XXI.	Xpert Xpress Sars-CoV-2		
Effective Date: 5/5/21	Reviewed: 5/2022		Discontinue Date:

A. Purpose/Clinical Usage

The Xpert Xpress SARS-CoV-2/Flu/RSV test is a rapid, multiplexed real-time RT-PCR test intended for the simultaneous qualitative detection of CoV-2 in either nasopharyngeal swab, nasal swab or nasal wash/aspirate specimens collected from individuals suspected of respiratory viral infection consistent with COVID-19. Viral infection due to SARS-CoV-2, influenza, and RSV can be similar.

Testing of nasopharyngeal or nasal swab specimens using the Xpert Xpress SARS-CoV-2/Flu/RSV test run on the GeneXpert Xpress System is authorized for use at the Point of Care (POC) setting operating under a CLIA Certificate of Waiver, Certificate of Compliance, or Certificate of Accreditation. Rusk State Hospital is authorized under a CLIA Certificate of Provider Performed Microscopy Procedures.

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 positive 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 epidemiological information.
Testing with the Xpert Xpress SARS-CoV-2/Flu/RSV test is intended for use to provide early detection and treatment.

B. Policy

COVID testing will be performed by designated staff that have completed annual competency and training on the GeneXpert Xpress system. The Xpert Xpress SARS-CoV-2/Flu/RSV test is only for use under the Food and Drug Administration's Emergency Use Authorization.

C. Clinical Significance

An outbreak of respiratory illness of unknown etiology in China was initially reported in December of 2019. A novel coronavirus has since spread globally, resulting in a pandemic of coronavirus disease COVID-19. COVID-19 is associated with a variety of clinical outcomes, including asymptomatic infection, pneumonia and respiratory failure, and in some cases, death.

D. Test Principle

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 Instrument Systems.

The GeneXpert Instrument Systems automate and integrate sample preparation, nucleic acid extraction and amplification, and detection of the target sequences in simple or complex samples using real-time PCR and RT-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.

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, nasal swab, or nasal wash/aspirate 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, nasal swab, or nasal wash/ aspirate specimen is collected and placed into a transport tube containing 3 mL of viral transport medium. 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 Instrument System platform, which performs hands-off, automated sample processing, and real-time RT-PCR for detection of viral RNA.

E. Specimen Collection/Storage/Rejection

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.

Dispose of specimens only after notification of the provider.

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

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. Break swab at the indicated break line and cap the specimen collection tube tightly.

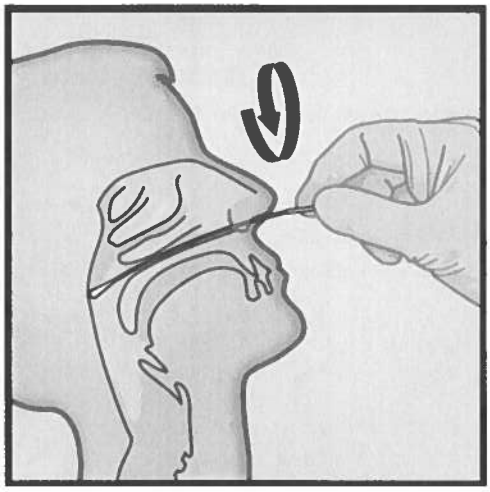

Figure 1. Nasopharyngeal Swab Collection

2. **Nasal Swab Collection Procedure**

   a. 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

   b. 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

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

3. **Nasal Wash/Aspirate Procedure**

Using a clean transfer pipette, transfer 600 µL of the sample into the tube containing 3 mL of viral transport medium and then cap the tube.

F. Reagents and Supplies

The Xpert Xpress SARS-CoV-2/Flu/RSV cartridge contains sufficient reagent to process a specimen or a quality control.

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

a. Bead 1, Bead 2, and Bead 3 (freeze-dried)	1 of each per cartridge
b. Lysis Reagent	1.0 mL per cartridge
c. Binding Reagent	1.0 mL per cartridge
d. Elution Reagent	3.0 mL per cartridge
e. Wash Reagent	0.4 mL per cartridge

2. Disposable Transfer Pipettes — 1

3.GeneXpert Instrument

G. Kit Storage and Stability

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.

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 expiration date.

Each single-use Xpert Xpress SARS-CoV-2/Flu/RSV cartridge is used to process one test. Do not reuse processed cartridges.

Each single-use disposable pipette is used to transfer one specimen. Do not reuse disposable pipettes.

Do not use a cartridge if it appears wet or if the lid seal appears to have been broken.

Wear clean lab coats and gloves. Change gloves between the handling of each specimen.

In the event of a spill of specimens or controls, wear gloves and absorb the spill with paper towels. Then, thoroughly clean the

contaminated area with an approved hospital cleaner. Follow the manufacturer's recommendations for decontamination of equipment.

H. Quality Control

1. Internal controls are run with each cartridge to ensure proper processing of the test procedure. Each cartridge includes a Sample Processing Control (SPC) and Probe Check Control (PCC). Please see the definitions below.
   a. **Sample Processing Control (SPC)** - This control detects sample-associated inhibition of the real-time PCR assay, ensures that the PCR temperature and time are appropriate for the amplification reaction, and that the PCR reagents are functional.
   b. **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.
2. External Controls are run monthly per assay. The instrument is set to lock any patient tests until these controls have been completed, and they are within range.
   a. Go to **Home** in the GeneXpert System window and choose **QC.**
   b. Select either **POSITIVE** or **NEGATIVE** for the control type that will be tested.
   c. Touch **Sample ID** and enter the corresponding NEGATIVE CONTROL or POSITIVE

CONTROL. Touch **Continue** when you are finished.

d. Continue with steps 6-10 of **(K) Procedure.**

I. Patient Preparation

The person collecting the sample must identify the patient using two unique identifiers and following the National Patient Safety Goals.

Inform patient of the purpose of test and the steps involved in collection of the specimen.

J. Procedure

Wear a clean lab coat and gloves for performing this test. Treat all biological specimens, including used cartridges, as if capable of transmitting infectious agents.

1. Touch the **User Name** field on the Xpress instrument, and the virtual keyboard appears. Enter your **User Name** and **Password** in the provided fields, and then touch X button at the far right of the keyboard. The keyboard disappears, and the **LOGIN** button is visible. Touch the **LOGIN** button to complete the process.
2. Go to **Home** in the GeneXpert System window and click **New Test.**
3. Type in the **Patient ID and Name**. This is the patient number beginning **679**. If typing the Patient ID, make sure the Patient ID is typed correctly. The Patient ID is shown on the left side of the View Results window and is associated with the test result. Use the employee ID if there is one available.
4. Type in the Sample ID. Use the accession number in this location. If typing the Sample ID, make sure the Sample ID is typed correctly. The Sample ID is shown on the left side of the View Results window and is associated with the test result.
5. Scan the barcode on the Xpert Xpress SARS-CoV-2/Flu/RSV cartridge. Using the barcode information, the software
automatically fills the boxes for the following fields: Reagent Lot ID, Cartridge SN, Expiration Date and Selected Assay.
6. Verify the correct test assay has been selected and Click **Confirm**.

If the barcode on the Xpert Xpress SARS-CoV-2/Flu/RSV <u>does not scan, then use a new cartridge</u>. Each cartridge can only be scanned ONE time.

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7. A video clip will appear on the screen showing the cartridge prep steps. **PREPARE THE SCANNED CARTRIDGE AT THIS TIME** according to the directions shown in the video and in the package insert.
8. Prepare the Cartridge.

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

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a. Remove a cartridge from the package.

b. Check the specimen transport tube is closed.

c. Mix specimen by rapidly inverting the specimen transport tube 5 times. Open cap on the specimen transport tube.

d. Open the cartridge lid.

e. Remove the transfer pipette from the wrapper.

f. 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.

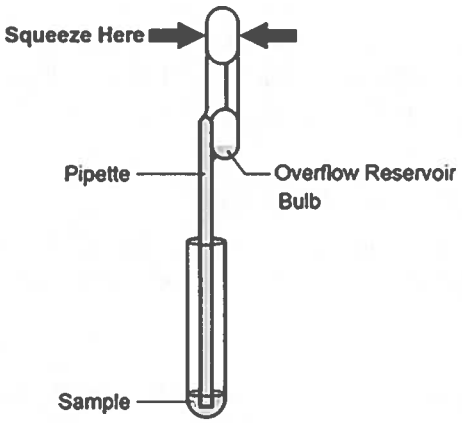

Figure 4. Transfer Pipette

g. 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. Check that the pipette does not contain bubbles.

h. To transfer the sample to the cartridge, squeeze the top bulb of the pipette completely again until it is fully flat to empty the contents of the pipette (300 µL) into the large opening (Sample Chamber) in the cartridge shown in Figure 5. Some liquid may remain in the overflow reservoir. Dispose of the used pipette.

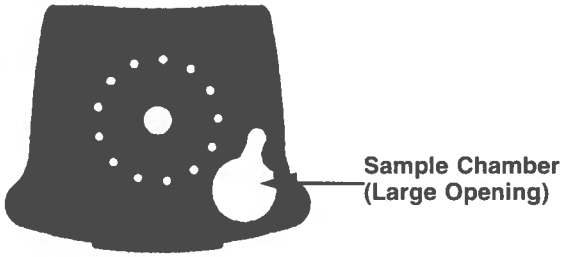

Figure 5. Xpert Xpress SARS-CoV-2/Flu/RSV Cartridge (Top View)

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.

i. Close the cartridge lid.

9. Touch the **Continue** button

10. Locate the module with the blinking green light, open the instrument module door and load

the cartridge with the label facing out. The **instrument will ONLY run the test in the module with the blinking light.**

11. Close the door. The test starts and the green light stops blinking. When the test is finished, the light turns off and the door will unlock. Remove the cartridge and dispose of as biohazard.

Do not turn off or unplug the instruments while a test is in progress. Turning off or unplugging the GeneXpert instrument or computer will stop the test.
If necessary, touch the STOP TEST button to cancel a test while it is loading. Note that you will not get a test result from a cancelled test.

At this point, while a test is running, another test can be started by returning to the Home screen.

Follow the proper COVID antigen reporting procedure and distribute results to infection control, the proper provider, the state department, and local health department, and any other indicated party. Results are documented on the log in the laboratory and entered in the lab computer.

K. Expected Results with Interpretation

The results are interpreted automatically by the GeneXpert 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.

Xpert Xpress_SARS-CoV-2_Flu_RSV Results and Interpretation

Result	Interpretation
SARS-CoV-2 POSITIVE	The SARS-CoV-2 target nucleic acids are detected.
SARS-CoV-2 NEGATIVE; Flu A NEGATIVE; Flu B NEGATIVE; RSV NEGATIVE	SARS-CoV-2, Flu A, Flu B and RSV target RNAs are not detected.
INVALID	SPC does not meet acceptance criteria and all targets not detected. Repeat test according to the Repeat Procedure according to the Retest procedure.
ERROR	Presence or absence of SARS-CoV-2, Flu A, Flu B and RSV nucleic acids cannot be determined. Repeat test according to the Retest Procedure.
NO RESULT	Presence or absence of SARS-CoV-2, Flu A, Flu B and RSV nucleic acids cannot be determined. Repeat test according to the Retest procedure.

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.

L. Retests

1. **Reasons to Repeat the Assay**

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

   a. An **INVALID** result indicates that the control SPC failed. The sample was not properly processed, PCR is inhibited, or the sample was not properly collected.

   b. An **ERROR** result could be due to, but not limited to, Probe Check Control failure, system component failure, no sample added, or the maximum pressure limits were exceeded.

   c. A **NO RESULT** indicates that insufficient data were collected. For example, cartridge failed integrity test, the operator stopped a test that was in progress, or a power failure occurred.

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

2. **Retest Procedure**

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

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

   c. Put on a clean pair of gloves. Obtain a new Xpert Xpress SARS-CoV-2/Flu/RSV cartridge and a new transfer pipette.

   d. Check the specimen transport tube or external control tube is closed.

   e. 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.

   f. Open the cartridge lid.

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

   h. Close the cartridge lid.

   i. Follow all **Procedure** steps above to load the prepared cartridge into the Xpert Xpress.

Follow the proper COVID reporting procedure and distribute results to infection control, the proper provider, the state, local health department, and any other indicated party. Results are documented on the manual log in the laboratory.

M. Limitations

- Please refer to the pamphlet insert for a full listing.
- Performance of the Xpert Xpress SARS-CoV-2/Flu/RSV test 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) and nasal wash/aspirate specimens 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 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.
- Modifications to the manufacturer's outlined procedures may alter the performance of the test.
- False negative results may occur if virus is present at levels below the analytical limit of detection.
- 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 monitoring treatment of infection.
- This test has not been evaluated for screening of blood or blood products for the 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.
- Recent patient exposure to Flu Mist® or other live attenuated influenza vaccines may cause inaccurate positive results.
- 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

N. Technical Assistance

Perform Maintenance Tasks and Document as described in the User's Guide.

In the event of a spill, clean the exterior areas.

If it is suspected that a spill has affected the interior of the instrument, **DO NOT** remove any of the exterior covers. **SHUT DOWN THE INSTRUMENT AND CONTACT Cepheid Technical Support for 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	+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/CustomerSupport.

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