GeneXpert
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Xpert® Xpress CoV-2/Flu/RSV *plus*

REF **XP3COV2/FLU/RSV-10**

Instructions for Use

For Use Under an Emergency Use Authorization (EUA) Only

For Use with GeneXpert® Dx or GeneXpert® Infinity Systems

IVD

Cepheid®

For Use Under an Emergency Use Authorization (EUA) Only **302-6991, Rev. C. July2023**

Trademark, Patents and Copyright Statements

See Section 25, Revision History for a description of changes.

Xpert® Xpress CoV-2/Flu/RSV *plus*

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

℞only

1 Proprietary Name

Xpert® Xpress CoV-2/Flu/RSV *plus*

2 Common or Usual Name

Xpert Xpress CoV-2/Flu/RSV *plus*

3 Intended Use

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

Testing of nasopharyngeal swab, anterior nasal swab, or nasal wash/aspirate specimens, 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 anterior nasal swab specimens, 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. The SARS-CoV-2, influenza A, influenza B and RSV RNA is generally detectable in upper respiratory specimens during the acute phase of infection. Positive results are indicative of active infection, 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.

Testing with the Xpert Xpress CoV-2/Flu/RSV *plus* test is intended for use by trained operators who are proficient in performing tests using either GeneXpert Dx, GeneXpert Infinity and/or GeneXpert Xpress systems. The Xpert Xpress CoV-2/Flu/RSV *plus* 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 via aerosolized droplets (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, the elderly, and those 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 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] RSV remains the leading cause for hospitalizations in infants worldwide.[7] 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 usually mirrors influenza as infections begin to rise during the fall and last through early spring.[5,6]

SARS-CoV-2, influenza, and RSV viruses can cause infections that present with very similar symptoms, making clinical differentiation between them very difficult.[8] Active surveillance programs in conjunction with infection prevention precautions are important components for preventing transmission of SARS-CoV-2, influenza and 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.

5 Principle of the Procedure

The Xpert Xpress CoV-2/Flu/RSV *plus* test is an automated *in vitro* diagnostic test for the simultaneous qualitative detection and differentiation of RNA from SARS-CoV-2, Flu A, Flu B, and RSV. The Xpert Xpress CoV-2/Flu/RSV *plus* test is performed on GeneXpert Instrument Systems (Dx and Infinity Systems). The primers and probes in the Xpert Xpress CoV-2/Flu/RSV *plus* test are designed to amplify and detect unique sequences in the following: nucleocapsid (N) and envelope (E) and RNA-dependent RNA polymerase (RdRP) genes of the SARS-CoV-2 virus genome, influenza A matrix (M), influenza A basic polymerase (PB2), influenza A acidic protein (PA), influenza B matrix (M), influenza B non-structural protein (NS), and the RSV A and RSV B nucleocapsid.

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. For a full description of the systems, see the *GeneXpert Dx System Operator Manual* or the *GeneXpert Infinity System Operator Manual*.

The Xpert Xpress CoV-2/Flu/RSV *plus* test includes reagents for the detection of SARS-CoV-2, Flu A, Flu B and RSV viral RNA in either nasopharyngeal swab, anterior 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 specimen is collected and placed into a transport tube containing 3 mL of viral transport medium or 2 mL of eNAT™. The specimen is briefly mixed by rapidly inverting the collection tube 5 times. Using the supplied transfer pipette, the sample is transferred to the sample chamber of the Xpert Xpress CoV-2/Flu/RSV *plus* 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.

6 Reagents and Instruments

6.1 Materials Provided

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

Xpert Xpress CoV-2/Flu/RSV *plus* Cartridges with 10 Integrated Reaction Tubes	
• 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 System only)	

Not Safety Data Sheets (SDS) are available at www.cepheid.com or www.cepheidinternational.com under the **SUPPORT** tab.

Not 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 CoV-2/Flu/RSV *plus* 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 Dx or GeneXpert Infinity systems (catalog number varies by configuration): GeneXpert instrument, computer, barcode scanner, operator manual.

  For GeneXpert Dx System: GeneXpert Dx software version 4.7b or higher

  For GeneXpert Infinity-80 and Infinity-48s systems: Xpertise software version 6.4b or higher

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)

eNAT Molecular Collection and Preservation Medium from Copan Italy S.p.A. (Brescia, IT):

- eNAT Molecular Collection and Preservation Medium, Copan Catalog #6U073S01
- eNAT Molecular Collection and Preservation Medium, Copan Catalog #6U074S01

10 Warnings and Precautions

10.1 General

- For *in vitro* diagnostic use.
- For emergency use only.
- For prescription use only.
- Positive results are indicative of presence of Flu A, Flu B, RSV, and/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.
- Treat all biological specimens, including used cartridges, as if capable of transmitting infectious agents. Because it is often impossible to know which might be infectious, all biological specimens should be handled using standard precautions. Guidelines for specimen handling are available from the U.S. Centers for Disease Control and Prevention[9] and the Clinical and Laboratory Standards Institute.[10]
- Follow safety procedures set by your institution for working with chemicals and handling biological specimens.
- Refer to Copan eNAT® Package Insert for safety and handling information.
- Avoid direct contact between guanidine thiocyanate and sodium hypochlorite (bleach) or other highly reactive reagents such as acids and bases. These mixtures could release noxious gas. 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 disposalof 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.
- This product has not been FDA cleared or approved, but has been authorized for emergency use by FDA under an EUA for use by authorized laboratories.
- This product has been authorized only for the 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.
- The emergency use of this product is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of in vitro diagnostics 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 declaration is terminated or authorization is revoked sooner.
- Testing of nasopharyngeal swab, anterior nasal swab, or nasal wash/aspirate specimens using the Xpert Xpress CoV-2/Flu/RSV *plus* 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 anterior nasal swab specimens using the Xpert Xpress CoV-2/Flu/RSV *plus* 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.

10.2 Specimens

- Maintain proper storage conditions during specimen transport to ensure the integrity of the specimen (see Section 12, Specimen Collection, Transport, and Storage). Specimen stability under shipping conditions other than those recommended has not been evaluated.

10.3 Assay/Reagent

- Do not open the Xpert Xpress CoV-2/Flu/RSV *plus* cartridge lid except when adding specimen.
- Do not use a cartridge that has been dropped after removing it from the packaging.
- Do not shake the cartridge. Shaking or dropping the cartridge after opening the cartridge lid may yield non-determinate results.
- Do not place the sample ID label on the cartridge lid or on the barcode label on the cartridge.
- Do not use a cartridge with a damaged barcode label.
- Do not use a cartridge that has a damaged reaction tube.
- Do not use reagents beyond their expiry date.
- Each single-use Xpert Xpress CoV-2/Flu/RSV *plus* cartridge is used to process one test. Do not reuse processed cartridges.
- Each single-use disposable pipette is used to transfer one specimen. Do not reuse disposable pipettes.
- Do not use a cartridge if it appears wet or if the lid seal appears to have been broken.
- Wear clean lab coats and gloves. Change gloves between the handling of each specimen.
- In the event of a spill of specimens or controls, wear gloves and absorb the spill with paper towels. Then, thoroughly clean the contaminated area with a 10% freshly prepared household chlorine bleach. Allow a minimum of two minutes of contact time. Ensure the work area is dry before using 70% denatured ethanol to remove bleach residue. Allow surface to dry completely before proceeding. Or, follow your institution's standard procedures for a contamination or spill event. For equipment, follow the manufacturer's recommendations for decontamination of equipment.

11 Chemical Hazards[11, 12]

- **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, Section 12.2 for nasal swab collection procedure, and Section 12.3 for nasal wash/aspirate procedure. Nasopharyngeal and nasal swab specimens can be stored at room temperature (15–30 °C) for up to 48 hours in viral transport medium or eNAT 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 and up to six days in eNAT until testing is performed on the GeneXpert Instrument Systems.

Nasal wash/aspirate specimens can be stored at room temperature (15-30 °C) for up to 48 hours in viral transport medium and refrigerated (2-8 °C) for up to seven days in viral transport medium.

Samples collected in viral transport medium and eNAT can be frozen at -80 °C and can undergo 1 freeze thaw/cycle. 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 2 mL of eNAT. 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).

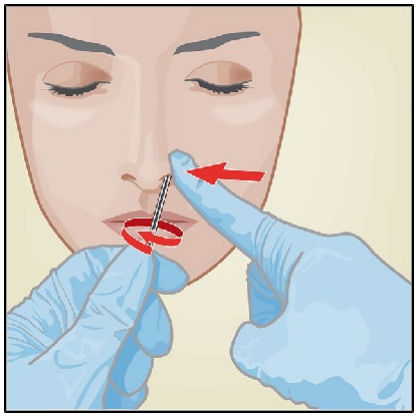


Figure 2. Nasal Swab Collection for First Nostril

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.

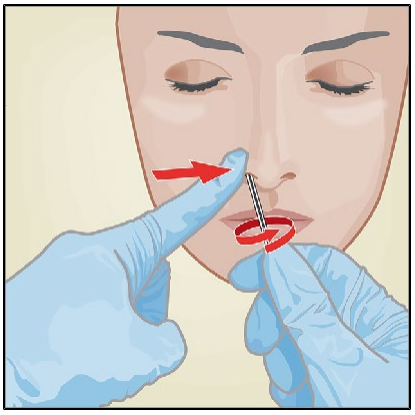


Figure 3. Nasal Swab Collection for Second Nostril

3. Remove and place the swab into the tube containing 3 mL of viral transport medium or 2 mL of eNAT.Break swab at the indicated break line and cap the specimen collection tube tightly.

12.3 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.

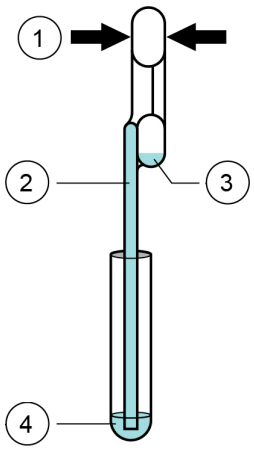
13 Procedure

13.1 Preparing the Cartridge

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

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

6. Squeeze the top bulb of the transfer pipette **completely until the top bulb is fully flat**. While continuing to hold the bulb fully flat, place the pipette tip in the specimen transport tube (see Figure 4).



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

Figure 4. Transfer Pipette

7. 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 4). Check that the pipette does not contain bubbles.
8. To transfer the sample to the cartridge, squeeze the top bulb of the pipette completely again until it is fully flat to empty the contents of the pipette (300 µL) into the large opening (Sample Chamber) of the cartridge shown in Figure 5. Some liquid may remain in the overflow reservoir. Dispose of the used pipette.

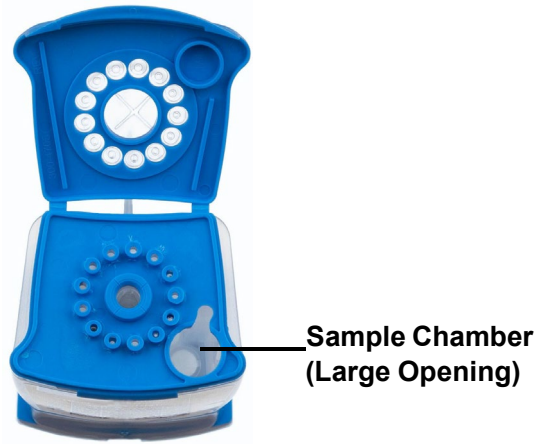


Figure 5. Xpert Xpress CoV-2/Flu/RSV *plus* Cartridge (Top View)

Not Take care to dispense the entire volume of liquid into the Sample Chamber. False negative results may occur if insufficient sample volume is added to the cartridge.

9. Close the cartridge lid.

13.2 External Controls

External controls described in Section 9 are available but not provided and may be used in accordance with local, state, and federal accrediting organizations, as applicable.

To run a control using the Xpert Xpress CoV-2/Flu/RSV *plus* test, perform the following steps:

1. Mix control by rapidly inverting the external control tube 5 times. Open cap on external control tube.
2. Open the cartridge lid.

3. Using a clean transfer pipette, transfer one draw of the external control sample (300 µL) into the large opening (Sample Chamber) in the cartridge shown in Figure 5.
4. Close cartridge lid.

13.3 Starting the Test

Note Before you start the test, make sure that the system contains modules with GeneXpert Dx software version 4.7b or higher or Infinity Xpertise software 6.4b or higher, and that the Xpert Xpress CoV-2/Flu/RSV *plus* Assay Definition File (ADF) is imported into the software.

This section lists the default steps to operate the GeneXpert Instrument System. For detailed instructions, see the *GeneXpert Dx System Operator Manual* or the *GeneXpert Infinity System Operator Manual*, depending on the model that is being used.

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

1. Turn on the GeneXpert Instrument System:
   - **GeneXpert Dx:**

     If using the GeneXpert Dx instrument, first turn on the instrument and then turn on the computer. Log into the Windows operating system. The GeneXpert software may launch automatically or may require double-clicking on the GeneXpert Dx shortcut icon on the Windows® desktop.

     or
   - **GeneXpert Infinity System:**

     If using the GeneXpert Infinity instrument, power up the instrument by turning the power switch clockwise to the **ON** position. On the Windows desktop, double-click the Xpertise Software shortcut icon to launch the software.
2. Log on to the System software. The login screen appears. Type your user name and password.
3. In the GeneXpert System window, click **Create Test** (GeneXpert Dx) or **Orders** followed by **Order Test** (Infinity).
4. Scan or type in the Patient ID (optional). 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.
5. Scan or type in the Sample ID. If typing the Sample ID, make sure the Sample ID is typed correctly. The Sample ID is shown on the left side of the View Results window and is associated with the test result.
6. Scan the barcode on the Xpert Xpress CoV-2/Flu/RSV *plus* 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.

Not If the barcode on the Xpert Xpress CoV-2/Flu/RSV *plus* cartridge does not scan, then repeat the test with a new cartridge.

7. Click **Start Test** (GeneXpert Dx) or **Submit** (Infinity) if Auto-Submit is not enabled. In the dialog box that appears, type your password, if required.

   For the GeneXpert Dx Instrument:

   a. Locate the module with the blinking green light, open the instrument module door and load the cartridge.
   b. 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.
   c. Dispose of used cartridges in the appropriate sample waste containers according to your institution's standard practices.

   or

   For the GeneXpert Infinity System:

   a. After clicking **Submit**, you will be asked to place the cartridge on the conveyor belt. After placing the cartridge, click OK to continue. The cartridge will be automatically loaded, the test will run, and the used cartridge will be placed onto the waste shelf for disposal.
   b. When all samples are loaded, click on the **End Order Test** icon.

Not 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.

14 Viewing and Printing Results

For detailed instructions on how to view and print the results, see the *GeneXpert Dx System Operator Manual* or the *GeneXpert Infinity System Operator Manual*.

15 Quality Control

15.1 Internal Controls

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

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

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

15.2 External Controls

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

Cepheid recommends that all laboratories perform external QC with each new lot and shipment of reagents, at a minimum, while running the Xpert Xpress CoV-2/Flu/RSV *plus* test under Emergency Use Authorization (EUA).

If the expected results for the external control materials are not obtained, repeat the external controls, prior to releasing patient results. If the expected results for the external control material are not obtained upon repeat, contact Cepheid Technical Support.

16 Interpretation of Results

The results are interpreted automatically by the GeneXpert System and are clearly shown in the **View Results** window. The Xpert Xpress CoV-2/Flu/RSV *plus* 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 Xpress SARS-CoV-2_Flu_RSV plus, Xpress SARS-CoV-2_Flu plus or Xpress SARS-CoV-2 plus test.

Table 1 shows the possible result outcomes when the Xpress SARS-CoV-2_Flu_RSV plus test mode is selected.

Table 1. Xpress SARS-CoV-2_Flu_RSV plus Possible Results and Interpretation

Result	Interpretation
SARS-CoV-2 POSITIVE	The SARS-CoV-2 target RNA is detected. ● 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	The Flu A target RNA is detected. ● 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	The Flu B target RNA is detected. ● 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	The RSV target RNA is detected. ● 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**	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. ● 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
INVALID	SPC does not meet acceptance criteria and all targets are not detected. Repeat test according to the Retest Procedure in Section 17.2 of the IFU. ● SPC: FAIL; SPC and SARS-CoV-2, Flu A, Flu B and RSV signals do not have a Ct within valid range and endpoint is below minimum setting ● Probe Check: PASS; all probe check results pass
ERROR	Presence or absence of SARS-CoV-2, Flu A, Flu B and RSV RNA cannot be determined. Repeat test according to the Retest Procedure in Section 17.2 of the IFU. ● SARS-CoV-2: NO RESULT ● Flu A: NO RESULT ● Flu B: NO RESULT ● RSV: NO RESULT ● SPC: NO RESULT ● Probe Check: FAIL[1]; all or one of the probe check results fail [1]If the probe check passes, the error is caused by the maximum pressure limit exceeding the acceptable range, no sample added, or by a system component failure.

Result	Interpretation
NO RESULT	Presence or absence of SARS-CoV-2, Flu A, Flu B and RSV RNA cannot be determined. Repeat test according to the Retest Procedure in Section 17.2 of the IFU. A **NO RESULT** indicates that insufficient data were collected. For example, the operator stopped a test that was in progress. ● SARS-CoV-2: NO RESULT ● Flu A: NO RESULT ● Flu B: NO RESULT ● RSV: NO RESULT ● SPC: NO RESULT ● Probe Check: NA
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 Xpress SARS-CoV-2_Flu plus test mode is selected.

Table 2. Xpress SARS-CoV-2_Flu plus Possible Results and Interpretation

Result	Interpretation
SARS-CoV-2 POSITIVE	The SARS-CoV-2 target RNA is detected. ● 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	The Flu A target RNA is detected. ● 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	The Flu B target RNA is detected. ● 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	SARS-CoV-2 target RNA is not detected; Flu A target RNA is not detected; Flu B target RNA is not detected. ● 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
INVALID	SPC does not meet acceptance criteria and all targets are not detected. Repeat test according to the Retest Procedure in Section 17.2 of the IFU. ● SPC: FAIL; SPC and SARS-CoV-2, Flu A and Flu B signals do not have a Ct within valid range and endpoint is below minimum setting. ● Probe Check: PASS; all probe check results pass

Result	Interpretation
ERROR	Presence or absence of SARS-CoV-2, Flu A and Flu B RNA cannot be determined. Repeat test according to the Retest Procedure in Section 17.2 of the IFU. ● SARS-CoV-2: NO RESULT ● Flu A: NO RESULT ● Flu B: NO RESULT ● SPC: NO RESULT ● Probe Check: FAIL[1]; all or one of the probe check results fail [1] If the probe check passes, the error is caused by the maximum pressure limit exceeding the acceptable range, no sample added, or by a system component failure.
NO RESULT	Presence or absence of SARS-CoV-2, Flu A and Flu B RNA cannot be determined. Repeat test according to the Retest Procedure in Section 17.2 of the IFU. A **NO RESULT** indicates that insufficient data were collected. For example, the operator stopped a test that was in progress. ● SARS-CoV-2: NO RESULT ● Flu A: NO RESULT ● Flu B: NO RESULT ● SPC: NO RESULT ● Probe Check: NA
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 Xpress SARS-CoV-2 plus test mode is selected.

Table 3. Xpress SARS-CoV-2 plus Possible Results and Interpretation

Result	Interpretation
SARS-CoV-2 POSITIVE	The SARS-CoV-2 target RNA is detected. ● 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	SARS-CoV-2 target RNA is not detected. ● 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
INVALID	SPC does not meet acceptance criteria and SARS-CoV-2 is not detected. Repeat test according to the Retest Procedure in Section 17.2 of the IFU. ● SPC: FAIL; SPC and SARS-CoV-2 signals do not have a Ct within valid range and endpoint is below minimum setting ● Probe Check: PASS; all probe check results pass

Result	Interpretation
ERROR	Presence or absence of SARS-CoV-2 RNA cannot be determined. Repeat test according to the Retest Procedure in Section 17.2 of the IFU. • SPC: NO RESULT • Probe Check: FAIL[1]; all or one of the probe check results fail [1] If the probe check passes, the error is caused by the maximum pressure limit exceeding the acceptable range, no sample added, or by a system component failure.
NO RESULT	Presence or absence of SARS-CoV-2 RNA cannot be determined. Repeat test according to the Retest Procedure in Section 17.2 of the IFU. A **NO RESULT** indicates that insufficient data were collected. For example, the operator stopped a test that was in progress. • SARS-CoV-2: NO RESULT • SPC: NO RESULT • Probe Check: NA

The Xpert Xpress CoV-2/Flu/RSV *plus* test can be run to detect SARS-CoV-2, Flu and RSV by selecting Xpress SARS-CoV-2_Flu_RSV plus from the Select Test menu; SARS-CoV-2 and Flu only by selecting Xpress SARS-CoV-2_Flu plus; or SARS-CoV-2 only by selecting Xpress SARS-CoV-2 plus. The Xpress SARS-CoV-2 plus test mode includes an Early Assay Termination (EAT) function that will provide earlier time to result 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.

17 Retests

17.1 Reasons to Repeat the Test

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

- An **INVALID** result indicates that the control SPC failed. The sample was not properly processed, PCR is inhibited, or the sample was not properly collected.
- An **ERROR** result could be due to, but not limited to, Probe Check Control failure, system component failure, no sample added, or the maximum pressure limits were exceeded.
- A **NO RESULT** indicates that insufficient data were collected. For example, cartridge failed integrity test, the operator stopped a test that was in progress, or a power failure occurred.

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

17.2 Retest Procedure

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

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

1. Put on a clean pair of gloves. Obtain a new Xpert Xpress CoV-2/Flu/RSV *plus* cartridge and a new transfer pipette.
2. Check the specimen transport tube or external control tube is closed.
3. Mix the sample by rapidly inverting the specimen transport medium tube or external control tube 5 times. Open the cap on the specimen transport tube or external control tube.
4. Open the cartridge lid.
5. Using a clean transfer pipette (supplied), transfer sample (one draw) to the sample chamber with the large opening in the cartridge.
6. Close the cartridge lid.

18 Limitations

- Performance of the Xpert Xpress CoV-2/Flu/RSV *plus* test has only been established in nasopharyngeal swab specimens. Use of the Xpert Xpress CoV-2/Flu/RSV *plus* 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 CoV-2/Flu/RSV *plus* test but performance with these specimen types has not been established.
- The performance of this test was established based on the evaluation of a limited number of clinical specimens. Clinical performance has not been established with all circulating variants but is anticipated to be reflective of the prevalent variants in circulation at the time and location of the clinical evaluation. Performance at the time of testing may vary depending on the variants circulating, including newly emerging strains of SARS-CoV-2 and their prevalence, which change over time.
- The performance of this device has not been assessed in a population vaccinated against COVID-19.
- As with any molecular test, mutations within the target regions of the Xpert Xpress CoV-2/Flu/RSV *plus* 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 CoV-2/Flu/RSV *plus* 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 infectivity. Detection of analyte target(s) does not imply that the corresponding virus(es) are infectious or are the causative agents for clinical symptoms.
- This test has been evaluated for use with human specimen material only.
- This test is a qualitative test and does not provide the quantitative value of detected organism present.
- This test has not been evaluated for monitoring treatment of infection.
- This test has not been evaluated for patients without signs and symptoms of respiratory tract 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.
- Results from analytical studies with contrived co-infected samples showed potential for competitive interference of influenza B or RSV A at low concentrations (~3X LoD) when influenza A concentration is >1.7e5 RNA copies/mL or 1.7e6 RNA copies/mL, respectively. In addition, there is potential for competitive interference of influenza B at low concentration (~3X LoD) when SARS-CoV-2 concentration is >1e5 RNA copies/mL.
- 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.
- Zicam at 15% (w/v) may interfere with the detection of low levels of influenza B and RSV A.
-
- As the Xpert Xpress CoV-2/Flu/RSV *plus* test does not differentiate between the N2, RdRP and E gene targets, the presence of other coronaviruses in the B lineage, Betacoronavirus genus, including SARS-CoV 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.

19 Conditions of Authorization for Laboratory and Patient Care Settings

The Cepheid Xpert Xpress CoV-2/Flu/RSV *plus* 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/in-vitro-diagnostics-euas.

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

- Authorized laboratories[a] using your product must include with test result reports 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 must use your product as outlined in the authorized labeling. 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 CoV-2/Flu/RSV *plus* test are not permitted.
- Authorized laboratories that receive your product must notify the relevant public health authorities of their intent to run your product prior to initiating testing.
- Authorized laboratories using your product must have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.
- Authorized laboratories must collect information on the performance of your product 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 RT-PCR techniques and 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 using your product must 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.

[a] 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 Xpress CoV-2/Flu/RSV *plus* 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 CoV-2/Flu/RSV plus 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.

20 Performance Characteristics

20.1 Clinical Evaluation

The performance of the Xpert Xpress CoV-2/Flu/RSV *plus* test was evaluated using archived clinical nasopharyngeal (NP) swab specimens in viral transport medium or universal transport medium. Archived specimens were selected consecutively by date and previously known analyte result. A total of 279 NP swab specimens were tested with Xpert Xpress CoV-2/Flu/RSV *plus* side by side with FDA authorized SARS-CoV-2 RT-PCR test and the FDA-cleared influenza/RSV molecular test in a randomized and blinded fashion.

Positive Percent Agreement (PPA), Negative Percent Agreement (NPA), and non-determinate rate were determined by comparing the results of the Xpert Xpress CoV-2/Flu/RSV *plus* test relative to the results of FDA authorized SARS-CoV-2 RT-PCR test for the SARS-CoV-2 target, and FDA-cleared influenza/RSV molecular test for the Flu A, Flu B, and RSV targets, respectively.

Xpert Xpress CoV-2/Flu/RSV *plus* demonstrated a PPA and NPA of 100.0% and 100.0% for SARS-CoV-2, respectively; 100.0% and 100.0% for Flu A, respectively; 100.0% and 100.0% for Flu B, respectively; 100.0% and 100.0% for RSV, respectively (Table 4). The initial non-determinate rate for the Xpert Xpress CoV-2/Flu/RSV *plus* test was 0.7% (2/279). On repeat testing, both (2)specimens yielded valid results. The final non-determinate rate for the Xpert Xpress CoV-2/Flu/RSV *plus* test was 0.0% (0/279).

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

Target	Number of Specimens	TP	FP	TN	FN	PPA (95% CI)	NPA (95% CI)
SARS-CoV-2	279	66	0	213	0	100.0% (94.5% - 100.0%)	100.0% (98.2% - 100.0%)
Flu A	264	51	0	213	0	100.0% (93.0% - 100.0%)	100.0% (98.2% - 100.0%)
Flu B	264	46	0	218	0	100.0% (92.3% - 100.0%)	100.0% (98.3% - 100.0%)
RSV	264	47	0	217	0	100.0% (92.4% - 100.0%)	100.0% (98.3% - 100.0%)
TP: True Positive; FP: False Positive; TN: True Negative; FN: False Negative; CI: Confidence Interval							

20.2 Prospective Clinical Evaluation

The clinical performance of the Xpert Xpress CoV-2/Flu/RSV plus test was evaluated in a multi-site, observational and method comparison study that included 33 geographically diverse sites in the United States (US) using specimens collected from individuals showing signs and symptoms of respiratory infection. Of the 33 sites, 5 sites participated in specimen collection only, 27 performed Xpert testing and specimen collection, and 1 site performed Xpert testing as well as comparator and discrepant testing.

Specimens tested included prospective clinical NPS and NS specimens collected in UTM/VTM. Prospectively collected fresh clinical specimens (Category I) tested in the study were from a larger US specimen collection protocol. Fresh (98.9%) and frozen (1.1%) specimens meeting the eligibility criteria were prospectively collected and tested in 2022. Due to low prevalence of Flu/RSV in 2022, archived prospectively collected frozen clinical specimens (Category II) collected during the 2016-2017 influenza season were used to supplement the sample size. These specimens represent contemporary Flu/RSV strains. Since these specimens were collected prior to the COVID-19 pandemic, they were expected to be negative for SARS-CoV-2 and therefore tested only for the Flu A, Flu B, and RSV targets. Available demographic data from the individuals from whom Category I and Category II specimens were collected are presented in Table 5.

Table 5. Demographic Summary for Category I and II Specimens

Prospectively Collected Fresh Specimens from 2022 (Category I)	NPS (N=2672)	NS (N=2659)	Overall (N=5331)
Gender			
Female	1568 (58.7%)	1634 (61.5%)	3202 (60.1%)
Male	1104 (41.3%)	1025 (38.5%)	2129 (39.9%)
Age Group (Years)			
≤5	9 (0.3%)	183 (6.9%)	192 (3.6%)
6-21	623 (23.3%)	562 (21.1%)	1185 (22.2%)
22-59	1676 (62.7%)	1553 (58.4%)	3229 (60.6%)
≥60	364 (13.6%)	361 (13.6%)	725 (13.6%)
Race			
American Indian or Alaska Native	5 (0.2%)	6 (0.2%)	11 (0.2%)
Asian	73 (2.7%)	80 (3.0%)	153 (2.9%)
Asian, White	8 (0.3%)	1 (0.0%)	9 (0.2%)
Black or African American	734 (27.5%)	730 (27.5%)	1464 (27.5%)
Black or African American, White	10 (0.4%)	12 (0.5%)	22 (0.4%)
Native Hawaiian or Other Pacific Islander	6 (0.2%)	2 (0.1%)	8 (0.2%)
Other Mixed (N ≤ 3)	4 (0.1%)	5 (0.2%)	9 (0.2%)
White	1685 (63.1%)	1641 (61.7%)	3326 (62.4%)
Participant Declined to Answer, or Unknown	147 (5.5%)	182 (6.8%)	329 (6.2%)
Ethnicity			
Hispanic	228 (8.5%)	213 (8.0%)	441 (8.3%)
Non-Hispanic	2333 (87.3%)	2323 (87.4%)	4656 (87.3%)
Participant Declined to Answer, or Unknown	111 (4.2%)	123 (4.6%)	234 (4.4%)
Specimen Testing			
Fresh	2641 (98.8%)	2631 (98.9%)	5272 (98.9%)
Frozen	31 (1.2%)	28 (1.1%)	59 (1.1%)
COVID-19 Vaccination Status			
Vaccinated	1969 (73.7%)	1865 (70.1%)	3834 (71.9%)
Not Vaccinated	665 (24.9%)	764 (28.7%)	1429 (26.8%)
Unknown	38 (1.4%)	30 (1.1%)	68 (1.3%)
Testing Environment			
CLIA Waiver	1603 (60.0%)	1619 (60.9%)	3222 (60.4%)

Prospectively Collected Fresh Specimens from 2022 (Category I)	NPS (N=2672)	NS (N=2659)	Overall (N=5331)
Laboratory/NPT	1069 (40.0%)	1040 (39.1%)	2109 (39.6%)
Prospectively Collected Frozen Specimens from 2016-2017 Influenza Season (Category II)	NPS Collected from One Nostril (N=422)	NS Collected from Both Nostrils (N=368)	Overall (N=790)
Gender			
Female	211 (50.0%)	223 (60.6%)	434 (54.9%)
Male	211 (50.0%)	145 (39.4%)	356 (45.1%)
Age Group (Years)			
≤5	164 (38.9%)	144 (39.1%)	308 (39.0%)
6-21	85 (20.1%)	72 (19.6%)	157 (19.9%)
22-59	134 (31.8%)	111 (30.2%)	245 (31.0%)
≥60	39 (9.2%)	41 (11.1%)	80 (10.1%)

Specimens were tested using Xpert Xpress CoV-2/Flu/RSV plus side-by-side with an FDA-cleared SARS-CoV-2 RT-PCR test and an FDA-cleared influenza/RSV RT-PCR test, in a randomized and blinded fashion.

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

Discrepant results between Xpert Xpress CoV-2/Flu/RSV plus and the comparator for the SARS-CoV-2 target were investigated using an FDA-authorized SARS-CoV-2 EUA test. Discrepant results between the Xpert Xpress CoV-2/Flu/RSV plus and the comparator for the Flu A/B/RSV targets were investigated using an FDA-cleared influenza/RSV RT-PCR test.

A total of 5051 specimens, including 2536 NPS and 2515 NS specimens that yielded valid results by both the Xpert Xpress CoV-2/Flu/RSV plus and the FDA-cleared SARS-CoV-2 RT-PCR tests, were included in the performance evaluation for SARS-CoV-2. A total of 5954 specimens, including 3011 NPS and 2943 NS specimens that yielded valid results by both the Xpert Xpress CoV2/Flu/RSV plus and the FDA-cleared influenza/RSV RT-PCR tests, were included in the performance evaluation for Flu A, Flu B, and RSV targets.

For the NPS specimens (fresh and frozen, combined), Xpert Xpress CoV-2/Flu/RSV plus demonstrated a PPA and NPA of 97.1% and 98.2% for SARS-CoV-2, respectively; 99.0% and 99.1% for Flu A, respectively; 96.6% and 100.0% for Flu B, respectively; 98.6% and 100.0% for RSV, respectively (Table 6). The initial non-determinate rate for the Xpert Xpress CoV-2/Flu/RSV plus test was 2.4% (74/3094). On repeat testing, 66 specimens yielded valid results. The final non-determinate rate for the Xpert Xpress CoV-2/Flu/RSV plus test was 0.3% (8/3094).

Table 6. Xpert Xpress CoV-2/Flu/RSV plus Performance Results for NPS Specimens

Target	Specimen Collection	Numbers of Specimens	TP	FP	TN	FN	PPA (%)	95%CI	NPA (%)	95%CI
SARS-CoV-2	Fresh	2505	454	37[a]	2000	14[b]	97	95.0 - 98.2	98.2	97.5 - 98.7
	Frozen	31	8	0	23	0	100	67.6 - 100.0	100	85.7 - 100.0
	Overall	2536	462	37	2023	14	97.1	95.1 - 98.2	98.2	97.5 - 98.7
Flu A	Fresh	2562	98	11[c]	2451	2[d]	98	93.0 - 99.4	99.6	99.2 - 99.8
	Frozen	449	93	13[e]	343	0	100	96.0 - 100.0	96.3	93.9 - 97.9
	Overall	3011	191	24	2794	2	99.0	96.3 - 99.7	99.1	98.7 - 99.4
Flu B	Fresh	2562	0	0	2562	0	NA	NA	100	99.9 - 100.0

	Frozen	449	57	0	390	2[f]	96.6	88.5 - 99.1	100	99.0 - 100.0
	Overall	3011	57	0	2952	2	96.6	88.5 - 99.1	100	99.9 - 100.0
RSV	Fresh	2562	12	0	2550	0	100	75.8 - 100.0	100	99.8 - 100.0
	Frozen	449	59	0	389	1[g]	98.3	91.1 - 99.7	100	99.0 - 100.0
	Overall	3011	71	0	2939	1	98.6	92.5 - 99.8	100	99.9 - 100.0

a. Discrepant test results based on an FDA-authorized EUA test: 15/37 SARS-CoV-2 positive; 22/37 SARS-CoV-2 negative

b. Discrepant test results based on an FDA-authorized EUA test: 3/14 SARS-CoV-2 positive; 10/14 SARS-CoV-2 negative; 1/14 invalid result

c. Discrepant test results based on an FDA-cleared test: 8/11 Flu A positive; 3/11 Flu A negative

d. Discrepant test results based on an FDA-cleared test: 1/2 Flu A positive; 1/2 Flu A negative

e. Discrepant test results based on an FDA-cleared test: 13/13 tests not performed due to specimens being stored for a longer duration than recommended per the package insert

f. Discrepant test results based on an FDA-cleared test: 2/2 test not performed due to specimens being stored for a longer duration than recommended per the package insert

g. Discrepant test results based on an FDA-cleared test: 1/1 test not performed due to specimens being stored for a longer duration than recommended per the package insert

For the NS specimens (fresh and frozen, combined), Xpert Xpress CoV-2/Flu/RSV plus demonstrated a PPA and NPA of 98.2% and 98.8% for SARS CoV-2, respectively; 98.0% and 99.3% for Flu A, respectively; 100.0% and 99.9% for Flu B, respectively; 95.8% and 100.0% for RSV, respectively (Table 7). The initial non-determinate rate for the Xpert Xpress CoV-2/Flu/RSV plus test was 2.4% (74/3027). On repeat testing, 57 specimens gave valid results upon retest. The final non-determinate rate for the Xpert Xpress CoV-2/Flu/RSV plus test was 0.6% (17/3027).

Table 7. Xpert Xpress CoV-2/Flu/RSV plus Performance Results for NS Specimens

Target	Specimen Collection	Numbers of Specimens	TP	FP	TN	FN	PPA (%)	95%CI	NPA (%)	95%CI
SARS-CoV-2	Fresh	2489	442	23[a]	2017	7[b]	98.4	96.8 - 99.2	98.9	98.3 - 99.2
	Frozen	26	6	1[c]	18	1[d]	85.7	48.7 - 97.4	94.7	75.4 - 99.1
	Overall	2515	448	24	2035	8	98.2	96.6 - 99.1	98.8	98.3 - 99.2
Flu A	Fresh	2553	130	6[e]	2413	4[f]	97.0	92.6 - 98.8	99.8	99.5 - 99.9
	Frozen	390	66	12[g]	312	0	100	94.5 - 100.0	96.3	93.6 - 97.9
	Overall	2943	196	18	2725	4	98.0	94.9 - 99.2	99.3	99.0 - 99.6
Flu B	Fresh	2553	0	0	2553	0	NA	NA	100	99.8 - 100.0
	Frozen	390	34	3[h]	353	0	100	89.8 - 100.0	99.2	97.6 - 99.7
	Overall	2943	34	3	2906	0	100	89.8 - 100.0	99.9	99.7 - 100.0
RSV	Fresh	2553	14	0	2538	1[i]	93.3	70.2 - 98.8	100	99.8 - 100.0
	Frozen	390	55	0	333	2[j]	96.5	88.1 - 99.0	100	98.9 - 100.0
	Overall	2943	69	0	2871	3	95.8	88.5 - 98.6	100	99.9 - 100.0

a. Discrepant test results based on an FDA-authorized EUA test: 6/23 SARS-CoV-2 positive; 14/23 SARS-CoV-2 negative; 2/23 invalid result; 1/23 discrepant testing was inadvertently not performed

b. Discrepant test results based on an FDA-authorized EUA test: 2/7 SARS-CoV-2 positive; 5/7 SARS-CoV-2 negative

c. Discrepant test results based on an FDA-authorized EUA test: 1/1 SARS-CoV-2 positive

d. Discrepant test results based on an FDA-authorized EUA test: 1/1 SARS-CoV-2 negative

e. Discrepant test results based on an FDA-cleared test: 5/6 Flu A positive; 1/6 Flu A negative

f. Discrepant test results based on an FDA-cleared test: 2/4 Flu A positive; 2/4 Flu A negative

g. Discrepant test results based on an FDA-cleared test: 12/12 tests not performed due to specimens being stored for a longer duration than recommended per the package insert

h. Discrepant test results based on an FDA-cleared test: 3/3 tests not performed due to specimens being stored for a longer duration than recommended per the package insert

i. Discrepant test results based on an FDA-cleared test: 1/1 RSV positive

j. Discrepant test results based on an FDA-cleared test: 2/2 test not performed due to specimens being stored for a longer duration than recommended per the package insert

The number of specimens with positive results for more than one target as detected by Xpert Xpress CoV-2/Flu/RSV plus is presented in Table 8 and Table 9, where bolded values indicate concordant results.

Table 8. Multi-Target Detection by Xpert Xpress CoV-2/Flu/RSV plus

Infection		Comparator Results						
		SARS-CoV-2 only	SARS-CoV-2 and Flu A	Flu A only	RSV only	Negative	Total	Co-Infection Rate (%)
Xpert Xpress CoV-2/Flu/RSV *plus*	SARS-CoV-2 only	**876**	1	0	0	57	934	0.3
	SARS-CoV-2 and Flu A	0	**2**	1	0	0	3	
	Flu A only	0	0	**220**	0	17	237	
	RSV only	0	0	0	**26**	0	26	
	Negative	22	0	5	1	**3693**	3721	
	Total	898	3	226	27	3767	4921	
	Co-Infection Rate (%)	0.3						

As presented in Table 8, a total of 4921 Category I specimens collected in 2022 yielded valid results for SARS-CoV-2, Flu A, and RSV targets for both the Xpert Xpress CoV-2/Flu/RSV plus test and the comparator test. The co-infection rate for Xpert Xpress CoV-2/Flu/RSV plus was 0.3% (3/1200) and the rate of co-infection by the comparator was 0.3% (3/1154).

Table 9. Flu A, Flu B, and RSV Multi-Target Detection by Xpert Xpress CoV-2/Flu/RSV plus

Infection		Comparator								
		Flu A only	Flu B Only	RSV Only	Flu A and Flu B	Flu A and RSV	Flu B and RSV	Negative	Total	Co-Infection Rate (%)
Xpert Xpress CoV-2/Flu/RSV *plus*	Flu A only	**381**	0	0	1	1	0	36	419	1.7
	Flu B Only	0	**85**	0	0	0	0	2	87	
	RSV Only	0	0	**135**	0	0	0	0	135	
	Flu A and Flu B	0	4	0	**1**	0	0	1	6	
	Flu A and RSV	0	0	1	0	**3**	0	0	4	
	Flu B and RSV	0	0	0	0	0	**1**	0	1	
	Negative	6	1	3	0	0	0	**5292**	5302	
	Total	387	90	139	2	4	1	5331	5954	
	Co-Infection Rate (%)	1.1								

As presented in Table 9, of the 5954 Category I and II specimens evaluated for Flu A, Flu B and RSV targets, the co-infection rate for Xpert Xpress CoV-2/Flu/RSV plus was 1.7% (11/652) and the rate of co-infection by the comparator was 1.1% (7/623).

20.3 Analytical Sensitivity (Limit of Detection)

The analytical sensitivity of the Xpert Xpress CoV-2/Flu/RSV *plus* test was first estimated using two reagent lots by testing limiting dilutions of seven respiratory viruses (NATtrol SARS-CoV-2, Flu A H1, Flu A H3, Flu B Victoria lineage, Flu B Yamagata lineage, 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 CoV-2/Flu/RSV *plus* reagents. The verified LoD values for the virusestested are summarized in Table 10.

Table 10. Xpert Xpress CoV-2/Flu/RSV *plus* Limit of Detection

Virus/Strain	LoD Concentration
SARS-CoV-2 (USA-WA1/2020)	138 copies/mL
Influenza A/Idaho/07/2018	0.007 $TCID_{50}$/mL
Influenza A/Hong Kong/45/2019	0.44 FFU/mL
Influenza B/Washington/2/2019	12.9 $CEID_{50}$/mL
Influenza B/Wisconsin/10/2016	2.4 $TCID_{50}$/mL
RSV A/2/Australia/61	0.33 $TCID_{50}$/mL
RSV B/9320/MA/77	0.37 $TCID_{50}$/mL

20.4 Analytical Reactivity (Inclusivity)

The inclusivity of Xpert Xpress CoV-2/Flu/RSV *plus* was evaluated on June 30th, 2021 using *in silico* analysis of the assay amplicons in relation to 1,566,123 SARS-CoV-2 sequences available in the GISAID gene database for three targets, E, N2and RdRP.

For analysis of the E target, 1,626 sequences were excluded due to ambiguous nucleotides, which reduced the total to 1,564,497 sequences. Of the 1,564,497 GISAID sequences, 1,555,036 (99.4%) were an exact match to the SARS-CoV-2 E target amplicon generated in the Xpert Xpress CoV-2/Flu/RSV *plus* test. Single nucleotide mismatches were

observed for 9,406 sequences and two mismatches were observed for 55 sequences. Of the 55 sequences with two or more mismatches,16 sequences contained 2 mismatches in the forward primer region, and three sequences contained 2

mismatches in the probe region. These double mismatches could have an impact on probe or reverse primer binding.

For analysis of the N2 target, 2,046 sequences were excluded due to ambiguous nucleotides, which reduced the total used in the evaluation to 1,564,077 sequences. Of the 1,564,077 GISAID sequences, 1,511,700 (96.65%) were an exact match to
the SARS-CoV-2 N2 target amplicon generated in the Xpert Xpress CoV-2/Flu/RSV *plus* test. Single nucleotide mismatches were observed for 50,466 sequences and two or three mismatches were observed for 1,911 sequences. For the 31 sequences with three variant positions, five sequences have two of the mismatched nucleotides in the probe region and two of the sequences have two of the mismatched nucleotides in the reverse primer region. These double mismatches could have an impact on probe or reverse primer binding. None of the other mismatches are predicted to have a negative impact on the performance of the assay.

The RdRP is amplified using a semi-nested primer/probe set; only the inner amplicon is used for the in silico analysis. For analysis of the RdRP target, 3,616 sequences were excluded due to ambiguous nucleotides, which reduced the total to 1,565,149 sequences. Of the 1,565,149 GISAID sequences, 1,550,310 (99.05%) were an exact match to the SARS-CoV-2
RdRP target amplicon generated in the Xpert Xpress CoV-2/Flu/RSV *plus* test. Single nucleotide mismatches were observedfor 14,791 sequences and two or more mismatches were observed for 48 sequences. Two sequences have 5 mismatches, three located in the probe region and two in the reverse primer region, and 19 sequences have two nucleotide mismatches in the forward primer or probe region. These mismatches could have an impact on probe or reverse primer binding. None of theother mismatches are predicted to have a negative impact on the performance of the assay.

In addition to the *in silico* analysis of the SARS-CoV-2 primers and probes for inclusivity, the inclusivity of the Xpert Xpress CoV-2/Flu/RSV *plus* test was evaluated by bench testing against multiple strains of SARS-CoV-2, 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 Yamagatalineages), and respiratory syncytial virus subgroups A and B (RSV A and RSV B) at levels near the analytical LoD. A

Total of 84 strains comprised of 5 SARS-CoV-2 virus strains, 4 SARS-CoV-2 in vitro RNA transcripts representing variant strains, 69 influenza viruses (48 influenza A and 21 influenza B) and 6 RSV strains (4 RSVA and 2 RSV B) were tested in this study with the Xpert Xpress CoV-2/Flu/RSV *plus* test. Three replicates were tested for each strain. All SARS-CoV-2, Flu and RSV strains tested positive in all three replicates. Results are shown in Table 11.

Table 11. Analytical Reactivity (Inclusivity) of the Xpert Xpress CoV-2/Flu/RSV *plus* Test

Virus	Strain	Tested Titer	SARS-CoV-2	Flu A	Flu B	RSV
SARS-CoV-2	NATtrol SARS-CoV-2 USA-WA1/2020	412 copies/mL	POS	NEG	NEG	NEG
	SARS-CoV-2/Hong Kong/VM20001061/2020	0.5 $TCID_{50}$/mL	POS	NEG	NEG	NEG
	SARS-CoV-2/Italy-INMI1	4 $TCID_{50}$/mL	POS	NEG	NEG	NEG
	SARS-CoV-2/South_Africa/ KRISP-K005325/2020	0.2 $TCID_{50}$/mL	POS	NEG	NEG	NEG
	SARS-CoV-2/England/ 204820464/2020	0.5 $TCID_{50}$/mL	POS	NEG	NEG	NEG
	SARS-CoV-2 RNA USA/WA2/2020(C09)[a]	100 copies/mL	POS	NEG	NEG	NEG
	SARS-CoV-2RNA/ England/205041766/ 2020(C14)[a]	100 copies/mL	POS	NEG	NEG	NEG
	SARS-CoV-2 RNA /England/ MILK-9E05B3/2020 (C15)[a]	200 copies/mL	POS	NEG	NEG	NEG
	SARS-CoV-2 RNA /Japan (Brazil)/IC-0564/2021 (C17)[a]	100 copies/mL	POS	NEG	NEG	NEG
Influenza A H1N1 (pre-2009)	A/swine/Iowa/15/30	30 $TCID_{50}$/mL	NEG	POS	NEG	NEG
	A/WS/33	5.0 $CEID_{50}$/mL	NEG	POS	NEG	NEG
	A/PR/8/34	20 $CEID_{50}$/mL	NEG	POS	NEG	NEG
	A/Mal/302/54	0.156 $CEID_{50}$/mL	NEG	POS	NEG	NEG
	A/Denver/1/57	10 $CEID_{50}$/mL	NEG	POS	NEG	NEG
	A/New Jersey/8/76	5.0 $CEID_{50}$/mL	NEG	POS	NEG	NEG
	A/New Caledonia/20/1999	0.10 $TCID_{50}$/mL	NEG	POS	NEG	NEG
	A/New York/55/2004	30 $TCID_{50}$/mL	NEG	POS	NEG	NEG
	A/Solomon Island/3/2006	0.0159 $TCID_{50}$/mL	NEG	POS	NEG	NEG
	A/Taiwan/42/06	0.0159 $TCID_{50}$/mL	NEG	POS	NEG	NEG
	A/Brisbane/59/2007	0.060 $TCID_{50}$/mL	NEG	POS	NEG	NEG
	A/Swine/NY/02/2009	20 $TCID_{50}$/mL	NEG	POS	NEG	NEG
Influenza A H1N1 (pdm2009)	A/Colorado/14/2012	0.13 $TCID_{50}$/mL	NEG	POS	NEG	NEG
	A/Michigan/45/2015	100 $CEID_{50}$/mL	NEG	POS	NEG	NEG
	A/Iowa/53/2015	100 $CEID_{50}$/mL	NEG	POS	NEG	NEG
	A/Michigan/272/2017	1.0 $TCID_{50}$/mL	NEG	POS	NEG	NEG

Virus	Strain	Tested Titer	SARS-CoV-2	Flu A	Flu B	RSV
	A/Idaho/07/2018	0.0159 $TCID_{50}$/mL	NEG	POS	NEG	NEG
	A/Wisconsin/505/2018	0.25 $TCID_{50}$/mL	NEG	POS	NEG	NEG
	A/Hawaii/66/2019	100 $CEID_{50}$/mL	NEG	POS	NEG	NEG
	A/Indiana/02/2020	NA[b]	NEG	POS	NEG	NEG
Influenza A H3N2 (Seasonal)	A/Aichi/2/68	2.0 $CEID_{50}$/mL	NEG	POS	NEG	NEG
	A/Hong Kong/8/68	2.0 $CEID_{50}$/mL	NEG	POS	NEG	NEG
	A/Port Chalmers/1/73	100 $CEID_{50}$/mL	NEG	POS	NEG	NEG
	A/Hawaii/15/2001	100 $CEID_{50}$/mL	NEG	POS	NEG	NEG
	A/Wisconsin/67/05[c]	0.22 $TCID_{50}$/mL	NEG	POS	NEG	NEG
	A/Brisbane/10/2007	0.025 $TCID_{50}$/mL	NEG	POS	NEG	NEG
	A/Minnesota/11/2010	30 $CEID_{50}$/mL	NEG	POS	NEG	NEG
	A/Indiana/08/2011	0.25 $TCID_{50}$/mL	NEG	POS	NEG	NEG
	A/Texas/50/2012	0.050 $TCID_{50}$/mL	NEG	POS	NEG	NEG
	A/Alaska/232/2015	20 $CEID_{50}$/mL	NEG	POS	NEG	NEG
	A/Singapore/ INFIMH-16-0019/2016	20 $CEID_{50}$/mL	NEG	POS	NEG	NEG
	A/Texas/71/2017	1.0 FFU/mL	NEG	POS	NEG	NEG
	A/Kansas/14/2017	1.0 FFU/mL	NEG	POS	NEG	NEG
	A/Wisconsin/04/2018	1.0 FFU/mL	NEG	POS	NEG	NEG
	A/Arizona/45/2018	2.0 FFU/mL	NEG	POS	NEG	NEG
	A/Hong Kong/45/2019	2.0 FFU/mL	NEG	POS	NEG	NEG
Avian influenza A[d]	A/Mallard/NY/6750/78 (H2N2)	<1 pg/µL	NEG	POS	NEG	NEG
	A/duck/Hunan/ 795/2002 (H5N1)	<1 pg/µL	NEG	POS	NEG	NEG
	A/Vietnam/1194/ 2004 (H5N1)	<1 pg/µL	NEG	POS	NEG	NEG
	A/Anhui/01/ 2005 (H5N1)	<1 pg/µL	NEG	POS	NEG	NEG
	A/Japanese white eye/Hong Kong/1038/2006 (H5N1)	<1 pg/µL	NEG	POS	NEG	NEG
	A/mallard/WI/34/75 (H5N2)	<1 pg/µL	NEG	POS	NEG	NEG
	A/chicken/CA431/00 (H6N2)	<1 pg/µL	NEG	POS	NEG	NEG
	A/duck/LTC-10-82743 (H7N2)	<1 pg/µL	NEG	POS	NEG	NEG
	A/chicken/New Jersey/15086/3 (H7N3)	<1 pg/µL	NEG	POS	NEG	NEG
	A/Anhui/1/2013 (H7N9)	0.612 ng/µL	NEG	POS	NEG	NEG
	A/Shanghai/1/ 2013 (H7N9)	NA[e]	NEG	POS	NEG	NEG

Virus	Strain	Tested Titer	SARS-CoV-2	Flu A	Flu B	RSV
	A/chicken/Korea/38349-p96323/1996 (H9N2)	<1 pg/µL	NEG	POS	NEG	NEG
Influenza B	B/Lee/40	1.0 PFU/mL	NEG	NEG	POS	NEG
	B/Allen/45	0.25 $CEID_{50}$/mL	NEG	NEG	POS	NEG
	B/GL/1739/54	0.50 $CEID_{50}$/mL	NEG	NEG	POS	NEG
	B/Maryland/1/59	1.0 $CEID_{50}$/mL	NEG	NEG	POS	NEG
	B/Taiwan/2/62	1.0 $CEID_{50}$/mL	NEG	NEG	POS	NEG
	B/Hong Kong/5/72	1.0 $CEID_{50}$/mL	NEG	NEG	POS	NEG
Influenza B Victoria Lineage	B/Panama/45/90	1.0 $TCID_{50}$/mL	NEG	NEG	POS	NEG
	B/Malaysia/2506/04	0.025 $TCID_{50}$/mL	NEG	NEG	POS	NEG
	B/Florida/02/06	0.025 $TCID_{50}$/mL	NEG	NEG	POS	NEG
	B/Brisbane/60/2008	0.05 $TCID_{50}$/mL	NEG	NEG	POS	NEG
	B/Maryland/15/2016	0.25 $TCID_{50}$/mL	NEG	NEG	POS	NEG
	B/Colorado/6/2017	0.25 $TCID_{50}$/mL	NEG	NEG	POS	NEG
	B/Hawaii/01/2018	8.0 $TCID_{50}$/mL	NEG	NEG	POS	NEG
	B/Missouri/12/2018(NA D197E)	10 $TCID_{50}$/mL	NEG	NEG	POS	NEG
	B/Washington/02/2019	60 $TCID_{50}$/mL	NEG	NEG	POS	NEG
Influenza B Yamagata Lineage	B/Florida/07/2004	0.50 $TCID_{50}$/mL	NEG	NEG	POS	NEG
	B/Florida/04/06	0.25 $TCID_{50}$/mL	NEG	NEG	POS	NEG
	B/Wisconsin/01/2010	0.50 $CEID_{50}$/mL	NEG	NEG	POS	NEG
	B/Wisconsin/10/2016	20 $TCID_{50}$/mL	NEG	NEG	POS	NEG
	B/Indiana/17/2017	10 $TCID_{50}$/mL	NEG	NEG	POS	NEG
	B/Oklahoma/10/2018	10 $TCID_{50}$/mL	NEG	NEG	POS	NEG
RSV A	RSV-A/NY	0.386 $TCID_{50}$/mL	NEG	NEG	NEG	POS
	RSV-A/WI-629.8.2/2007	0.50 $TCID_{50}$/mL	NEG	NEG	NEG	POS
	RSV-A/WI/629-11-1_2008	0.50 $TCID_{50}$/mL	NEG	NEG	NEG	POS
	RSV-A, Strain: 4/2015 Isolate #1	0.25 $TCID_{50}$/mL	NEG	NEG	NEG	POS
RSV B	RSV-B/WV14617/85	0.10 $TCID_{50}$/mL	NEG	NEG	NEG	POS
	RSV-B-CH93(18)-18-01	0.10 $TCID_{50}$/mL	NEG	NEG	NEG	POS

[a] *in vitro* RNA transcripts

[b] Titer A/Indiana/02/2020 virus was without titer and was diluted 100,000-fold in simulated background matrix for testing.

[c] One of three replicates reported ERROR. The run was successfully repeated to obtain three valid replicates.

[d] Purified viral RNA in simulated background matrix was used for avian influenza A viruses due to biosafety regulations.

[e] Inactivated avian influenza A (H7N9) viruses without viral titer was diluted 100,000-fold in simulated background matrix and tested due to biosafety regulations.

20.5 Analytical Specificity (Exclusivity)

An *in silico* analysis for possible cross-reactions with all the organisms listed in Table 12 was conducted by mapping the SARS-CoV-2 primers and probes in the Xpert Xpress CoV-2/Flu/RSV *plus* 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 12 is expected based on the *in silico* analysis.

Table 12. Microorganisms Analyzed in the *in silico* Analysis for the SARS-CoV-2 Target

Microorganisms from the Same Genetic Family	High Priority Organisms
Human coronavirus 229E	Adenovirus (e.g. C1 Ad. 71)
Human coronavirus OC43	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
	Chlamydia pneumoniae
	Haemophilus influenzae
	Legionella pneumophila
	Mycobacterium tuberculosis
	Streptococcus pneumoniae
	Streptococcus pyogenes
	Bordetella pertussis
	Mycoplasma pneumoniae
	Pneumocystis jirovecii (PJP)
	Parechovirus
	Candida albicans
	Corynebacterium diphtheriae
	Legionella non-*pneumophila*
	Bacillus anthracis (Anthrax)
	Moraxella catarrhalis
	Neisseria elongata and *N. meningitidis*
	Pseudomonas aeruginosa
	Staphylococcus epidermidis
	Streptococcus salivarius
	Leptospira
	Chlamydia psittaci
	Coxiella burnetii (Q-Fever)

Microorganisms from the Same Genetic Family	High Priority Organisms
	Staphylococcus aureus

In addition to the *in silico* analysis of the SARS-CoV-2 primers and probes for cross-reactivity, the analytical specificity of the Xpert Xpress CoV-2/Flu/RSV *plus* test was evaluated by bench-testing a panel of 48 microorganisms comprising 4 human coronaviruses, 1 MERS coronavirus and 43 common respiratory pathogens or those potentially encountered in the nasopharynx. The panel was tested in different pools of microorganisms; if a pool produced a positive result, then each member of the pool would have been tested individually. Three replicates of each pool were tested. A sample was considered negative if all three replicates were negative. The bacterial and yeast strains were tested at concentrations of ≥ 1 x 10^6 CFU/mL with the exception of *Chlamydia pneumoniae* which was tested at 1.2 x 10^6 IFU/mL and Lactobacillus reuteri which was tested at 5 x 10^7 copies/mL of genomic DNA. Viruses were tested at concentrations of ≥ 1 x 10^5 $TCID_{50}$/mL. The analytical specificity was 100%. Results are shown in Table 13.

Table 13. Respiratory Microorganisms and Human Coronavirus Tested, Concentrations and Xpert Xpress CoV-2/Flu/RSV *plus* Test Results

Strain	Tested Concentration	SARS-CoV-2	Flu A	Flu B	RSV
Negative Control	NA	NEG	NEG	NEG	NEG
Positive Control	NA	POS	POS	POS	POS
Human coronavirus NL63	1.17e5 $TCID_{50}$/mL	NEG	NEG	NEG	NEG
MERS-coronavirus	1.17e5 $TCID_{50}$/mL	NEG	NEG	NEG	NEG
Human coronavirus 229E	1.21e5 $TCID_{50}$/mL	NEG	NEG	NEG	NEG
Human coronavirus OC43	1.02e5 $TCID_{50}$/mL	NEG	NEG	NEG	NEG
Human coronavirus HKU1	1.23e6 copies/mL	NEG	NEG	NEG	NEG
Adenovirus Type 1	4.07e5 $TCID_{50}$/mL	NEG	NEG	NEG	NEG
Adenovirus Type 7	1.14e5 $TCID_{50}$/mL	NEG	NEG	NEG	NEG
Cytomegalovirus	1.0e5 $TCID_{50}$/mL	NEG	NEG	NEG	NEG
Echovirus	1.14e5 $TCID_{50}$/mL	NEG	NEG	NEG	NEG
Enterovirus	2.80e5 $TCID_{50}$/mL	NEG	NEG	NEG	NEG
Epstein Barr Virus	5.60e6 $TCID_{50}$/mL	NEG	NEG	NEG	NEG
HSV	1.97e5 $TCID_{50}$/mL	NEG	NEG	NEG	NEG
Human metapneumovirus	4.07e5 $TCID_{50}$/mL	NEG	NEG	NEG	NEG
Human parainfluenza Type 1	1.0e5 $TCID_{50}$/mL	NEG	NEG	NEG	NEG
Human parainfluenza Type 2	1.2e5 $TCID_{50}$/mL	NEG	NEG	NEG	NEG
Human parainfluenza Type 3	1.2e5 $TCID_{50}$/mL	NEG	NEG	NEG	NEG
Human parainfluenza Type 4	1.19e6 $TCID_{50}$/mL	NEG	NEG	NEG	NEG
Measles	1.2e5 $TCID_{50}$/mL	NEG	NEG	NEG	NEG
Mumps virus	1.2e5 $TCID_{50}$/mL	NEG	NEG	NEG	NEG
Rhinovirus Type 1A	1.0e5 $TCID_{50}$/mL	NEG	NEG	NEG	NEG
Acinetobacter baumannii	1.30e7 CFU/mL	NEG	NEG	NEG	NEG
Bordetella pertussis	6.40e7 CFU/mL	NEG	NEG	NEG	NEG

Strain	Tested Concentration	SARS-CoV-2	Flu A	Flu B	RSV
Burkholderia cepacia	1.90e8 CFU/mL	NEG	NEG	NEG	NEG
Candida albicans	6.30e6 CFU/mL	NEG	NEG	NEG	NEG
Candida parapsilosis	1.45e6 CFU/mL	NEG	NEG	NEG	NEG
Citrobacter freundii	1.73e8 CFU/mL	NEG	NEG	NEG	NEG
Corynebacterium sp.	1.27e7 CFU/mL	NEG	NEG	NEG	NEG
Enterococcus faecalis	5.87e7 CFU/mL	NEG	NEG	NEG	NEG
Escherichia coli	1.55e8 CFU/mL	NEG	NEG	NEG	NEG
Hemophilus influenzae	6.62e6 CFU/mL	NEG	NEG	NEG	NEG
Lactobacillus reuteri	5.0e7 copies/mL	NEG	NEG	NEG	NEG
Legionella spp.	1.42e8 CFU/mL	NEG	NEG	NEG	NEG
Moraxella catarrhalis	2.46e6 CFU/mL	NEG	NEG	NEG	NEG
Mycoplasma pneumoniae	2.7e6 CFU/mL	NEG	NEG	NEG	NEG
Neisseria meningitides	4.2e6 CFU/mL	NEG	NEG	NEG	NEG
Neisseria mucosa	1.0e8 CFU/mL	NEG	NEG	NEG	NEG
Propionibacterium acnes	8.25e7 CFU/mL	NEG	NEG	NEG	NEG
Pseudomonas aeruginosa	1.05e7 CFU/mL	NEG	NEG	NEG	NEG
Staphylococcus haemolyticus	2.66e6 CFU/mL	NEG	NEG	NEG	NEG
Staphylococcus aureus	5.87e7 CFU/mL	NEG	NEG	NEG	NEG
Staphylococcus epidermidis	2.47e7 CFU/mL	NEG	NEG	NEG	NEG
Streptococcus agalactiae	1.75e7 CFU/mL	NEG	NEG	NEG	NEG
Streptococcus pneumoniae	2.26e7 CFU/mL	NEG	NEG	NEG	NEG
Streptococcus pyogenes	9.0e6 CFU/mL	NEG	NEG	NEG	NEG
Streptococcus salivarius	4.19e6 CFU/mL	NEG	NEG	NEG	NEG
Streptococcus sanguinis	8.67e6 CFU/mL	NEG	NEG	NEG	NEG
Chlamydia pneumoniae	1.20e6 CFU/mL	NEG	NEG	NEG	NEG
Mycobacterium tuberculosis (avirulent)	1.20e6 CFU/mL	NEG	NEG	NEG	NEG

20.6 Microbial Interference

Microbial interference of the Xpert Xpress CoV-2/Flu/RSV *plus* test caused by the presence of bacterial or viral strains that might be encountered in human upper respiratory tract specimens, was evaluated by testing a panel of 10 commensal microorganisms, consisting of 7 viral strains and 3 bacterial strains. Contrived samples consisted of SARS-CoV-2, Flu A, Flu B, RSV A, or RSV B viruses seeded at 3x the Limit of Detection (LoD) into simulated nasopharyngeal swab (NPS)/ nasal swab (NS) matrix in the presence of Adenovirus Type 1C, Human Coronavirus OC43, Rhinovirus Type 1A, Human metapneumovirus, Human parainfluenza Types 1, 2, and 3 (each seeded at $1x10^5$ units/mL), *Hemophilus influenzae* (seeded at $1x10^6$ CFU/mL), *Staphylococcus aureus* or *Staphylococcus epidermidis* (each seeded at $1x10^7$ CFU/mL).

Replicates of 8 positive samples were tested for each target virus (SARS-CoV-2, Flu A, Flu B, RSV A, or RSV B) and each potential microbial interference strain combination. For each target, all 8 of 8 replicate samples were correctly identified using the Xpert Xpress CoV-2/Flu/RSV *plus* test. No interference by the commensal viral or bacterial strains was reported.

20.7 Competitive Interference

Competitive interference of the Xpert Xpress CoV-2/Flu/RSV *plus* caused by co-infections were evaluated by testing contrived samples of individual SARS-CoV-2, Flu A, Flu B or RSV strains at 3X LoD in the presence of different target strains at a higher concentration in a simulated background matrix. The concentration at 3X LoD was 414 copies/mL for SARS-CoV-2 (inactivated USA-WA1/2020); 0.021 $TCID_{50}$/mL for Flu A/Idaho/072018, 38.7 $CEID_{50}$/mL for Flu B/Washington/2/2019; 0.99 $TCID_{50}$/mL for RSV A/2/Australia/61), and 1.11 $TCID_{50}$/mL for RSV B/9320/MA/77. The competitive strains were evaluated at 10^5 or higher titer units (copies/mL, $TCID_{50}$/mL, $CEID_{50}$/mL or PFU/mL). The corresponding concentration of RNA (copies/mL) for the Flu and RSV strains was determined by droplet digital PCR (ddPCR). Replicates of 3 were tested for each target strain and each competitive strain combination. The virus at high concentration shows no competitive inhibitory effects if 3 of 3 replicates for the target strain report positive results. If the results reported less than 3 of 3 positive replicates, the concentration of the competing virus was reduced by 10-fold increments until no interference was observed. Below is a summary of the results:

Table 14. Summary of Competitive Interference Study with Flu A at High Concentration

Test Viruses at 3X LoD	Interferent Virus	Correct Calls (n/3)			
		at 1.7e8 RNA copies/mL	at 1.7e7 RNA copies/mL	at 1.7e6 RNA copies/mL	at 1.7e5 RNA copies/mL
Flu B	Flu A	0/3	0/3	2/3	3/3
RSV A		0/3	0/3	3/3	Not tested
RSV B		3/3	Not tested	Not tested	Not tested
SARS-CoV-2		3/3	Not tested	Not tested	Not tested

Table 15. Summary of Competitive Interference Study with Flu B at High Concentration

Test Viruses at 3X LoD	Interferent Virus	Correct Calls (n/3) at 1.4e5 RNA copies/mL
Flu A	Flu B	3/3
RSV A		3/3
RSV B		3/3
SARS-CoV-2		3/3

Table 16. Summary of Competitive Interference Study with RSV A at High Concentration

Test Viruses at 3X LoD	Interferent Virus	Correct Calls (n/3) at 4.6e6 RNA copies/mL
Flu A	RSV A	3/3
Flu B		3/3
SARS-CoV-2		3/3

Table 17. Summary of Competitive Interference Study with RSV B at High Concentration

Test Viruses at 3X LoD	Interferent Virus	Correct Calls (n/3) at 1.9e5 RNA copies/mL
Flu A	RSV B	3/3
Flu B		3/3
SARS-CoV-2		3/3

Table 18. Summary of Competitive Interference Study with SARS-CoV-2 at High Concentration

Test Viruses at 3X LoD	Interferent Virus	Correct Calls (n/3)	
		at 1e6 RNA copies/mL	at 1e5 RNA copies/mL
Flu A	SARS-CoV-2	3/3	Not tested
Flu B		1/3	3/3
RSV A		3/3	Not tested
RSV B		3/3	Not tested

The study showed that Flu A/Idaho/07/2018 at concentrations above 1.7e5 RNA copies/mL inhibited detection of Flu B at 3X LoD, and at concentrations above 1.7e6 RNA copies/mL inhibited detection of RSV A at 3X LoD (Table 14). In addition, SARS-CoV-2 at concentrations above 1e5 RNA copies/mL inhibited detection of Flu B at 3X LoD (Table 18). No other competitive interference was observed for the potential co-infections tested in the study at the concentrations tested.

20.8 Potentially Interfering Substances

Substances that could be present in the nasopharynx (or introduced during specimen collection and handling) and potentially interfere with accurate detection of SARS-CoV-2, Flu A, Flu B and RSV were evaluated with direct testing on the Xpert Xpress CoV-2/Flu/RSV *plus*.

Potentially interfering substances in the nasal passage and nasopharynx may include, but are not limited to: blood, nasal secretions or mucus, and nasal and throat medications used to relieve congestion, nasal dryness, irritation, or asthma and allergy symptoms, as well as antibiotics and antivirals. Positive and negative samples were prepared in simulated nasopharyngeal swab (NPS)/ nasal swab (NS) matrix. Negative samples (N = 8) were tested in the presence of each substance to determine the effect on the performance of the sample processing control (SPC). Positive samples (N = 8) were tested per substance with viruses spiked at 3x the LoD determined for each strain. Positive samples tested with the Xpert Xpress CoV-2/Flu/RSV *plus* included one SARS-CoV-2, one influenza A H1N1, one influenza A H3N2, one influenza B and two RSV (RSV A and RSV B) strains. The substances, with active ingredients, that were evaluated are listed in Table 19.

Table 19. Potentially Interfering Substances Tested

Substance ID	Substance/Class	Substance/Active Ingredient
No substance	Control	Copan Universal Transport Medium (UTM)
Albuterol Sulfate	Beta-adrenergic bronchodilator	Albuterol Sulfate (5mg/mL)
Afrin	Nasal Spray	Oxymetazoline, 0.05%
BD Universal Transport Medium	Transport Media	N/A
Copan 3U045N.PH (Cepheid Swab/M)	Transport Media	N/A
Blood	Blood	Blood (Human)
Fluticasone Propionate Nasal Spray	Nasal corticosteroid	Fluticasone Propionate

Substance ID	Substance/Class	Substance/Active Ingredient
Menthol	Throat lozenges, oral anesthetic and analgesic	Benzocaine, Menthol
Mucin	Mucin	Purified Mucin protein (Bovine or porcine submaxillary gland)
Mupirocin	Antibiotic, nasal ointment	Mupirocin (20 mg/g=2%)
PHNY	Nasal Drops	Phenylephrine, 1%
Saline	Saline Nasal Spray	Sodium Chloride (0.65%)
Remel M4RT	Transport Media	N/A
Remel M5	Transport Media	N/A
Tamiflu	Anti-viral drugs	Zanamivir
Tobramycin	Antibacterial, systemic	Tobramycin
Zicam	Nasal Gel	Luffa opperculata, Galphimia glauca, Histaminum hydrochloricum Sulfur (0.05%)
Zinc	Zinc supplement	Zinc Gluconate

The results from the study (Table 20) show that for most cases, 8 out of 8 replicates reported positive results for each combination of virus and substance tested and no interference was observed. When Zicam was initially tested at 15% w/v, interference was observed in the detection of Flu B and RSV A. However, when Zicam was tested at 7.5% w/v, no interference was observed.

Table 20. Mean Ct values for Xpert Xpress CoV-2/Flu/RSV *plus* Targets Tested in the Presence of Potentially Interfering Substances

Substance	Concentration Tested	Number of Correct Results/Number Tested					
		SARS-CoV-2/ USA-WA-1	Influenza A/Idaho/07/ 2018	H3N2 Flu A/ Hong Kong/ 45/2019	Flu B/ Washington /02/2019	RSV A/2/ Australia/61	RSV B/9320/ MA/77
Control Simulated NPS/NS Matrix (No substance)	100% (v/v)	8/8	8/8	8/8	8/8	8/8	8/8
Afrin	15% (v/v)	8/8	8/8	8/8	8/8	8/8	8/8
Albuterol Sulfate	0.83 mg/mL	8/8	8/8	8/8	8/8	8/8	8/8
BD Universal Transport Medium	N/A	8/8	8/8	8/8	8/8	8/8	8/8
Blood	2% (v/v)	8/8	8/8	8/8	8/8	8/8	8/8
Copan Swab M	N/A	8/8	8/8	8/8	8/8	8/8	8/8
Fluticasone Propionate Nasal Spray	5 µg/mL	8/8	8/8	8/8	8/8	8/8	8/8
Menthol	1.7 mg/mL	8/8	8/8	8/8	8/8	8/8	8/8
Mucin	0.1% (w/v)	8/8	8/8	8/8	8/8	8/8	8/8
Mupirocin	10 mg/mL	8/8	8/8	8/8	8/8	8/8	8/8

Substance	Concentration Tested	Number of Correct Results/Number Tested					
		SARS-CoV-2/ USA-WA-1	Influenza A/Idaho/07/ 2018	H3N2 Flu A/ Hong Kong/ 45/2019	Flu B/ Washington /02/2019	RSV A/2/ Australia/61	RSV B/9320/ MA/77
PHNY	15% (v/v)	8/8	8/8	8/8	8/8	8/8	8/8
Remel M4RT	N/A	8/8	8/8	8/8	8/8	8/8	8/8
Remel M5	N/A	8/8	8/8	8/8	8/8	8/8	8/8
Saline	15% (v/v)	8/8	8/8	8/8	8/8	8/8	8/8
Tamiflu	7.5 mg/mL	8/8	8/8	8/8	8/8	8/8	8/8
Tobramycin	4 µg/mL	8/8	8/8	8/8	8/8	8/8	8/8
Zicam	15% (w/v)	8/8	8/8	8/8	5/8[a]	7/8[b]	8/8
Zinc	0.1 µg/mL	8/8	8/8	8/8	8/8	8/8	8/8

[a] With 15% (w/v) Zicam, a statistically significant difference was observed between the control mean Ct and the test mean Ct. Testing was repeated with 7.5% (w/v) Zicam and no clinically significant difference was observed between the control mean Ct and the test mean Ct.

[b] With 15% (w/v) Zicam, a statistically significant difference was observed between the control mean Ct and the test mean Ct. Testing was repeated with 7.5% (w/v) Zicam and no statistically significant difference was observed between the control mean Ct and the test mean Ct.

20.9 Carry-over Contamination

A study was conducted to assess whether the single-use, self-contained Xpert Xpress CoV-2/Flu/RSV *plus* cartridge prevents specimen and amplicon carryover by testing a negative sample immediately after testing of a very high positive sample in the same GeneXpert module. The negative sample used in this study consisted of simulated NPS/NS matrix and the positive sample consisted of high Flu B and high SARS-CoV-2 virus concentrations (Flu B/Wisconsin/10/2016 at 1.0e6 $TCID_{50}$/mL and inactivated SARS-CoV-2 USA-WA1/2020 at 1e4 copies/mL) seeded into negative NPS/NS matrix. The negative sample was tested in a GeneXpert module at the start of the study. Following the initial testing of the negative sample, the high positive sample was processed in the same GeneXpert module immediately followed by another negative sample. This was repeated 20 times in the same module, resulting in 20 positives and 21 negatives for the module. The study was repeated using a second GeneXpert module for a total of 40 positive and 42 negative samples. All 40 positive samples were correctly reported as **SARS-CoV-2 POSITIVE**; **Flu A NEGATIVE**; **Flu B POSITIVE**; **RSV NEGATIVE**. All 42 negative samples were correctly reported as **SARS-CoV-2 NEGATIVE**; **Flu A NEGATIVE**; **Flu B NEGATIVE**; **RSV NEGATIVE** with the Xpert Xpress CoV-2/Flu/RSV *plus* test. No specimen or amplicon carry-over contamination was observed in this study.

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22 Cepheid Headquarters Locations

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23 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

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Email: support@cepheideurope.com

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

24 Table of Symbols

Symbol	Meaning
	Catalog number
	*In vitro* diagnostic medical device
	Do not reuse
	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

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For use under Emergency Use Authorization (EUA) Only

25 Revision History

Description of Changes: 302-6991, Rev. B to Rev. C

Purpose: To address Conditions of Authorization for the Xpert Xpress CoV-2/Flu/RSV *plus* test

Section	Description of Change
5	Removed reference to saline as a transport medium.
10	Added instructions to refer to Copan eNAT package insert for safety and handling and to avoid direct contact between guanidine thiocyanate and sodium hypochlorite
12	Removed references to saline as a transport medium. Updated to include frozen storage claim.
18	Removed reference to saline as a transport medium.
20.1	Specified initial non-determinate rate and added final non-determinate rate.
20.2	Section added to include results of prospective clinical evaluation.
20.8	Potentially interfering substances was updated to make a correction: Afrin from Anefrin
25	Updated Revision History section.

ENGLISH

READ BEFORE USING THIS KIT: NEW ASSAY DEFINITION FILE (ADF)

- An updated ADF file has been released as part of our continuous product improvement efforts.
- Cartridges from this lot of Xpert® **Xpress** CoV-2/Flu/RSV ***plus*** require the import of ADF version 2 (called Xpress_SARS-CoV-2_Flu_RSV_plus_2.zip) provided online at https://www.cepheid.com/coronavirus-product-resources. If you cannot download the ADF, you may order a CD with the ADF here https://www.cepheid.com/en/contact/request-cd-international or request a CD from Technical Support.
- All customers connected to a Laboratory Information System (LIS) may need to verify LIS outputs to ensure that they are consistent with instrument result outputs. Run quality assurance checks as determined by your institution's policy.
- The ADF update does not change the product intended use. Assay re-verification is based on your institution's requirements.

For All Users:

- The updated ADF can be run with both new and previous lots of product.
- When ready to import this ADF, DO NOT manually delete the old ADF version. Follow the ADF Import Instructions located on the product page.
- The existing LIS Test Codes will be imported automatically into the ADF. LIS result outputs must be verified to be consistent with instrument result outputs. Run quality assurance checks as determined by your institution's policy.
- If for some reason you believe you must revert to the older ADF, please contact Cepheid Technical Support for assistance:
  - Cepheid Technical Support (U.S.): + 1 888 838 3222
  - Cepheid Technical Support (Europe): + 33 563 82 53 19
- For use under Emergency Use Authorization (EUA) only.
- For prescription use only.
- For in vitro diagnostic use.
- This product has not been FDA cleared or approved but has been authorized for emergency use by FDA under an EUA for use by authorized laboratories.
- This product has been authorized only for the detection and differentiation of nucleic acids from SARS-CoV-2, influenza A, influenza B, and respiratory syncytial virus (RSV), not for any other viruses or pathogens.
- The emergency use of this product is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of in vitro diagnostics 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. § 360bbb3(b)(1), unless the declaration is terminated or authorization is revoked sooner.