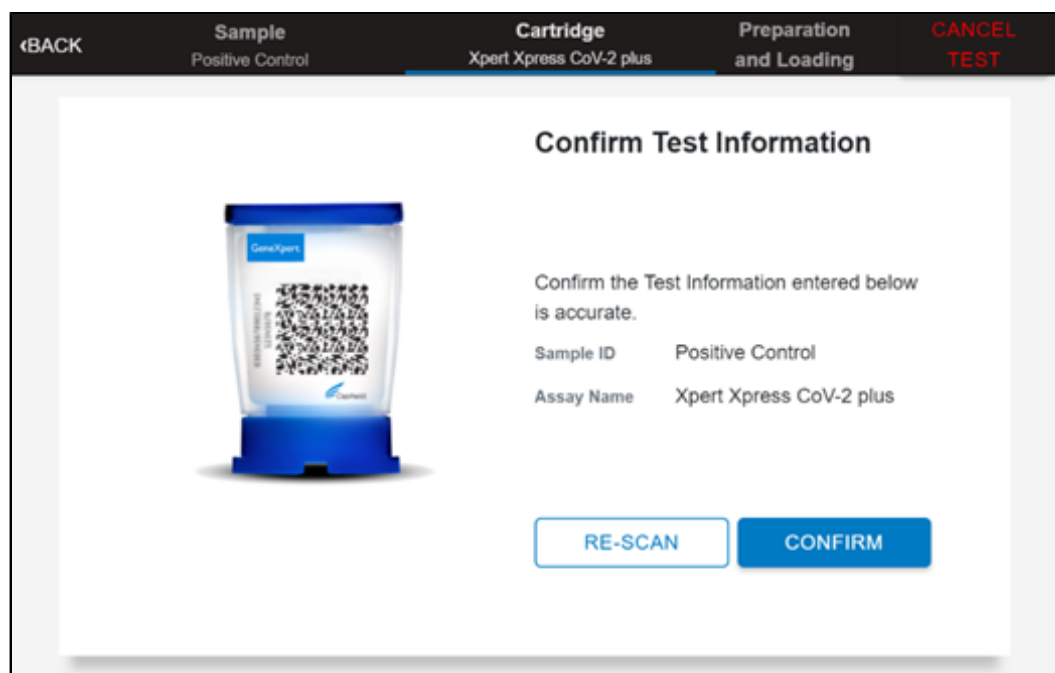


Figure 25. Confirm Test Information

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 26).

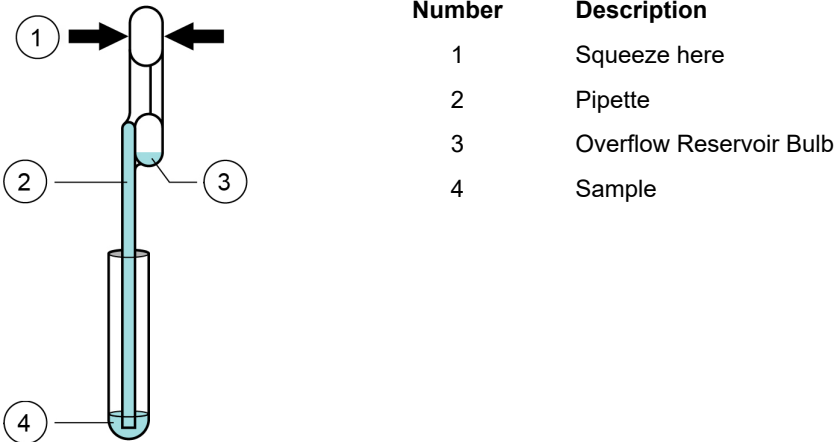


Figure 26. Transfer Pipette

- 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 26). 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 27. Dispose of the used pipette.

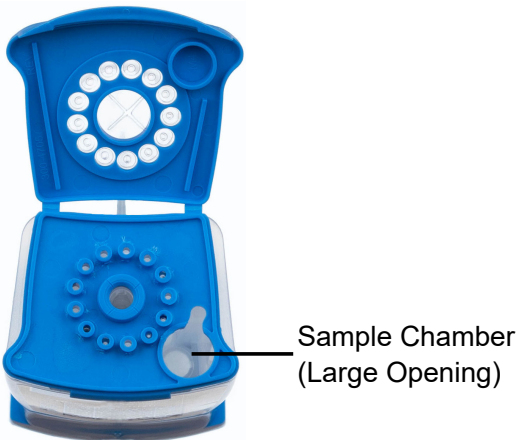


Figure 27. Xpert Xpress CoV-2 plus Cartridge (Top View)

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 28).
2. Open the module door with the flashing green light.

Flashing Green Light



Figure 28. 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 Starting a Test, Section 16.2 Preparing the Specimen, and Section 16.4 Loading the Cartridge.
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 29).

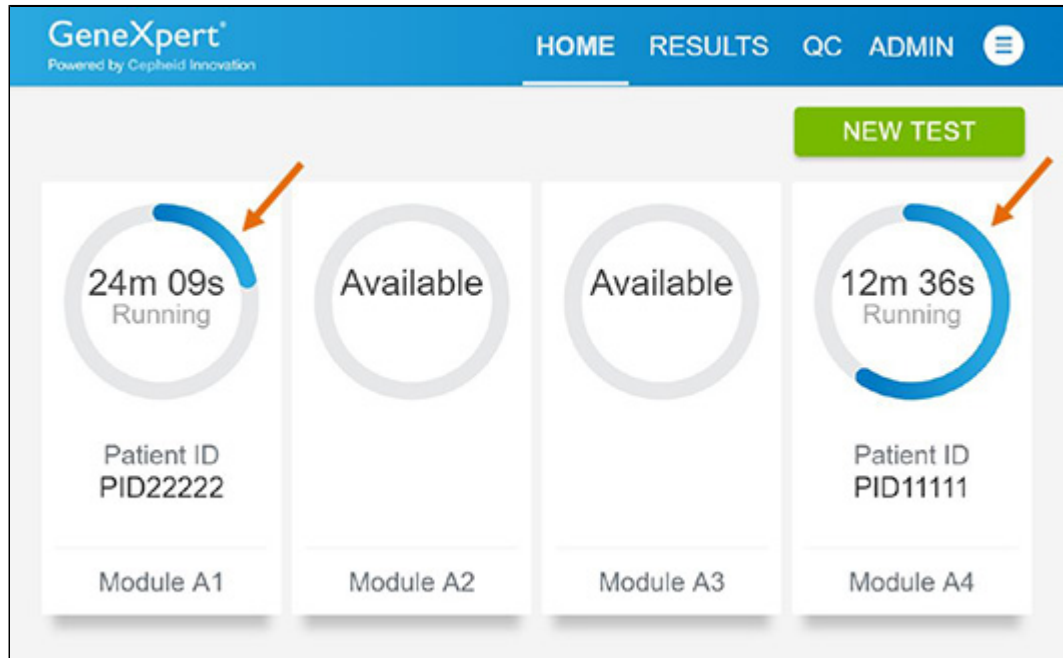


Figure 29. Home Screen showing Two Tests Running

- After a test has completed, the module icon text changes to **Complete** (see Figure 30). Touch **Complete View Results** to view test results.

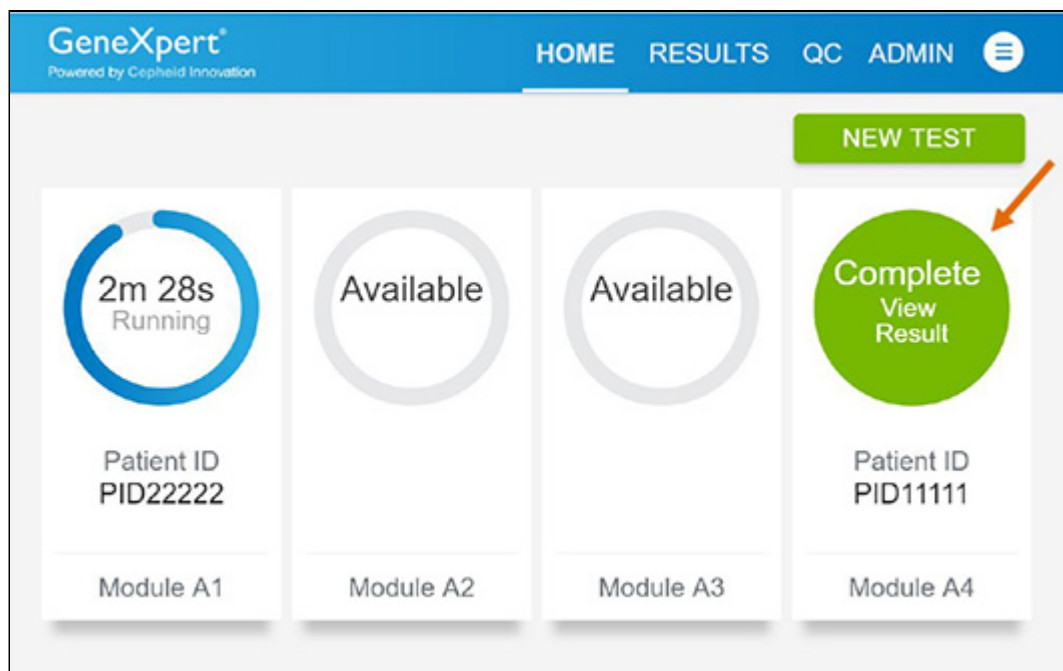


Figure 30. Home Screen with One of Two Tests Completed

16.6 Viewing Test Results

- Touch the **RESULTS** button located on the panel at the top of the screen (see Figure 31). The Results screen appears (see Figure 32). 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,

| 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 31. Results Screen

2. Touch the desired result to open the Test Result screen (see Figure 32).
3. To view test report, touch the **REPORT** button then swipe across the screen from left to right to minimize screen and view report.

Test Completed

Module A3

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

Test Disclaimer

Test Methodology: RT-PCR For In Vitro Diagnostic Use Only.
For use under the Emergency Use Authorization (US).

Figure 32. 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 Instrument 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 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 Clinical Evaluation

21.1 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 swab (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 SARS-CoV-2 RT-PCR test (listed in ARTG) as comparator method 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 RT-PCR comparator method 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%) |

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 Analytical Performance

22.1 Analytical Sensitivity (Limit of Detection)

22.1.1 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 NATrol 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 three clinical NPS matrices (UTM/VTM, saline, eNAT). The concentration level with observed hit rates greater than or equal to 95% in the 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 5).

Table 5. Xpert Xpress CoV-2 *plus* Limit of Detection for Nasopharyngeal Swab

| 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 |

| Concentration (copies/mL) | E gene | | | N2 gene | | | RdRP gene | | |
|------------------------------|------------|------------|---------|------------|------------|---------|------------|------------|---------|
| | # Positive | % Positive | Mean Ct | # Positive | % Positive | Mean Ct | # Positive | % Positive | Mean Ct |
| 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.

22.1.2 Analytical Sensitivity (Limit of Detection) for Nasal Swab

The analytical sensitivity of the Xpert Xpress CoV-2 *plus* test was first estimated by testing limiting dilutions of a NATrol inactivated SARS-CoV-2 virus in pooled negative clinical NS-UTM/VTM matrix, using two reagent lots and 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 LoD point estimates and 95% upper and lower confidence intervals (CI) for individual SARS-CoV-2 targets (E, N2 and RdRP) in clinical NS-UTM/VTM matrix were determined using Probit regression analysis and the point estimated LoD values were 97, 462 and 157 copies/mL for the E target, N2 target and RdRP target, respectively (Table 6). The estimated LoD value of the weakest target gene (N2) was verified using two lots of Xpert Xpress CoV-2 *plus* reagents in replicates of 20 for in clinical NS-UTM/VTM matrix. The claimed LoD is 462 copies/ mL.

Table 6. Xpert Xpress CoV-2 *plus* Limit of Detection for Nasal Swab

| Concentration (copies/mL) | E gene | | | N2 gene | | | RdRP gene | | |
|------------------------------|------------|------------|---------|------------|------------|---------|------------|------------|---------|
| | # Positive | % Positive | Mean Ct | # Positive | % Positive | Mean Ct | # Positive | % Positive | Mean Ct |
| 10 ^a | 10 | 50 | 39.1 | 0 | 0 | 0 | 8 | 40 | 41.7 |
| 20 | 9 | 45 | 39.5 | 0 | 0 | 0 | 8 | 40 | 41.3 |
| 30 | 16 | 80 | 38.2 | 0 | 0 | 0 | 8 | 40 | 41.4 |
| 40 | 17 | 85 | 38.1 | 0 | 0 | 0 | 15 | 75 | 41.0 |
| 50 ^a | 20 | 100 | 38.1 | 0 | 0 | 0 | 12 | 60 | 40.5 |
| 70 ^a | 17 | 85 | 37.5 | 1 | 5 | 44.8 | 14 | 70 | 39.9 |
| 100 | 20 | 100 | 37.2 | 1 | 5 | 41.2 | 20 | 100 | 40.3 |
| 200 | 20 | 100 | 35.6 | 9 | 45 | 40.1 | 20 | 100 | 38.0 |
| 300 | 19 | 95 | 34.9 | 13 | 65 | 39.7 | 20 | 100 | 37.6 |

| Concentration (copies/mL) | E gene | | | N2 gene | | | RdRP gene | | |
|------------------------------|------------|------------|---------|------------|------------|---------|------------|------------|---------|
| | # Positive | % Positive | Mean Ct | # Positive | % Positive | Mean Ct | # Positive | % Positive | Mean Ct |
| 400 | 20 | 100 | 34.3 | 20 | 100 | 38.8 | 20 | 100 | 36.7 |
| 500 | 20 | 100 | 34.1 | 19 | 95 | 38.6 | 20 | 100 | 36.6 |
| 600 | 20 | 100 | 33.8 | 20 | 100 | 38.4 | 20 | 100 | 36.2 |
| 700 | 20 | 100 | 33.6 | 20 | 100 | 38.1 | 20 | 100 | 36.1 |

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

22.2 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 |
|----------------------------|---|-------------------------|----------------------|-----------------------|
| 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 10,178,602 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 |
| 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 | 3/3 | 3/3 | 3/3 |
| 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 |

| 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 |
| 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

22.3 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> |

| Microorganisms from the Same Genetic Family | High Priority Organisms |
|---|-------------------------------------|
| | <i>Haemophilus influenzae</i> |
| | <i>Lactobacillus</i> sp. |
| | <i>Legionella non-pneumophila</i> |
| | <i>Legionella pneumophila</i> |
| | <i>Leptospira</i> |
| | <i>Moraxella catarrhalis</i> |
| | <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</i> sp |
| | <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 |
| 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 | | | | |

| 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 |
| 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 | | | | |
| 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 | 1.1e6 CFU/mL | NEG | 0/3 | 0/3 | 0/3 |
| <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</i> (avirulent) | 11 | 1.1e6 CFU/mL | NEG | 0/3 | 0/3 | 0/3 |
| <i>Mycoplasma pneumoniae</i> | | 1.1e6 CFU/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 |
| <i>Neisseria mucosa</i> | | 1.1e6 CFU/mL | | | | |
| <i>Propionibacterium acnes</i> (= <i>Cutibacterium acnes</i>) Z144 | | 1.1e6 CFU/mL | | | | |
| <i>Pseudomonas aeruginosa</i> , Z139 | | 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 |
| <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 | | | | |
| <i>Pneumocystis jirovecii</i> (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 meningitidis</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

22.4 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 Type 1A 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.

22.5 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 |

| Substance ID | Substance/Class | Substance/Active Ingredient | Concentrations Tested |
|---|---|--|----------------------------|
| 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) |
| 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 ^b |
| 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 ^b |
| 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 |

| Substance | Concentration Tested | Number of Correct Results/Number Tested | | | |
|---|----------------------------|---|-----|-----|------|
| | | SARS-CoV-2 (USA/WA/1/2020) | E | N2 | RdRP |
| 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 |
| 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.

22.6 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.

22.7 Reproducibility

The reproducibility of the Xpert Xpress CoV-2 *plus* test was established at three (3) sites using a 3-member panel including one negative sample, one low positive (~1.5X LoD) sample and one moderate positive (~3X LoD) sample. The negative sample consisted of simulated matrix without target microorganism or target RNA. The positive samples were contrived samples in a simulated matrix using inactivated NATtrol SARS-CoV-2 (ZeptoMetrix).

Testing was conducted over six (6) days, using three (3) lots of Xpert Xpress CoV-2 *plus* cartridges at three (3) participating sites each with two (2) operators to yield a total of 144 observations per panel member (3 Sites x 2 Operators x 3 Lots x 2 Days/Lot x 2 Runs x 2 Replicates = 144 observations/panel member). The results from the study are summarized in Table 15.

Table 15. Summary of the Reproducibility Results - % Agreement

| Panel Member | Site 1 | | | Site 2 | | | Site 3 | | | % Total Agreement and 95% CI by Panel Member |
|---------------------------|-----------------|------------------|------------------|-----------------|-----------------|-----------------|-----------------|------------------------------|-----------------|--|
| | Op1 | Op2 | Site | Op1 | Op2 | Site | Op1 | Op2 | Site | |
| Negative | 100% (24/24) | 95.8% (23/24) | 97.9% (47/48) | 100% (24/24) | 100% (24/24) | 100% (48/48) | 100% (24/24) | 100% (23/23) ^a | 100% (47/47) | 99.3% (142/143) [96.1%-99.9%] |
| SARS-CoV-2 Low Pos | 100% (24/24) | 100% (24/24) | 100% (48/48) | 100% (24/24) | 100% (24/24) | 100% (48/48) | 100% (24/24) | 100% (24/24) | 100% (48/48) | 100% (144/144) [97.4%-100%] |
| SARS-CoV-2 Mod Pos | 100% (24/24) | 100% (24/24) | 100% (48/48) | 100% (24/24) | 100% (24/24) | 100% (48/48) | 100% (24/24) | 100% (24/24) | 100% (48/48) | 100% (144/144) [97.4%-100%] |

^a One sample was non-determinate on both initial and retest and was excluded from the analyses.

23 References

1. Centers for Disease Control and Prevention. <https://www.cdc.gov/coronavirus/2019-ncov/index.html>. Accessed February 9, 2020.
2. bioRxiv. (<https://www.biorxiv.org/content/10.1101/2020.02.07.937862v1>). Accessed March 3, 2020.
3. 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).
4. Occupational Safety and Health Standards, Hazard Communication, Toxic and Hazard Substances (March 26, 2012) (29 C.F.R., pt. 1910, subpt. Z).

24 Cepheid Headquarters Location

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25 Technical Assistance

Before Contacting Us

Collect the following information before contacting Cepheid Technical Support:














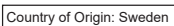
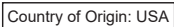
- Product name
- Lot number
- Serial number of the instrument
- Error messages (if any)
- Software version and, if applicable, Computer Service Tag Number

Australia

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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

26 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 |
|  | Country of Origin: Sweden |
|  | Country of Origin: United States of America |



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IVD

27 Revision History

Description of Changes: 303-2899, Rev. B to C

| Section | Description of Change |
|--|---|
| Materials Provided | Clarified the animal origin of the protein stabilizer used in the product. |
| Warnings and Precautions - Assay/ Reagent | Removed two cartridge images that do not apply to this product. |
| Analytical Performance - Analytical Sensitivity (Limit of Detection) for Nasopharyngeal Swab | <p>Corrections made based on source report:</p> <ul style="list-style-type: none"> Updated the number of clinical NPS matrices from 'two' to 'three' for LoD value determination. Replaced 'estimated LoD determination' with 'LoD determination' in the concentration level statement. |
| Potentially Interfering Substances | <p>Corrections made to Table 13 based on source report:</p> <ul style="list-style-type: none"> Mucin (Type I-S) - For 1.25 mg/mL concentration, the footnote for 'Number of Correct Results/Number Tested' is updated from 'a' to 'b'. Snuff - For 0.5% (w/v) mg/mL concentration, the footnote for 'Number of Correct Results/Number Tested' is updated from 'a' to 'b'. |
| Cepheid Headquarters Location | Removed the European Headquarters address. |
| Table of Symbols | Added the symbols for Country of Origin: Sweden and United States of America. |