

Xpert[®] Xpress SARS-CoV-2

REF XPRSARS-COV2-10

Instructions for Use

For Use with GeneXpert Dx or GeneXpert Infinity Systems

CE **IVD**

Trademark, Patents, and Copyright Statements

Cepheid[®], the Cepheid logo, GeneXpert[®], and Xpert[®] are trademarks of Cepheid, registered in the U.S. and other countries.

All other trademarks are the property of their respective owners.

THE PURCHASE OF THIS PRODUCT CONVEYS TO THE BUYER THE NON-TRANSFERABLE RIGHT TO USE IT IN ACCORDANCE WITH THESE INSTRUCTIONS FOR USE. NO OTHER RIGHTS ARE CONVEYED EXPRESSLY, BY IMPLICATION OR BY ESTOPPEL. FURTHERMORE, NO RIGHTS FOR RESALE ARE CONFERRED WITH THE PURCHASE OF THIS PRODUCT.

© 2020–2023 Cepheid

See Section 26, Revision History for a description of changes.

Xpert[®] Xpress SARS-CoV-2

1 Proprietary Name

Xpert[®] Xpress SARS-CoV-2

2 Common or Usual Name

Xpert Xpress SARS-CoV-2

3 Intended Use

The Xpert Xpress SARS-CoV-2 test is a real-time RT-PCR test intended for the qualitative detection of nucleic acid from the SARS-CoV-2 in nasopharyngeal swab and nasal swab specimens collected from individuals who are suspected of COVID-19 infection.

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

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

The Xpert Xpress SARS-CoV-2 test is intended to be performed by trained users in both laboratory and near patient testing settings.

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 was later renamed SARS-CoV-2 by the International Committee for Taxonomy of Viruses (ICTV).² The WHO declared the outbreak a global health emergency on January 30, 2020. SARS-CoV-2 has been responsible for over a million reported cases of Coronavirus infectious disease 2019 (COVID-19) worldwide. The morbidity and mortality of COVID-19 varies by patient age and risk factors, with the elderly and those with co-morbidities such as hypertension, diabetes, and respiratory disease at most risk.

The Xpert Xpress SARS-CoV-2 test 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 SARS-CoV-2 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 (NP) swab and nasal swab specimens.

5 Principle of the Procedure

The Xpert Xpress SARS-CoV-2 test is an automated *in vitro* diagnostic test for qualitative detection of nucleic acid from SARS-CoV-2. The Xpert Xpress SARS-CoV-2 test is performed on GeneXpert Instrument Systems.

The GeneXpert Instrument Systems automate and integrate sample preparation, nucleic acid extraction and amplification, and detection of the target sequences in simple or complex samples using real-time PCR assays. The systems consist of an instrument, computer, and preloaded software for running tests and viewing the results. The systems require the use of

single-use disposable cartridges that hold the RT-PCR reagents and host the RT-PCR process. Because the cartridges are self-contained, cross-contamination between samples is minimized. For a full description of the systems, see the *GeneXpert Dx System Operator Manual* or the *GeneXpert Infinity System Operator Manual*.

The Xpert Xpress SARS-CoV-2 test includes reagents for the detection of RNA from SARS-CoV-2 in NP swab or nasal swab specimen. A Sample Processing Control (SPC) and a Probe Check Control (PCC) are also included in the cartridge utilized by the GeneXpert instrument. 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 NP swab or nasal swab specimen is collected and placed into a transport tube containing 3 mL of viral transport medium or 3 mL of saline. 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 SARS-CoV-2 cartridge. The Xpert 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.

6 Materials Provided

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

Xpert Xpress SARS-CoV-2 Cartridges with Integrated Reaction Tubes	10
Bead 1, Bead 2, and Bead 3 (freeze-dried)	1 of each per cartridge
Lysis Reagent	1.5 mL per cartridge
Binding Reagent	1.5 mL per cartridge
Elution Reagent	3.0 mL per cartridge
Disposable Transfer Pipettes	10-12 per kit
CD	1 per kit
Assay Definition File (ADF)	
Instructions to import ADF into the software	
Flyer	1 per kit
Directions to locate the product insert on www.cepheid.com .	

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

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

7 Storage and Handling

- Store the Xpert Xpress SARS-CoV-2 cartridges at 2-28 °C.
- Do not open a 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

- 0.85% (w/v) saline, 3 mL
- Nasopharyngeal Sample Collection Kit for Viruses (Cepheid P/N SWAB/B-100, SWAB/M-100, Copan P/N 305C) or equivalent
- Nasal Sample Collection Kit for Viruses (Cepheid P/N SWAB/F-100, Copan P/N 346C) or equivalent
- Alternatively, swabs and transport medium can be obtained separately:
 - Nylon flocked swab (Copan P/N 502CS01, 503CS01) or equivalent
 - Viral transport medium, 3 mL (Copan P/N 330C) or equivalent
- GeneXpert Dx System or GeneXpert Infinity System (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

9 Materials Available but Not Provided

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

10 Warnings and Precautions

10.1 General

- For *in vitro* diagnostic use.
- Positive results are indicative of presence of SARS-CoV-2-RNA.
- Report all positive results to the appropriate health authorities as required.
- 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 Prevention³ and the Clinical and Laboratory Standards Institute.⁴
- Follow safety procedures set by your institution for working with chemicals and handling biological specimens.
- 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 SARS-CoV-2 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.
- Each single-use Xpert Xpress SARS-CoV-2 cartridge is used to process one test. Do not reuse processed cartridges.
- Each single-use disposable pipette is used to transfer one specimen. Do not reuse disposable pipettes.

- Do not use a cartridge if it appears wet or if the lid seal appears to have been broken.
- Wear clean lab coats and gloves. Change gloves between the handling of each specimen.
- In the event of a spill of specimens or controls, wear gloves and absorb the spill with paper towels. Then, thoroughly clean the contaminated area with a 10% freshly prepared household chlorine bleach. Allow a minimum of two minutes of contact time. Ensure the work area is dry before using 70% denatured ethanol to remove bleach residue. Allow surface to dry completely before proceeding. Or, follow your institution's standard procedures for a contamination or spill event. For equipment, follow the manufacturer's recommendations for decontamination of equipment.
- Biological specimens, transfer devices, and used cartridges should be considered capable of transmitting infectious agents requiring standard precautions. Follow your institution's environmental waste procedures for proper disposal of used cartridges and unused reagents. These materials may exhibit characteristics of chemical hazardous waste requiring specific disposal. If country or regional regulations do not provide clear direction on proper disposal, biological specimens and used cartridges should be disposed per WHO [World Health Organization] medical waste handling and disposal guidelines.

11 Chemical Hazards^{5,6}

Signal Word: WARNING

UN GHS Hazard Statements

- Harmful if swallowed.
- May be harmful in contact with skin.
- Causes eye irritation.

UN GHS Precautionary Statements Prevention

- Wash hands thoroughly after handling.

Response

- Call a POISON CENTER or doctor/physician if you feel unwell.
- If skin irritation occurs: Get medical advice/attention.
- IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
- If eye irritation persists: Get medical advice/attention.

12 Specimen Collection, Transport, and Storage

Proper specimen collection, storage, and transport are critical to the performance of this test. Inadequate specimen collection, improper specimen handling and/or transport may yield a false result. See Section 12.1. Nasopharyngeal Swab Collection Procedure and Section 12.2. Nasal Swab Collection Procedure.

Nasopharyngeal swab and nasal swab specimens can be stored in viral transport medium or saline, at room temperature (15-30 °C) for up to 8 hours and refrigerated (2-8 °C) up to 7 days until testing is performed on the GeneXpert Instrument 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

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 the tube containing 3mL of viral transport medium or 3 mL of saline. Break swab at the indicated break line and cap the specimen collection tube tightly.



Figure 1. Nasopharyngeal Swab Collection

12.2 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).

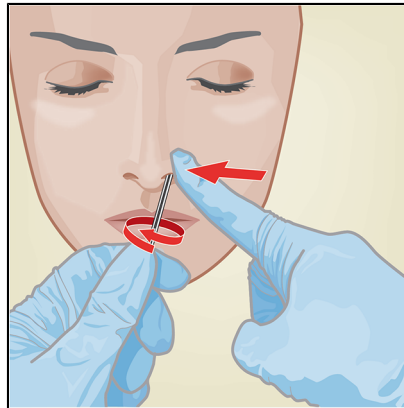


Figure 2. Nasal Swab Collection for First Nostril

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.

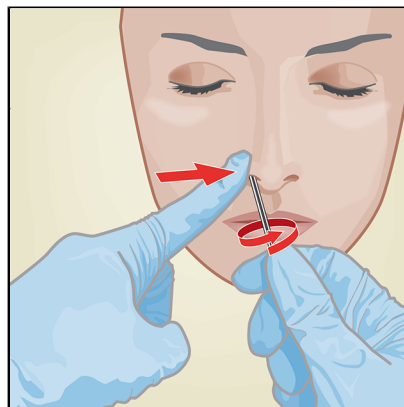


Figure 3. Nasal Swab Collection for Second Nostril

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

13 Procedure

13.1 Preparing the Cartridge

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

1. Remove a cartridge from the package.
2. Check the specimen transport tube is closed.
3. Mix specimen by rapidly inverting the specimen transport tube 5 times. Open the cap on the specimen transport tube.
4. Open the cartridge lid.
5. Remove the transfer pipette from the wrapper.
6. 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 4).

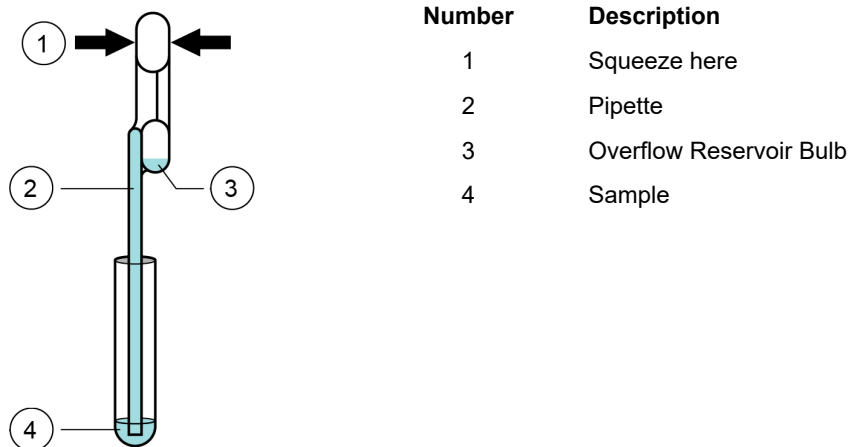


Figure 4. Transfer Pipette

7. Release the top bulb of the pipette to fill the pipette before removing from the tube. After filling pipette, excess sample will be seen in the overflow reservoir bulb of the pipette (see Figure 4). Check that the pipette does not contain bubbles.
8. To transfer the sample to the cartridge, squeeze the top bulb of the transfer pipette completely again to empty the contents of the pipette (300 μ L) into the large opening (Sample Chamber) in the cartridge shown in Figure 5. Dispose of the used pipette.

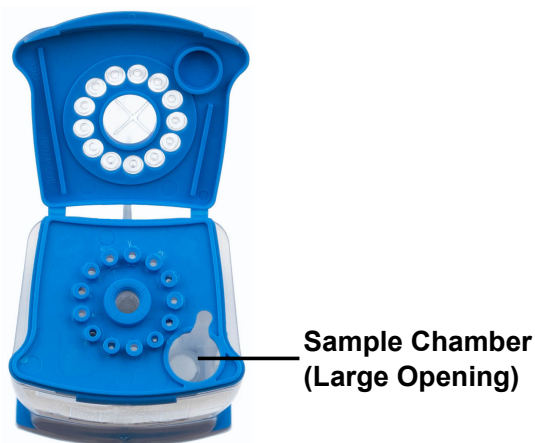


Figure 5. Xpert Xpress SARS-CoV-2 Cartridge (Top View)

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.

9. Close the cartridge lid.

13.2 External Controls

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

To run a control using the Xpert Xpress SARS-CoV-2 test, perform the following steps:

1. Mix control by rapidly inverting the external control tube 5 times. Open cap on external control tube.
2. Open the cartridge lid.
3. Using a clean transfer pipette, transfer one draw of the external control sample (300 µL) into the large opening (Sample Chamber) in the cartridge shown in Figure 5.
4. Close cartridge lid.

14 Running the Test

- For the GeneXpert Dx System, see Section 14.1.
- For the GeneXpert Infinity System, see Section 14.2.

14.1 GeneXpert Dx System

14.1.1 Starting the Test

Before you start the test, make sure that:

- Important**
- The system is running the correct GeneXpert Dx software version shown in section - Materials Required but Not Provided.
 - The correct assay definition file is imported into the software.
-

This section lists the basic steps for running the test. For detailed instructions, see the *GeneXpert Dx System Operator Manual*.

Note The steps you follow can be different if the system administrator changed the default workflow of the system.

1. Turn on the GeneXpert Dx System, then turn on the computer and log on. The GeneXpert software will launch automatically. If it does not, double-click the GeneXpert Dx software shortcut icon on the Windows® desktop.
 2. Log on using your username and password.
 3. In the **GeneXpert System** window, click **Create Test**.
The **Create Test** window displays. The **Scan Patient ID barcode** dialog box displays.
 4. Scan or type in the Patient ID. If typing the Patient ID, make sure the Patient ID is typed correctly.
The Patient ID is associated with the test results and displays in the **View Results** window and all the reports. The **Scan Sample ID barcode** dialog box displays.
 5. Scan or type in the Sample ID. If typing the Sample ID, make sure the Sample ID is typed correctly.
The Sample ID is associated with the test results and displays in the **View Results** window and all the reports. The **Scan Cartridge Barcode** dialog box displays.
 6. Scan the barcode on the cartridge. Using the barcode information, the software automatically fills the boxes for the following fields: Select Assay, Reagent Lot ID, Cartridge SN, and Expiration Date.
-

Note If the barcode on the cartridge does not scan, then repeat the test with a new cartridge. If you have scanned the cartridge barcode in the software and the assay definition file is not available, a screen displays indicating the assay definition file is not loaded on the system. If this screen displays, contact Cepheid Technical Support.

7. Click **Start Test**. In the dialog box that displays, type your password, if required.
8. Open the instrument module door with the blinking green light and load the cartridge.
9. Close the door. The test starts and the green light stops blinking.

When the test is finished, the light turns off.

10. Wait until the system releases the door lock before opening the module door, then remove the cartridge.
11. Dispose of the used cartridges in the appropriate specimen waste containers according to your institution's standard practices.

14.1.2 Viewing and Printing Results

This section lists the basic steps for viewing and printing results. For more detailed instructions on how to view and print the results, see the *GeneXpert Dx System Operator Manual*.

1. Click the **View Results** icon to view results.
2. Upon completion of the test, click the **Report** button of the **View Results** window to view and/or generate a PDF report file.

14.2 GeneXpert Infinity System

14.2.1 Starting the Test

Before you start the test, make sure that:

- Important**
- The system is running the correct Xpertise software version shown in section - Materials Required but Not Provided.
 - The correct assay definition file is imported into the software.

This section lists the basic steps for running the test. For detailed instructions, see the *GeneXpert Infinity System Operator Manual*.

Note The steps you follow can be different if the system administrator changed the default workflow of the system.

1. Power up the instrument. The Xpertise software will launch automatically. If it does not, double-click the Xpertise software shortcut icon on the Windows® desktop.
2. Log on to the computer, then log on to the GeneXpert Xpertise software using your user name and password.
3. In the **Xpertise Software Home** workspace, click **Orders** and in the **Orders** workspace, click **Order Test**. The **Order Test - Patient ID** workspace displays.
4. Scan or type in the Patient ID. If typing the Patient ID, make sure the Patient ID is typed correctly. The Patient ID is associated with the test results and displays in the **View Results** window and all the reports.
5. Enter any additional information required by your institution, and click the **CONTINUE** button. The **Order Test - Sample ID** workspace displays.
6. Scan or type in the Sample ID. If typing the Sample ID, make sure the Sample ID is typed correctly. The Sample ID is associated with the test results and displays in the **View Results** window and all the reports.
7. Click the **CONTINUE** button. The **Order Test - Assay** workspace displays.
8. Scan the barcode on the cartridge. Using the barcode information, the software automatically fills the boxes for the following fields: Select Assay, Reagent Lot ID, Cartridge SN, and Expiration Date.

Note If the barcode on the cartridge does not scan, then repeat the test with a new cartridge. If you have scanned the cartridge barcode in the software and the assay definition file is not available, a screen displays indicating the assay definition file is not loaded on the system. If this screen displays, contact Cepheid Technical Support.

After the cartridge is scanned, the **Order Test - Test Information** workspace displays.

9. Verify that the information is correct, and click **Submit**. In the dialog box that displays, type your password, if required.
10. Place the cartridge on the conveyor belt. The cartridge automatically loads, the test runs, and the used cartridge are placed into the waste container.

14.2.2 Viewing and Printing Results

This section lists the basic steps for viewing and printing results. For more detailed instructions on how to view and print the results, see the *GeneXpert Infinity System Operator Manual*.

1. In the **Xpertise Software Home** workspace, click the **RESULTS** icon. The Results menu displays.
2. In the Results menu, select the **VIEW RESULTS** button. The **View Results** workspace displays showing the test results.
3. Click the **REPORT** button to view and/or generate a PDF report file.

15 Quality Control

15.1 Internal Controls

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

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

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

15.2 External Controls

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

To run a control using the Xpert Xpress SARS-CoV-2 test, perform the following steps:

1. Mix control by rapidly inverting the external control tube 5 times. Open cap on external control tube.
2. Open the cartridge lid.
3. Using a clean transfer pipette, transfer one draw of the external control sample (300 µL) into the large opening (Sample Chamber) in the cartridge shown in Figure 5.
4. Close cartridge lid.

16 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 PRESUMPTIVE POS	-	+	+/-
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	<p>The 2019 novel coronavirus (SARS-CoV-2) target nucleic acids are detected.</p> <ul style="list-style-type: none"> • 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 POS	<p>The 2019 novel coronavirus (SARS-CoV-2) nucleic acids may be present. Sample should be retested according to the Retest Procedure in Section 17.2. 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. • SPC: NA; SPC is ignored because a target amplification has occurred. • Probe Check: PASS; all probe check results pass.
SARS-CoV-2 NEGATIVE	<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.
INVALID	<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 (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.

Result	Interpretation
ERROR	<p>Presence or absence of the 2019 novel coronavirus (SARS-CoV-2) nucleic acids cannot be determined. Repeat test according to the Retest Procedure (Section 17.2).</p> <ul style="list-style-type: none"> • SARS-CoV-2: NO RESULT • SPC: NO RESULT • Probe Check: FAIL; all or one of the probe check results fail.¹ <p>¹ If the probe check passes, the error is caused by the maximum pressure limit exceeding the acceptable range, no sample added, or by a system component failure.</p>
NO RESULT	<p>Presence or absence of the 2019 novel coronavirus (SARS-CoV-2) nucleic acids cannot be determined. Repeat test according to the Retest Procedure (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)

The Xpert Xpress SARS-CoV-2 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 full 45 PCR cycles have been completed. When SARS-CoV-2 titers are high enough to initiate the EAT function, the SPC amplification curve may not be seen and its results may not be reported.

17 Retests

17.1 Reasons to Repeat the Assay

If any of the test results mentioned below occur, repeat the test once according to instructions in Section 17.2, Retest Procedure.

- A **PRESUMPTIVE POS** result indicates the 2019 novel coronavirus (SARS-CoV-2) nucleic acids may be present. Only one of the SARS-CoV-2 nucleic acid target was detected (E gene) while the other SARS-CoV-2 nucleic acid target (N2 gene) was not detected.
- An **INVALID** result indicates that the control SPC failed. The sample was not properly processed, PCR is inhibited, or the sample was not properly collected.
- An **ERROR** result could be due to, but not limited to, Probe Check Control failure, system component failure, no sample added, or the maximum pressure limits were exceeded.
- A **NO RESULT** indicates that insufficient data were collected. For example, cartridge failed integrity test, 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.

17.2 Retest Procedure

To retest a non-determinate result (**INVALID**, **NO RESULT**, or **ERROR**), or a **PRESUMPTIVE POS** result, use a new cartridge.

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

1. Put on a clean pair of gloves. Obtain a new Xpert Xpress SARS-CoV-2 cartridge and a new transfer pipette.
2. Check the specimen transport tube or external control tube is closed.
3. Mix the sample by rapidly invert the specimen transport medium tube or external control tube 5 times. Open the cap on the specimen transport tube or external control tube.
4. 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.

18 Limitations

- 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.
- 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 SARS-CoV-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.

19 Performance Characteristics

19.1 Clinical Evaluation

The performance of the Xpert Xpress SARS-CoV-2 test was evaluated using archived clinical nasopharyngeal (NP) swab specimens in viral transport medium. A total of 45 SARS-CoV-2 positive and 45 SARS-CoV-2 negative NP swab specimens were tested with Xpert Xpress SARS-CoV-2 in a randomized and blinded fashion.

All the 45 SARS-CoV-2 positive specimens and 30 of the 45 SARS-CoV-2 negative specimens were collected during COVID-19 pandemic in the US and had previously been characterized as positive or negative for SARS-CoV-2 by an EUA RT-PCR test. Fifteen of the 45 SARS-CoV-2 negative NP swab specimens were collected before December 2019 and are expected to be negative for SARS-CoV-2.

Positive Percent Agreement (PPA) and Negative Percent Agreement (NPA) were determined by comparing the results of the Xpert Xpress SARS-CoV-2 test relative to the expected results. Results of these 90 archived clinical NP swab specimens are shown in Table 3. The PPA was 97.8% (95% CI: 88.4% - 99.6%) and the NPA was 95.6% (95% CI: 85.2% - 98.8%).

Table 3. Xpert Xpress SARS-CoV-2 Performance Results

	Expected Results			
		Positive	Negative	Total
Xpert Xpress SARS-CoV-2	Positive	44 ^a	2 ^b	46
	Negative	1	43	44
	Total	45	45	90
	PPA	97.8% (95% CI: 88.4% - 99.6%)		
NPA	95.6% (95% CI: 85.2% - 98.8%)			

a. One specimen was reported as "SARS-CoV-2 Presumptive Pos" in initial testing and yielded a "SARS-CoV-2 Positive" test result upon retesting.

b. The two false positive specimens were collected during the COVID-19 pandemic.

20 Analytical Performance

20.1 Analytical Sensitivity (Limit of Detection)

Studies were performed to determine the analytical limit of detection (LoD) of the Xpert Xpress SARS-CoV-2. The LoD of Xpert Xpress SARS-CoV-2 was established using one lot of reagent and limiting dilutions of live SARS-CoV-2 virus (USA_WA1/2020) prepared in viral transport medium and NP swab clinical matrix. The concentration level with observed

hit rates greater than or equal to 95% in the LoD determination study were 0.0050 and 0.0200 PFU/mL for the N2 target and E target, respectively (Table 4). Verification of the estimated LoD claim was performed on one reagent lot in replicates of 20 prepared in pooled NP swab clinical matrix. The LoD is the lowest concentration (reported as PFU/mL) of live SARS-CoV-2 virus samples that can be reproducibly distinguished from negative samples $\geq 95\%$ of the time with 95% confidence. The claimed LoD is 0.0200 PFU/mL (Table 4).

Table 4. LoD Determination Using USA WA1/2020 Strain

Strain	Concentration (PFU/mL)	Total Valid Results	Hit Rate (%)	Hit Rate (%)	Mean Ct	Mean Ct
			N2 Target	E Target	N2 Target	E Target
SARS-CoV-2 virus (USA_WA1/2020)	0.0200	20	100	95.0	38.3	36.4
	0.0050	22	95.5	68.2	40.5	39.1
	0.0025	22	90.9	36.4	41.5	39.6
	0.0010	22	50.0	18.2	42.0	42.0
	0.0005	22	45.5	18.2	41.7	41.5
	0.0003	22	18.2	4.5	42.1	44.9
	0.0001	22	9.1	0	42.9	N/A
	0	0	0	0	N/A	N/A

20.2 Analytical Reactivity (Inclusivity)

The inclusivity of Xpert Xpress SARS-CoV-2 was evaluated using *in silico* analysis of the assay primers and probes in relation to 36,863 SARS-CoV-2 sequences available in the GISAID gene database for two targets, E and N2.

For the E target, 142 matching sequences were excluded due to ambiguity codes, which reduced the total to 36,721 sequences. Xpert Xpress SARS-CoV-2 had 99.4% match to the sequences with the exception of 187 sequences that had a single mismatch and 18 sequences with additional mismatches. Of the 18 sequences with additional mismatches, one sequence contained 2 mismatches in the forward primer region, three sequences contained a 5-nucleotide gap, 2 sequences contained multiple mismatches at the 3' end of the amplicon, and twelve sequences contained a 'AA' dinucleotide but this lies between the oligonucleotides used in the assay. None of these mismatches are expected to affect the performance of the assay.

For the N2 target, 132 matching sequences were excluded due to ambiguity codes, which reduced the total to 36,731 sequences. Xpert Xpress SARS-CoV-2 had 98.9% match to the sequences with the exception of 262 sequences that had a single mismatch and one sequence contained 3 mismatches. None of these mismatches are predicted to have a negative impact on the performance of the assay.

20.3 Analytical Specificity (Exclusivity)

An *in silico* analysis for possible cross-reactions with all the organisms listed in Table 5 was conducted by mapping primers and probes in the Xpert Xpress SARS-CoV-2 test individually to the sequences downloaded from the GISAID database. E primers and probes are not specific for SARS-CoV-2 and will detect human and bat SARS-coronavirus. No potential cross reactivity with other organisms listed in Table 5 is predicted based on the *in silico* analysis.

Table 5. Xpert Xpress SARS-CoV-2 Analytical Specificity Microorganisms

Microorganisms from the Same Genetic Family	High Priority Organisms
Human coronavirus 229E	Adenovirus (e.g. C1 Ad. 71)
Human coronavirus OC43	Human Metapneumovirus (hMPV)
Human coronavirus HKU1	Parainfluenza virus 1-4
Human coronavirus NL63	Influenza A

Microorganisms from the Same Genetic Family	High Priority Organisms
SARS-coronavirus	Influenza B
MERS-coronavirus	Influenza C
Bat coronavirus	Enterovirus (e.g. EV68)
	Respiratory syncytial virus
	Rhinovirus
	<i>Chlamydia pneumoniae</i>
	<i>Haemophilus influenzae</i>
	<i>Legionella pneumophila</i>
	<i>Mycobacterium tuberculosis</i>
	<i>Streptococcus pneumoniae</i>
	<i>Streptococcus pyogenes</i>
	<i>Bordetella pertussis</i>
	<i>Mycoplasma pneumoniae</i>
	<i>Pneumocystis jirovecii</i> (PJP)
	Parechovirus
	<i>Candida albicans</i>
	<i>Corynebacterium diphtheriae</i>
	<i>Legionella non-pneumophila</i>
	<i>Bacillus anthracis</i> (Anthrax)
	<i>Moraxella catarrhalis</i>
	<i>Neisseria elongata</i> and <i>N. meningitidis</i>
	<i>Pseudomonas aeruginosa</i>
	<i>Staphylococcus epidermidis</i>
	<i>Staphylococcus salivarius</i>
	<i>Leptospira</i>
	<i>Chlamydia psittaci</i>
	<i>Coxiella burnetii</i> (Q-Fever)
	<i>Staphylococcus aureus</i>

20.4 Interfering Substances

Potentially interfering substances studies have been conducted for previous Xpert Flu/RSV tests developed for the GeneXpert Instrument System, including Xpert Xpress Flu/RSV and Xpert Flu/RSV XC tests and assay interference was not observed in these studies. Further testing evaluating potentially interfering substances was not conducted with the Xpert Xpress SARS-CoV-2 test. The Xpert Xpress SARS-CoV-2 test uses conventional well-established nucleic acid extraction methods that are utilized with the Xpert Xpress Flu/RSV and Xpert Flu/RSV XC tests. In addition, the Xpert Flu/RSV tests are validated for use with the same specimen types, nasopharyngeal swab specimens, as the Xpert Xpress SARS-CoV-2 test. Therefore, assay interference from these substances is not expected for the Xpert Xpress SARS-CoV-2 test.

20.5 Carry-over Contamination Study

Carry-over studies have been conducted for previous Xpert tests developed for the GeneXpert system, including Xpert Xpress Flu/RSV, and no contamination due to carry-over was observed. Further testing for carry-over contamination was not conducted for Xpert Xpress SARS-CoV-2. To minimize test-to-test contamination, specimen and fluids including amplicons are contained within the single-use, disposable cartridge. The self-contained cartridge design prevents the GeneXpert instrument coming into contact with any fluids within the cartridge. Precise fluidic handling within the enclosed cartridge is driven by the syringe and valve, commanded by the assay definition file (ADF) and automated by the GeneXpert instrument. No manual pipetting step is required other than the addition of the specimen to the cartridge by the user prior to the cartridge being placed on the instrument. Once the specimen is added to the cartridge the lid is closed. Thus the instrument and cartridge design are a closed system which minimizes the potential for carry-over.

21 Reproducibility

The reproducibility of the Xpert Xpress SARS-CoV-2 test was established at three sites using a 5-member panel including one negative sample, two low positive (~1.5x LoD) and two moderate positive (~3x LoD) samples. The negative sample consisted of simulated matrix without target microorganism or target RNA. The positive samples were contrived samples in a simulated matrix using either AccuPlex™ SARS-CoV-2 reference material (targeting the N2 and E genes) or inactivated SARS-CoV Urbani strain (targeting the E gene).

Testing was conducted over six (6) days, using three (3) lots of Xpert Xpress SARS-CoV-2 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 Reps = 144 observations/panel member). The results from the study are summarized in Table 6.

Table 6. Summary of Reproducibility Results - % Agreement by Study Site/Operator

Sample ID	Site 1			Site 2			Site 3			% Total Agreement ^a by Sample
	Op1	Op2	Site	Op1	Op2	Site	Op1	Op2	Site	
Negative	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)
SARS-CoV-2 Low Pos	100% (24/24)	100% (24/24)	100% (48/48)	100% (24/24)	95.8% (23/24)	97.9% (47/48)	95.8% (23/24)	100% (24/24)	97.9% (47/48)	98.6% (142/144)
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)
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)
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)

a. Agreement was calculated as the percentage of observed results that were in agreement with the expected results.

22 References

- Centers for Disease Control and Prevention. <https://www.cdc.gov/coronavirus/2019-ncov/index.html>. Accessed February 9, 2020.
- bioRxiv. (<https://www.biorxiv.org/content/10.1101/2020.02.07.937862v1>). Accessed March 3, 2020.
- Centers for Disease Control and Prevention. Biosafety in Microbiological and Biomedical laboratories (refer to latest edition). <http://www.cdc.gov/biosafety/publications/>
- Clinical and Laboratory Standards Institute. Protection of Laboratory Workers from Occupationally Acquired Infections; Approved Guideline. Document M29 (refer to latest edition).
- REGULATION (EC) No 1272/2008 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 16 December 2008 on the classification labeling and packaging of substances and mixtures amending and repealing, List of Precautionary Statements, Directives 67/548/EEC and 1999/45/EC (amending Regulation (EC) No 1907/2007).
- Occupational Safety and Health Standards, Hazard Communication, Toxic and Hazard Substances (March 26, 2012) (29 C.F.R., pt. 1910, subpt. Z).

23 Cepheid Headquarters Locations

Corporate Headquarters

Cepheid
904 Caribbean Drive
Sunnyvale, CA 94089
USA

Telephone: + 1 408 541 4191
Fax: + 1 408 541 4192
www.cepheid.com

European Headquarters

Cepheid Europe SAS
Vira Solelh
81470 Maurens-Scopont
France

Telephone: + 33 563 825 300
Fax: + 33 563 825 301
www.cepheidinternational.com

24 Technical Assistance

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

United States


















Telephone: + 1 888 838 3222
Email:
techsupport@cepheid.com

France

Telephone: + 33 563 825 319
Email:
support@cepheideurope.com

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

25 Table of Symbols

Symbol	Meaning
	Catalog number
	<i>In vitro</i> diagnostic medical device
	Do not reuse
	Batch code
	CE marking – European Conformity
	Authorized Representative in the European Community
	Consult instructions for use
	Caution
	Manufacturer
	Country of manufacture
	Contains sufficient for <i>n</i> tests
	Control
	Expiration date
	Temperature limitation
	Biological risks
	Authorized Representative in Switzerland
	Importer



Cepheid
904 Caribbean Drive
Sunnyvale, CA 94089
USA

Phone: + 1 408 541 4191

Fax: + 1 408 541 4192



Cepheid Europe SAS
Vira Solelh
81470 Maurens-Scopont
France

Phone: + 33 563 825 300

Fax: + 33 563 825 301



Cepheid Switzerland GmbH
Zürcherstrasse 66
Postfach 124, Thalwil
CH-8800
Switzerland



Cepheid Switzerland GmbH
Zürcherstrasse 66
Postfach 124, Thalwil
CH-8800
Switzerland



26 Revision History

Description of Changes: From 302-3787 Rev. C. to Rev. D.

Purpose: Minor updates.

Section	Description of Change
Throughout	Removed nasal wash/aspirate.
14	Separated procedures for GeneXpert Dx System and GeneXpert Infinity System. Revised GeneXpert Infinity System procedure.
26	Added Revision History section.