

GeneXpert.
Powered By CEPHEID INNOVATION

Xpert[®] Xpress SARS-CoV-2/Flu/RSV

Instructions for Use

For Use Under an Emergency Use Authorization (EUA) Only



XPCOV2/FLU/RSV-10

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



For use under an Emergency Use
Authorization (EUA) Only



For *In Vitro* Diagnostic use

302-4419, Rev. C January 2021

Trademark, Patents and Copyright Statements

Cepheid[®], the Cepheid logo, GeneXpert[®] and Xpert[®] are trademarks of Cepheid.
Windows[®] is a trademark of Microsoft Corporation.

THE PURCHASE OF THIS PRODUCT CONVEYS TO THE BUYER THE NON-TRANSFERABLE RIGHT TO USE IT IN ACCORDANCE WITH THIS 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.

Copyright © 2021 Cepheid. All rights reserved.



Cepheid
904 Caribbean Drive
Sunnyvale, CA 94089 USA
Phone: +1 408 541 4191
Fax: +1 408 541 4192

Xpert Xpress SARS-CoV-2/Flu/RSV

For use under the Emergency Use Authorization (EUA) only.

1 Proprietary Name

Xpert® Xpress SARS-CoV-2/Flu/RSV

2 Common or Usual Name

Xpert Xpress SARS-CoV-2/Flu/RSV

3 Intended Use

The Xpert Xpress SARS-CoV-2/Flu/RSV test is a rapid, multiplexed real-time RT-PCR test intended for the simultaneous qualitative detection and differentiation of SARS-CoV-2, influenza A, influenza B, and respiratory syncytial virus (RSV) viral RNA in either nasopharyngeal swab, nasal swab or nasal wash/ aspirate specimens collected from individuals suspected of respiratory viral infection consistent with COVID-19 by their healthcare provider.¹ Clinical signs and symptoms of respiratory viral infection due to SARS-CoV-2, influenza, and RSV can be similar.

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

Testing of nasopharyngeal or nasal swab specimens using the Xpert Xpress SARS-CoV-2/Flu/RSV test run on the GeneXpert Xpress System (Tablet and Hub Configurations) is authorized for use at the Point of Care (POC), i.e., in patient care settings operating under a CLIA Certificate of Waiver, Certificate of Compliance, or Certificate of Accreditation.

Results are for the simultaneous detection and differentiation of SARS-CoV-2, influenza A virus, influenza B virus and RSV nucleic acids in clinical specimens and is not intended to detect influenza C virus. SARS-CoV-2, influenza A, influenza B and RSV RNA identified by this test are generally detectable in upper respiratory specimens during the acute phase of infection. Positive results are indicative of the presence of the identified virus, but do not rule out bacterial infection or co-infection with other pathogens not detected by the test.

Clinical correlation with patient history and other diagnostic information is necessary to determine patient infection status. The agent detected may not be the definite cause of disease. Laboratories within the United States and its territories are required to report all SARS-CoV-2 results to the appropriate public health authorities.

Negative results do not preclude SARS-CoV-2, influenza A virus, influenza B virus and/or RSV 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/or epidemiological information.

¹ For this EUA, a healthcare provider includes, but is not limited to, physicians, nurses, pharmacists, technologists, laboratory directors, epidemiologists, or any other practitioners or allied health professionals.

Xpert Xpress SARS-CoV-2/Flu/RSV

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

4 Summary and Explanation

An outbreak of respiratory illness of unknown etiology in Wuhan City, Hubei Province, China was initially reported to the World Health Organization (WHO) on December 31, 2019.¹ Chinese authorities identified a novel coronavirus (2019-nCoV), which has since spread globally, resulting in a pandemic of coronavirus disease 2019 (COVID-19). 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 International Committee on Taxonomy of Viruses (ICTV) renamed the virus SARS-CoV-2.²

Influenza, or the flu, is a contagious viral infection of the respiratory tract. Transmission of influenza is primarily airborne (i.e., coughing or sneezing) and the peak of transmission usually occurs in the winter months. Symptoms commonly include fever, chills, headache, malaise, cough and sinus congestion. Gastrointestinal symptoms (i.e., nausea, vomiting or diarrhea) may also occur, primarily in children, but are less common. Symptoms generally appear within two days of exposure to an infected person. Pneumonia may develop as a complication due to influenza infection, causing increased morbidity and mortality in pediatric, elderly, and immunocompromised populations.^{3, 4}

Influenza viruses are classified into types A, B, and C, the former two of which cause the most human infections. Influenza A (Flu A) is the most common type of influenza virus in humans and is generally responsible for seasonal flu epidemics and potentially pandemics. Flu A viruses can also infect animals such as birds, pigs, and horses. Infections with influenza B (Flu B) virus are generally restricted to humans and less frequently cause epidemics.⁵ Flu A viruses are further divided into subtypes on the basis of two surface proteins: hemagglutinin (H) and neuraminidase (N). Seasonal flu is normally caused by influenza A subtypes H1, H2, H3, N1 and N2.

Respiratory Syncytial Virus (RSV), a member of the *Pneumoviridae* family (formerly *Paramyxoviridae*), consisting of two strains (subgroups A and B) is also the cause of a contagious disease that affects primarily infants, and the elderly who are immunocompromised (e.g. patients with chronic lung disease or undergoing treatment for conditions that reduce the strength of their immune system).⁶ The virus can remain infectious for hours on countertops and toys and can cause both upper respiratory infections, such as colds, and lower respiratory infections manifesting as bronchiolitis and pneumonia.⁶ By the age of two years, most children have already been infected by RSV and because only weak immunity develops, both children and adults can be re-infected.⁶ Symptoms appear four to six days after infection and are usually self-limiting, lasting approximately one to two weeks in infants. In adults, infection lasts about 5 days and presents as symptoms consistent with a cold, such as rhinorrhea, fatigue, headache, and fever. The RSV season mirrors influenza somewhat as infections begin to rise during the fall through early spring.^{5, 6}

Active surveillance programs in conjunction with infection prevention precautions are important components for preventing transmission of SARS-CoV-2, influenza and RSV.

Xpert Xpress SARS-CoV-2/Flu/RSV

The use of assays providing rapid results to identify patients infected with these viruses can be an important factor for effective control, proper choice of treatment, and prevention of widespread outbreaks.

The Xpert Xpress SARS-CoV-2/Flu/RSV test is a molecular *in vitro* diagnostic test that aids in the detection and differentiation of RNA from Flu A, Flu B, RSV and SARS-CoV-2 virus and is based on widely used nucleic acid amplification technology. The Xpert Xpress SARS-CoV-2/Flu/RSV test contains primers and probes and internal controls used in RT-PCR for the *in vitro* qualitative detection and differentiation of RNA from Flu A, Flu B, RSV and SARS-CoV-2 virus in upper respiratory specimens.

5 Principle of the Procedure

The Xpert Xpress SARS-CoV-2/Flu/RSV test is an automated *in vitro* diagnostic test for qualitative detection and differentiation of RNA from Flu A, Flu B, RSV and SARS-CoV-2 virus. The Xpert Xpress SARS-CoV-2/Flu/RSV test is performed on GeneXpert Xpress System.

The GeneXpert Xpress System 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 SARS-CoV-2/Flu/RSV test includes reagents for the detection of RNA from Flu A, Flu B, RSV and SARS-CoV-2 virus in either nasopharyngeal swab or nasal swab specimens. 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 nasopharyngeal swab or nasal swab specimen is collected and placed into a transport tube containing 3 mL of viral transport medium or 3mL 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/Flu/RSV cartridge. The GeneXpert cartridge is loaded onto the GeneXpert Xpress System platform, which performs hands-off, automated sample processing, and real-time RT-PCR for detection of viral RNA.

Xpert Xpress SARS-CoV-2/Flu/RSV

6 Reagents and Instruments

6.1 Materials Provided



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

Xpert Xpress SARS-CoV-2/Flu/RSV Cartridges with Integrated Reaction Tubes

10

- Bead 1, Bead 2, and Bead 3 (freeze-dried) **1 of each per cartridge**
- Lysis Reagent **1.0 mL per cartridge**
- Binding Reagent **1.0 mL per cartridge**
- Elution Reagent **3.0 mL per cartridge**
- Wash Reagent **0.4 mL per cartridge**

Disposable Transfer Pipettes

10-12 per kit

Flyer

1 per kit

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

Quick Reference Instructions

2 per kit

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

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

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

7 Storage and Handling



- Store the Xpert Xpress SARS-CoV-2/Flu/RSV 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

- 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,

Xpert Xpress SARS-CoV-2/Flu/RSV

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

External controls in the form of inactivated virus(es) are available from ZeptoMetrix (Buffalo, NY).

- External Positive Control: Catalog # NATFRC-6C (NATtrol Flu/RSV/SARS-CoV-2)
- External Negative Control: Catalog # NATCV9-6C (Coxsackievirus A9)

10 Warnings and Precautions

10.1 General

- For *in vitro* diagnostic use.
- For emergency use only.
- Positive results are indicative of presence of Flu A, Flu B, RSV, or SARS-CoV-2 RNA.
- Laboratories within the United States and its territories are required to report all SARS-CoV-2 results to the appropriate public health authorities.
- Performance characteristics of this test have been established with the specimen types listed in the Intended Use Section only. The performance of this assay with other specimen types or samples has not been evaluated.
-  Treat all biological specimens, including used cartridges, as if capable of transmitting infectious agents. Because it is often impossible to know which might be infectious, all biological specimens should be handled using standard precautions. Guidelines for specimen handling are available from the U.S. Centers for Disease Control and Prevention⁷ and the Clinical and Laboratory Standards Institute.⁸
- 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.

Xpert Xpress SARS-CoV-2/Flu/RSV

10.3 Assay/Reagent

- Do not open the Xpert Xpress SARS-CoV-2/Flu/RSV 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.
- ② • Each single-use Xpert Xpress SARS-CoV-2/Flu/RSV cartridge is used to process one test. Do not reuse processed cartridges.
- ② • 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^{9,10}

- **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 nasal swab collection procedure.



Nasopharyngeal and nasal swab specimens can be stored at room temperature (15–30 °C) for up to 24 hours in viral transport medium or 48 hours in saline until testing is performed on the GeneXpert Instrument Systems. Alternatively, nasopharyngeal and nasal swab specimens can be stored refrigerated (2–8 °C) up to seven days in viral transport medium or saline until testing is performed on the GeneXpert Xpress System.

Refer to the CDC Interim Guidelines for Collecting, Handling, and Testing Clinical Specimens from Persons Under Investigation (PUIs) for Coronavirus Disease 2019 (COVID-19)

<https://www.cdc.gov/coronavirus/2019-nCoV/lab/guidelines-clinical-specimens.html>.

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

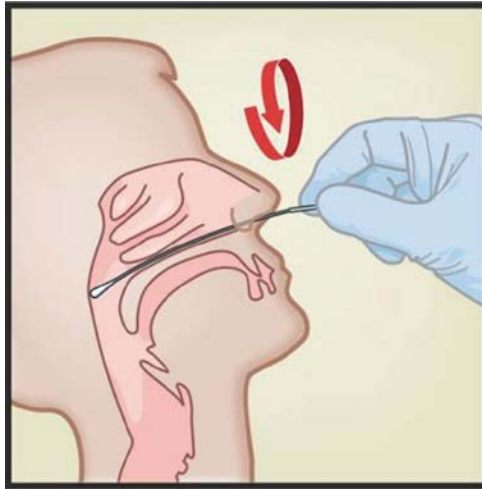


Figure 1. Nasopharyngeal Swab Collection

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 3mL of saline. 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 SARS-CoV-2/Flu/RSV 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).

Tablet Configuration



Hub Configuration



Figure 4. Tablet and Hub System Configurations

Xpert Xpress SARS-CoV-2/Flu/RSV

- 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.

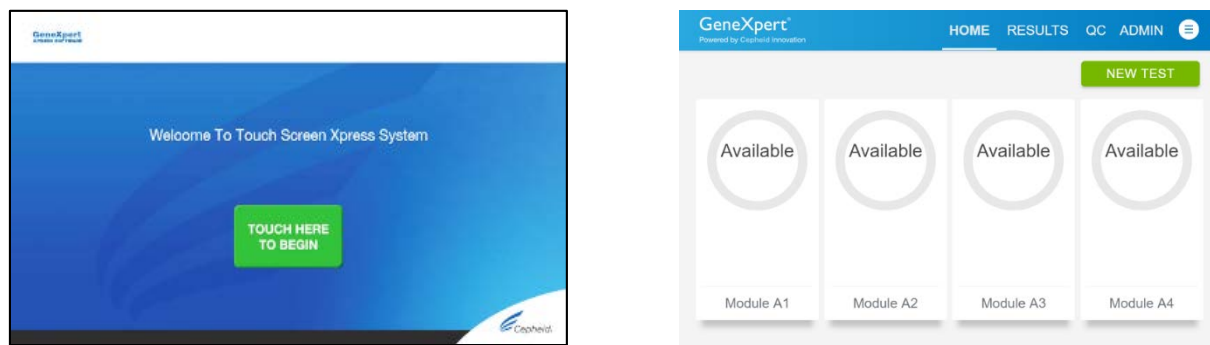
13.2 Starting the Hub Configuration

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).

Xpert Xpress SARS-CoV-2/Flu/RSV



Software Version 5.0 or Software Version 5.1

Software Version 6.1 or Higher

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).

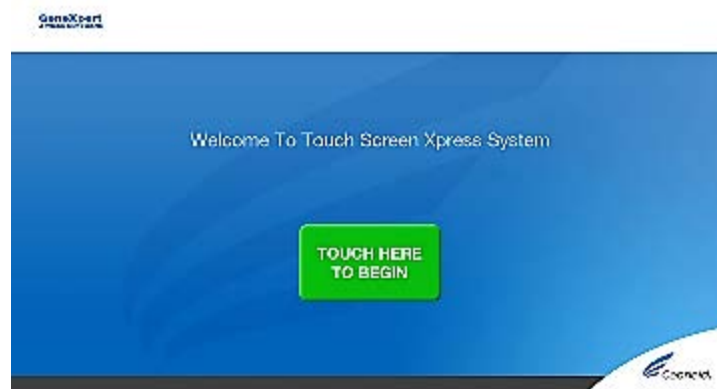


Figure 6. Welcome Screen

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.

Xpert Xpress SARS-CoV-2/Flu/RSV

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.

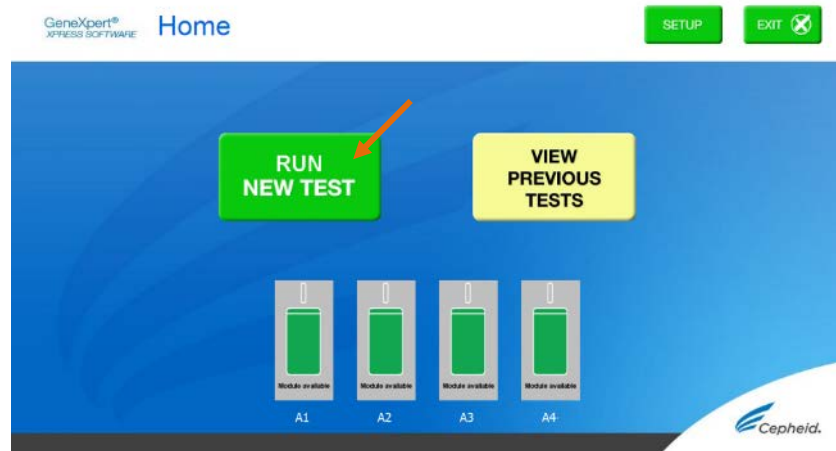


Figure 7. RUN NEW TEST button on Home Screen (GeneXpert Xpress IV screen shown)

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 at the frequency noted below.

- Each time a new lot of Xpert Xpress SARS-CoV-2/Flu/RSV kits is received.
- Each time a new shipment of Xpert Xpress SARS-CoV-2/Flu/RSV 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.

Xpert Xpress SARS-CoV-2/Flu/RSV

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 SARS-CoV-2/Flu/RSV 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.
 - SARS-CoV-2, Flu A, Flu B and RSV: Select **Xpert Xpress_SARS-CoV-2_Flu_RSV**
 - SARS-CoV-2 and Flu only: Select **Xpert Xpress_SARS-CoV-2_Flu**
 - SARS-CoV-2 only: Select **Xpert Xpress_SARS-CoV-2**

Only the test result for the assay selected at this step will be collected once the test is started. SARS-CoV-2, Flu A, Flu B, and RSV results will only be collected if the Xpert Xpress_SARS-CoV-2_Flu_RSV assay is selected.

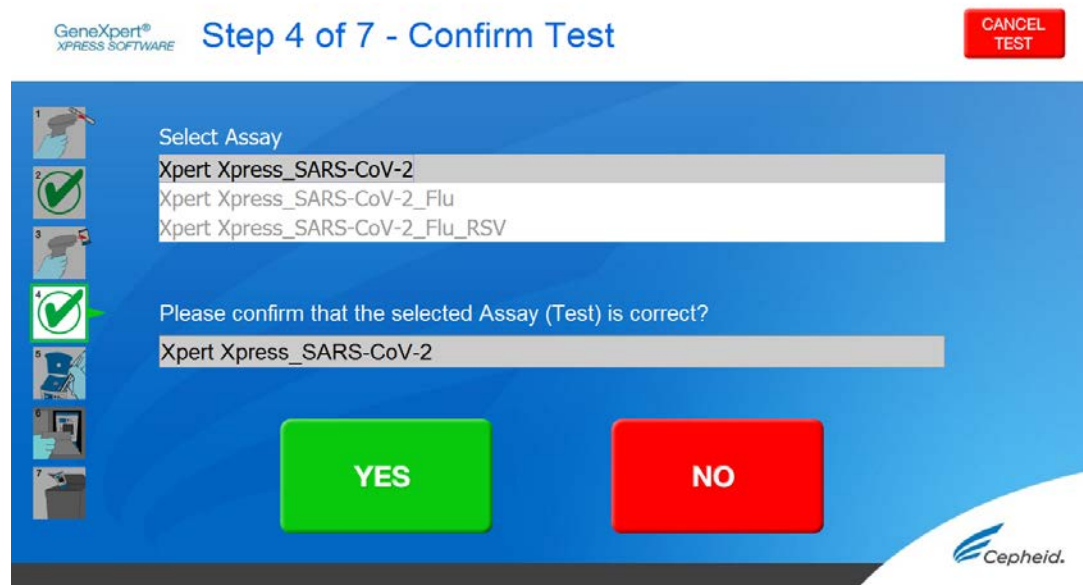


Figure 8. Confirm Test Screen – Select Assay

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.

Xpert Xpress SARS-CoV-2/Flu/RSV

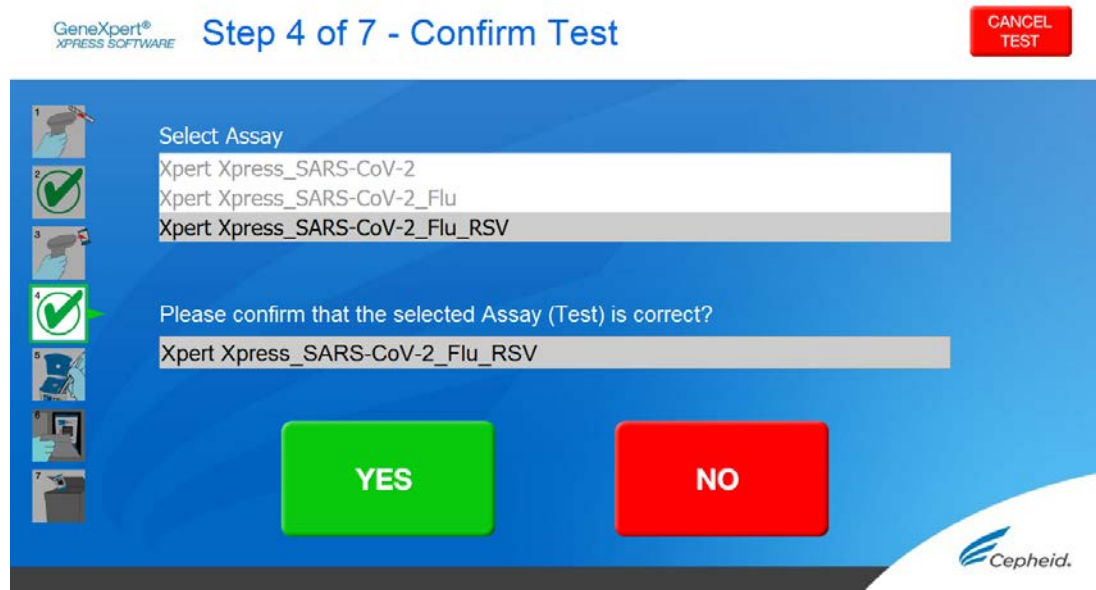


Figure 9. Confirm Test Screen



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).

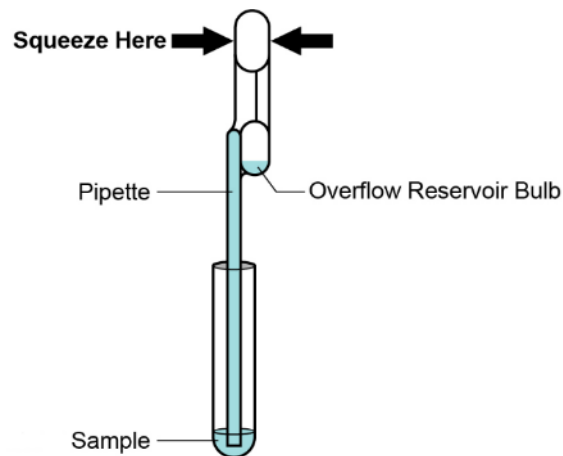


Figure 10. Transfer Pipette

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 μ L) 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.

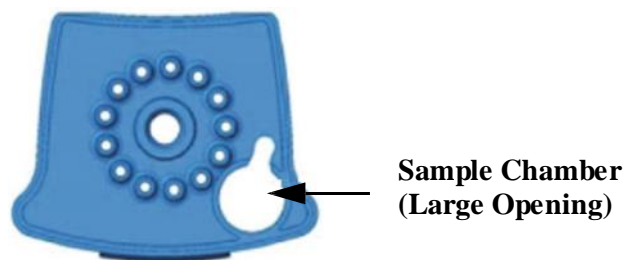


Figure 11. Xpert Xpress SARS-CoV-2/Flu/RSV Cartridge (Top View)

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.

Xpert Xpress SARS-CoV-2/Flu/RSV

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 SARS-CoV-2/Flu/RSV 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 Start 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.

Xpert Xpress SARS-CoV-2/Flu/RSV

15.3 Results of Past Tests

1. Touch the **VIEW PREVIOUS TESTS** button on the Home screen shown in Figure 12.

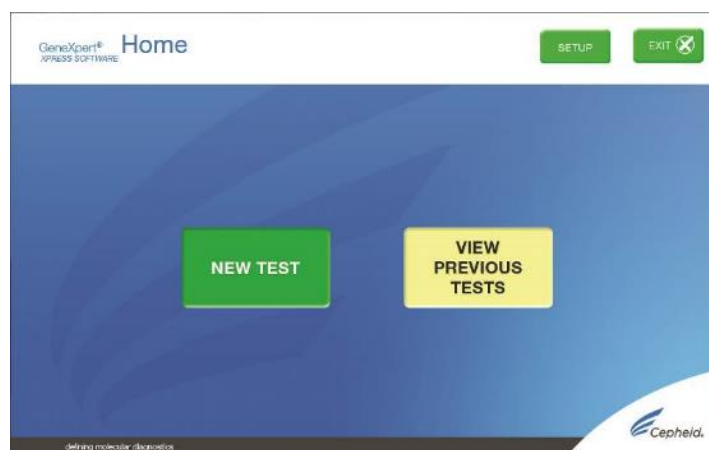


Figure 12. **VIEW PREVIOUS TESTS** button on Home Screen

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

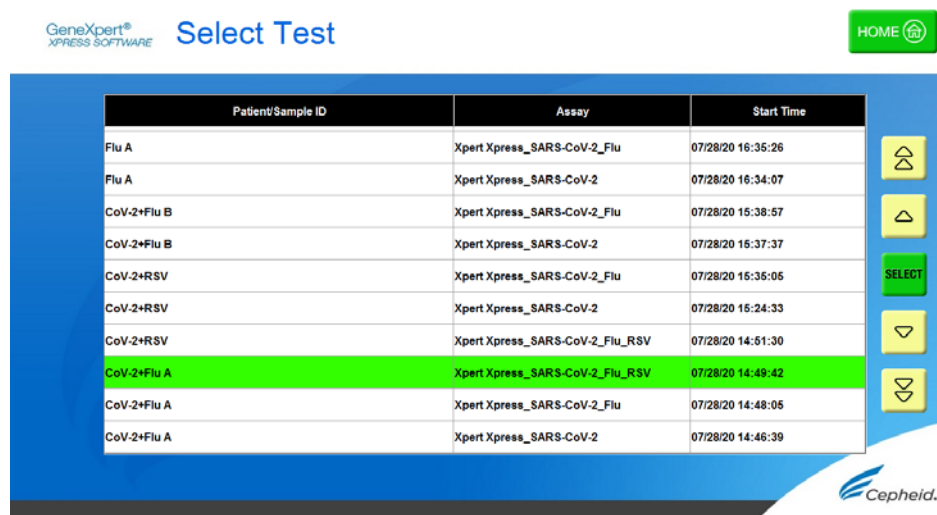


Figure 13. **SELECT** button

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.

Xpert Xpress SARS-CoV-2/Flu/RSV

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).

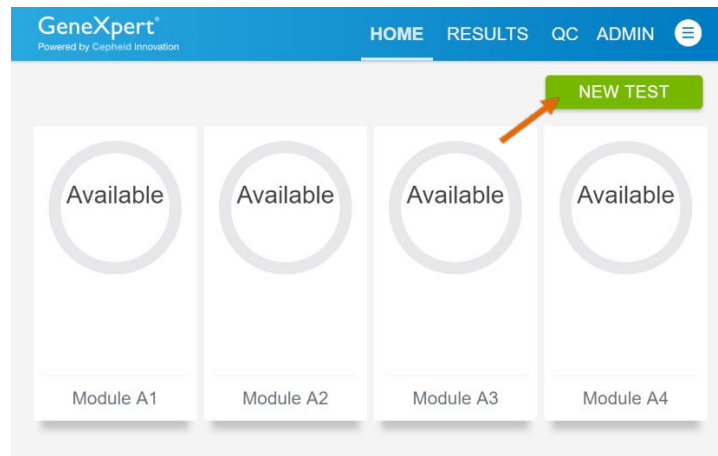


Figure 14. Home Screen

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.

Xpert Xpress SARS-CoV-2/Flu/RSV

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 SARS-CoV-2/Flu/RSV 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.

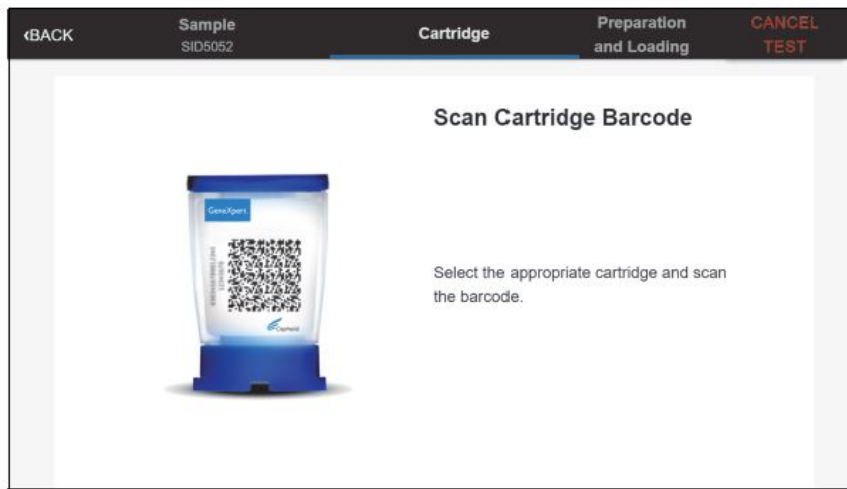


Figure 16. Scan Cartridge Barcode Screen

5. Select the appropriate cartridge with the sample and scan the cartridge barcode. After scanning, the Select Test screen appears.
6. Select the test to run (see Figure 17):
 - SARS-CoV-2, Flu A, Flu B and RSV: Select **Xpert Xpress_SARS-CoV-2_Flu_RSV**
 - SARS-CoV-2 and Flu only: Select **Xpert Xpress_SARS-CoV-2_Flu**
 - SARS-CoV-2 only: Select **Xpert Xpress_SARS-CoV-2**

Only the test result for the assay selected at this step will be collected once the test is started. SARS CoV-2, Flu A, Flu B, and RSV results will only be collected if the Xpert Xpress_SARS-CoV-2_Flu_RSV assay is selected.

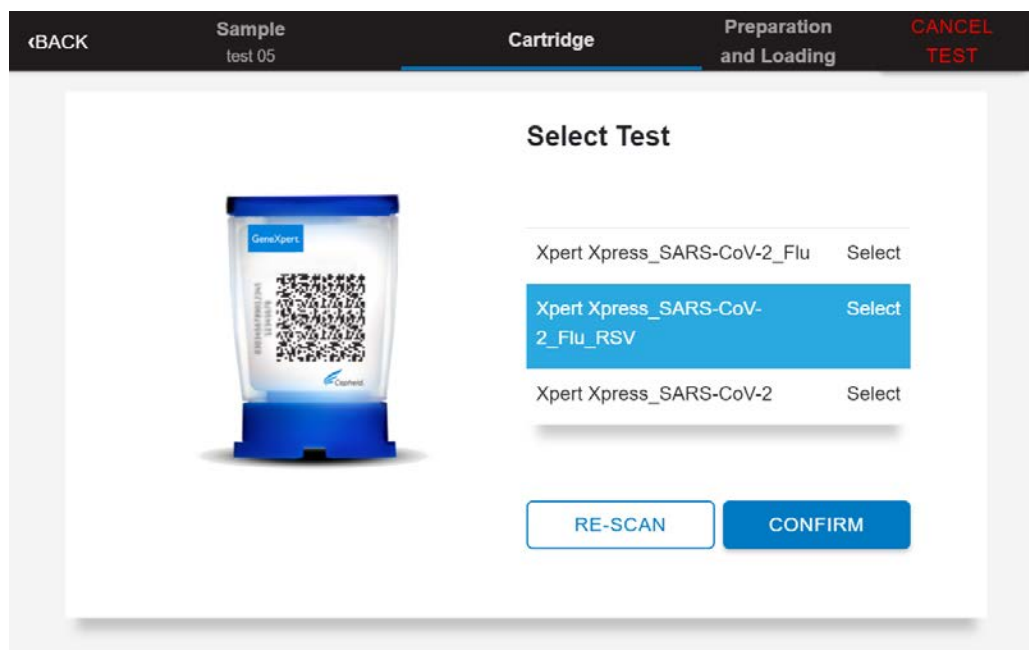


Figure 17. Select Test Screen

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

Confirm Test Information

Confirm the Test Information entered below is accurate.

Patient ID	PID12345
Sample ID	SID12345
Assay Name	Xpert Xpress_SARS-CoV-2_Flu_RSV

RE-SCAN CONFIRM

Figure 18. Confirm Test Information Screen

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

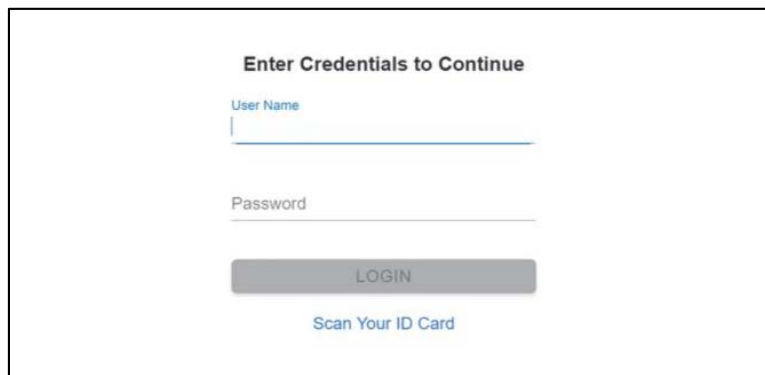


Figure 19. Enter Credentials to Continue Screen

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



Figure 20. Cartridge Preparation Screen

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

Note Do not place unwrapped pipette on the workbench.

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

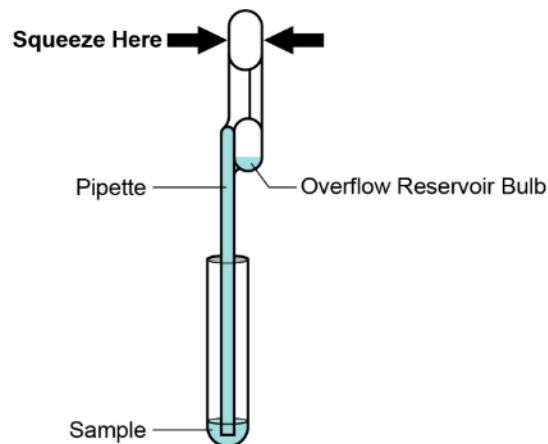


Figure 21. Transfer Pipette

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

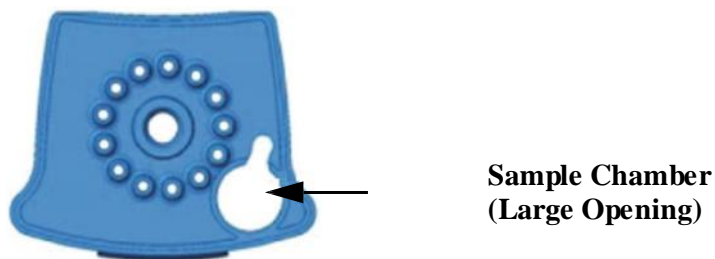


Figure 22. Xpert Xpress SARS-CoV-2/Flu/RSV Cartridge (Top View)

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.

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

Xpert Xpress SARS-CoV-2/Flu/RSV

16.3 Running External Controls

It is recommended that external controls be tested at the frequency noted below.

- Each time a new lot of Xpert Xpress SARS-CoV-2/Flu/RSV kits is received.
 - Each time a new shipment of Xpert Xpress SARS-CoV-2/Flu/RSV kits is received even if it is the same lot previously received.
 - Each time a new operator is performing the test (i.e., operator who has not performed the test recently)
 - When problems (storage, operator, instrument, or other) are suspected or identified
 - If otherwise required by your institution's standard Quality Control (QC) procedures
1. Put on a new pair of gloves if performing a new test. Touch the **QC** button on the Home screen (see Figure 23).

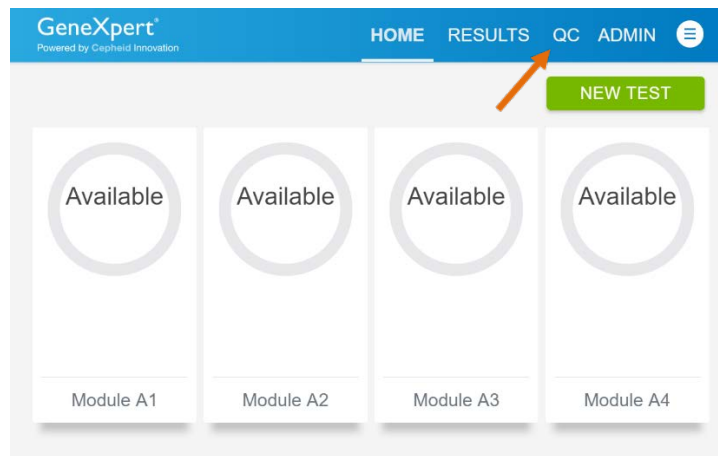


Figure 23. Home Screen

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

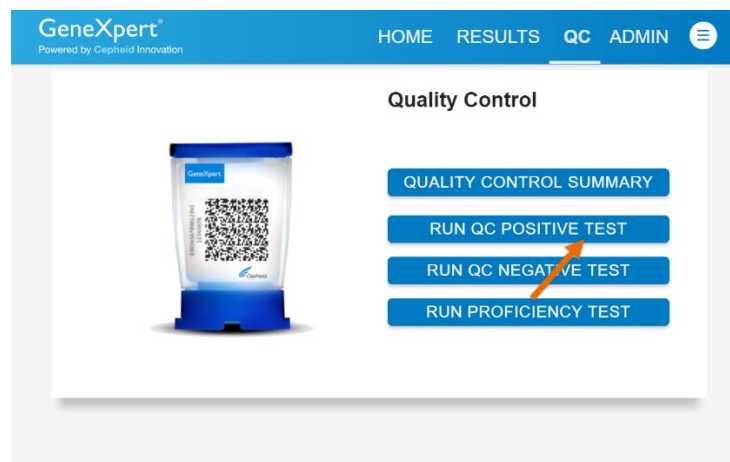


Figure 24. Quality Control Screen

Xpert Xpress SARS-CoV-2/Flu/RSV

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



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 SARS-CoV-2/Flu/RSV cartridge does not scan or scanning the barcode results in an error message stating that the cartridge is expired, then repeat the test with a new cartridge.

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

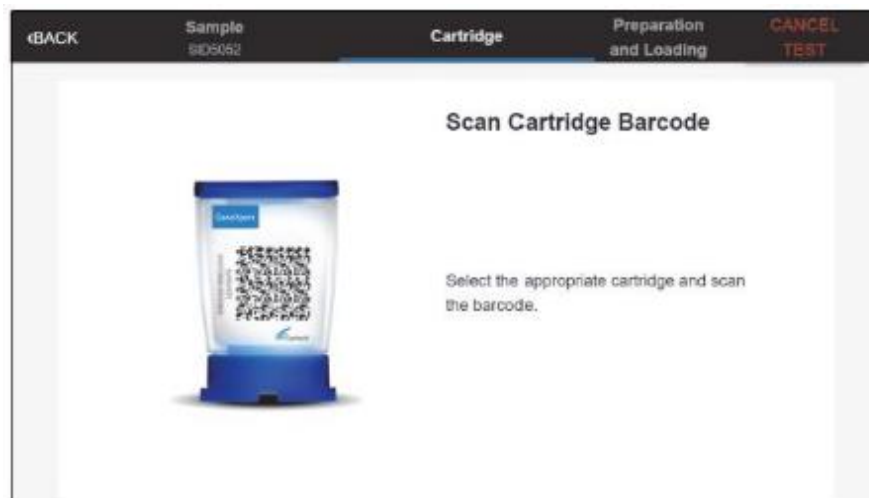


Figure 25. Scan Cartridge Barcode Screen

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

Confirm Test Information

Confirm the Test Information entered below is accurate.

Sample ID	Positive Control
Assay Name	Xpert Xpress_SARS-CoV-2_Flu_RSV



Figure 26. Confirm Test Information

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

Note Do not place unwrapped pipette on the workbench.

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

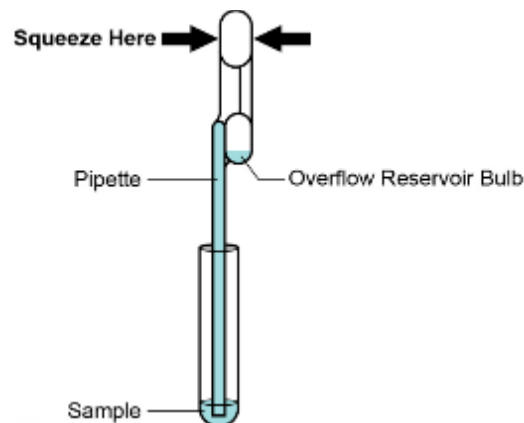


Figure 27. Transfer Pipette

Xpert Xpress SARS-CoV-2/Flu/RSV

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

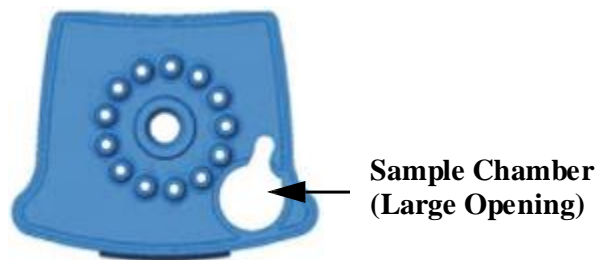


Figure 28. Xpert Xpress SARS-CoV-2/Flu/RSV Cartridge (Top View)

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

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

16.4 Loading the Cartridge

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

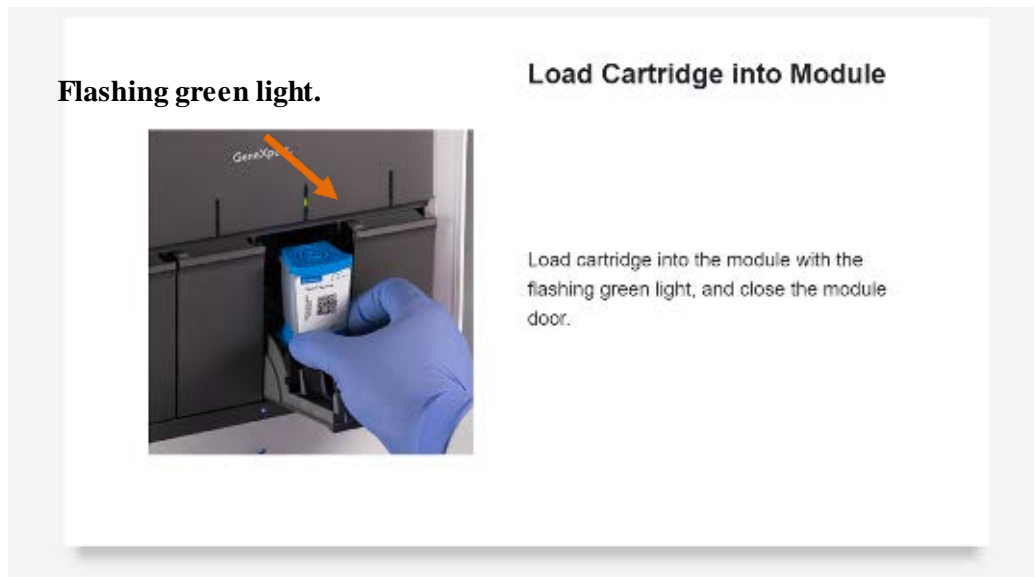


Figure 29. Load Cartridge into Module Screen


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

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

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


6. 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.

7. Open the module door, remove the used cartridge, and properly dispose of the cartridge according to your institution's policy.
8. Touch **HOME** to go back to the Home screen.
9. 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 30).

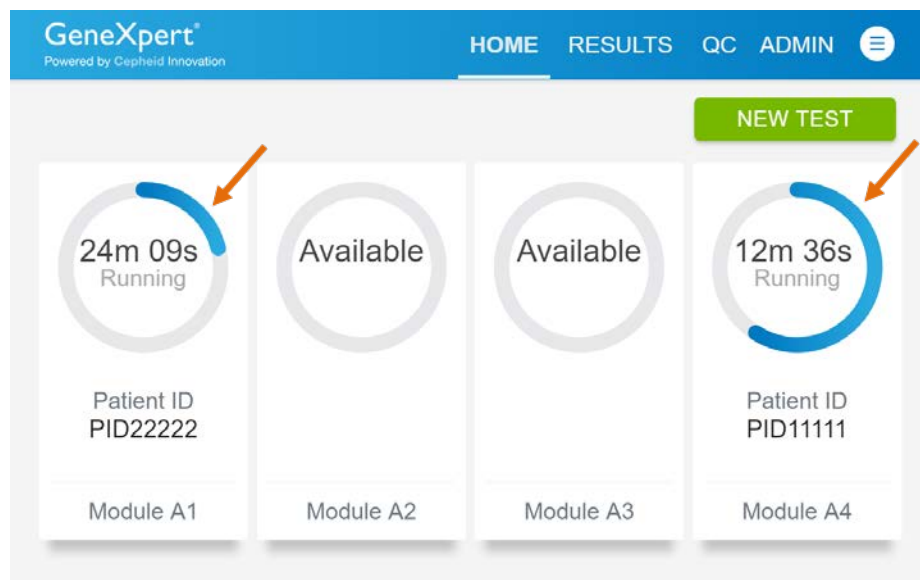


Figure 30. Home Screen showing Two Tests Running

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

Xpert Xpress SARS-CoV-2/Flu/RSV

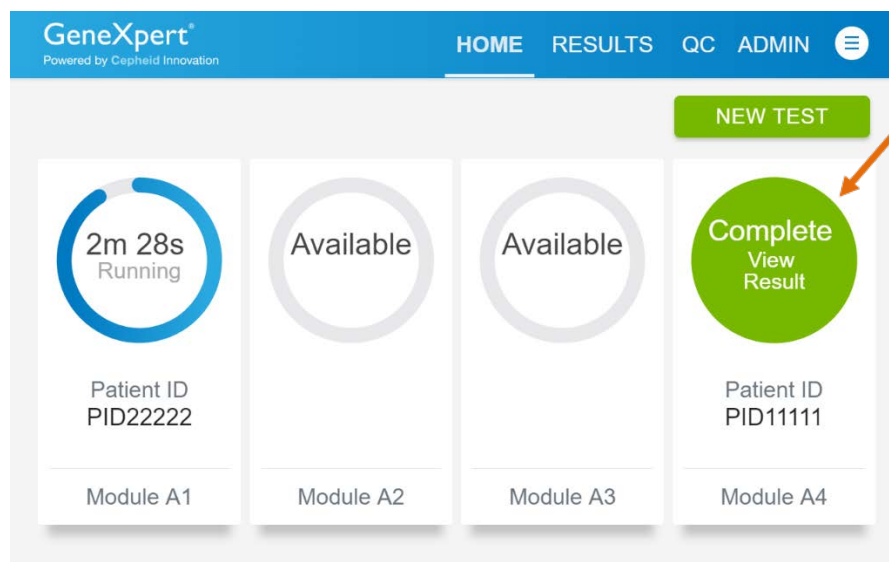


Figure 31. Home Screen with One of Two Tests Completed

16.6 Viewing Test Results

1. 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.

The image shows the GeneXpert Results screen. At the top is a blue header with the GeneXpert logo and navigation tabs: HOME, RESULTS, QC, ADMIN. Below the header is a 'Results' section with a filter bar and a table of test results. The filter bar includes 'Filter: Start Date', 'End Date', 'Assay Name', 'Test Type', a search bar, and an 'EXPORT' button. The table has columns: Select All, Patient ID, Sample ID, Test Type, Assay Name, Start Date & Time, Reagent Lot, and Result. The results are sorted by date and time.

Select All	Patient ID	Sample ID	Test Type	Assay Name	Start Date & Time	Reagent Lot	Result
<input type="checkbox"/>		test 06	Specimen	Xpert Xpress_SARS-CoV-2_Flu_RSV	07/27/20 14:05:02	00501	SARS-CoV-2 POSITIVE; Flu A NEGATIVE; Flu B NEGATIVE; RSV NEGATIVE
<input type="checkbox"/>		test 07	Specimen	Xpert Xpress_SARS-CoV-2_Flu_RSV	07/27/20 14:05:59	00501	SARS-CoV-2 POSITIVE; Flu A NEGATIVE; Flu B NEGATIVE; RSV NEGATIVE
<input type="checkbox"/>		test 08	Specimen	Xpert Xpress_SARS-CoV-2_Flu_RSV	07/27/20 14:07:01	00501	SARS-CoV-2 POSITIVE; Flu A NEGATIVE; Flu B NEGATIVE; RSV NEGATIVE
<input type="checkbox"/>		test 2	Specimen	Xpert Xpress_SARS-CoV-2_Flu_RSV	07/25/20 11:32:27	00501	SARS-CoV-2 NEGATIVE; Flu A NEGATIVE;

Figure 32. Results Screen

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

Test Completed	
Module A4	Result
Sample ID	Patient ID
test 06	SARS-CoV-2 POSITIVE;
Test Type	Flu A NEGATIVE;
Specimen	Flu B NEGATIVE;
Assay Name	RSV NEGATIVE
Xpert Xpress SARS-CoV-2_Flu_RSV	
User	Start Date & Time
CLINICAL AFFAIRS DO NOT DELETE	07/27/20 14:05:02
REPORT	
Test Disclaimer	
For In Vitro Diagnostic Use Only. For use under the Emergency Use Authorization (US).	

Figure 33. Test Result Screen (Example)

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

17 Quality Control

17.1 Internal Controls

CONTROL

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

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

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

17.2 External Controls

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

Xpert Xpress SARS-CoV-2/Flu/RSV

18 Interpretation of Results

The results are interpreted automatically by the GeneXpert Xpress System and are clearly shown in the **View Results** window. The Xpert Xpress SARS-CoV-2/Flu/RSV test provides test results based on the detection of respective gene targets according to the algorithms.

The format of the test results presented will vary depending on the user's choice to run either an Xpert Xpress_SARS-CoV-2_Flu_RSV, Xpert Xpress_SARS-CoV-2_Flu or Xpert Xpress_SARS-CoV-2 test.

Table 1 shows the possible result outcomes when the Xpert Xpress_SARS-CoV-2_Flu_RSV test mode is selected.

Table 1. Xpert Xpress_SARS-CoV-2/Flu/RSV Possible Results and Interpretation

Result	Interpretation
SARS-CoV-2 POSITIVE	<p>The 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.• SPC: NA (not applicable); SPC is ignored because SARS-CoV-2 target amplification occurred.• Probe Check: PASS; all probe check results pass.
Flu A POSITIVE	<ul style="list-style-type: none">• The Flu A signal for either the Flu A1 RNA target or the Flu A2 RNA target or signals for both RNA targets has a Ct within the valid range and endpoint above the threshold setting.• SPC – NA; SPC is ignored because the Flu A target amplification occurred.• Probe Check – PASS; all probe check results pass.
Flu B POSITIVE	<ul style="list-style-type: none">• The Flu B signal has a Ct within the valid range and endpoint above the minimum setting.• SPC: NA; SPC is ignored because Flu B target amplification occurred.• Probe Check: PASS; all probe check results pass.
RSV POSITIVE	<ul style="list-style-type: none">• The RSV signal has a Ct within the valid range and endpoint above the minimum setting.• SPC: NA; SPC is ignored because RSV target amplification occurred.• Probe Check: PASS; all probe check results pass.
SARS-CoV-2 NEGATIVE; Flu A NEGATIVE; Flu B NEGATIVE; RSV NEGATIVE	<p>SARS-CoV-2 target RNA is not detected; Flu A target RNA is not detected; Flu B target RNA is not detected; RSV target RNA is not detected.</p> <ul style="list-style-type: none">• SARS-CoV-2, Flu A, Flu B and RSV target RNAs are not detected.• SPC – PASS; SPC has a Ct within the valid range and endpoint above the minimum setting.• Probe Check – PASS; all probe check results pass.
NO RESULT- REPEAT TEST	<p>If result is NO RESULT - REPEAT TEST, retest with a new cartridge according to the Retest Procedure in Section 19.2. If retest is NO RESULT - REPEAT TEST, obtain a new specimen for testing.</p>

Xpert Xpress SARS-CoV-2/Flu/RSV

Result	Interpretation
INSTRUMENT ERROR	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.
If the SPC is negative and the results for any of the targets are positive, the results for all targets are considered valid.	

If only one viral target is positive but coinfection with multiple targets is suspected, the sample should be re-tested with another FDA cleared, approved, or authorized test, if coinfection would change clinical management.

Table 2 shows the possible result outcomes when the Xpert Xpress_SARS-CoV-2_Flu test mode is selected.

Table 2. Xpert Xpress_SARS-CoV-2_Flu Possible Results and Interpretation

Result	Interpretation
SARS-CoV-2 POSITIVE	<p>The 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. SPC: NA (not applicable); SPC is ignored because SARS-CoV-2 target amplification occurred. Probe Check: PASS; all probe check results pass.
Flu A POSITIVE	<ul style="list-style-type: none"> The Flu A signal for either the Flu A1 RNA target or the Flu A2 RNA target or signals for both RNA targets has a Ct within the valid range and endpoint above the threshold setting. SPC – NA; SPC is ignored because the Flu A target amplification occurred. Probe Check – PASS; all probe check results pass.
Flu B POSITIVE	<ul style="list-style-type: none"> The Flu B signal has a Ct within the valid range and endpoint above the minimum setting. SPC: NA; SPC is ignored because Flu B target amplification occurred. Probe Check: PASS; all probe check results pass.
SARS-CoV-2 NEGATIVE; Flu A NEGATIVE; Flu B NEGATIVE	<p>SARS-CoV-2 target RNA is not detected; Flu A target RNA is not detected; Flu B target RNA is not detected.</p> <ul style="list-style-type: none"> SARS-CoV-2, Flu A and Flu B target RNAs are not detected. SPC – PASS; SPC has a Ct within the valid range and endpoint above the minimum setting. Probe Check – PASS; all probe check results pass.
NO RESULT- REPEAT TEST	If result is NO RESULT - REPEAT TEST , retest with a new cartridge according to the Retest Procedure in Section 19.2. If retest is NO RESULT - REPEAT TEST , obtain a new specimen for testing.

Xpert Xpress SARS-CoV-2/Flu/RSV

Result	Interpretation
INSTRUMENT ERROR	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.
If the SPC is negative and the results for any of the targets are positive, the results for all targets are considered valid.	

If only one viral target is positive but coinfection with multiple targets is suspected, the sample should be re-tested with another FDA cleared, approved, or authorized test, if coinfection would change clinical management.

Table 3 shows the possible result outcomes when the Xpert Xpress_SARS-CoV-2 test mode is selected.

Table 3. Xpert Xpress_SARS-CoV-2 Possible Results and Interpretation

Result	Interpretation
SARS-CoV-2 POSITIVE	<p>The 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. • SPC: NA (not applicable); SPC is ignored because SARS-CoV-2 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"> • SARS-CoV-2 target RNA is not detected. • SPC – PASS; SPC has a Ct within the valid range and endpoint above the minimum setting. • Probe Check – PASS; all probe check results pass.
NO RESULT-REPEAT TEST	If result is NO RESULT - REPEAT TEST , retest with a new cartridge according to the Retest Procedure in Section 19.2. If retest is NO RESULT - REPEAT TEST , obtain a new specimen for testing.
INSTRUMENT ERROR	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.

The Xpert Xpress SARS-CoV-2/Flu/RSV test can be run to detect SARS-CoV-2, Flu and RSV by selecting Xpert Xpress_SARS-CoV-2_Flu_RSV from the Select Test menu; SARS-CoV-2 and Flu only by selecting Xpert Xpress_SARS-CoV-2_Flu; or SARS-CoV-2 only by selecting Xpert Xpress_SARS-CoV-2. The Xpert Xpress_SARS-CoV-2 test mode

Xpert Xpress SARS-CoV-2/Flu/RSV

includes an Early Assay Termination (EAT) function which will provide earlier time to results in high titer specimens if the signal from the SARS-CoV-2 target 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.

19 Retests

19.1 Reasons to Repeat the Test

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

- An **INSTRUMENT ERROR** result could be due to, but not limited to, a 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, no sample added, 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 Technical Support for assistance.

19.2 Retest Procedure

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

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

1. Put on a clean pair of gloves. Obtain a new Xpert Xpress SARS-CoV-2/Flu/RSV 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 by lifting the front of 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 SARS-CoV-2/Flu/RSV has only been established in nasopharyngeal swab specimens. Use of the Xpert Xpress SARS-CoV-2/Flu/RSV test with other specimen types has not been assessed and performance characteristics are unknown.
- Nasal swabs (self-collected under supervision of, or collected by, a healthcare provider) are considered acceptable specimen types for use with the Xpert Xpress SARS-CoV-2/Flu/RSV test but performance with these specimen types has not been established.
- As with any molecular test, mutations within the target regions of Xpert Xpress SARS-CoV-2/Flu/RSV could affect primer and/or probe binding resulting in failure to detect the presence of virus.
- As with any molecular test, mutations within the target regions of the Xpert Xpress SARS-CoV-2/Flu/RSV test could affect primer and/or probe binding resulting in failure to detect the presence of virus or the virus being detected less predictably.
- 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.
- False negative results may occur if virus is present at levels below the analytical limit of detection.
- Negative results do not preclude SARS-CoV-2, influenza or RSV infection and should not be used as the sole basis for treatment or other patient management decisions.
- Results from the Xpert Xpress SARS-CoV-2/Flu/RSV test should be correlated with the clinical history, epidemiological data, and other data available to the clinician evaluating the patient.
- Viral nucleic acid may persist *in vivo*, independent of virus viability. 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 patients without signs and symptoms of respiratory tract infection.
- 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

Xpert Xpress SARS-CoV-2/Flu/RSV

presence of SARS-CoV-2, influenza or RSV.

- 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.
- Results from analytical studies with contrived co-infected samples showed potential for competitive interference when SARS-CoV-2, influenza or RSV was present at 1X LoD levels.
- Cross-reactivity with respiratory tract organisms other than those described herein can lead to erroneous results.
- Recent patient exposure to FluMist® or other live attenuated influenza vaccines may cause inaccurate positive results.
- As the Xpert Xpress SARS-CoV-2/Flu/RSV test does not differentiate between the N2 and E gene targets, the presence of other coronaviruses in the B lineage, *Betacoronavirus* genus, including SARS-CoV-1 may cause a false positive result. None of these other coronaviruses is known to currently circulate in the human population.
- This test is not intended to differentiate RSV subgroups, influenza A subtypes or influenza B lineages. If differentiation of specific RSV or influenza subtypes and strains is needed, additional testing, in consultation with state or local public health departments, is required.
- Specimen transport media that contain guanidine thiocyanate (GTC) may interfere with the test causing false negative results.
- The performance of this device has not been assessed in a population vaccinated against COVID-19.
- This test has not been FDA cleared or approved.
- This test has been authorized by FDA under an EUA for use by authorized laboratories.
- This test has been authorized only for the simultaneous qualitative detection and differentiation of nucleic acids from SARS-CoV-2, influenza A, influenza B, and respiratory syncytial virus (RSV), and not for any other viruses or pathogens.
- This test is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of in vitro diagnostic tests for detection and/or diagnosis of COVID-19 under Section 564(b)(1) of the Federal Food, Drug and Cosmetic Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.

Xpert Xpress SARS-CoV-2/Flu/RSV

21 Conditions of Authorization for Laboratory and Patient Care Settings

The Cepheid Xpert Xpress SARS-CoV-2/Flu/RSV Letter of Authorization, along with the authorized Fact Sheet for Healthcare Providers, the authorized Fact Sheet for Patients and authorized labeling are available on the FDA website:

<https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/vitro-diagnostics-euas>.

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

- Authorized laboratoriesⁱⁱ using your product will include with result reports of the Xpert Xpress SARS-CoV-2/Flu/RSV test, all authorized Fact Sheets. Under exigent circumstances, other appropriate methods for disseminating these Fact Sheets may be used, which may include mass media.
- Authorized laboratories using your product will use your product as outlined in the Xpert Xpress SARS-CoV-2/Flu/RSV Instructions for Use - For Use with GeneXpert Dx or GeneXpert Infinity systems. Deviations from the authorized procedures, including the authorized instruments, authorized extraction methods, authorized clinical specimen types, authorized control materials, authorized other ancillary reagents and authorized materials required to use the Xpert Xpress SARS-CoV-2/Flu/RSV test are not permitted.
- Authorized laboratories operating under a CLIA Certificate of Waiver, Certificate of Compliance, or Certificate of Accreditation using your product will use your product as outlined in the Xpress SARS-CoV-2/Flu/RSV Instructions for Use - For Use with GeneXpert Xpress System and associated Quick Reference Instructions for Xpert Xpress SARS-CoV-2/Flu/RSV and GeneXpert Xpress System (Hub configuration), and Quick Reference Instructions for Xpert Xpress SARS-CoV-2/Flu/RSV and GeneXpert Xpress System (Tablet configuration). Deviations from the authorized procedures, including the authorized instruments, authorized extraction methods, authorized clinical specimen types, authorized control materials, authorized other ancillary reagents and authorized materials required to use your product are not permitted.
- Authorized laboratories that receive your product will notify the relevant public health authorities of their intent to run your product prior to initiating testing.
- Authorized laboratories using the Xpert Xpress SARS-CoV-2/Flu/RSV test will have a process in place for reporting test results to healthcare providers and relevant public health

ⁱⁱ The letter of authorization refers to “authorized laboratories as follows: (1) testing of nasopharyngeal swab, nasal swab, or nasal wash/aspirate specimens using the Xpert SARS-CoV-2/Flu/RSV test run on the GeneXpert Dx and GeneXpert Infinity systems is limited to laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. § 263a, that meet requirements to perform high or moderate complexity tests and (2) testing of nasopharyngeal or nasal swab specimens using the Xpert Xpress SARS-CoV-2/Flu/RSV test run on the GeneXpert Xpress System (Tablet and Hub Configurations) is authorized for use at the Point of Care (POC), i.e., in patient care settings operating under a CLIA Certificate of Waiver, Certificate of Compliance, or Certificate of Accreditation.

Xpert Xpress SARS-CoV-2/Flu/RSV

authorities, as appropriate.

- Authorized laboratories will collect information on the performance of the test and report to DMD/OHT7-OIR/OPEQ/CDRH (via email: CDRH-EUA-Reporting@fda.hhs.gov) and Cepheid (+ 1 888 838 3222 or techsupport@cepheid.com) any suspected occurrence of false positive or false negative results and significant deviations from the established performance characteristics of the test of which they become aware.
- All operators using your product must be appropriately trained in performing and interpreting the results of your product, use appropriate personal protective equipment when handling this kit, and use your product in accordance with the authorized labeling.
- Cepheid, authorized distributors, and authorized laboratories and patient care settings using your product will ensure that any records associated with this EUA are maintained until otherwise notified by FDA. Such records will be made available to FDA for inspection upon request.

Xpert Xpress SARS-CoV-2/Flu/RSV

22 Performance Characteristics

22.1 Clinical Evaluation

The performance of the Xpert Xpress SARS-CoV-2/Flu/RSV test was evaluated using archived clinical nasopharyngeal (NP) swab specimens in viral transport medium. Archived specimens were selected consecutively by date and previously known analyte result. A total of 240 NP swab specimens were tested with Xpert Xpress SARS-CoV-2/Flu/RSV side by side with a SARS-CoV-2 EUA RT-PCR test and the FDA-cleared Xpert Xpress Flu/RSV test in a randomized and blinded fashion.

Positive Percent Agreement (PPA) and Negative Percent Agreement (NPA) were determined by comparing the results of the Xpert Xpress SARS-CoV-2/Flu/RSV test relative to the results of a SARS-CoV-2 EUA RT-PCR test for the SARS-CoV-2 target, and Xpert Xpress Flu/RSV for the Flu A, Flu B, and RSV targets, respectively.

Xpert Xpress SARS-CoV-2/Flu/RSV demonstrated a PPA and NPA of 97.9% and 100.0% for SARS-CoV-2, respectively; 100.0% and 100.0% for Flu A, respectively; 100.0% and 99.0% for Flu B, respectively; 100.0% and 100.0% for RSV, respectively (Table 4).

Table 4. Xpert Xpress SARS-CoV-2/Flu/RSV Performance Results

Target	Number of Specimens	TP	FP	TN	FN	PPA (95% CI)	NPA (95% CI)
SARS-CoV-2	240	46	0	193	1	97.9% (88.9% - 99.6%)	100.0% (98.1% - 100.0%)
Flu A	240	48	0	192	0	100.0% (92.6% - 100.0%)	100.0% (98.0% - 100.0%)
Flu B	240	46	2	192	0	100.0% (92.3% - 100.0%)	99.0% (96.3% - 99.7%)
RSV	240	47	0	193	0	100.0% (92.4% - 100.0%)	100.0% (98.1% - 100.0%)

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

22.2 Analytical Sensitivity (Limit of Detection)

The analytical sensitivity of the Xpert Xpress SARS-CoV-2/Flu/RSV test was assessed with one lot of reagent and limiting dilutions of the six respiratory viruses (NATrol SARS-CoV-2, Flu A H1, Flu A H3, Flu B, RSV A and RSV B) into pooled negative clinical NP swab matrix following the guidance in Clinical and Laboratory Standards Institute (CLSI) document EP17-A2. The estimated LoD values as determined by Probit regression analysis were verified using two lots of Xpert Xpress SARS-CoV-2/Flu/RSV reagents. The verified LoD values for the viruses tested are summarized in Table 5.

Table 5. Xpert Xpress SARS-CoV-2/Flu/RSV Limit of Detection

Virus/Strain	LoD Concentration
SARS-CoV-2 (USA-WA1/2020)	131 copies/mL
Influenza A/California/7/2009	0.004 TCID ₅₀ /mL
Influenza A/Victoria/361/2011	0.087 TCID ₅₀ /mL
Influenza B/Mass/2/2012	0.04 TCID ₅₀ /mL
RSV A/2/Australia/61	0.43 TCID ₅₀ /mL
RSV B/Wash/18537/62	0.22 TCID ₅₀ /mL

22.3 Analytical Reactivity (Inclusivity)

The inclusivity of Xpert Xpress SARS-CoV-2/Flu/RSV was evaluated using *in silico* analysis of the assay amplicons in relation to 48,461 SARS-CoV-2 sequences available in the GISAID gene database for two targets, E and N2.

For analysis of the E target, 113 sequences were excluded due to ambiguous nucleotides, which reduced the total to 48,348 sequences. Of the 48,348 GISAID sequences, 48,108 (99.5%) were an exact match to the SARS-CoV-2 E target amplicon generated in the Xpert Xpress SARS-CoV-2/Flu/RSV test. Single nucleotide mismatches were observed for 223 sequences and two mismatches were observed for 17 sequences. Of the 17 sequences with two mismatches, two sequences contained 2 mismatches in the forward primer region, three sequences have a 'GA' dinucleotide in the reverse primer, and twelve sequences contained a 'AA' dinucleotide that lies between the oligonucleotides used in the assay. None of these mismatches are expected to affect the performance of the assay.

For analysis of the N2 target, 129 sequences were excluded due to ambiguous nucleotides, which reduced the total used in the evaluation to 48,332 sequences. Of the 48,332 GISAID sequences, 47,962 (99.2%) were an exact match to the SARS-CoV-2 N2 target amplicon generated in the Xpert Xpress SARS-CoV-2/Flu/RSV test. Single nucleotide mismatches were observed for 369 sequences and three (3) mismatches were observed for one sequence. For the one sequence with three variant positions, two of the mismatched nucleotides are in the probe region and could have an impact on probe binding. None of the other mismatches are predicted to have a negative impact on the performance of the assay.

The inclusivity of the Xpert Xpress SARS-CoV-2/Flu/RSV for Flu and RSV viruses are as reported for the analytical reactivity evaluation of the Xpert Xpress Flu/RSV test.

Xpert Xpress Flu/RSV test was evaluated against multiple strains of influenza A H1N1 (seasonal pre-2009), influenza A H1N1 (pandemic 2009), influenza A H3N2 (seasonal), avian influenza A (H5N1, H5N2, H6N2, H7N2, H7N3, H2N2, H7N9, and H9N2), influenza B (representing strains from both Victoria and Yamagata lineages), and respiratory syncytial virus subgroups A and B (RSV A and RSV B) at levels near the analytical LoD. A total of 53 strains comprised of 48 influenza viruses (35 influenza A and 13 influenza B) and 5 RSV strains were tested in this study with the Xpert Xpress Flu/RSV test. Three replicates were tested for each strain. All Flu and RSV strains tested positive in all three replicates, except for one Flu A H1N1 strain (A/New Jersey/8/76), which tested positive in 2 of 3 replicates at 0.1 TCID₅₀/mL. Results are shown in Table 6. Predicted cross reactivity from *in silico* analyses showed 100% sequence homology for additional pH1N1 strains.

Xpert Xpress SARS-CoV-2/Flu/RSV

Table 6. Analytical Reactivity (Inclusivity) of the Xpert Xpress Flu/RSV Test

Virus	Strain	Target Concentration	Result		
			Flu A	Flu B	RSV
No Template Control		N/A	NEG	NEG	NEG
Influenza A H1N1 (pre-2009)	A/swine/Iowa/15/30	0.1 TCID ₅₀ /mL	POS	NEG	NEG
	A/WS/33	0.1 TCID ₅₀ /mL	POS	NEG	NEG
	A/PR/8/34	0.1 TCID ₅₀ /mL	POS	NEG	NEG
	A/Mal/302/54	0.1 TCID ₅₀ /mL	POS	NEG	NEG
	A/Denver/1/57	0.1 TCID ₅₀ /mL	POS	NEG	NEG
	A/New Jersey/8/76	0.1 TCID ₅₀ /mL	POS	NEG	NEG
	A/New Caledonia/20/1999	0.1 TCID ₅₀ /mL	POS	NEG	NEG
	A/New York/55/2004	0.1 TCID ₅₀ /mL	POS	NEG	NEG
	A/Solomon Island/3/2006	0.1 TCID ₅₀ /mL	POS	NEG	NEG
	A/Taiwan/42/06	0.1 TCID ₅₀ /mL	POS	NEG	NEG
	A/Brisbane/59/2007	0.1 TCID ₅₀ /mL	POS	NEG	NEG
Influenza A H1N1 (pdm2009)	A/swine/NY/02/2009	0.1 TCID ₅₀ /mL	POS	NEG	NEG
	A/Colorado/14/2012	0.1 TCID ₅₀ /mL	POS	NEG	NEG
	A/Washington/24/2012	0.1 TCID ₅₀ /mL	POS	NEG	NEG
Influenza A H3N2 (Seasonal)	A/Aichi/2/68	2.0 TCID ₅₀ /mL	POS	NEG	NEG
	A/Hong Kong/8/68	2.0 TCID ₅₀ /mL	POS	NEG	NEG
	A/Port Chalmers/1/73	2.0 TCID ₅₀ /mL	POS	NEG	NEG
	A/Hawaii/15/2001	2.0 TCID ₅₀ /mL	POS	NEG	NEG
	A/Wisconsin/67/05	2.0 TCID ₅₀ /mL	POS	NEG	NEG
	A/Brisbane/10/2007	2.0 TCID ₅₀ /mL	POS	NEG	NEG
	A/Minnesota/11/2010 (H3N2)v	2.0 TCID ₅₀ /mL	POS	NEG	NEG
	A/Indiana/08/2011 (H3N2)v	2.0 TCID ₅₀ /mL	POS	NEG	NEG
	A/Texas/50/2012	2.0 TCID ₅₀ /mL	POS	NEG	NEG
Avian influenza A	A/duck/Hunan/795/2002 (H5N1)	≤ 1pg/μL ^a	POS	NEG	NEG
	A/chicken/Hubei/327/2004 (H5N1)	≤ 1pg/μL ^a	POS	NEG	NEG
	A/Anhui/01/2005 (H5N1)	≤ 1pg/μL ^a	POS	NEG	NEG
	A/Japanese white eye/Hong Kong/1038/2006 (H5N1)	≤ 1pg/μL ^a	POS	NEG	NEG
	A/mallard/WI/34/75 (H5N2)	≤ 1pg/μL ^a	POS	NEG	NEG
	A/chicken/CA431/00 (H6N2)	≤ 1pg/μL ^a	POS	NEG	NEG
	A/duck/LTC-10-82743/1943 (H7N2)	≤ 1pg/μL ^a	POS	NEG	NEG
	A/chicken/NJ/15086-3/94 (H7N3)	≤ 1pg/μL ^a	POS	NEG	NEG
	A/Anhui/1/2013 (H7N9)	N/A ^b	POS	NEG	NEG
	A/Shanghai/1/2013 (H7N9)	N/A ^b	POS	NEG	NEG
	A/chicken/Korea/38349-p96323/ 1996 (H9N2)	≤ 1pg/μL ^a	POS	NEG	NEG
	A/Mallard/NY/6750/78 (H2N2)	≤ 1pg/μL ^a	POS	NEG	NEG
Influenza B	B/Lee/40	1.0 TCID ₅₀ /mL	NEG	POS	NEG
	B/Allen/45	1.0 TCID ₅₀ /mL	NEG	POS	NEG
	B/GL/1739/54	1.0 TCID ₅₀ /mL	NEG	POS	NEG
	B/Maryland/1/59	1.0 TCID ₅₀ /mL	NEG	POS	NEG
	B/Panama/45/90 ^c	1.0 TCID ₅₀ /mL	NEG	POS	NEG
	B/Florida/07/2004 ^d	1.0 TCID ₅₀ /mL	NEG	POS	NEG
	B/Florida/02/06 ^c	1.0 TCID ₅₀ /mL	NEG	POS	NEG

Xpert Xpress SARS-CoV-2/Flu/RSV

Virus	Strain	Target Concentration	Result		
			Flu A	Flu B	RSV
	B/Florida/04/06 ^d	1.0 TCID ₅₀ /mL	NEG	POS	NEG
	B/Hong Kong/5/72	1.0 TCID ₅₀ /mL	NEG	POS	NEG
	B/Wisconsin/01/2011 ^d	1.0 TCID ₅₀ /mL	NEG	POS	NEG
	B/Malaysia/2506/04 ^c	1.0 TCID ₅₀ /mL	NEG	POS	NEG
	B/Taiwan/2/62	1.0 TCID ₅₀ /mL	NEG	POS	NEG
	B/Brisbane/60/2008 ^c	1.0 TCID ₅₀ /mL	NEG	POS	NEG
RSV A	RSV-A/NY (Clinical unknown)	3.0 TCID ₅₀ /mL	NEG	NEG	POS
	RSV-A/WI/629-8-2/2007	3.0 TCID ₅₀ /mL	NEG	NEG	POS
	RSV-A/WI/629-11-1/2008	3.0 TCID ₅₀ /mL	NEG	NEG	POS
RSV B	RSV-B/WV14617/85	7.0 TCID ₅₀ /mL	NEG	NEG	POS
	RSV-B/CH93(18)-18	7.0 TCID ₅₀ /mL	NEG	NEG	POS

- a. Purified viral RNA in simulated background matrix was used for avian influenza A viruses due to biosafety regulations.
b. Inactivated avian influenza A (H7N9) viruses without viral titer was diluted 100,000-fold in simulated background matrix and tested due to biosafety regulations.
c. Known Victoria lineage.
d. Known Yamagata lineage.

22.4 Analytical Specificity (Exclusivity)

An *in silico* analysis for possible cross-reactions with all the organisms listed in Table 7 was conducted by mapping primers and probes in the Xpert Xpress SARS-CoV-2/Flu/RSV 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 unintended cross reactivity with other organisms listed in Table 7 is expected based on the *in silico* analysis.

Table 7. Xpert Xpress SARS-CoV-2/Flu/RSV 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 viruses 1-4
Human coronavirus NL63	Influenza A
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)

Xpert Xpress SARS-CoV-2/Flu/RSV

Microorganisms from the Same Genetic Family	High Priority Organisms
	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>Streptococcus salivarius</i>
	<i>Leptospira</i>
	<i>Chlamydia psittaci</i>
	<i>Coxiella burnetii</i> (Q-Fever)
	<i>Staphylococcus aureus</i>

The analytical specificity of the Xpert Xpress SARS-CoV-2/Flu/RSV for Flu A, Flu B and RSV viruses are as reported for the analytical exclusivity evaluation of the Xpert Xpress Flu/RSV test. The analytical specificity of the Xpert Xpress Flu/RSV test was evaluated by testing a panel of 44 cultures consisting of 16 viral, 26 bacterial, and two yeast strains representing common respiratory pathogens or those potentially encountered in the nasopharynx. Three replicates of each bacterial and yeast strain were tested at concentrations of $\geq 1 \times 10^6$ CFU/mL with the exception of one strain that was tested at 1×10^5 CFU/mL (*Chlamydia pneumoniae*). Three replicates of each virus were tested at concentrations of $\geq 1 \times 10^5$ TCID₅₀/mL. The analytical specificity was 100%. Results are shown in Table 8.

Table 8. Analytical Specificity of the Xpert Xpress Flu/RSV Test

Organism	Concentration	Influenza A	Influenza B	RSV
<i>No Template Control</i>	N/A	NEG	NEG	NEG
Adenovirus Type 1	1.12E+06 TCID ₅₀ /mL	NEG	NEG	NEG
Adenovirus Type 7	1.87E+05 TCID ₅₀ /mL	NEG	NEG	NEG
Human coronavirus OC43	2.85E+05 TCID ₅₀ /mL	NEG	NEG	NEG
Human coronavirus 229E	1.00E+05 TCID ₅₀ /mL	NEG	NEG	NEG
Cytomegalovirus	1.00E+05 TCID ₅₀ /mL	NEG	NEG	NEG
Echovirus	3.31E+07 TCID ₅₀ /mL	NEG	NEG	NEG
Enterovirus	3.55E+05 TCID ₅₀ /mL	NEG	NEG	NEG
Epstein Barr Virus	7.16E+07 TCID ₅₀ /mL	NEG	NEG	NEG
Herpes simplex virus	8.90E+05 TCID ₅₀ /mL	NEG	NEG	NEG
Measles	6.31E+05 TCID ₅₀ /mL	NEG	NEG	NEG
Human metapneumovirus	1.00E+05 TCID ₅₀ /mL	NEG	NEG	NEG
Mumps virus	6.31E+06 TCID ₅₀ /mL	NEG	NEG	NEG

Xpert Xpress SARS-CoV-2/Flu/RSV

Organism	Concentration	Influenza A	Influenza B	RSV
Human parainfluenza virus Type 1	1.15E+06 TCID ₅₀ /mL	NEG	NEG	NEG
Human parainfluenza virus Type 2	6.31E+05 TCID ₅₀ /mL	NEG	NEG	NEG
Human parainfluenza virus Type 3	3.55E+06 TCID ₅₀ /mL	NEG	NEG	NEG
Rhinovirus Type 1A	1.26E+05 TCID ₅₀ /mL	NEG	NEG	NEG
<i>Acinetobacter baumannii</i>	1.00E+06 CFU/mL	NEG	NEG	NEG
<i>Burkholderia cepacia</i>	3.30E+06 CFU/mL	NEG	NEG	NEG
<i>Candida albicans</i>	3.20E+06 CFU/mL	NEG	NEG	NEG
<i>Candida parapsilosis</i>	3.00E+06 CFU/mL	NEG	NEG	NEG
<i>Bordetella pertussis</i>	3.30E+06 CFU/mL	NEG	NEG	NEG
<i>Chlamydia pneumoniae</i>	1.00E+05 CFU/mL	NEG	NEG	NEG
<i>Citrobacter freundii</i>	3.30E+06 CFU/mL	NEG	NEG	NEG
<i>Corynebacterium sp.</i>	3.30E+06 CFU/mL	NEG	NEG	NEG
<i>Escherichia coli</i>	1.00E+07 CFU/mL	NEG	NEG	NEG
<i>Enterococcus faecalis</i>	1.30E+06 CFU/mL	NEG	NEG	NEG
<i>Hemophilus influenzae</i>	1.00E+06 CFU/mL	NEG	NEG	NEG
<i>Lactobacillus reuteri</i>	1.00E+06 CFU/mL	NEG	NEG	NEG
<i>Legionella spp.</i>	1.00E+06 CFU/mL	NEG	NEG	NEG
<i>Moraxella catarrhalis</i>	1.00E+07 CFU/mL	NEG	NEG	NEG
<i>Mycobacterium tuberculosis</i> (avirulent)	1.00E+06 CFU/mL	NEG	NEG	NEG
<i>Mycoplasma pneumoniae</i>	1.00E+06 CFU/mL	NEG	NEG	NEG
<i>Neisseria meningitidis</i>	2.15E+06 CFU/mL	NEG	NEG	NEG
<i>Neisseria mucosa</i>	1.00E+07 CFU/mL	NEG	NEG	NEG
<i>Propionibacterium acnes</i>	2.40E+07 CFU/mL	NEG	NEG	NEG
<i>Pseudomonas aeruginosa</i>	3.70E+06 CFU/mL	NEG	NEG	NEG
<i>Staphylococcus aureus</i> (protein A producer)	2.20E+06 CFU/mL	NEG	NEG	NEG
<i>Staphylococcus epidermidis</i>	3.40E+06 CFU/mL	NEG	NEG	NEG
<i>Staphylococcus haemolyticus</i>	4.00E+06 CFU/mL	NEG	NEG	NEG
<i>Streptococcus agalactiae</i>	3.50E+06 CFU/mL	NEG	NEG	NEG
<i>Streptococcus pneumoniae</i>	1.00E+06 CFU/mL	NEG	NEG	NEG
<i>Streptococcus pyogenes</i>	1.00E+07 CFU/mL	NEG	NEG	NEG
<i>Streptococcus salivarius</i>	1.00E+07 CFU/mL	NEG	NEG	NEG
<i>Streptococcus sanguinis</i>	3.10E+06 CFU/mL	NEG	NEG	NEG

Xpert Xpress SARS-CoV-2/Flu/RSV

22.5 Competitive Interference

Competitive interference of the Xpert Xpress SARS-CoV-2/Flu/RSV caused by co-infections were evaluated by testing individual SARS-CoV-2, Flu A, Flu B or RSV strains at 1X LoD in the presence of different target strains at a higher concentration in a simulated background matrix. The concentration at LoD was 131 copies/mL for SARS-CoV-2 and ranged from 0.004 TCID₅₀/mL to 0.43 TCID₅₀/mL for the Flu and RSV strains; the competitive strains were evaluated at 10⁴ titer units (copies/mL, TCID₅₀/mL, CEID₅₀/mL or PFU/mL). The corresponding concentration of RNA (copies/mL) for the Flu and RSV strains was determined by ddPCR.

Analytical competitive interference was assessed using a strain of SARS-CoV-2 (inactivated USA-WA1/2020), Flu A H3 (H3/Victoria/361/2011), Flu B (B/Mass/02/2012), RSV A (RSV-A/2/Australia/61), and RSV B (RSV-B/Wash/18537/62). Replicates of 20 were tested for each target strain and each competitive strain combination. The normal binomial distribution with 20 replicate samples at LoD is between 17 and 20 positive results based on the binomial distribution with N=20, $p=0.95$ ($X \sim \text{Bin}(20, 0.95)$). Therefore, sets of 20 with 16 or less positives would be rare and an indication of a competitive inhibitory effect due to high levels of a competing analyte. Below is a summary of the results:

Table 9. Summary of Results for Competitive Interference

		Correct Calls (n/20)					
		Test Strain at LoD and Interferent at:					
Test Strain at LoD	Interferent Strain	10 ⁴ * (2.1e7 cp/mL)	10 ³ * (2.1e6 cp/mL)	10 ² * (2.1e5 cp/mL)	10* (2.1e4 cp/mL)	1* (2.1e3 cp/mL)	0.1* (2.1e2 cp/mL)
Flu B	Flu A	6/20	20/20				
RSV A	Flu A	9/20	17/20				
RSV B	Flu A	11/20	18/20				
SARS-CoV-2	Flu A	6/20	17/20	20/20			
Test Strain at LoD	Interferent Strain	10 ⁴ * (5.2e7 cp/mL)	10 ³ * (5.2e6 cp/mL)	10 ² * (5.2e5 cp/mL)	10* (5.2e4 cp/mL)	1* (5.2e3 cp/mL)	0.1* (5.2e2 cp/mL)
Flu A	Flu B	1/20	4/20	8/20	9/19	15/20	20/20
RSV A	Flu B	0/20	0/20	3/20	18/20		
RSV B	Flu B	7/20	8/20	11/20	18/20		
SARS-CoV-2	Flu B	3/20	4/20	11/20	17/20	20/20	
Test Strain at LoD	Interferent Strain	10 ⁴ * (3.7e7 cp/mL)	10 ³ * (3.7e6 cp/mL)	10 ² * (3.7e5 cp/mL)	10* (3.7e4 cp/mL)	1* (3.7e3 cp/mL)	0.1* (3.7e2 cp/mL)
Flu A	RSV A	15/20	12/20	20/20			
Flu B	RSV A	15/20	17/20				
SARS-CoV-2	RSV A	17/20	19/20				
Test Strain at LoD	Interferent Strain	10 ⁴ * (1.1e7 cp/mL)	10 ³ * (1.1e6 cp/mL)	10 ² * (1.1e5 cp/mL)	10* (1.1e4 cp/mL)	1* (1.1e3 cp/mL)	0.1* (1.1e2 cp/mL)
Flu A	RSV B	9/20	7/20	6/20	14/20	20/20	
Flu B	RSV B	10/20	10/20	16/20	19/20		
SARS-CoV-2	RSV B	17/20	16/20	15/20	20/20		

Xpert Xpress SARS-CoV-2/Flu/RSV

Test Strain at LoD	Interferent Strain	Correct Calls (n/20)					
		Test Strain at LoD and Interferent at:					
		10 ⁴ *	10 ³ *	10 ² *	10*	1*	0.1*
Flu A	SARS-CoV-2	19/20					
Flu B	SARS-CoV-2	18/20					
RSV A	SARS-CoV-2	19/20					
RSV B	SARS-CoV-2	19/20					

* Units for the concentration of each organism are as follows: Flu A H3 – CEID₅₀/mL; Flu B and RSV B – TCID₅₀/mL; RSV A – PFU/mL; SARS-CoV-2 – copies/mL

Italicized font indicates inhibitory effects

Bold font indicates no inhibition (SARS-CoV-2 tested to ≥19/20)

Flu A/Victoria/361/2011 at a concentration of 1 x 10⁴ CEID₅₀/mL (2.1e7 copies/mL), inhibited Flu B, RSV A, RSV B and SARS-CoV-2 at the LoD.

Flu B/Mass/2/2012 at concentrations shown in Table 9, inhibited SARS-CoV-2, Flu A, RSV A and RSV B at concentrations at the LoD of those targets.

RSV A/2/Australia/61 at a concentration of 1 x 10⁴ PFU/mL (3.7e7 copies/mL), inhibited SARS-CoV-2, Flu A and Flu B at the LoD.

RSV-B/Wash/18537/62 at concentrations shown in Table 9, inhibited SARS-CoV-2, Flu A and Flu B at concentrations at the LoD of those targets.

22.6 Potentially Interfering Substances

Potentially interfering substances that could be present in the nasopharynx (or introduced during specimen collection and handling) and interfere with accurate detection of SARS-CoV-2, Flu A, Flu B and RSV were evaluated with select direct testing on the Xpert Xpress SARS-CoV-2/Flu/RSV. Additional substances have also been previously evaluated on the Xpert Xpress Flu/RSV assay.

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 nasal 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 viruses spiked at 3x the analytical LoD determined for each strain. Positive samples tested with the Xpert Xpress SARS-CoV-2/Flu/RSV included one SARS-CoV-2, two influenza A, one influenza B and two RSV (RSV A and RSV B) strains, whereas those tested with the Xpert Xpress Flu/RSV consisted of six influenza (four influenza A and two influenza B) and four RSV (two RSV A and two RSV B). The substances evaluated are listed in Table 10 with active ingredients and final concentrations tested shown. None of the substances caused interference of the assay performance at the concentrations tested in this study. All positive and negative replicates were correctly identified by the Xpert Xpress SARS-CoV-2/Flu/RSV and/or Xpert Xpress Flu/RSV tests.

Xpert Xpress SARS-CoV-2/Flu/RSV

Table 10. Potentially Interfering Substances in the Xpert Xpress SARS-CoV-2/Flu/RSV Test and/or Xpert Xpress Flu/RSV Test

Substance/Class	Description/Active Ingredient	Concentration Tested
Control	Simulated nasal matrix	100% (v/v)
Beta-adrenergic bronchodilator ^a	Albuterol Sulfate	0.83 mg/mL (equivalent to 1 dose per day)
Blood	Blood (Human)	2% (v/v)
BD Universal Transport System	Transport Media	100% (v/v)
Remel M4 [®]	Transport Media	100% (v/v)
Remel M4RT [®]	Transport Media	100% (v/v)
Remel M5 [®]	Transport Media	100% (v/v)
Remel M6 [®]	Transport Media	100% (v/v)
Throat lozenges, oral anesthetic and analgesic ^a	Benzocaine, Menthol	1.7 mg/mL
Mucin ^a	Purified Mucin protein (Bovine or porcine submaxillary gland)	0.1% (w/v) ^b
Antibiotic, nasal ointment ^a	Mupirocin	10 mg/mL
Saline Nasal Spray ^a	Sodium Chloride (0.65%)	15% (v/v)
Anefrin Nasal Spray	Oxymetazoline, 0.05%	15% (v/v)
PHNY Nasal Drops	Phenylephrine, 0.5%	15% (v/v)
Tamiflu anti-viral drugs ^a	Zanamivir	7.5 mg/mL
Antibacterial, systemic	Tobramycin	4 µg/mL
Zicam Nasal Gel	Luffa operculata, Galphimia glauca, Histaminum hydrochloricum Sulfur	15% (w/v)
Nasal corticosteroid	Fluticasone Propionate	5 µg/mL

a. Substances/active ingredients and concentrations specifically evaluated with the Xpert Xpress SARS-CoV-2/Flu/RSV test.

b. No interference to the Xpert Xpress Flu/RSV performance observed at a concentration of 2.5%

22.7 Carry-Over Contamination

Carry-over studies to establish that single-use, self-contained GeneXpert cartridges prevent carry-over contamination have been conducted for previous Xpert tests developed for the GeneXpert systems, including the Xpert Xpress Flu/RSV. The studies demonstrated that a negative sample when preceded by very a high positive sample in the same GeneXpert module resulted in no carry-over.

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. Petric M, Comanor L, Petti CA. Role of the laboratory in diagnosis of influenza during seasonal epidemics and potential pandemics. *J Infect Dis*. 2006;194:S98-110.
4. Schweiger B, Zadow I, Heckler R, et al. Application of a fluorogenic PCR assay for typing and subtyping of influenza viruses in respiratory samples. *J Clin Micro*. 2000;38:1552-1558.
5. <http://www.cdc.gov/flu/about/viruses/types.htm>. Accessed on May 19, 2016.
6. <http://www.cdc.gov/RSV/index.html>. Accessed on March 14, 2013.
7. Centers for Disease Control and Prevention. *Biosafety in Microbiological and Biomedical laboratories* (refer to latest edition). <http://www.cdc.gov/biosafety/publications/>
8. Clinical and Laboratory Standards Institute. *Protection of Laboratory Workers from Occupationally Acquired Infections; Approved Guideline*. Document M29 (refer to latest edition).
9. 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).
10. 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 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

25 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

Region	Telephone	Email
US	+ 1 888 838 3222	techsupport@cepheid.com
France	+ 33 563 825 319	support@cepheideurope.com
Australia New Zealand	1800 130 821 0800 001 028	techsupportANZ@cepheid.com

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 re-use
	Batch code
	Consult instructions for use
	Caution
	Manufacturer
	Country of manufacture
	Contains sufficient for <n> tests
	Control
	Expiration date
	Temperature limitation
	Biological risks
	For prescription use only



Cepheid
904 Caribbean Drive
Sunnyvale, CA 94089 USA
Phone: +1 408 541 4191
Fax: +1 408 541 4192



For use under Emergency Use Authorization (EUA) Only