

SARS-COV-2 (Coronavirus) Testing Protocol for PICTS using GeneXpert Systems

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Pacific
Community
Communauté
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World Health
Organization
Representative Office
for the South Pacific

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SARS-COV-2 (Coronavirus) Testing

1.0 Background:

The SARS-COV-2, the virus causing COVID-19 was detected as the causative agent for the cluster of pneumonia cases that were reported in Wuhan China on 31 December 2019 [1]. The novel coronavirus genome was first made publicly available on 22nd January 2020 [2]. On 30 January 2020 WHO declares this first outbreak of novel coronavirus a 'public health emergency of international concern' [3]. On 21 March 2020 the Cepheid Company manufacturing GeneXpert and cartridges received FDA Emergency Use Authorization for SARS-COV-2 Coronavirus testing [4]. The test is for use under the Emergency Use Authorization (EUA) only. The user should be trained in the procedure and to wear the appropriate protective attire for safety when handling patient samples. This test developed by Cepheid, is for nasopharyngeal swabs/or nasal wash/ aspirate specimens collected from individuals suspected of COVID-19 by their healthcare provider. The test is suitable for testing of nasopharyngeal swab and nasal wash/aspirate specimens only [5].

2.0 Principle of Test:

Nasopharyngeal swab specimen and/or nasal wash/aspirate specimen collected is placed into a viral transport tube containing 3 mL transport medium. The specimen is then 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 SARS-CoV-2 cartridge. The GeneXpert cartridge is loaded onto the GeneXpert Instrument System platform, which performs hands-off, automated sample processing, and real-time RT-PCR for detection of viral RNA specific for SARS-COV-2 [6].

3.0 Important Notes on Storage, Handling & Warnings: (adapted from Cepheid Quick Reference for Xpert® Xpress SARS-CoV-2 and GeneXpert Xpress System)

3.1 Specimen Collection, Transport, Storage and Handling

- Proper specimen collection, storage, and transport are critical to the performance of this test.
- Refer to **Annex 1: Nasopharyngeal Swab Collection**.
- All COVID-19 samples should be transported in biohazard zipped-lock bags with separate form compartment and placed in Bio Bottles.
- 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 handled using standard precautions. Guidelines for specimen handling are available from the U.S. Centers for Disease Control and Prevention [7] and the Clinical and Laboratory Standards Institute [8].
- Nasopharyngeal swab specimens can be stored at room temperature (15–30 °C) for up to 8 hours and refrigerated (2–8 °C) up to seven days until testing is performed on the GeneXpert Instrument Systems.
- Follow safety procedures set by your institution for working with chemicals and handling biological specimens.
- Wear gloves. Change gloves between processing each sample.

- Handling of samples and transferring into test cartridge should be carried out in well maintained and regularly serviced Class II Biosafety Cabinet.
- In the event of a spill of specimens or control; where possible isolate the area, wear gloves and quickly cover spills with absorbable disposable material (paper towels) to absorb spills and stop it from spreading. Pour adequate 10% hypochlorite solution (freshly prepared household chlorine bleach) on the tissue covering spills to inactivate the infectious agent, allow at least two minutes contact time, then carefully collect soaked tissues and dispose into biohazard waste bag. Thoroughly clean the contaminated area with a 10% hypochlorite solution. 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 decontamination, 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 or follow WHO guidelines on proper handling and disposal of medical waste.

3.2 Storage of GeneXpert Cartridges

- Store the Xpert Xpress SARS-CoV-2 cartridges at 2-28°C.

3.3 Materials Required but Not Provided

- GeneXpert Dx or GeneXpert Infinity systems (catalog number varies by configuration): GeneXpert instrument, computer, barcode scanner, operator manual.
- For GeneXpert Dx System: GeneXpert Dx software version 4.7b or higher.
- For GeneXpert Infinity-80 and Infinity-48s systems: Xpertise software version 6.4b or higher.

3.4 Materials Available but Not Provided

- SeraCare AccuPlex™ Reference Material Kit, catalog number 0505-0126 (Order Code CEPHEID)

3.5 Warnings

- DO NOT use a cartridge that is wet or has leaked
- DO NOT use a cartridge that has been dropped.
- DO NOT open a cartridge lid until you are ready to perform testing.
- DO NOT shake or tilt the cartridge after adding the sample.
- DO NOT reuse disposable pipettes or cartridges.
- DO NOT turn off or unplug the instrument while a test is in progress as this will stop the test.
- Do not use a cartridge that has a missing or damaged reaction tube.

3.6 Importing Assay Definition Files (ADF)

It is important to import ADF prior to proceeding with testing. To perform this procedure, use the assay definition CD provided inside the Cepheid GeneXpert assay kit and also refer to document titled **"Assay Import Instructions"** provided separately.

4.0 Method:

Please follow testing procedure according to type of configuration you have on your GeneXpert i.e for **Hub configuration, follow testing procedure outlined on pages 4- 13. For Tablet configuration, follow testing procedure shown on pages 14-23 of this SOP.**

4.1 Procedure for GeneXpert Xpress System (Hub configuration)

(adapted from Cepheid Quick Reference for Xpert® Xpress SARS-CoV-2 and GeneXpert Xpress System)

4.2 Starting the Software

- a. Put on a pair of clean gloves.
- b. Turn on the GeneXpert Xpress instrument.
- c. Turn on the Hub computer. The Windows lock screen appears. Swipe up to continue.
- d. Enter the Windows password and touch the arrow next to the password field.
- e. The GeneXpert Xpress Software login screen appears.
- f. Manually enter username and password in Step 2a, or if enabled, scan your ID card in Step 2b.

4.3 Enter Password

- a. Touch the Username field to display the virtual keyboard.
- b. Enter your username and password.
- c. Touch the X in the upper right of the virtual keyboard. Touch the Login button.

4.2 Scan ID Card (for countries with new Xpress GeneXpert)

If enabled, log in by scanning the barcode on your institutional ID, as shown below.



4.3 Home Screen Displays

The Home screen will display the module status and the NEW TEST button.

5.0 Testing Patient's Sample

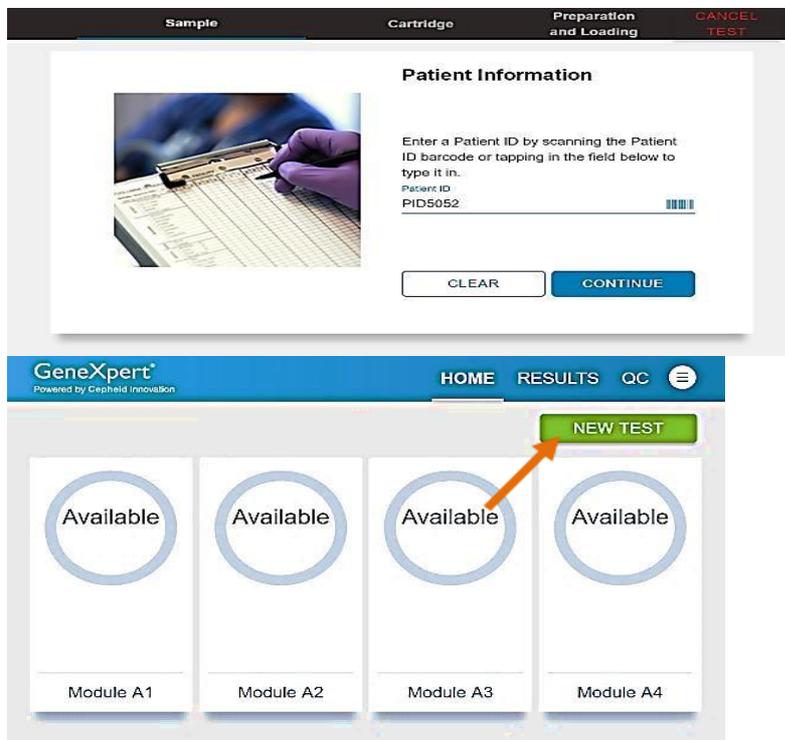
Before you begin

- a. Refer to the package insert for more information.
- b. Read through this entire Quick Reference Instructions before beginning a test.
- c. Instructions on how to prepare the specimen and the cartridge (presented below) are also shown in a video within the software.

- d. Start the test within 30 minutes of adding the specimen to the cartridge.
- e. The recommended environmental operating conditions for Xpert Xpress SARS-CoV-2 are 15-30°C, 20-80% relative humidity.

5.1 Start a test

- a. Touch NEW TEST on the Home screen
- b. Check that the specimen tube cap is closed.



5.2(a) Enter/Scan and touch CONTINUE.

Confirm Patient ID



5.2 (b) Enter/Scan and touch CONTINUE Confirm Sample ID

5.3 Scan and Confirm Cartridge

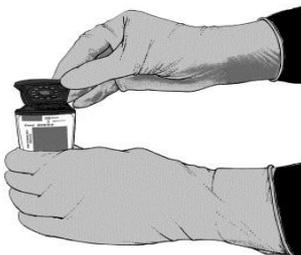




* If applicable enter your username and password

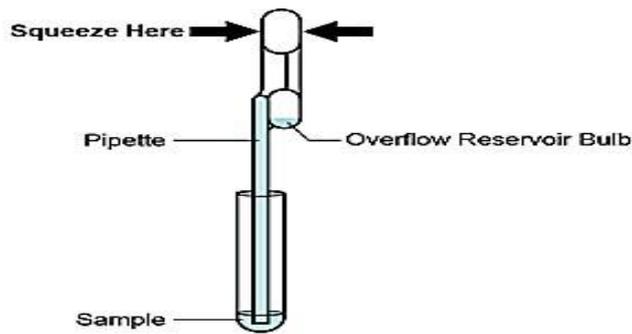
6.0 Mixing Specimen (Steps 6.0 to 8.0 will be carried out inside the Class II Biosafety Cabinet)

- Watch video before performing Steps 6.0, 7.0, and 8.0. The video will repeat. Touch the **CONTINUE** button to exit video.
- Mix specimen by rapidly inverting the specimen transport tube 5 times. Open the cap on the specimen transport tube.
- Open the cartridge lid.



7.0 Fill Pipette with Sample

- Remove the pipette from the wrapper.
- Squeeze the top bulb of the pipette **completely** and place the pipette tip in the specimen transport tube.
- Release the top bulb of the pipette to fill the pipette with sample from the patient specimen tube.



8.0 Transfer Sample to Cartridge

Squeeze the top bulb of the pipette completely again to empty the contents of the pipette into the large cartridge opening (Sample Chamber).



9.0 Close cartridge Lid

a. Close the cartridge lid.



b. Dispose of the used pipette in an appropriate waste container.

c. Wipe outside of cartridge with 70% alcohol and apply alcohol to gloves to disinfect. Wait for 30 seconds before removing cartridge from Biosafety cabinet and placing into the GeneXpert.

10.0 Load Cartridge

- a. Open the instrument door with the blinking green light.
- b. Load the cartridge with barcode facing the operator on the cartridge bay platform.



- c. Close the door until it clicks.



11.0 Remove Cartridge and View Results

- a. When the test is completed, the screen text will change to COMPLETE and the door unlocks.
- b. To view test report, touch the REPORT button then swipe across the screen from left to right to minimize screen and view report.
- c. Dispose of the cartridge and gloves according to your institution's policy
- d. To log out, tap the User Menu icon , then tap Logout

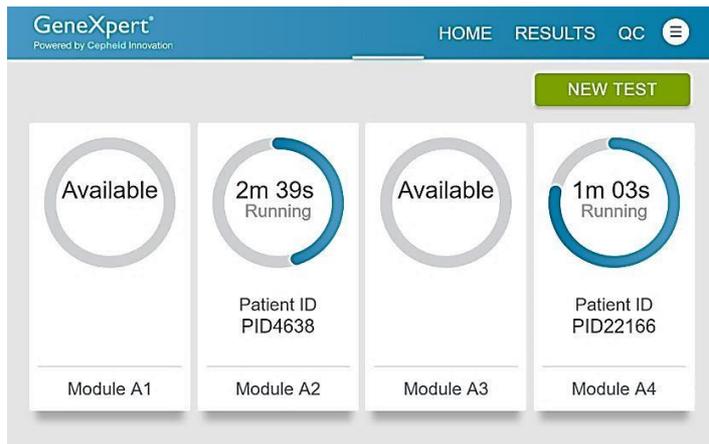
12.0 How to View Status of Tests in Progress and Completed Tests

Touch the **HOME** button to view the status of the tests in progress or completed tests.

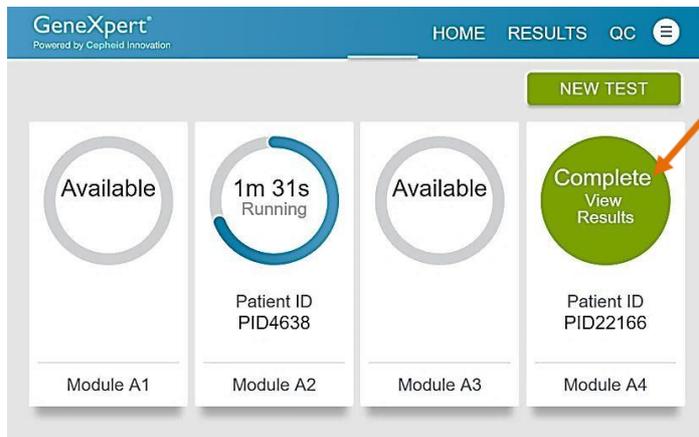


13.0 To view Tests in Progress

Tests in progress are shown on the HOME screen with a circular graphic indicator around each test and the Patient ID number below the module graphic. Touch the corresponding circular indicator to view the details.



14.0 To view Results of Completed Tests



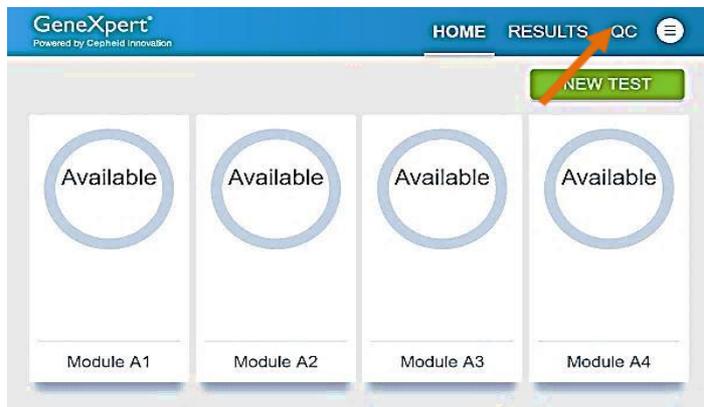
15.0 How to Run External Controls – Positive and Negative Controls

It is recommended that external controls (SeraCare AccuPlex™ Reference Material Kit, catalog number 0505-126) be tested at the frequency noted below.

- a. Each time a new lot of Xpert Xpress SARS-CoV-2 is received.
- b. Each time a new shipment of Xpert Xpress SARS-CoV-2 is received even if it is the same lot
- c. Each time a new operator is performing the test (i.e., operator who has not performed the test before).
- d. When problems (storage, operator, instrument, or other) are suspected or identified.
- e. If otherwise required by your institution's standard Quality Control (QC) procedures. previously received.

16.0 Running Controls

- Put on a new pair of gloves if performing a new test.
- Touch **QC** on the **Home** screen or touch **QC** on the Test Running screen.

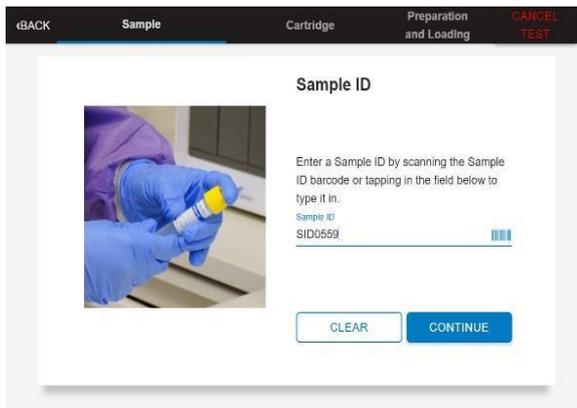


- Select **RUN POSITIVE CONTROL**, **RUN NEGATIVE CONTROL** or **RUN PROFICIENCY TEST** option.



17.0 Enter and Confirm Sample ID

- On the Sample ID screen, type Negative Control for the Negative Control or Positive Control for the Positive Control, or scan sample ID barcode if available.
- Touch **CONTINUE** if the displayed information is correct.
- Verify Sample ID and touch **CONFIRM**.



18.0 Scan and Confirm Cartridge

- a. Scan the barcode on the cartridge with the scanner.
- b. Touch **CONFIRM** if the displayed information is correct.
- c. If applicable, enter your username and password.



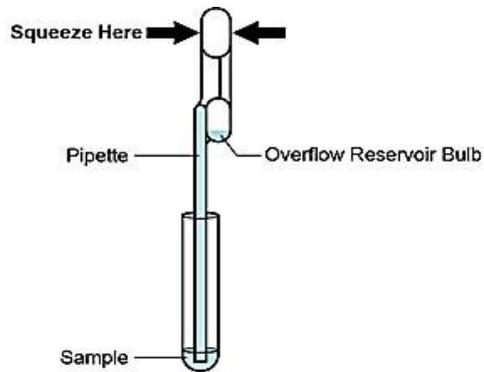
19.0 Mixing Sample (Steps 19.0 to 21.0 will be done inside the Class II Safety Cabinet)

- a. Watch video before performing Steps 20.0, 21.0, and 22.0. The video will repeat. Touch the **CONTINUE** button to exit video.
- b. Mix control by rapidly inverting the quality control tube 5 times. Open the cap on the quality control tube.
- c. Open the cartridge lid.



20.0 Fill Pipette with Control

- Remove the pipette from the wrapper.
- Squeeze the top bulb of the pipette completely and place the pipette tip in the quality control tube.
- Release the top bulb of the pipette to fill the pipette with the quality control.



21.0 Transfer Control to Cartridge

- Squeeze the top bulb of the pipette completely again to empty the contents of the pipette into the large cartridge opening (Sample Chamber).



- Close the cartridge lid



- Dispose of the used pipette in an appropriate waste container.

- d. Wipe outside of cartridge with 70% alcohol and apply alcohol to gloves to disinfect. Wait for 30 seconds before removing cartridge from Biosafety cabinet and placing into the GeneXpert.

22.0 Load Cartridge

- a. Open the instrument door with the blinking green light.
- b. Load the cartridge with barcode facing the operator on the cartridge bay platform.
- c. Close the door until it clicks.



23.0 Remove Cartridge and View Results

- a. When the test is completed, the screen text will change to COMPLETE and the door unlocks.
- b. To view test report, touch the **REPORT** button then swipe across the screen from left to right to minimize screen and view report.
- c. Dispose of the cartridge and gloves according to your institution's policy.
- d. Repeat steps in this section to test the second control tube starting with Step 1, Start a Test before testing patient samples.
- e. To log out, tap the User Menu icon , then tap Logout.

24.0 Procedure for GeneXpert Xpress System (Tablet configuration)



24.1 Storage and Handling

- Wear gloves. Change gloves between processing each sample.
- Store the Xpert Xpress SARS-CoV-2 cartridges at 2-28°C.

24.2 Warnings

- DO NOT use a cartridge that is wet or has leaked.
- DO NOT use a cartridge that has been dropped.
- DO NOT open a cartridge lid until you are ready to perform testing.
- DO NOT shake or tilt the cartridge after adding the sample.
- DO NOT reuse disposable pipettes or cartridges.
- DO NOT turn off or unplug the instrument while a test is in progress as this will stop the test.
- Do not use a cartridge that has a missing or damaged reaction tube.

25.0 How to Start the Software

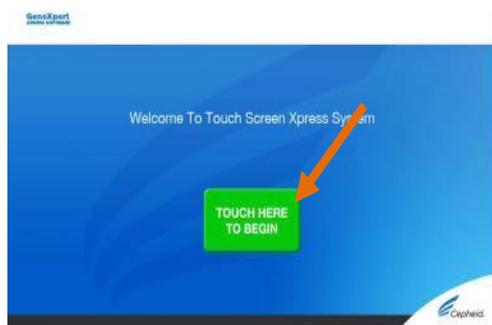
- a. Put on a pair of clean gloves.
 - b. Turn on the GeneXpert Xpress instrument (GeneXpert Xpress II or GeneXpert Xpress IV).
 - c. Turn on the computer.
- Windows 7: The Windows 7 account screen appears. Touch the Cepheid Admin icon to continue.
 - Windows 10: The Windows lock screen appears. Swipe up to continue.

26.0 Enter Password

- a. Touch **Password** to display the keyboard.
- b. Enter your password.
- c. Touch the arrow button at the right of the password entry area.

27.0 Touch Begin Button

- a. Press the **TOUCH HERE TO BEGIN** button.
- b. If applicable, enter your user name and password.



28.0 Home Screen Display

The Home screen will be displayed with the **VIEW PREVIOUS TESTS** button appearing initially. The **RUN NEW TEST** button will appear on the Home screen within 1 minute. (GeneXpert Xpress IV screen shown below).



29.0 How to Test a Patient Specimen

Before you begin

- Refer to the package insert for more information.
- Read through this entire Quick Reference Instructions before beginning a test.
- Instructions on how to prepare the specimen and the cartridge (presented below) are also shown in a video within the software.
- Start the test within 30 minutes of adding the specimen to the cartridge.
- The recommended environmental operating conditions for Xpert Xpress SARS-CoV-2 are 15-30°C, 20-80% relative humidity.

30.0 Start a Test

- Touch **RUN NEW TEST** on the Home screen (GeneXpert Xpress IV screen shown below).
- Check that the specimen tube cap is closed.



31.0 Enter & Confirm Patient/Sample ID.

- 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.
- Touch the **YES** button to confirm that the Patient/Sample ID is correct.



32.0 Scan and Confirm Cartridge.

- Remove a cartridge and a transfer pipette from the cartridge kit box.
- Scan the barcode on the cartridge with the scanner. Touch **YES** if the displayed information is correct.
- If applicable, enter your username and password.



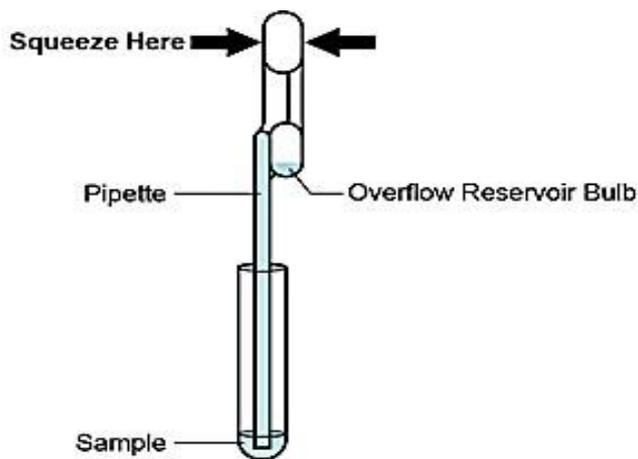
33.0 Watch Video. Mix Specimen. (Steps 33.0 to 35.0 will be done inside the Class II Safety Cabinet)

- Watch video before performing Steps **34.0**, **35.0**, and **36.0**. The video will repeat. Touch the **SKIP VIDEO AND CONTINUE** button to exit video.
- Mix specimen by rapidly inverting the specimen transport tube 5 times. Open the cap on the specimen transport tube.
- Open the cartridge lid.



34.0 Fill Pipette with Sample.

- a. Remove the pipette from the wrapper.
- b. Squeeze the top bulb of the pipette completely and place the pipette tip in the specimen transport tube.
- c. Release the top bulb of the pipette to fill the pipette with sample from the patient specimen tube.



35.0 Transfer Sample to Cartridge.

- a. Squeeze the top bulb of the pipette completely again to empty the contents of the pipette into the large cartridge opening (Sample Chamber).

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.



Sample Chamber (Large Opening)

- b. Close the cartridge lid. Dispose of the used pipette in an appropriate waste container.



- c. Wipe outside of cartridge with 70% alcohol and apply alcohol to gloves to disinfect. Wait for 30 seconds before removing cartridge from Biosafety cabinet and placing into the GeneXpert.

36.0 Load Cartridge.

- a. Open the instrument door with the blinking green light.
- b. Load the cartridge with barcode facing the operator on the cartridge bay platform



- d. Close the door until it clicks.



37.0 Remove Cartridge. View Results.

- a. When the test is completed, the door will unlock, and the **Remove Cartridge** screen will be displayed.
- b. Follow the on-screen instructions to remove the cartridge. Touch **CONTINUE** to view the result of the test.
- c. To print the results, touch the **PRINT RESULT** button.



- e. Dispose of the cartridge and gloves according to your institution's policy.

38.0 How to Start a New Test.

- a. Put on a new pair of gloves if performing a new test.
- b. Touch the **HOME** button to go to the Home Screen.



- c. Start a new test following the steps in this section starting with Step **30.0**, Start a Test. Or for starting a test while a test is running or a new test with another user, see Step **39.0**

39.0 Starting Another Test While a Test is Running

- a. Put on a new pair of gloves if performing a new test.
- b. Touch the **HOME** button to go to the Home Screen.



- c. Touch the **SIGN OUT** button to log out previous user, if applicable.
- d. Start a new test following the steps in this section starting with **Step 31.0, Start a Test.**

40.0 How to View Status of Tests in Progress and Completed Tests

40.1 Touch HOME Button

Touch the **HOME** button to view the status of tests in progress or completed tests.



40.2 View Test in Progress.

To view a test in progress, touch the **Test in progress, touch for status** button. The time remaining to complete the testing will be displayed on the progress bar at the bottom of the **Test in Progress** screen.

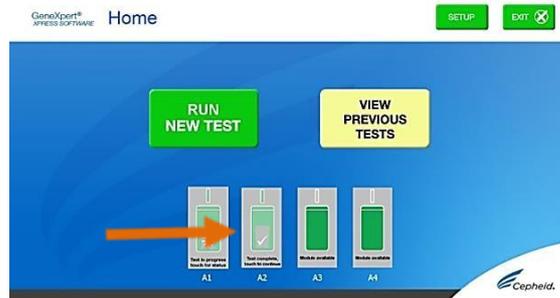
“Test in progress, touch for status”
button



40.3 View Completed Tests.

When a test is completed, touch the **Test complete, touch to continue** button. The **Remove Cartridge** screen will be displayed. Follow the on-screen instructions to remove the cartridge. Touch the **CONTINUE** button to view the result of the test.

“Test complete, touch to
continue” button



41.0 How to Run External Controls – Positive and Negative Controls

It is recommended that external controls (SeraCare AccuPlex™ Reference Material Kit, catalog number 0505-126) be tested at the frequency noted below.

- Each time a new lot of Xpert Xpress SARS-CoV-2 is received.
- Each time a new shipment of Xpert Xpress SARS-CoV-2 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 before).
- When problems (storage, operator, instrument, or other) are suspected or identified.
- If otherwise required by your institution's standard Quality Control (QC) procedures.

41.1 Start a Test

- Put on a pair of clean gloves.
- Have a new Xpert Xpress SARS-CoV-2 cartridge, a control tube, and a transfer pipette ready.
- Touch **RUN NEW TEST** on the home screen (GeneXpert Xpress IV shown below).



41.2 Enter & Confirm Patient/Sample ID.

- Touch the **NO** button if there is no Sample ID barcode.
- Type **negative** control for the Negative External Control or **positive** control for the Positive External Control in the Sample ID field. Touch the **OK** button.
- Touch the **YES** button to confirm that the Patient/Sample ID is correct.



41.3 Scan and Confirm Cartridge.

- Remove a cartridge and a transfer pipette from the cartridge kit box.
- Scan the barcode on the cartridge with the scanner. Touch **YES** if the displayed information is correct.
- If applicable, enter your username and password.



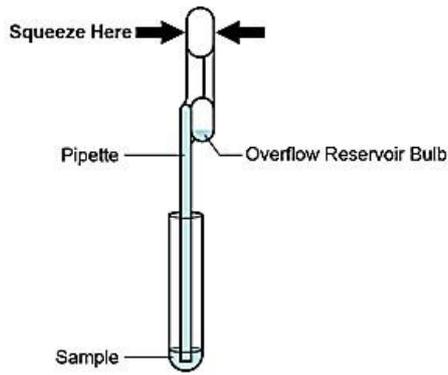
41.4 Watch Video. Mix Control. (Steps 41.4 to 41.6 will be carried out inside the Class II Biosafety Cabinet)

- Watch video before performing **Steps 41.5, 41.6, and 41.7**. The video will repeat. Touch the **SKIP VIDEO AND CONTINUE** button to exit video.
- Mix control by rapidly inverting the quality control tube 5 times. Open the cap on the quality control tube.
- Open the cartridge lid.



41.5 Fill Pipette with Control

- Remove the pipette from the wrapper.
- Squeeze the top bulb of the pipette completely and place the pipette tip in the quality control tube.
- Release the top bulb of the pipette to fill the pipette with sample from the quality control tube.



41.6 Transfer Control to Cartridge.

- a. Squeeze the top bulb of the pipette completely again to empty the contents of the pipette into the large cartridge opening (Sample Chamber).



Sample Chamber (Large Opening)

- a. Close the cartridge lid. Dispose of the used pipette in an appropriate waste container



- b. Wipe outside of cartridge with 70% alcohol and apply alcohol to gloves to disinfect. Wait for 30 seconds before removing cartridge from Biosafety cabinet and placing into the GeneXpert.

41.7 Load Cartridge.

- a. Open the instrument door with the blinking green light.
- b. Load the cartridge with barcode facing the operator on the cartridge bay platform. Do not try to insert the cartridge past the cartridge bay platform.



- c. Close the door until it clicks.



41.8 Remove Cartridge. View Results.

- a. When the test is completed, the door will unlock and the **Remove Cartridge** screen will be displayed.
- b. Follow the on-screen instructions to remove the cartridge. Touch **CONTINUE** to view the result of the test.



- c. To print the results, touch the **PRINT RESULT** button.
- d. Dispose of the cartridge and gloves according to your institution's policy.
- e. Touch the **HOME** button to go to the Home Screen.
- f. Repeat steps in this section to test the second control tube starting with **Step 31.0 Start a Test** before testing patient samples.

42.0 POSSIBLE RESULTS:

SARS-COV-2 NEGATIVE	SARS-COV-2 (coronavirus) target RNA is not detected
SARS-COV-2 POSITIVE	SARS-COV-2 (coronavirus) target RNA is detected
SARS-COV-2 PRESUMPTIVE POSITIVE	If the result is SARS-CoV-2 PRESUMPTIVE POSITIVE , then retest with a new cartridge. If the retest is SARS CoV-2 PRESUMPTIVE POSITIVE , collect new specimen and REPEAT TEST.
NO RESULT REPEAT TEST	If the result is NO RESULT- REPEAT TEST with a new cartridge. If the retest is NO RESULT , collect new specimen and REPEAT TEST.
INSTRUMENT ERROR	Result is an instrument error. Touch CLEAR ERROR and follow the on-screen instructions. When the Home screen appears, repeat the test using a new cartridge.

Note: If an incorrect result is provided for the external control, repeat the external control run. If repeated control runs do not produce the expected results, contact Cepheid Technical Support at (888) 838-3222.

43.0 Quality Control & Interpretation of Results

For more information on Quality Control and Interpretation of Results, refer to **Annex 2**

44.0 SARS-COV-2 Verification Procedure

For information on GeneXpert Express SARS-COV-2 Verification Procedure, refer to **Annex 3**

45.0 Limitation

- Performance of the Xpert Xpress SARS-CoV-2 has only been established in nasopharyngeal swab specimens. Specimen types other than nasopharyngeal swab may give inaccurate results.
- A false negative result may occur if a specimen is improperly collected, transported or handled. False negative results may also occur if inadequate numbers of organisms are present in the specimen.
- As with any molecular test, mutations within the target regions of Xpert Xpress SARSCoV-2 could affect primer and/or probe binding resulting in failure to detect the presence of virus.
- This test cannot rule out diseases caused by other bacterial or viral pathogens.

46.0 Technical Support - Region

For any queries or troubleshooting that you may encounter, please contact the following

WHO:

RAIKABAKABA, Asaeli Babiau at raikabakabaa@who.int

For PNG and supply logistics

UNDP:

Mr Imran Khan at imran.khan@undp.org

For supplies and software issues.

Mr Praneel Maharaj at praneel.maharaj@undp.org

For Kiribati and Tuvalu

SPC:

Dr Eka Buadromo at ekab@spc.int

[For Fiji, Tonga, Samoa and Cook Islands](#)

Mr Tebuka Toatu at tebukat@spc.int

For Tokelau and Niue

Mr Vijesh Lal at vijeshl@spc.int

For Nauru, Solomon Islands, Vanuatu and Wallis & Futuna

PIHOA:

Ms Vasiti Uluiviti at vasitiu@pihoa.org

For the 6 USAPIs

46.1 Technical Support - Cepheid Headquarters Locations

Corporate Headquarters	European Headquarters
Cepheid 904 Caribbean Drive Sunnyvale, CA 94089 USA	Cepheid Europe SAS Vira Solelh 81470 Maurens-Scopont France
Telephone: +1 408 541 4191	Telephone: +33 563 825 300
Fax: +1 408 541 4192	Fax: +33 563 825 301
www.cepheid.com	www.cepheidinternational.com/

Before contacting Cepheid Technical Support, collect the following information:

- Product name
- Lot number

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

Annexes:

Annex 1(a): Nasopharyngeal Swab Collection Procedure (adapted from Cepheid Instruction Package Insert)

Insert the swab into either nostril, passing it into the posterior nasopharynx (see Figure 1). Rotate swab by firmly brushing against the nasopharynx several times. Remove and place the swab into a viral transport tube (3 mL). Break swab at the indicated break line and cap the specimen collection tube tightly.

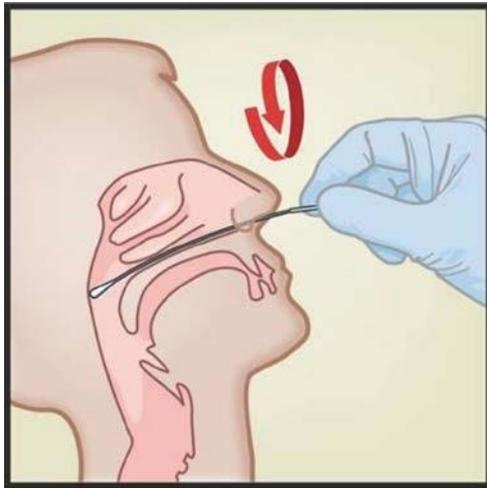


Figure 1. Nasopharyngeal Swab Collection

Annex 1(b): Nasal Wash/Aspirate Collection Procedure (adapted from Cepheid Instruction Package Insert)

Using a clean 300 μ L transfer pipette (supplied), transfer 600 μ L of the sample (two draws, using the same transfer pipette) into the 3 mL Xpert Viral Transport Medium tube and then cap the tube.

Annex 1(c): Mid-Turbinate Swab Collection Procedure

1. Insert the mid-turbinate swab into either nostril, passing it into the mid-turbinate area (see Figure 2). Rotate swab by firmly brushing against the mid-turbinate area several times.
2. Remove and place the swab into the tube containing 3 ml of viral transport medium. Break swab at the indicated break line and cap the specimen collection tube tightly.

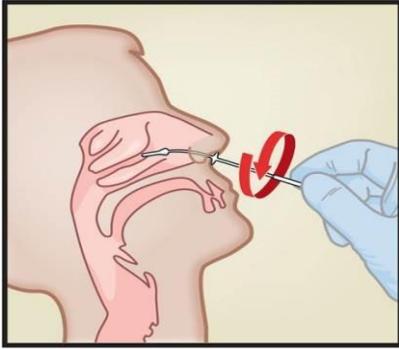


Figure 2: Mid-Turbinate Specimen Collection

Annex 2(a): Quality Control

a. Internal Controls

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

- Sample Processing Control (SPC) – Ensures that the sample was processed correctly. The SPC verifies that sample processing is adequate. Additionally, this control detects sample-associated inhibition of the real-time PCR assay, ensures that the PCR reaction conditions (temperature and time) are appropriate for the amplification reaction, and that the PCR reagents are functional. The SPC should be positive in a negative sample and can be negative or positive in a positive sample. The SPC passes if it meets the validated acceptance criteria.
- Probe Check Control (PCC) – Before the start of the PCR reaction, the GeneXpert System measures the fluorescence signal from the probes to monitor bead rehydration, reaction tube filling, probe integrity, and dye stability. The PCC passes if it meets the validated acceptance criteria.

b. External Controls

External controls may be used in accordance with local, state and federal accrediting organizations as applicable.

Annex 2(b): Interpretation of Results

The results are interpreted automatically by the GeneXpert System and are clearly shown in the

View Results window. The Xpert Xpress SARS-CoV-2 test provides test results based on the detection of two gene targets according to the algorithms shown in **Table 1**.

Table 1. Xpert Xpress SARS-CoV-2 Possible Results

Result Text	N2	E	SPC
SARS-CoV-2 POSITIVE	+	+	+/-
SARS-CoV-2 POSITIVE	+	-	+/-
SARS-CoV-2 PRESUMPTIVE POSITIVE	-	+	+/-
SARS-CoV-2 NEGATIVE	-	-	+
INVALID	-	-	-

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

Table 2. Xpert Xpress SARS-CoV-2 Results and Interpretation

Result	Interpretation
SARS-CoV-2 POSITIVE	<ul style="list-style-type: none"> The 2019 novel coronavirus (SARS-CoV-2) target nucleic acids are detected. The SARS-CoV-2 signal for the N2 nucleic acid target or signals for both nucleic acid targets (N2 and E) have a Ct within the valid range and endpoint above the minimum setting SPC: NA; SPC is ignored because coronavirus target amplification occurred Probe Check: PASS; all probe check results pass
SARS-CoV-2 PRESUMPTIVE POSITIVE	<p>The 2019 novel coronavirus (SARS-CoV-2) nucleic acids may be present. Sample should be retested. For samples with a repeated Presumptive Positive result, additional confirmatory testing may be conducted, if it is necessary to differentiate between SARS-CoV-2 and SARS-CoV-1 or other Sarbecovirus currently unknown to infect humans, for epidemiological purposes or clinical management.</p> <ul style="list-style-type: none"> The SARS-CoV-2 signal for only the E nucleic acid target has a Ct within the valid range and endpoint above the minimum setting <p>SPC: NA; SPC is ignored because a target amplification has occurred.</p> <p>Probe Check: PASS; all probe check results pass</p>

<p>SARS-CoV-2 NEGATIVE</p>	<p>The 2019 novel coronavirus (SARS-CoV-2) target nucleic acids are not detected.</p> <ul style="list-style-type: none"> • The SARS-CoV-2 signals for two nucleic acid targets (N2 and E) 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
<p>INVALID</p>	<p>SPC does not meet acceptance criteria. Presence or absence of the 2019 novel coronavirus (SARS-CoV-2) nucleic acids cannot be determined. Repeat test according to the Retest Procedure in IFU (Section 17.2).</p> <ul style="list-style-type: none"> • SPC: FAIL; SPC and SARS-CoV-2 signals do not have a Ct within valid range and endpoint below minimum setting • Probe Check – PASS; all probe check results pass
<p>ERROR</p>	<p>Presence or absence of the 2019 novel coronavirus (SARS-CoV-2) nucleic acids cannot be determined. Repeat test according to the Retest Procedure in IFU (Section 17.2).</p> <ul style="list-style-type: none"> • SARS-CoV-2: NO RESULT • SPC: NO RESULT Probe Check: FAIL1; all or one of the probe check results fail <p>1 If the probe check passes, the error is caused by the maximum pressure limit exceeding the acceptable range or by a system component failure.</p>
<p>NO RESULT</p>	<p>Presence or absence of the 2019 novel coronavirus (SARS-CoV-2) nucleic acids cannot be determined. Repeat test according to the Retest Procedure in IFU (Section 17.2). A NO RESULT indicates that insufficient data were collected. For example, the operator stopped a test that was in progress.</p> <ul style="list-style-type: none"> • SARS-CoV-2: NO RESULT • SPC: NO RESULT • Probe Check: NA (not applicable)

Annex 3: Verification Procedure

Required Materials

- AccuPlex™ SARS-CoV-2 Reference Material kit. SeraCare Material Number: 05050126 (5 x 1.5 mL vials, positive reference material; 5 x 1.5 mL vials, negative reference material). The positive reference material consists of recombinant Sindbis virus particles with sequences from the SARS-CoV-2 genome including the E gene, RdRp (RNA dependent RNA polymerase) gene, ORF1a gene, and N gene.
- Five negative clinical nasopharyngeal swab specimens in viral transport medium from patients not suspected of COV (~ 3 mL each), which could be residual specimens from other diagnostic testing.
- Three sterile, screw-capped test tubes; approximately 2 mL capacity and test tube rack
- Sterile disposable pipet tips or pipetman capable of delivering 0.25 mL and 0.3 mL of samples
- 24 Xpert Xpress SARS-CoV-2 cartridges (excluding the cartridges used for external control testing – at least 2 additional cartridges)

Precautions

The AccuPlex SARS-CoV-2 Reference Material contains recombinant virus that is heat-treated and replication-defective. However, the reference material should be handled as infectious materials using standard precautions and in accordance with Good Laboratory Practices to avoid contamination of laboratory equipment and reagents that could cause false positive results.

Store verification materials at appropriate temperatures per the manufacturer's storage requirements and hold on ice when thawed.

External Controls Testing

1. Test one positive and one negative external control listed in Section 9 of the Xpert Xpress SARS-CoV-2 instructions for use (IFU) according to the retest procedure described in the IFU.
2. Once the correct results have been obtained for the external controls, proceed with the verification procedure. If external control test results fail to give expected results, contact Cepheid Technical Support.

Verification Procedure: Accuracy, Reportable, and Reference Ranges

1. Label 20 of the Xpert Xpress SARS-CoV-2 cartridges #1 to #20.
2. Label three sterile, screw-capped test tubes "A", "B", and "C".
 - a. Create a 1:2 dilution of the positive AccuPlex reference material (**DILUTED positive**) in a test tube by taking 1.0 ml of the AccuPlex material and adding 1.0 mL of a negative patient specimen (can be pooled negative specimens). Label this test tube "A". Cap the test tube tightly. Mix thoroughly. The total volume in the test tube A will be 2.0 mL.
3. Using pipet provided in Xpert kit, add 0.3 mL from Test Tube A to cartridges #6 to #10 (note there will be approximately 0.5 mL remaining in Test Tube A).

4. Next, prepare a pool of AccuPlex **UNDILUTED positive** reference material by pipetting out 1 mL from each of two AccuPlex positive reference material vials to a separate test tube. Label this test tube "B".
5. Using pipet provided in Xpert kit, add 0.3 mL of **UNDILUTED positive** reference material (Test tube B) to cartridges #1 to #5. (note there will be remaining approximately 0.5 mL volume remaining in Test Tube B).
6. Next, prepare a pool of AccuPlex **NEGATIVE** reference material by pipetting out 1 mL from each of two AccuPlex negative reference material vials to a separate test tube. Label this test tube "C".
7. Using pipet provided in Xpert kit, add 0.3 mL of AccuPlex negative reference material (from Test Tube C) to cartridges #11 to #15 (note there will be approximately 0.5 mL volume remaining in test tube C).
8. Using pipet provided in Xpert kit, add 0.3 mL of negative NP sample in viral transport medium matrix (5 clinical specimens) to cartridges #16 to #20 (each clinical specimen added to different cartridge).
9. Run the Xpert cartridges as per the product IFU.
10. Fill out the results in the Table below.

% Overall Agreement					
Cartridge #/Date	SARS-CoV-2 Positive Sample Testing Result	% Agreement (Acceptance criteria – 100% for specimens 1-5; 80% for specimens 6-10)	Cartridge #/Date	SARS-COV-2 Negative Sample Testing Result	% Agreement (Acceptance criteria – 100%)
#1/			#11/		
#2/			#12/		
#3/			#13/		
#4/			#14/		
#5/			#15/		
#6/			#16/		
#7/			#17/		
#8/			#18/		
#9/			#19/		
#10/			#20/		
Comments			Comments		

Expected Results

Undiluted and 1:2 diluted positive samples should be positive for SARS-CoV-2. Negative samples (AccuPlex reference material and patient specimens) should be negative for SARS-CoV-

2.

Acceptance criteria for the testing are:

1. 100% of tests results should be in agreement with the expected results for the undiluted positive samples and negative samples.
2. $\geq 4/5$ (80%) of test results should be in agreement with the expected results for the diluted positive samples.

If test results fail to meet expected results, contact Cepheid Technical Support.

Verification Procedure: Reproducibility

1. Select two operators to repeat the Xpert SARS-CoV-2 test on selected vials of AccuPlex positive reference material and AccuPlex negative reference material.
2. Using pipet provided, Operator #1 add 0.3 mL of AccuPlex positive reference material to cartridge #21. Operator #2 add 0.3 mL of AccuPlex positive to cartridge #22.
3. Using pipet provided, Operator #1 add 0.3 mL of AccuPlex negative reference material to cartridge #23. Operator #2 add 0.3 mL of AccuPlex negative to cartridge #24.
4. Fill out results in the Table below:

Reproducibility					
Cartridge #/Date	SARS-CoV-2 Positive Sample Testing Results	% Agreement (Acceptance criteria – 100%)	Cartridge #/Date	SARS-COV-2 Negative Sample Testing Results	% Agreement (Acceptance criteria – 100%)
Operator 1: #21/			Operator 1: #23/		
Operator 2: #22/			Operator 2: #24/		

Expected Results

Acceptance criteria for the testing are: All replicates of the positive samples should be 100% positive, and all replicates of the negative samples should be 100% negative.

If test results fail to meet expected results, contact Cepheid Technical Support.

Annex 4: Acronyms

Acronym	Meaning
COVID-19	Coronavirus Disease 2019. It is a respiratory disease caused by a new coronavirus identified in December, 2019
Hub	Also called a network hub and is a common connection point for devices in a network.
IFU	Instruction for use
SARS-COV-2	Severe Acute Respiratory Syndromme Coronavirus 2. It is the the type of coronavirus that causes COVID-19
UTM/VTM	Universal Transport Medium or often referred to also as Viral Transport Medium

References:

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This document has been developed in accordance with global guidance and contextualized to the Pacific context by the, Pacific Island Health Officers Association (PIHOA), Pacific Community (SPC), United Nations Development Programme (UNDP) and the World Health Organization (WHO) from the COVID-19 Pacific Joint Incident Management Team



Pacific
Community
Communauté
du Pacifique



World Health
Organization
Representative Office
for the South Pacific