GeneXpert®
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Xpert® Xpress Flu/RSV

REF **XPRSFLU/RSV-CE-10**

Instructions For Use

IVD CE

Cepheid®

In Vitro Diagnostic Medical Device

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Trademark, Patents, and Copyright Statements

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

Xpert® Xpress Flu/RSV

For *In Vitro* Diagnostic Use

1 Proprietary Name

Xpert® Xpress Flu/RSV

2 Common or Usual Name

Xpert Xpress Flu/RSV

3 Intended Use

The Cepheid Xpert® Xpress Flu/RSV test, performed on the GeneXpert® Instrument Systems, is an automated, multiplex real-time, reverse transcriptase polymerase chain reaction (RT-PCR) assay intended for the *in vitro* qualitative detection and differentiation of influenza A, influenza B, and respiratory syncytial virus (RSV) viral RNA. The Xpert Xpress Flu/RSV test uses nasopharyngeal (NP) swab and nasal swab (NS) specimens collected from patients of all ages with signs and symptoms of respiratory infection. The Xpert Xpress Flu/RSV test is intended as an aid in the diagnosis of influenza and respiratory syncytial virus infections in conjunction with clinical and epidemiological risk factors.

Negative results do not preclude influenza virus or RSV infection and should not be used as the sole basis for treatment or other patient management decisions.

Performance characteristics for influenza A were established during the 2015-2016 influenza season for NP swab specimens and the 2016-2017 influenza season for NS specimens.. When other novel influenza A viruses are emerging, performance characteristics may vary.

If infection with a novel influenza A virus is suspected based on current clinical and epidemiological screening criteria recommended by public health authorities, specimens should be collected with appropriate infection control precautions for novel virulent influenza viruses and sent to state or local health departments for testing. Viral culture should not be attempted in these cases unless a BSL 3+ facility is available to receive and culture specimens.

4 Summary and Explanation

Influenza, or the flu, is a contagious viral infection of the respiratory tract. Transmission of influenza is primarily airborne (i.e., coughing or sneezing) and the peak of transmission usually occurs in the winter months. Symptoms commonly include fever, chills, headache, malaise, cough and sinus congestion. Gastrointestinal symptoms (i.e., nausea, vomiting or diarrhea) may also occur, primarily in children, but are less common. Symptoms generally appear within two days of exposure to an infected person. Pneumonia may develop as a complication due to influenza infection, causing increased morbidity and mortality in pediatric, elderly, and immunocompromised populations.[1,2]

Influenza viruses are classified into types A, B, and C, the former two of which cause the most human infections. Influenza A is the most common type of influenza virus in humans, and is generally responsible for seasonal flu epidemics and potentially pandemics. Influenza A viruses can also infect animals such as birds, pigs, and horses. Infections with influenza B virus are generally restricted to humans and are a rare cause of epidemics. Influenza 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 subtypes H1, H2, H3, N1 and N2. In addition to seasonal flu, a novel H1N1 strain was identified in humans in the United States in early 2009.[3]

Respiratory Syncytial Virus (RSV), a member of the *Pneumoviridae* family (formerly *Paramyxoviridae*), consisting of two strains (subgroups A and B) is also a contagious disease that affects primarily infants, the elderly, and other adults that tend to be immunocompromised in some way.[3] The virus can remain infectious for hours on countertops and toys and can cause both upper respiratory infections, such as colds, and lower respiratory infections manifesting as bronchiolitis and pneumonia.[4] 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 reinfected.[3] Symptoms appear four to six days after infection and are usually self-limiting, lasting approximately one to two weeks. In adults, infection lasts about 5 days and presents as symptoms consistent with a cold, such as rhinorrhea, fatigue, headache, and fever. The RSV season mirrors influenza somewhat as infections begin to rise during the fall through early spring.[3,4]

Active surveillance programs in conjunction with infection prevention precautions are important components for preventing transmission of influenza and RSV. The use of assays providing rapid results to identify patients infected with these seasonal viruses is also an important factor for effective control, proper choice of treatment, and prevention of widespread outbreaks.

5 Principle of the Procedure

The Xpert Xpress Flu/RSV test is an automated *in vitro* diagnostic test for qualitative detection of influenza A, influenza B, and RSV viral RNA. The test is performed on Cepheid GeneXpert Instrument Systems.

The GeneXpert Instrument Systems automate and integrate sample extraction, nucleic acid purification and amplification, and detection of target sequences from clinical specimens by using reverse transcription (conversion of RNA templates into DNA) followed by real-time PCR. The primers and probes in the Xpert Xpress Flu/RSV test are designed to amplify and detect unique sequences in the genes that encode the following proteins: 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 systems consist of an instrument, personal computer, and preloaded software for running tests and viewing the results. Each test requires the use of a single-use disposable GeneXpert cartridge that contains target-specific reagents and carries out the RT-PCR and PCR processes. Because the cartridges are self-contained, the risk of cross-contamination between samples is minimized. For a full description of the systems, refer to the appropriate GeneXpert Dx System Operator Manual or GeneXpert Infinity System Operator Manual.

The Xpert Xpress Flu/RSV test includes reagents for the detection and differentiation of influenza A, influenza B, and RSV viral RNA directly from NP swab and NS specimens from patients with signs and symptoms of respiratory tract infection. A Sample Processing Control (SPC) and a Probe Check Control (PCC) are also included in the cartridge. The SPC is present to control for an adequate amplification process and to monitor for the presence of inhibitors in the PCR reaction. The PCC verifies reagent rehydration, PCR tube filling in the cartridge, probe integrity, and dye stability.

The Xpert Xpress Flu/RSV test can be run to detect Flu A, Flu B, and RSV by selecting **Xpert Xpress Flu-RSV** from the Select Assay menu; Flu A and Flu B only by selecting **Xpert Xpress_Flu**; or RSV only by selecting **Xpert Xpress_RSV**. Xpert Xpress Flu and Xpert Xpress RSV tests have an Early Assay Termination (EAT) function that enables early result reporting. EAT is activated when the pre-determined threshold for a positive test result is reached before the full 40 PCR cycles have been completed. When Flu A or Flu B viral titers are high enough to generate very early cycle thresholds (Cts) with the Xpert Xpress Flu test, SPC amplification curves will not be seen and their results will not be reported. When RSV titers are high enough to generate very early Cts with the Xpert Xpress RSV test, SPC amplification curves will not be seen and their results will not be reported.

The specimens for testing (NP swabs or NS) should be collected according to the institution's standard procedures and placed into the Xpert Nasopharyngeal Sample Collection Kit for Viruses or the Xpert Nasal Sample Collection Kit for Viruses (viral transport tubes containing 3 mL transport medium). Following brief mixing by inverting the viral transport tube five times, the medium containing the virus suspension is transferred to the sample chamber of the disposable Xpert Xpress Flu/RSV cartridge. The user initiates a test from the system user interface and places the cartridge into the GeneXpert instrument, which performs nucleic acid preparation and real-time, multiplex RT-PCR for detection of viral RNA. On this platform, sample preparation, reverse transcription, amplification, and real-time detection are all fully-automated and completely integrated. Test results are obtained in approximately 30 minutes.

The results are interpreted by the GeneXpert software from measured fluorescent signals and embedded calculation algorithms and are shown in the "View Results" window in tabular and graphic formats. The Xpert Xpress Flu/RSV test provides test results for influenza A, influenza B, and RSV. It also reports if the test is invalid, error or no result.

6 Reagents and Instruments

6.1 Materials Provided

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

Xpert Xpress Flu/RSV Cartridges with Integrated Reaction Tubes	**10**
• Bead 1, Bead 2, and Bead 3 (freeze-dried)	1 of each per cartridge
• Lysis Reagent (Guanidinium thiocyanate)	1.5 mL per cartridge
• Binding Reagent	1.5 mL per cartridge
• Elution Reagent	3.0 mL per cartridge
Disposable 300 µL Transfer Pipettes	**1 bag of 12 per kit**
CD	**1 per kit**

- Assay Definition Files (ADF)
- Instructions to import ADF into GeneXpert Dx and Xpertise software
- Instructions for Use (Package Insert)

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

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

7 Storage and Handling

- Store the Xpert Xpress Flu/RSV cartridges at 2–28 °C until the expiration date provided on the label.
- Do not open a cartridge lid until you are ready to perform testing.
- Do not use cartridges that have passed the expiration date.
- Do not use a cartridge that has leaked.

8 Materials Required but Not Provided

- Nasopharyngeal Sample Collection Kit for Viruses (Cepheid P/N SWAB/B-100, Copan P/N 305C) or equivalent.
- Nasal Sample Collection Kit for Viruses (Cepheid P/N SWAB/F-100, Copan P/N 346C) or equivalent.
- Alternatively, swabs and transport medium can be obtained separately:
  - Nylon flocked swab (Copan P/N 502CS01, 503CS01) or equivalent
  - Viral transport medium, 3 mL (Copan P/N 330C) or equivalent
- GeneXpert Dx System or GeneXpert Infinity Systems (catalog number varies by configuration): GeneXpert Instrument, computer, barcode scanner, and operator manual.
  - For GeneXpert Dx System: GeneXpert Dx software version 4.7b or higher
  - For GeneXpert Infinity-80 and Infinity 48s Systems: Xpertise 6.4b or higher
- Printer: If a printer is required, contact Cepheid Technical Support to arrange for the purchase of a recommended printer.

9 Warnings and Precautions

9.1 General

- For *in vitro* Diagnostic Use
- 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 treated with standard precautions.
- Guidelines for specimen handling are available from the U.S. Centers for Disease Control and Prevention[5] and the Clinical and Laboratory Standards Institute.[6,7]
- If infection with a novel influenza A virus is suspected based on current clinical and epidemiological screening criteria recommended by public health authorities, specimens should be collected with appropriate infection control precautions for novel virulent influenza viruses and sent to state or local health departments for testing. Viral culture should not be attempted in these cases unless a BSL 3+ facility is available to receive and culture specimens.
- Performance characteristics of this test have been established with the specimen types listed in the Intended Use Section only. The performance of this assay with other specimen types or samples has not been evaluated.
- Follow your institution's safety procedures for working with chemicals and handling biological samples.
- Biological specimens, transfer devices, and used cartridges should be considered capable of transmitting infectious agents requiring standard precautions. Follow your institution’s environmental waste procedures for proper disposal of used cartridges and unused reagents. These materials may exhibit characteristics of chemical hazardous waste requiring specific national or regional disposal procedures. If national 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.

9.2 Specimen

- Specimen collection and handling procedures require specific training and guidance.
- Specimens must be collected and tested before the expiration date of the viral transport medium tube included in the required collection kit.
- Maintain proper storage conditions during specimen transport to ensure the integrity of the specimen (see Section 11). Specimen stability under shipping conditions other than those recommended has not been evaluated.
- Proper sample collection, storage, and transport are essential for correct results.

9.3 Assay/Reagent

- The assay has been validated using Cepheid GeneXpert software version 4.7b or higher and Xpertise software version 6.4b or higher. Cepheid will validate future software versions for use with the Xpert Xpress Flu/RSV test.
- When performing a test in the Xpert Xpress RSV test mode, a sample that is positive for influenza A or influenza B will show growth curves and Ct values for these analytes but test results will not be reported (Figure 20).
- When performing a test in the Xpert Xpress RSV test mode, a sample strongly positive for influenza A or influenza B may cause the SPC to fail; if the sample is RSV negative, a valid result (**RSV NEGATIVE**) will be reported not an **INVALID** result.
- Performance may be impacted when using frozen specimens.
- Do not substitute Xpert Xpress Flu/RSV reagents with other reagents.
- Do not open the Xpert Xpress Flu/RSV cartridge lid except when adding sample.
- Do not use a cartridge that has been dropped after removing from the kit or shaken after the cartridge lid has been opened. Shaking or dropping the cartridge after opening the lid may yield false or non-determinate results.
- Do not place the sample ID label on the cartridge lid or on the barcode label.
- Do not use a cartridge that has a damaged reaction tube.
- Each single-use Xpert Xpress Flu/RSV cartridge is used to process one test. Do not reuse cartridges.
- A 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.
- Good laboratory practices, including changing gloves between handling patient specimens, are recommended to avoid contamination of specimens or reagents.
- Wear clean laboratory coats and gloves. In the event of contamination of the work area or equipment with samples or controls, thoroughly clean the contaminated area with a 1:10 dilution of household chlorine bleach and then 70% denatured ethanol. Wipe work surfaces dry completely before proceeding.

10 Chemical Hazards[8,9]

- 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**
    - 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.
    - Call a POISON CENTER or doctor/physician if you feel unwell.

11 Specimen Collection, Transport and Storage

Specimens can be collected following the user institution's standard procedures and placed into the Xpert Viral Transport Medium or Copan UTM (Universal Transport Medium, 3 mL tube with transport medium). Specimens should be transported at 2–8 °C.

Specimens can be stored at room temperature (15–30 °C) for up to 24 hours and refrigerated (2–8 °C) up to seven days until testing is performed on the GeneXpert.

Proper specimen collection, storage, and transport are critical to the performance of this test.

12 Procedure

12.1 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. Mix specimen by inverting the Xpert Viral Transport Medium or Copan UTM tube five times.
3. Open the cartridge lid. Using a clean 300 µL transfer pipette (supplied), transfer 300 µL (one draw) of the specimen from the transport medium tube to the sample chamber by expressing the fluid into the large opening in the cartridge (Figure 1).
4. Close the cartridge lid.

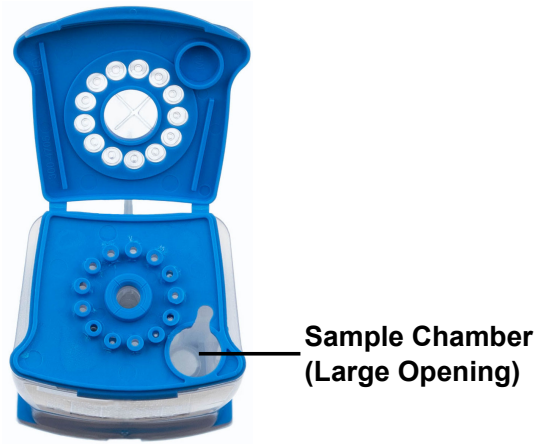

Figure 1. Xpert Xpress Flu/RSV Cartridge (Top View)

12.2 Starting the Test

Important **Before starting the test, make sure that the Xpert Xpress Flu/RSV Assay Definition File is imported into the software. This section lists the basic steps of running the test. For detailed instructions, see the *GeneXpert Dx System Operator Manual* or the *GeneXpert Infinity System Operator Manual,* depending on the model being used.**

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

1. Turn on the GeneXpert instrument system:
   - If using the GeneXpert Dx instrument, first turn on the GX Dx instrument and then turn on the computer. The GeneXpert Dx software will launch automatically or may require double-clicking the GeneXpert Dx software shortcut icon on the Windows® desktop.

     or
   - If using the GeneXpert Infinity instrument, power up the instrument. The GeneXpert software will launch automatically or may require double clicking the Xpertise software shortcut icon on the Windows® desktop.
2. Log on to the GeneXpert Instrument System software using your user name and password.
3. In the GeneXpert System window, click **Create Test** (GeneXpert Dx) or click **Orders** and **Order Test** (Infinity). The **Create Test** window opens.
4. Scan 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 results.
5. Scan in Sample ID or type 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 results.
6. Scan the barcode on the Xpert Xpress Flu/RSV cartridge. Using the barcode information, the software automatically fills the boxes for the following fields: Reagent Lot ID, Cartridge SN, and Expiration Date.

Note If the barcode on the Xpert Xpress Flu/RSV cartridge does not scan, then repeat the test with a new cartridge.

7. Make the appropriate selection from the Select Assay menu, as shown in Figure 2.
   - Flu A, Flu B and RSV: Select **Xpert Xpress Flu-RSV**
   - Flu A and Flu B only: Select **Xpert Xpress_Flu**
   - RSV only: Select **Xpert Xpress_RSV**

   Only the test result for the test selected at this step will be collected once the test is started. Flu A, Flu B, and RSV results will only be collected if Xpert Xpress Flu-RSV is selected.

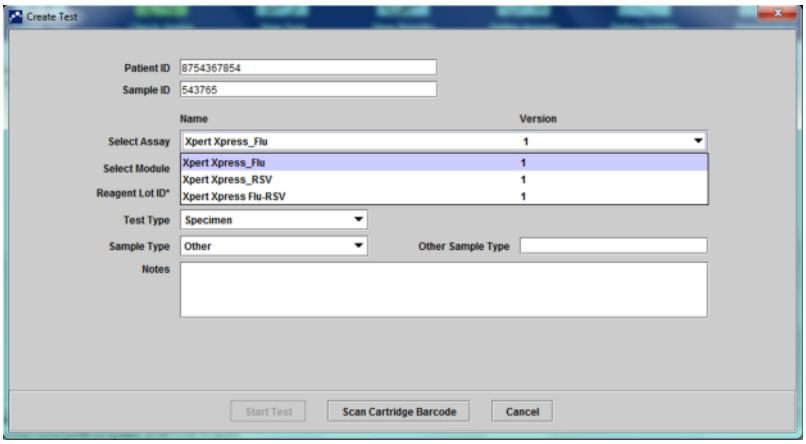

Figure 2. Create Test Window; Select Assay Menu

8. Click **Start Test** (GeneXpert Dx) or **Submit** (Infinity). Type your password in the dialog box that appears.
9. For the GeneXpert Infinity System, place the cartridge on the conveyor belt. The cartridge will be automatically loaded, the test will run, and the used cartridge will be placed into the waste container.

   or

   For the GeneXpert Dx Instrument:

   a) Open the instrument module door with the blinking green light 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.
   c) Wait until the system releases the door lock before opening the module door and removing the cartridge.
   d) Dispose of used cartridges in the appropriate specimen waste container according to your institution's standard practices.

13 Viewing and Printing Results

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

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

14 Quality Control

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

- **Sample Processing Control (SPC)**—Ensures the sample was processed correctly. The SPC is an Armored RNA® control that is included in each cartridge to verify adequate processing of the sample. The SPC verifies that release of RNA from the influenza and RSV viruses has occurred if the organism is present and verifies that the specimen processing is adequate. Additionally, this control detects specimen-associated inhibition of the RT-PCR and PCR reactions. 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. If the sample is negative for Flu and RSV viruses and the SPC fails, the result will be **INVALID**.

The assay result is **INVALID** if all targets are reported negative and the SPC does not meet the validated acceptance criteria. Thus, when performing a test in the Xpert Xpress RSV Assay mode, a sample strongly positive for influenza A or influenza B may cause the SPC to fail; if the sample is RSV negative, a valid result (**RSV NEGATIVE**) will be reported not an **INVALID** result.

- **Probe Check Control (PCC, QC1, QC2)**—Before the start of the PCR reaction, the GeneXpert Instrument System measures the fluorescence signal from the first PCC (QC1 and QC2) performed before the reverse transcription step. QC1 checks for the presence of the EZR bead and QC2 checks for the presence of the TSR bead. The second PCC (Flu A 1, Flu A 2, Flu B, RSV, and SPC) is performed after the reverse transcription step and before PCR begins. The

PCC monitors bead rehydration, reaction tube filling, probe integrity, and dye stability. The PCC passes if it meets the validated acceptance criteria.

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

15 Interpretation of Results

The Xpert Xpress Flu/RSV test has two channels (Flu A 1 and Flu A 2) to detect most influenza A strains. All influenza A strains detected by the Xpert Xpress Flu/RSV test are reported as **Flu A POSITIVE**. The Xpert Xpress Flu/RSV test requires either the Flu A 1 or Flu A 2 channel to be positive in order for a **Flu A POSITIVE** test result to be reported. Table 1 below lists all the possible test results for Flu A.

Table 1. Possible Test Results for Flu A for Flu A 1 and Flu A 2 Channels

Flu A Test Result	Flu A 1 Channel	Flu A 2 Channel
Flu A POSITIVE	POS	POS/NEG
	POS/NEG	POS
Flu A NEGATIVE	NEG	NEG

The results reported from testing with the Xpert Xpress Flu/RSV test are interpreted automatically by the GeneXpert Instrument System from measured fluorescent signals and embedded calculation algorithms and are clearly shown in the View Results window. All the possible results are shown in Table 2.

Table 2. All Possible Final Test Results for the Xpert Xpress Flu/RSV

Result Text	Flu A 1	Flu A 2	Flu B	RSV	SPC
Flu A POSITIVE; Flu B NEGATIVE; RSV NEGATIVE	POS	POS/NEG	NEG	NEG	POS/NEG
	POS/NEG	POS			
Flu A POSITIVE; Flu B POSITIVE; RSV NEGATIVE	POS	POS/NEG	POS	NEG	POS/NEG
	POS/NEG	POS			
Flu A POSITIVE; Flu B NEGATIVE; RSV POSITIVE	POS	POS/NEG	NEG	POS	POS/NEG
	POS/NEG	POS			
Flu A POSITIVE; Flu B POSITIVE; RSV POSITIVE	POS	POS/NEG	POS	POS	POS/NEG
	POS/NEG	POS			
Flu A NEGATIVE; Flu B POSITIVE; RSV NEGATIVE	NEG	NEG	POS	NEG	POS/NEG
Flu A NEGATIVE; Flu B NEGATIVE; RSV POSITIVE	NEG	NEG	NEG	POS	POS/NEG
Flu A NEGATIVE; Flu B POSITIVE; RSV POSITIVE	NEG	NEG	POS	POS	POS/NEG
Flu A NEGATIVE; Flu B NEGATIVE; RSV NEGATIVE	NEG	NEG	NEG	NEG	POS
INVALID	NEG	NEG	NEG	NEG	NEG
ERROR	NO RESULT	NO RESULT	NO RESULT	NO RESULT	NO RESULT
NO RESULT	NO RESULT	NO RESULT	NO RESULT	NO RESULT	NO RESULT

See Table 3, Table 4 and Table 5 and Figure 3 through Figure 20 for specific examples and to interpret test result statements for the Xpert Xpress Flu/RSV, Xpert Xpress Flu, and Xpert Xpress RSV tests. The format of the test results presented will vary depending on the user's choice to run either an Xpert Xpress Flu/RSV, Xpert Xpress Flu, or Xpert Xpress RSV selected assay.

Table 3. Xpert Xpress Flu/RSV Test Results and Interpretation

Result	Interpretation
Flu A POSITIVE; Flu B NEGATIVE; RSV NEGATIVE See Figure 3.	Flu A target RNA is detected; Flu B target RNA is not detected; RSV target RNA is not detected. ● The Flu A target has a Ct within the valid range and endpoint above the threshold setting. ● SPC – NA (not applicable); SPC is ignored because the Flu A target amplification may compete with this control. ● Probe Check – PASS; all probe check results pass.
Flu A POSITIVE; Flu B POSITIVE; RSV NEGATIVE** See Figure 4.	Flu A target RNA is detected; Flu B target RNA is detected; RSV target RNA is not detected. Repeat test according to the instructions in Section 16.2. ● The Flu A target has a Ct within the valid range and endpoint above the threshold setting. ● The Flu B target has a Ct within the valid range and endpoint above the threshold setting. ● SPC – NA (not applicable); SPC is ignored because the Flu A and Flu B target amplification may compete with this control. ● Probe Check – PASS; all probe check results pass.
Flu A POSITIVE; Flu B NEGATIVE; RSV POSITIVE** See Figure 5.	Flu A target RNA is detected; Flu B target RNA is not detected; RSV target RNA is detected. Repeat test according to the instructions in Section 16.2. ● The Flu A target has a Ct within the valid range and endpoint above the threshold setting. ● The RSV target has a Ct within the valid range and endpoint above the threshold setting. ● SPC – NA (not applicable); SPC is ignored because the Flu A and RSV target amplification may compete with this control. ● Probe Check – PASS; all probe check results pass.
Flu A POSITIVE; Flu B POSITIVE; RSV POSITIVE** See Figure 6.	Flu A target RNA is detected; Flu B target RNA is detected; RSV target RNA is detected. Repeat test according to the instructions in Section 16.2. ● The Flu A target has a Ct within the valid range and endpoint above the threshold setting. ● The Flu B target has a Ct within the valid range and endpoint above the threshold setting. ● The RSV target has a Ct within the valid range and endpoint above the threshold setting. ● SPC – NA (not applicable); SPC is ignored because the Flu A, Flu B, and RSV target amplification may compete with this control. ● Probe Check – PASS; all probe check results pass.
Flu A NEGATIVE; Flu B POSITIVE; RSV NEGATIVE See Figure 7.	Flu A target RNA is not detected; Flu B target RNA is detected; RSV target RNA is not detected. ● The Flu B target has a Ct within the valid range and endpoint above the threshold setting. ● SPC – NA (not applicable); SPC is ignored because the Flu B target amplification may compete with this control. ● Probe Check – PASS; all probe check results pass.

Result	Interpretation
Flu A NEGATIVE; Flu B NEGATIVE; RSV POSITIVE See Figure 8.	Flu A target RNA is not detected; Flu B target RNA is not detected; RSV target RNA is detected. ● The RSV target has a Ct within the valid range and endpoint above the threshold setting. ● SPC – NA (not applicable); SPC is ignored because the RSV target amplification may compete with this control. ● Probe Check – PASS; all probe check results pass.
Flu A NEGATIVE; Flu B POSITIVE; RSV POSITIVE** See Figure 9.	Flu A target RNA is not detected; Flu B target RNA is detected; RSV target RNA is detected. Repeat test according to the instructions in Section 16.2. ● The Flu B target has a Ct within the valid range and endpoint above the threshold setting. ● The RSV target has a Ct within the valid range and endpoint above the threshold setting. ● SPC – NA (not applicable); SPC is ignored because the Flu B and RSV target amplification may compete with this control. ● Probe Check – PASS; all probe check results pass.
Flu A NEGATIVE; Flu B NEGATIVE; RSV NEGATIVE See Figure 10.	Flu A target RNA is not detected; Flu B target RNA is not detected; RSV target RNA is not detected. ● 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 threshold setting. ● Probe Check – PASS; all probe check results pass.
INVALID See Figure 11.	SPC does not meet acceptance criteria. Presence or absence of the target RNAs cannot be determined. Repeat test according to the instructions in Section 16.2.
ERROR See Figure 12.	Presence or absence of Flu A, Flu B, and/or RSV target RNA cannot be determined. Repeat test according to the instructions in Section 16.2. ● Flu A – NO RESULT ● Flu B – NO RESULT ● RSV – NO RESULT ● SPC – NO RESULT ● Probe Check – FAIL*; all or one of the probe check results fail. * If the probe check passed, the error is caused by the maximum pressure limit exceeding the acceptable range or by a system component failure.
NO RESULT See Figure 13.	Presence or absence of Flu A, Flu B, and/or RSV target RNA cannot be determined. Repeat test according to the instructions in the Section 16.2. A NO RESULT indicates that insufficient data were collected. For example, the operator stopped a test that was in progress or a power failure occurred. ● Flu A – NO RESULT ● Flu B – NO RESULT ● RSV – NO RESULT ● SPC – NO RESULT ● Probe Check – NA (not applicable)

Note ** Because the incidence of co-infection with two or more viruses (Influenza A and Influenza B) within a single specimen is low, it is recommended that repeat testing is performed according to the instructions in Section 16.2.

Table 4. Xpert Xpress Flu Test Results and Interpretation

Result	Interpretation
Flu A POSITIVE; Flu B NEGATIVE See Figure 14.	Flu A target RNA is detected; Flu B target RNA is not detected. ● The Flu A target has a Ct within the valid range and endpoint above the threshold setting. ● SPC: NA (not applicable); SPC is ignored because the Flu A and Flu B target amplification may compete with this control. ● Probe Check: PASS; all probe check results pass.
Flu A NEGATIVE; Flu B POSITIVE See Figure 15.	Flu A target RNA is not detected; Flu B target RNA is detected. ● The Flu B target has a Ct within the valid range and endpoint above the threshold setting. ● SPC: NA (not applicable); SPC is ignored because the Flu B target amplification may compete with this control. ● Probe Check: PASS; all probe check results pass.
Flu A POSITIVE; Flu B POSITIVE See Figure 16.	Flu A target RNA is detected; Flu B target RNA is detected. Repeat test according to the instructions in Section 16.2. ● The Flu A target has a Ct within the valid range and endpoint above the threshold setting. ● The Flu B target has a Ct within the valid range and endpoint above the threshold setting. ● SPC: NA (not applicable); SPC is ignored because the Flu A and Flu B target amplification may compete with this control. ● Probe Check: PASS; all probe check results pass.
Flu A NEGATIVE; Flu B NEGATIVE See Figure 17.	Flu A target RNA is not detected; Flu B target RNA is not detected. ● Flu A and Flu B target RNAs are not detected. ● SPC: PASS; SPC has a Ct within the valid range and endpoint above the threshold setting. ● Probe Check: PASS; all probe check results pass.
ERROR	Presence or absence of Flu A and/or Flu B target RNA cannot be determined. Repeat test according to the instructions in Section 16.2. ● Flu A: NO RESULT ● Flu B: NO RESULT ● SPC: NO RESULT ● Probe Check: FAIL*; all or one of the probe check results fail. * If the probe check passed, the error is caused by the maximum pressure limit exceeding the acceptable range or by a system component failure.
NO RESULT	Presence or absence of Flu A and/or Flu B target RNA cannot be determined. Repeat test according to the instructions in Section 16.2. A **NO RESULT** indicates that insufficient data were collected. For example, the operator stopped a test that was in progress or a power failure occurred. ● Flu A: NO RESULT ● Flu B: NO RESULT ● SPC: NO RESULT ● Probe Check: NA (not applicable)

Note Because the incidence of co-infection with two or more viruses (Influenza A and Influenza B) within a single specimen is low, it is recommended that repeat testing is performed according to the instructions in Section 16.2.

Table 5. Xpert Xpress RSV Test Results and Interpretation

Result	Interpretation
RSV POSITIVE See Figure 18.	RSV target RNA is detected. • The RSV target has a Ct within the valid range and endpoint above the threshold setting. • SPC: NA (not applicable); SPC is ignored because the RSV target amplification may compete with this control. • Probe Check: PASS; all probe check results pass.
RSV NEGATIVE See Figure 19 and Figure 20.	RSV target RNA is not detected. • RSV target RNA is not detected. • SPC: PASS; SPC has a Ct within the valid range and endpoint above the threshold setting. • Probe Check: PASS; all probe check results pass.
ERROR	Presence or absence of RSV target RNA cannot be determined. Repeat test according to the instructions in Section 16.2. • RSV: NO RESULT • SPC: NO RESULT • Probe Check: FAIL*; all or one of the probe check results fail. * If the probe check passed, the error is caused by the maximum pressure limit exceeding the acceptable range or by a system component failure.

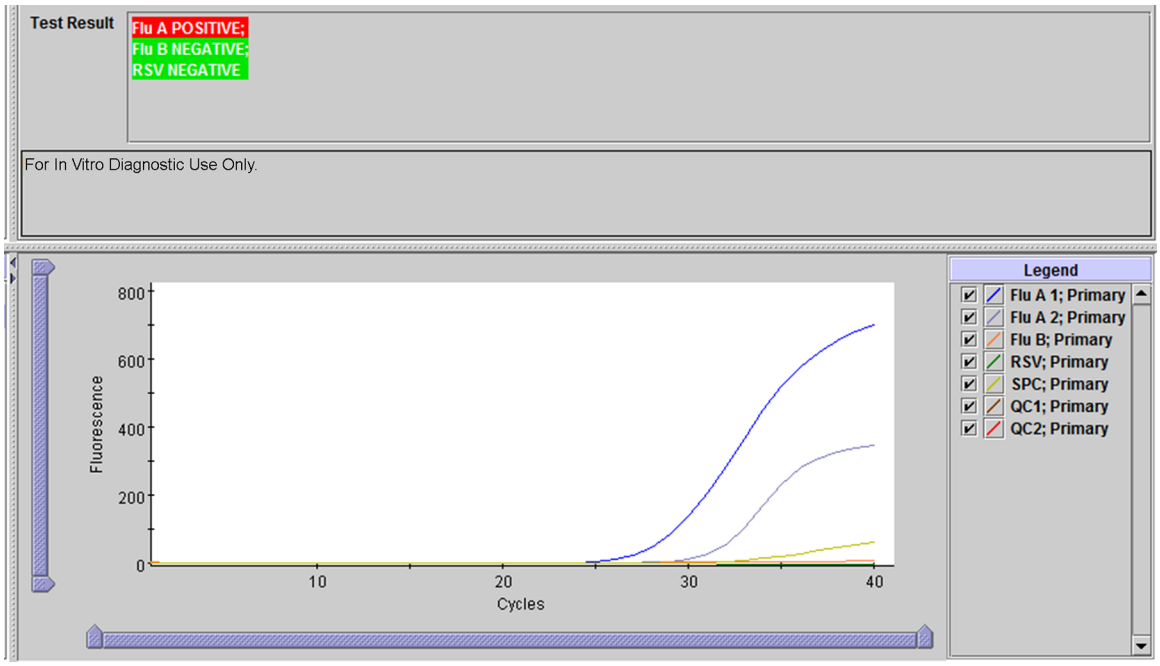

Figure 3. Xpert Xpress Flu/RSV CE-IVD: An Example of a Positive Result for Flu A

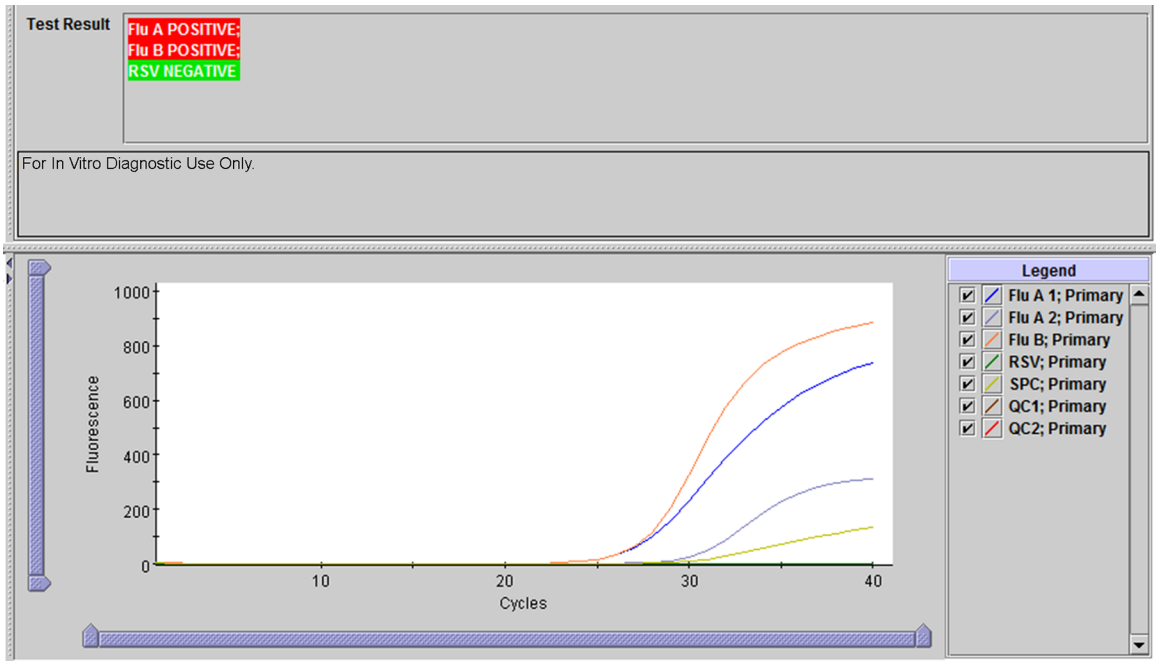

Figure 4. Xpert Xpress Flu/RSV CE-IVD: An Example of a Positive Result for Flu A and Flu B

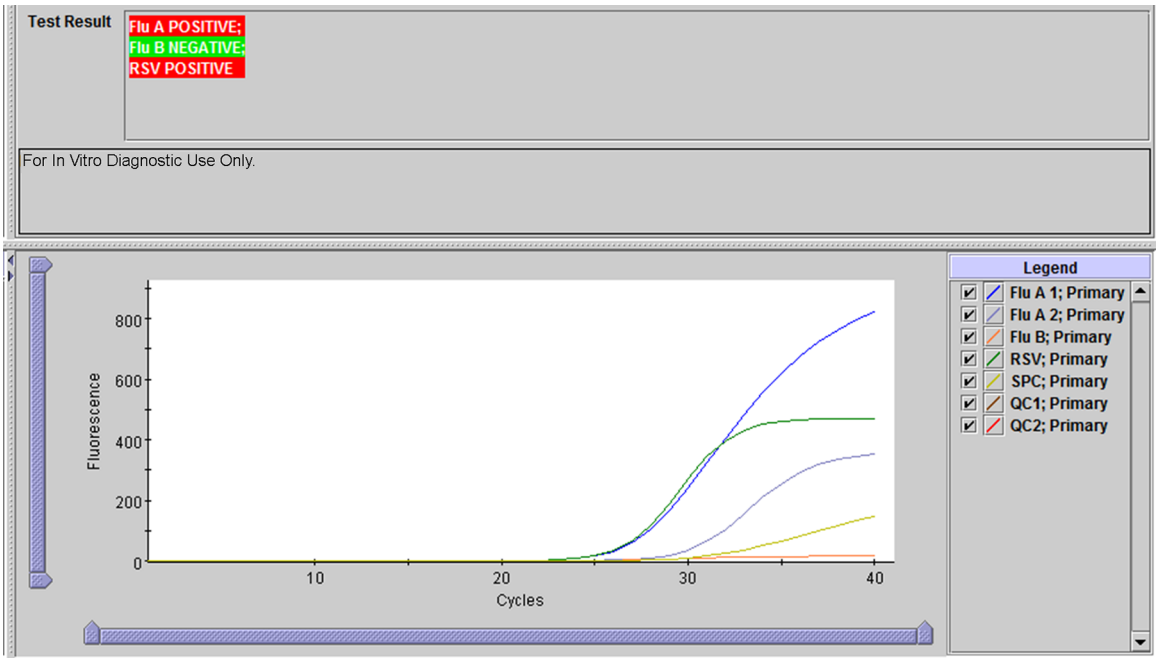

Figure 5. Xpert Xpress Flu/RSV CE-IVD: An Example of a Positive Result for Flu A and RSV

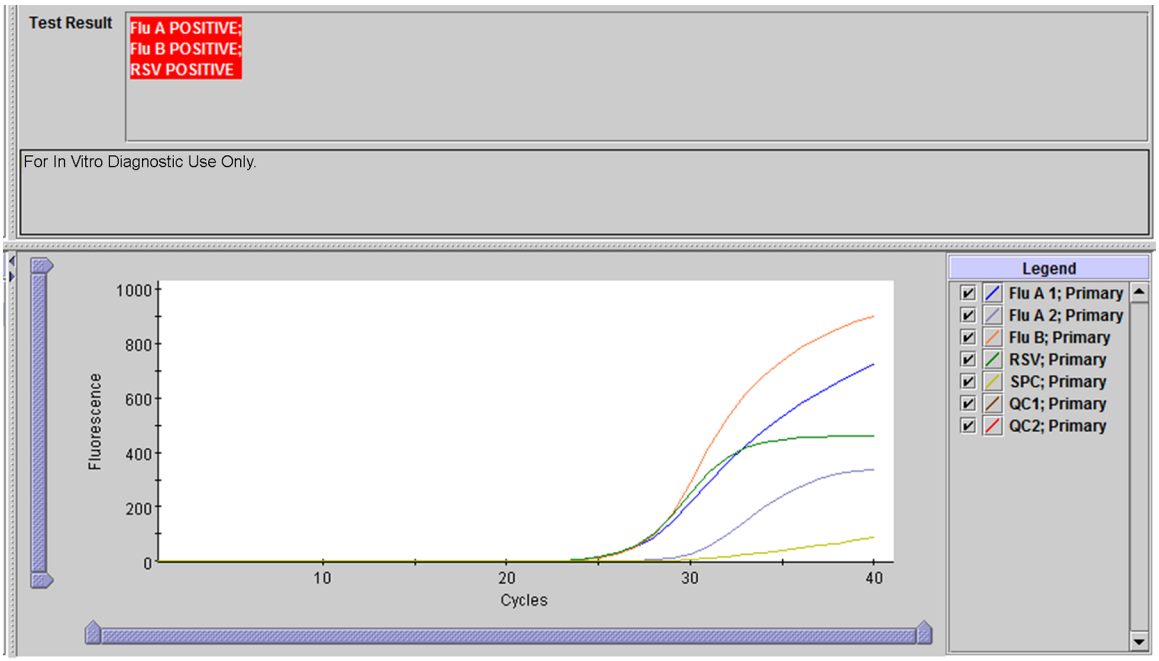

Figure 6. Xpert Xpress Flu/RSV CE-IVD: An Example of a Positive Result for Flu A, Flu B and RSV

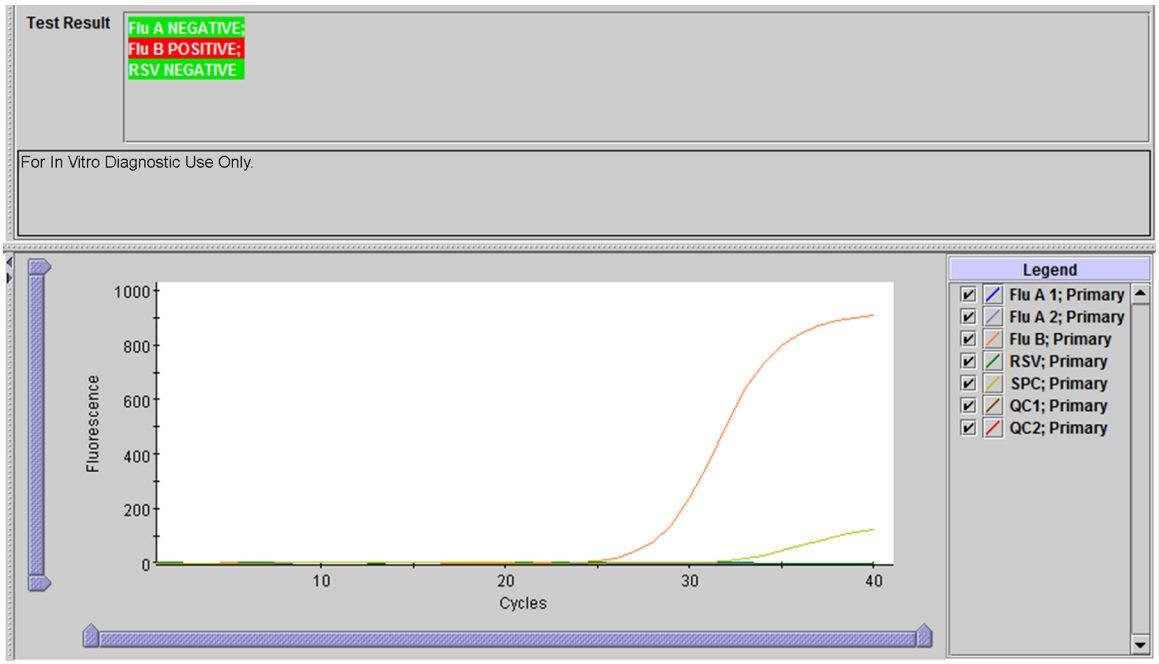

Figure 7. Xpert Xpress Flu/RSV CE-IVD: An Example of a Positive Result for Flu B

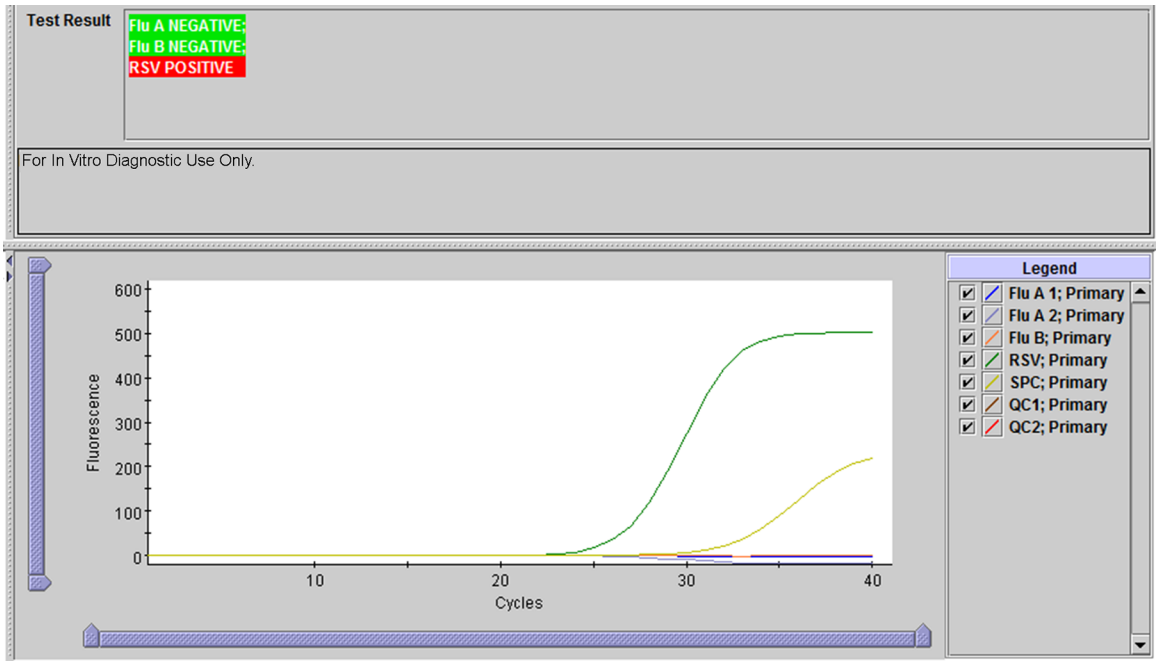

Figure 8. Xpert Xpress Flu/RSV CE-IVD: An Example of a Positive Result for RSV

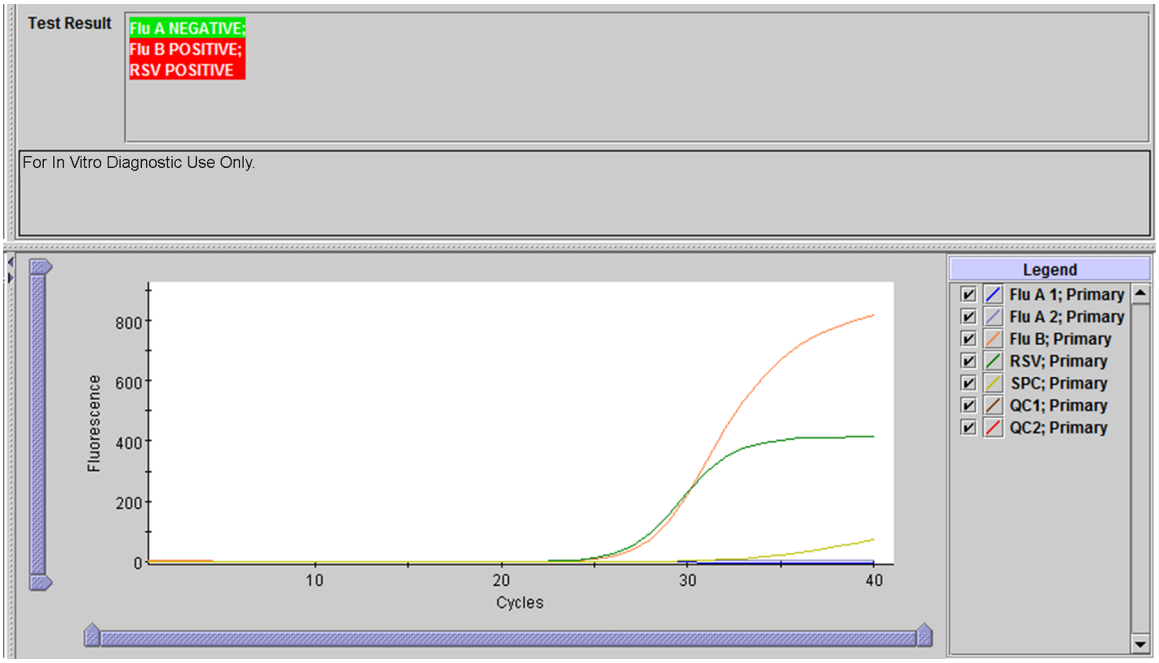

Figure 9. Xpert Xpress Flu/RSV CE-IVD: An Example of a Positive Result for Flu B and RSV

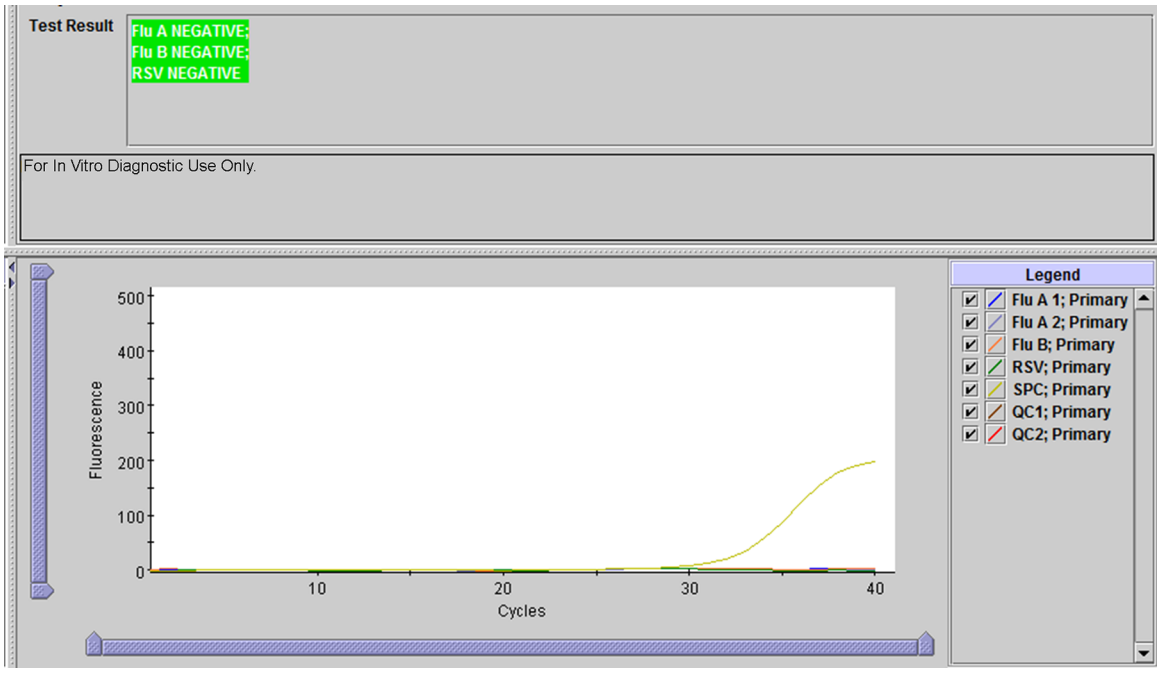

Figure 10. Xpert Xpress Flu/RSV CE-IVD: An Example of a Negative Result for Flu A, Flu B, and RSV

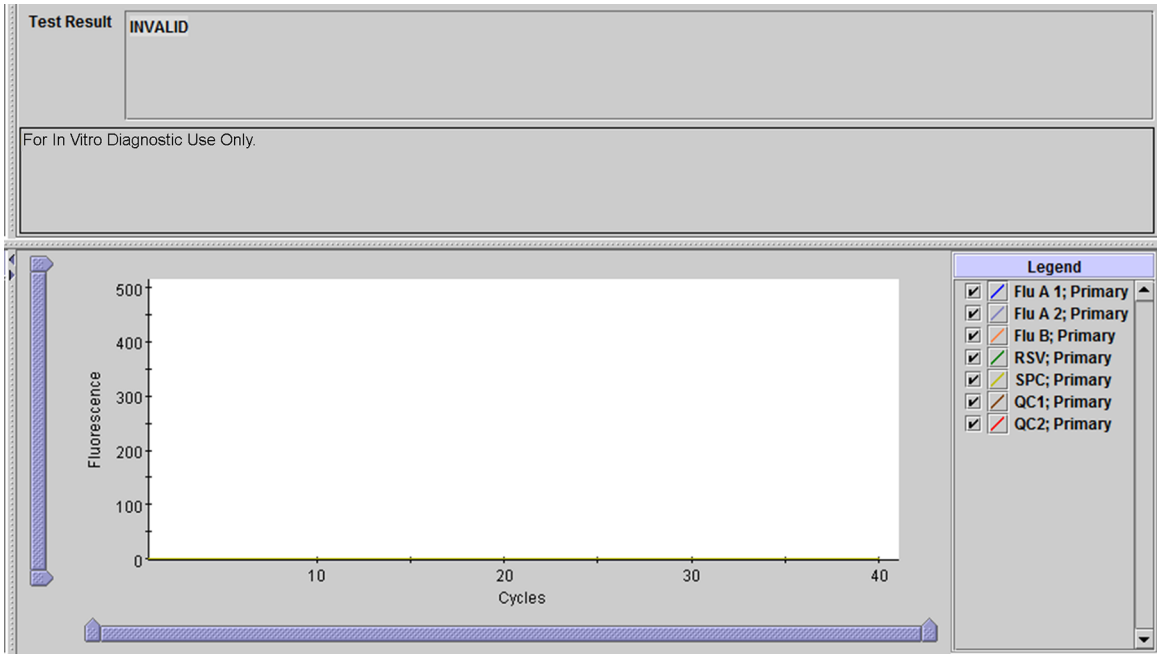

Figure 11. Xpert Xpress Flu/RSV CE-IVD: An Example of an Invalid Result (SPC does not meet acceptance criteria)

Figure 12. Xpert Xpress Flu/RSV CE-IVD: An Example of an Error

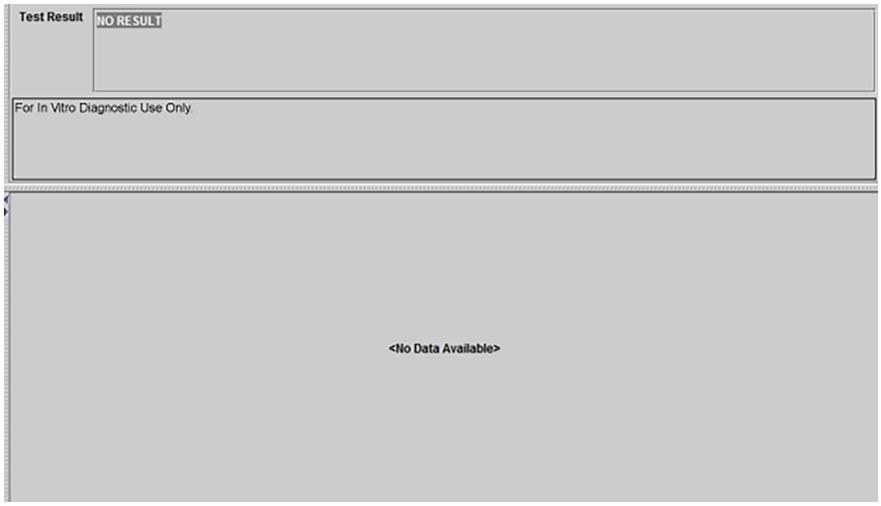

Figure 13. Xpert Xpress Flu/RSV CE-IVD: An Example of a No Result

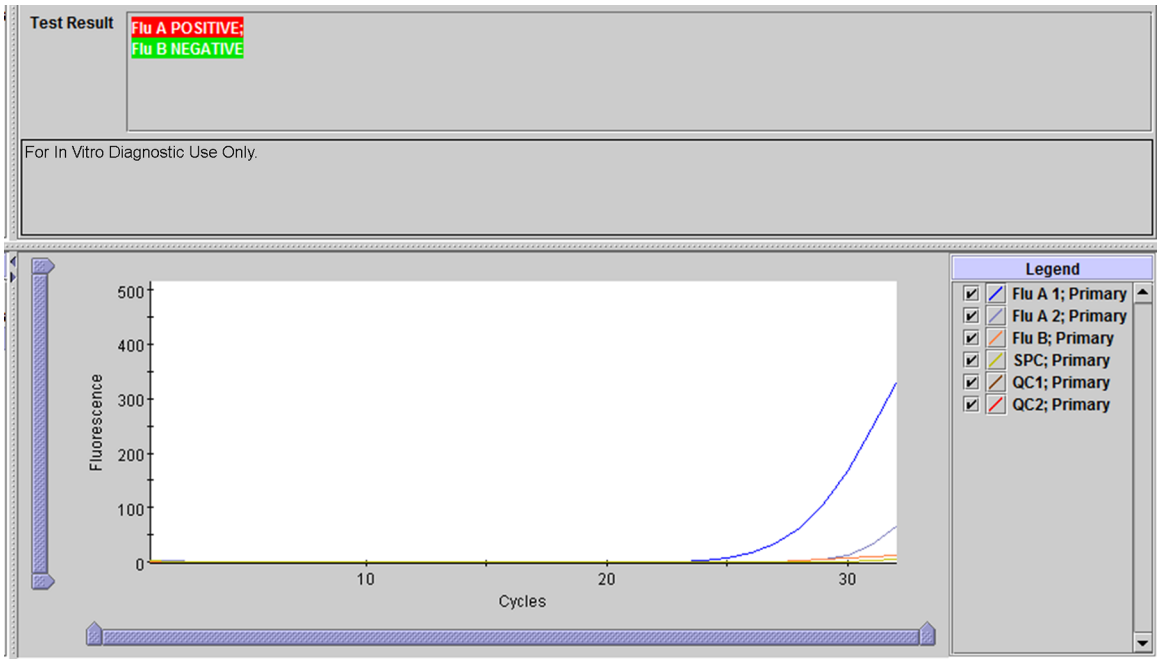

Figure 14. Xpert Xpress Flu CE-IVD: An Example of a Positive Result for Flu A

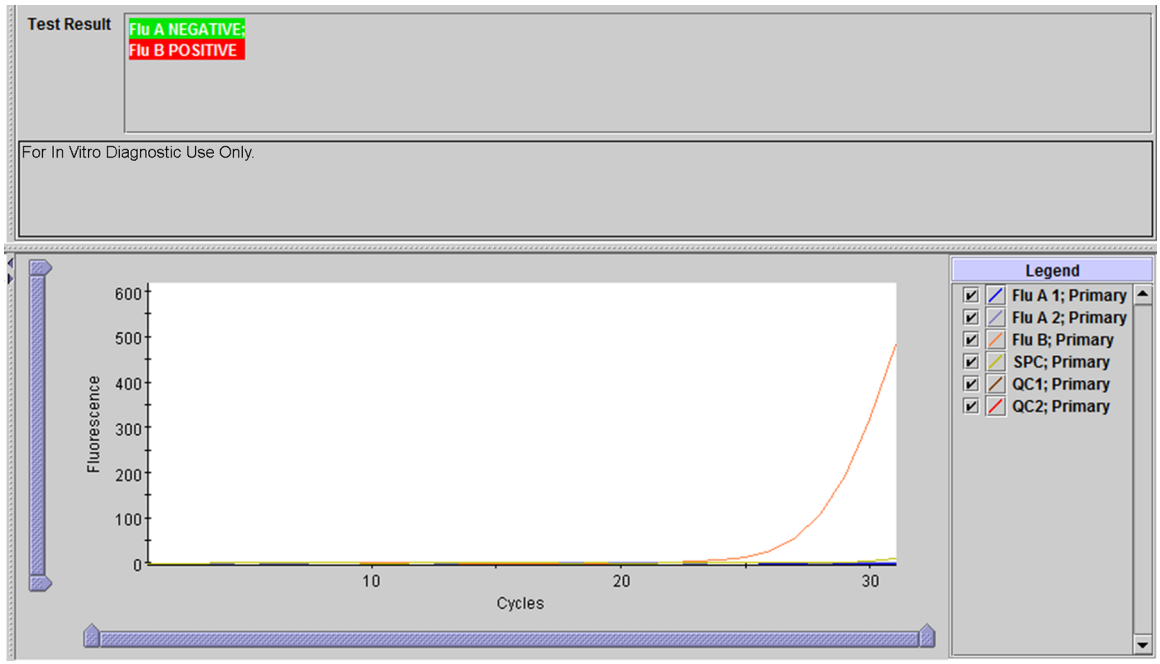

Figure 15. Xpert Xpress Flu CE-IVD: An Example of a Positive Result for Flu B

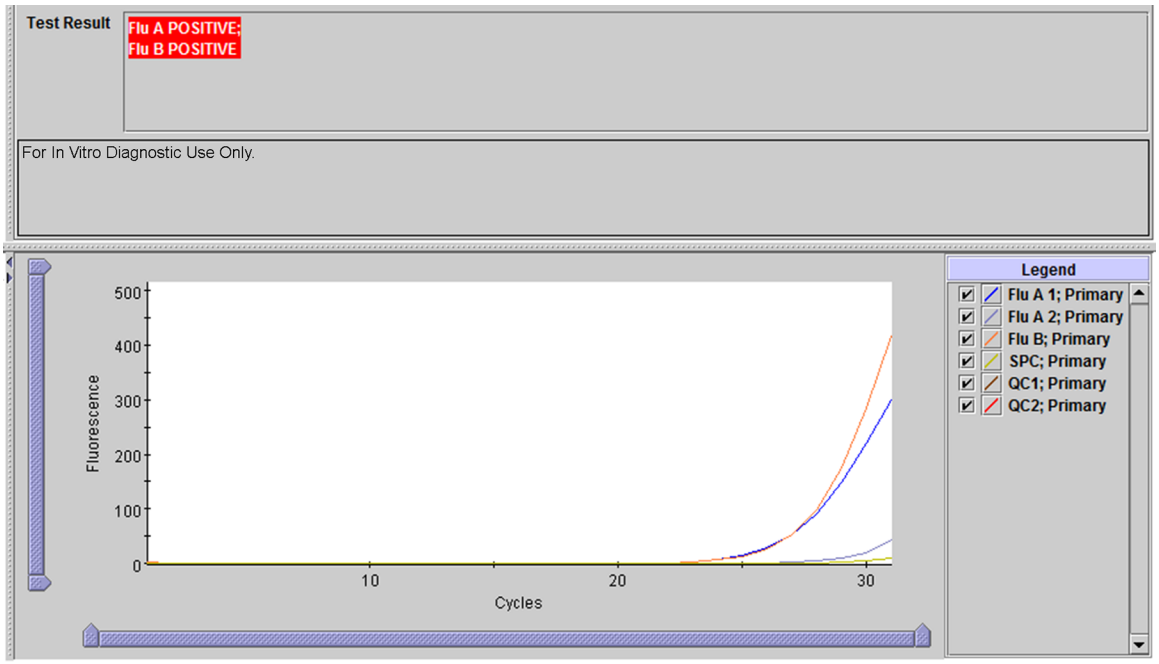

Figure 16. Xpert Xpress Flu CE-IVD: An Example of a Positive Result for Flu A and Flu B

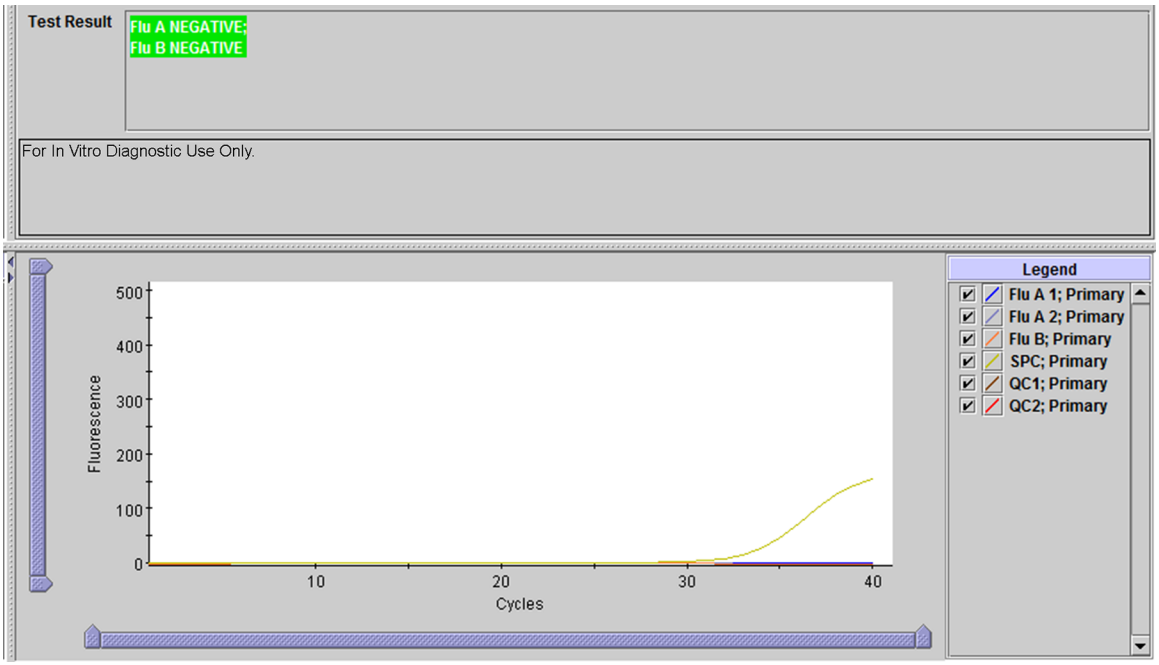

Figure 17. Xpert Xpress Flu CE-IVD: An Example of a Negative Result for Flu A and Flu B

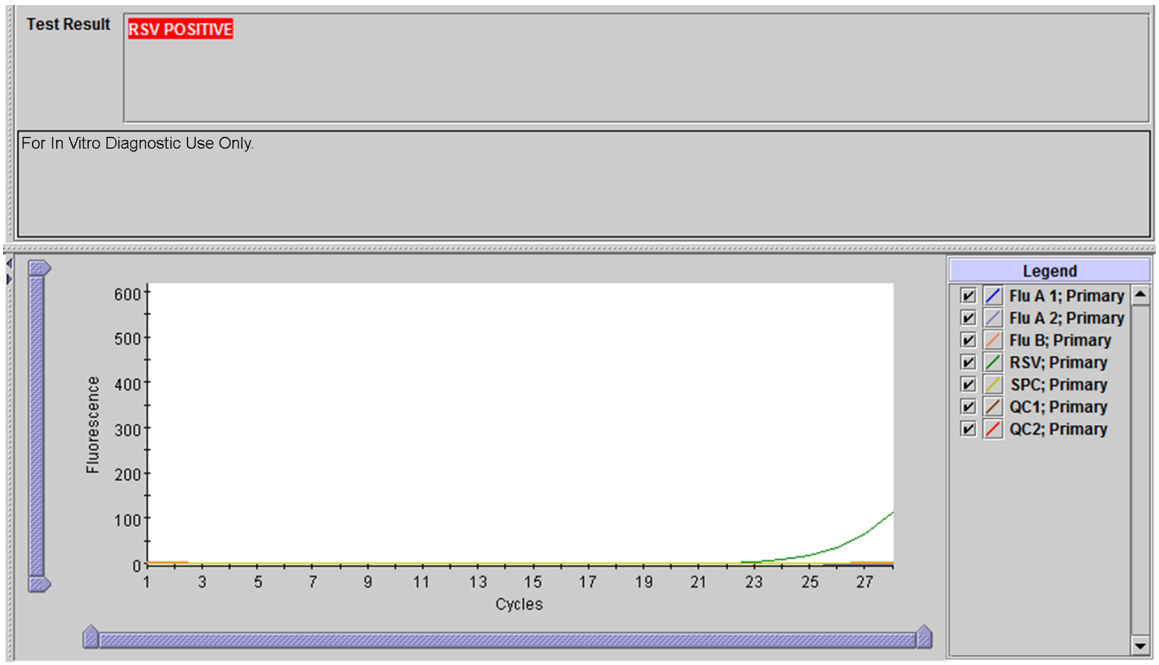

Figure 18. Xpert Xpress RSV CE-IVD: An Example of a Positive Result for RSV

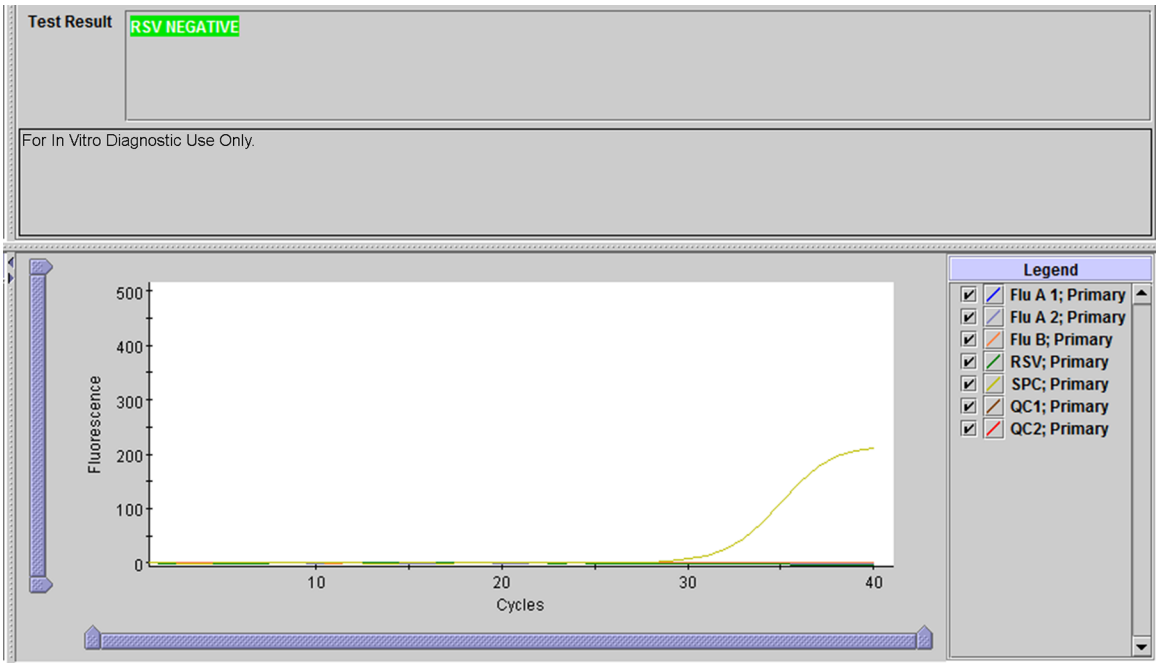

Figure 19. Xpert Xpress RSV CE-IVD: An Example of a Negative Result for RSV

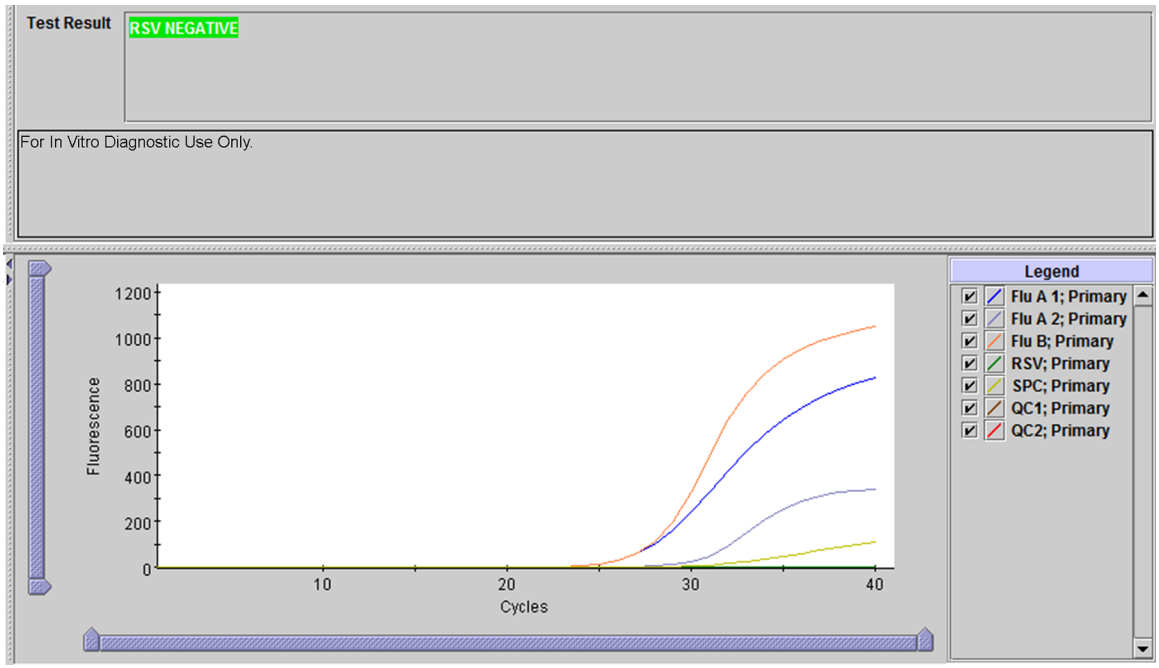

Figure 20. Xpert Xpress RSV CE-IVD: An Example of a Negative Result for RSV (Sample containing Flu A and Flu B targets)

16 Retests

16.1 Reasons to Repeat the Assay

If any of the test results mentioned below occur, repeat the test according to instructions in the Section 16.2.

- Because the incidence of co-infection with two or more viruses (Influenza A, Influenza B, and RSV) is low, it is recommended that specimens undergo repeat testing if nucleic acids from two or more analytes are detected in a single specimen. Repeat test according to the instructions in Section 16.2.
- An **INVALID** result indicates that the control SPC failed. The sample was not properly processed or PCR is inhibited, or the sample was not properly collected.
- An **ERROR** result could be due to, but not limited to, PCC failed or the maximum pressure limits were exceeded.
- A **NO RESULT** indicates that insufficient data were collected. For example, the operator stopped a test that was in progress or a power failure occurred.

16.2 Retest Procedure

For retest of an indeterminate result or a result indicating co-infection, use a new cartridge (do not re-use the cartridge).

Use 300 µL of the left over specimen from the original transport medium tube.

1. Remove a new cartridge from the kit.
2. Mix the specimen by inverting the Xpert Swab Transport Medium tube five times.
3. Open the cartridge lid. Use a clean 300 µL transfer pipette (supplied) to transfer 300 µL of the sample to the chamber by expressing the fluid into the large opening in the cartridge (Figure 1).
4. Close the cartridge lid.
5. Follow the procedure in Starting the Test.

17 Limitations

- The performance of the Xpert Xpress Flu/RSV test was validated using the procedures provided in this package insert only. Modifications to these procedures may alter the performance of the test.
- Results from the Xpert Xpress Flu/RSV test should be interpreted with other laboratory and clinical data available to the clinician.
- Erroneous test results might occur from improper specimen collection; failure to follow the recommended sample collection, handling, and storage procedures; technical error; sample mix-up; or because the number of organisms in the specimen is too low to be detected by the test. 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 influenza virus or RSV infection and should not be used as the sole basis for treatment or other patient management decisions.
- Results from analytical studies show potential for competitive inhibition in specimens with two different viruses.
- When using the Xpert Xpress Flu/RSV test in the Flu Only mode, in the event of a mixed infection one of the two infections may be reported as **NEGATIVE**.
- Results from the Xpert Xpress Flu/RSV test should be correlated with the clinical history, epidemiological data, and other data available to the clinician evaluating the patient.
- Viral nucleic acid may persist *in vivo*, independent of virus viability. Detection of analyte target(s) does not imply that the corresponding virus(es) are infectious or are the causative agents for clinical symptoms.
- This test has been evaluated for use with human specimen material only.
- If the virus mutates or there are other sequence changes in the target region, influenza virus and/or RSV may not be detected, or may be detected less predictably.
- Positive and negative predictive values are highly dependent on prevalence. The assay performance was established during the 2015-2016 influenza season for NP swab specimens and during the 2016-2017 influenza season for NS specimens. The performance may vary depending on the prevalence of the different viruses and population tested.
- This test is a qualitative test and does not provide the quantitative value of detected organism present.
- This test has not been evaluated for patients without signs and symptoms of influenza or RSV infection.
- This test has not been evaluated for monitoring treatment of influenza or RSV infection.
- This test has not been evaluated for screening of blood or blood products for the presence of influenza or RSV.
- This test cannot rule out diseases caused by other bacterial or viral pathogens.
- 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.
- Cross-reactivity with respiratory tract organisms other than those described herein can lead to erroneous results.
- This assay has not been evaluated for immunocompromised individuals.
- Recent patient exposure to FluMist® or other live attenuated influenza vaccines may cause inaccurate positive results.
- Although this test has been shown to detect A/H1N1 (pre-2009 pandemic), A/H7N9 (detected in China in 2013) and A/H3N2v viruses cultured from positive human respiratory specimens, the performance characteristics of this device with clinical specimens that are positive for the A/H1N1 (pre-2009 pandemic), A/H7N9 (detected in China in 2013) and A/H3N2v viruses have not been established.
- This test is not intended to differentiate Influenza A subtypes or Influenza B lineages. If differentiation of specific influenza subtypes and strains is needed, additional testing, in consultation with state or local public health departments, is required.

18 Expected Values

The Xpert Xpress Flu/RSV clinical study included a total of 2051 NP swab specimens.

The number and percentage of cases positive for one or more of influenza A, influenza B, and RSV in NP swab specimens as determined by the Xpert Xpress Flu/RSV test are shown by age category in Table 6.

Table 6. Age Group Flu A, Flu B, and RSV Positive by Xpert Xpress Flu/RSV Test – NP Swab Specimens[a]

Age Group	Number of Patients	% of Total	Flu A		Flu B		RSV	
			Number of Positives	Positivity Rate	Number of Positives	Positivity Rate	Number of Positives	Positivity Rate
≤5 years	360	17.6%	25	6.9%	18	5.0%	28	7.8%
6-21 years	225	11.0%	18	8.0%	30	13.3%	7	3.1%
22-59 years	729	35.5%	52	7.1%	26	3.6%	15	2.1%
≥60 years	736	35.9%	32	4.3%	22	3.0%	26	3.5%
Unknown	1	<0.1%	0	0.0%	0	0.0%	0	0.0%
Total	2051	100%	127	6.2%	96	4.7%	76	3.7%

[a] Two subjects had multi-infections by Xpert Xpress Flu/RSV Test and are therefore counted more than once in this table: Flu A & RSV POS [(1); Flu A POS by comparator assay], and Flu A & Flu B POS [(1); Flu A POS by comparator assay].

The Xpert Xpress Flu/RSV clinical study included a total of 1598 NS specimens for evaluation of influenza A and influenza B detection.

The number and percentage of cases positive for one or more of influenza A and influenza B in NS specimens as determined by the Xpert Xpress Flu/RSV test are shown by age category in Table 7.

Table 7. Age Group Flu A and Flu B Positive by Xpert Xpress Flu/RSV Test – NS Specimens [a]

Age Group (years)	Number of Patients	% of Total	Flu A		Flu B	
			Number of Positives	Positivity Rate	Number of Positives	Positivity Rate
≤5	604	37.8%	67	11.1%	26	4.3%
6-21	273	17.1%	66	24.2%	26	9.5%
22-59	554	34.7%	58	10.5%	19	3.4%
≥60	167	10.5%	30	18.0%	3	1.8%
Total	1598	100%	221	13.8%	74	4.6%

[a] One subject had multi-infection by the Xpert Xpress Flu/RSV Test and was therefore counted more than once in this table. The sample was Flu B POS by comparator method.

The Xpert Xpress Flu/RSV clinical study included a total of 1543 NS specimens for evaluation of RSV detection.

The number and percentage of cases positive for RSV in NS specimens as determined by the Xpert Xpress Flu/RSV Test are shown by age category in Table 8.

Table 8. Age Group RSV Positive by Xpert Xpress Flu/RSV Test – NS Specimens

Age Group (years)	Number of Patients	% of Total	RSV	
			Number of Positives	Positivity Rate
≤5	587	38.0%	230	39.2%
6-21	254	16.5%	11	4.3%
22-59	537	34.8%	19	3.5%
≥60	165	10.7%	21	12.7%
Total	1543	100%	281	18.2%

19 Performance Characteristics

19.1 Clinical Performance

Performance characteristics of the Xpert Xpress Flu/RSV test were evaluated at eleven institutions in the U.S. during the 2015-2016 influenza season for NP swab specimens and at fourteen institutions in the U.S. during the 2016-2017 influenza season for NS specimens.

Specimens were collected from the following:

- Individuals exhibiting signs and symptoms of respiratory infection who provided informed consent for the collection of a NP swab or NS specimen.
- Individuals with signs and symptoms of respiratory infection and whose routine care called for collection of NP swab specimens for influenza and/or RSV testing. Aliquots of leftover routine care specimens were obtained for testing with the Xpert Xpress Flu/RSV test and comparator test, and patient management continued at the site per the standard practice.

The Xpert Xpress Flu/RSV test performance was compared to FDA-cleared molecular comparator test. Bi-directional sequencing was performed on specimens where the Xpert Xpress Flu/RSV test and the comparator test were discrepant, and is provided for informational purposes only.

19.2 Overall Results - NP Swab Specimens

A total of 2051 NP swab specimens were tested for influenza A, influenza B and RSV by the Xpert Xpress Flu/RSV test and the comparator assay. Of the 2051 NP swab specimens, 1139 were fresh, prospectively collected and 912 were consecutively collected, frozen specimens.

For the fresh, prospectively collected NP swab specimens, the Xpert Xpress Flu/RSV test demonstrated a PPA and NPA of 94.6% and 99.4%, detection of influenza A; 100% and 99.2% for influenza B, respectively; and 100% and 99.8%, for RSV, respectively, relative to the comparator assay (Table 9).

For the consecutively collected, frozen NP swab specimens, the Xpert Xpress Flu/RSV test demonstrated a PPA and NPA of 100% and 98.0% for the detection of influenza A, respectively; 100% and 99.0% for influenza B, respectively; and 97.9% and 98.7% for RSV, respectively, relative to the comparator assay (Table 9).

For the combined dataset, the Xpert Xpress Flu/RSV test demonstrated a PPA and NPA of 98.1% and 98.8% for the detection of influenza A, respectively; 100% and 99.1% for influenza B respectively; and 98.4% and 99.3% for RSV, respectively, relative to the comparator assay (Table 9).

Table 9. Xpert Xpress Flu/RSV Test Performance

Collection Type	Target	n	TP	FN	TN	FP	PPA (95% CI)	NPA (95% CI)
Fresh	Flu A	1139	35	2[a]	1095	7[b]	94.6% (82.3 - 98.5)	99.4% (98.7 - 99.7)
	Flu B	1139	42	0	1088	9[c]	100.0% (91.6 - 100.0)	99.2% (98.4 - 99.6)
	RSV	1139	17	0	1120	2[d]	100.0% (81.6 - 100.0)	99.8% (99.4 - 100.0)
Frozen Consecutively Collected	Flu A	912	68	0	827	17[e]	100.0% (94.7 - 100.0)	98.0% (96.8 - 98.7)
	Flu B	912	36	0	867	9[f]	100.0% (90.4 - 100.0)	99.0% (98.1 - 99.5)
	RSV	912	46	1[g]	854	11[h]	97.9% (88.9 - 99.6)	98.7% (97.7 - 99.3)
Combined	Flu A	2051	103	2[a]	1922	24[i]	98.1% (93.3 - 99.5)	98.8% (98.2 - 99.2)
	Flu B	2051	78	0	1955	18[j]	100.0% (95.3 - 100.0)	99.1% (98.6 - 99.4)
	RSV	2051	63	1[g]	1974	13[k]	98.4% (91.7 - 99.7)	99.3% (98.9 - 99.6)

[a] Testing results by sequencing: 2 of 2 were Flu A Negative.

[b] Testing results by sequencing: 3 of 7 were Flu A Positive; 3 of 7 were Flu A Negative; 1 of 7 insufficient specimen for sequencing.

[c] Testing results by sequencing: 6 of 9 were Flu B Positive; 2 of 9 were Flu B Negative; 1 of 9 insufficient specimen for sequencing.

[d] Testing results by sequencing: 0 of 2 were RSV Positive; 1 of 2 was RSV Negative; 1 of 2 insufficient specimen for sequencing.

[e] Testing results by sequencing: 7 of 17 were Flu A Positive; 7 of 17 were Flu A Negative; 3 of 17 insufficient specimen for sequencing.

[f] Testing results by sequencing: 7 of 9 were Flu B Positive; 0 of 9 were Flu B Negative; 2 of 9 insufficient specimen for sequencing.

[g] Testing results by sequencing: 1 of 1 was RSV Negative.

[h] Testing results by sequencing: 3 of 11 were RSV Positive; 2 of 11 were RSV Negative; 6 of 11 insufficient specimen for sequencing.

[i] Testing results by sequencing: 10 of 24 were Flu A Positive; 10 of 24 were Flu A Negative; 4 of 24 insufficient specimen for sequencing.

[j] Testing results by sequencing: 13 of 18 were Flu B Positive; 2 of 18 were Flu B Negative; 3 of 18 insufficient specimen for sequencing.

[k] Testing results by sequencing: 3 of 13 were RSV Positive; 3 of 13 were RSV Negative; 7 of 13 insufficient specimen for sequencing.

In addition, 98 pre-selected frozen NP swab specimens were collected and tested. The results of this testing were analyzed separately and are as follows: the Xpert Xpress Flu/RSV test demonstrated a PPA and NPA of 100% and 97.8%, for influenza A, respectively; 100% and 96.6% for influenza B, respectively; and 100% and 100%, for RSV, respectively, relative to the comparator assay.

19.3 Overall Results - NS Specimens

A total of 1598 NS specimens were tested for influenza A and influenza B by the Xpert Xpress Flu/RSV test and the comparator assay. A total of 1543 NS specimens were tested for RSV by the Xpert Xpress Flu/RSV test and the comparator assay.

The Xpert Xpress Flu/RSV test demonstrated a PPA and NPA relative to the comparator method of 98.9% and 97.5%, for detection of Flu A, respectively; 98.4% and 99.3% for Flu B, respectively; and 98.2% and 99.1%, for detection of RSV, respectively (Table 10).

Table 10. Xpert Xpress Flu/RSV Test Performance on NS Specimens

Target[a]	N	TP	FN	TN	FP	PPA (95% CI)	NPA (95% CI)
Flu A	1598	186	2[b]	1375	35[c]	98.9% (96.2 - 99.7)	97.5% (96.6 - 98.2)
Flu B	1598	63	1[d]	1523	11[e]	98.4% (91.7 - 99.7)	99.3% (98.7 - 99.6)
RSV	1543	269	5[f]	1257	12[g]	98.2% (95.8 - 99.2)	99.1% (98.4 - 99.5)

[a] Five specimens were positive for both Flu A and Flu B by Xpert.

[b] Testing results by sequencing: 1 of 2 Flu A NEG; 1 of 2 Flu A POS.

[c] Testing results by sequencing: 17 of 35 Flu A NEG; 11 of 35 Flu A POS; 7 of 35 inconclusive.

[d] Testing results by sequencing: 1 of 1 inconclusive.

[e] Testing results by sequencing: 5 of 11 Flu B POS; 6 of 11 inconclusive.

[f] Testing results by sequencing: 3 of 5 RSV NEG; 1 of 5 inconclusive; 1 of 5 not done.

[g] Testing results by sequencing: 5 of 12 RSV NEG; 3 of 12 RSV POS; 4 of 12 inconclusive.

19.4 Indeterminate Rate

Of the Xpert Xpress Flu/RSV test runs performed with eligible NP swab and NS specimens, 97.8% (3594/3674) of these specimens were successful on the first attempt. The remaining 80 gave indeterminate results on the first attempt (39 **ERROR**, 32 **INVALID**, and 9 **NO RESULT**). Sixty of the 80 indeterminate cases were retested, of which 54 yielded valid results upon repeat testing; 20 specimens were not retested. The overall rate of assay success was 99.3% (3649/3674). The overall indeterminate rate was 0.7% (25/3674) with a 95% CI 0.5 - 1.0%.

20 Analytical Performance

20.1 Analytical Sensitivity (Limit of Detection)

Studies were performed to determine the analytical limit of detection (LoD) of the Xpert Xpress Flu/RSV test with two lots of reagents across three testing days. The higher LoD observed per strain and per lot was selected for verification. Verification of the estimated LoD claim was performed on one reagent lot across a minimum of three testing days. LoD was established using two influenza A H3N2 strains, two influenza A 2009 H1N1 strains, two influenza B strains, two respiratory syncytial virus A (RSV A) strains and two respiratory syncytial virus B (RSV B) strains. Viruses were diluted into negative pooled NP swab and negative pooled NS clinical matrices for testing. The LoD is defined as the lowest concentration (tissue culture infective dose, TCID50/mL) per sample that can be reproducibly distinguished from negative samples with 95% confidence or the lowest concentration at which 19 of 20 replicates were positive. Each strain was tested in replicates of 20 per concentration of virus in NP swab clinical and NS matrix. The LoD point values for each strain tested in NP swab and NS clinical matrices are summarized in Table 11, Table 12, Table 13, Table 14 and Table 15.

Table 11. Confirmed LoD ($TCID_{50}$/mL): Influenza A 2009 H1N1

Virus Strain	Confirmed LoD Probit ($TCID_{50}$/mL)	
	NP Swab	NS
Influenza A/California/7/2009	0.020	0.018
Influenza A/Florida/27/2011	0.040	0.04

Table 12. Confirmed LoD ($TCID_{50}$/mL): Influenza A H3N2

Virus Strain	Confirmed LoD Probit ($TCID_{50}$/mL)	
	NP Swab	NS
Influenza A/Perth/16/2009	0.013	0.006
Influenza A/Victoria/361/2011	0.750	0.21

Table 13. Confirmed LoD ($TCID_{50}$/mL): Influenza B

Virus Strain	Confirmed LoD Probit ($TCID_{50}$/mL)	
	NP Swab	NS
Influenza B/Mass/2/2012	0.400	0.07
Influenza B/Wisconsin/01/2011	0.190	0.17

Table 14. Confirmed LoD ($TCID_{50}$/mL) Respiratory Syncytial Virus A

Virus Strain	Confirmed LoD Probit ($TCID_{50}$/mL)	
	NP Swab	NS
RSV A/2/Australia/61	0.870	0.32
RSV A/Long/MD/56	1.100	0.45

Table 15. Confirmed LoD ($TCID_{50}$/mL): Respiratory Syncytial Virus B

Virus Strain	Confirmed LoD Probit ($TCID_{50}$/mL)	
	NP Swab	NS
RSV B/Wash/18537/62	0.790	0.29
RSV B/9320/MA/77	2.300	0.35

20.2 Analytical Specificity (Exclusivity)

The analytical specificity of the Xpert Xpress Flu/RSV test was evaluated by testing a panel of 44 cultures consisting of 16 viral, 26 bacterial, and two yeast strains representing common respiratory pathogens or those potentially encountered in the nasopharynx. Three replicates of all bacterial and yeast strains were tested at concentrations of $\geq 1 \times 10^6$ CFU/mL with the exception of one strain that was tested at 1×10^5 CFU/mL (*Chlamydia pneumoniae*). Three replicates of all viruses were tested at concentrations of $\geq 1 \times 10^5$ $TCID_{50}$/mL. The analytical specificity was 100%. Results are shown in Table 16.

Table 16. Analytical Specificity of the Xpert Xpress Flu/RSV Test

Organism	Concentration	Result		
		Influenza A	Influenza B	RSV
No Template Control	N/A	NEG	NEG	NEG
Adenovirus Type 1	1.12E+06 $TCID_{50}$/mL	NEG	NEG	NEG
Adenovirus Type 7	1.87E+05 $TCID_{50}$/mL	NEG	NEG	NEG
Human coronavirus OC43	2.85E+05 $TCID_{50}$/mL	NEG	NEG	NEG
Human coronavirus 229E	1.00E+05 $TCID_{50}$/mL	NEG	NEG	NEG

Organism	Concentration	Result		
		Influenza A	Influenza B	RSV
Cytomegalovirus	1.00E+05 $TCID_{50}$/mL	NEG	NEG	NEG
Echovirus	3.31E+07 $TCID_{50}$/mL	NEG	NEG	NEG
Enterovirus	3.55E+05 $TCID_{50}$/mL	NEG	NEG	NEG
Epstein Barr Virus	7.16E+07 $TCID_{50}$/mL	NEG	NEG	NEG
HSV	8.90E+05 $TCID_{50}$/mL	NEG	NEG	NEG
Measles	6.31E+05 $TCID_{50}$/mL	NEG	NEG	NEG
Human metapneumovirus	1.00E+05 $TCID_{50}$/mL	NEG	NEG	NEG
Mumps virus	6.31E+06 $TCID_{50}$/mL	NEG	NEG	NEG
Human parainfluenza Type 1	1.15E+06 $TCID_{50}$/mL	NEG	NEG	NEG
Human parainfluenza Type 2	6.31E+05 $TCID_{50}$/mL	NEG	NEG	NEG
Human parainfluenza Type 3	3.55E+06 $TCID_{50}$/mL	NEG	NEG	NEG
Rhinovirus Type 1A	1.26E+05 $TCID_{50}$/mL	NEG	NEG	NEG
Acinetobacter baumannii	1.00E+06 CFU/mL	NEG	NEG	NEG
Burkholderia cepacia	3.30E+06 CFU/mL	NEG	NEG	NEG
Candida albicans	3.20E+06 CFU/mL	NEG	NEG	NEG
Candida parapsilosis	3.00E+06 CFU/mL	NEG	NEG	NEG
Bordetella pertussis	3.30E+06 CFU/mL	NEG	NEG	NEG
Chlamydia pneumoniae	1.00E+05 CFU/mL	NEG	NEG	NEG
Citrobacter freundii	3.30E+06 CFU/mL	NEG	NEG	NEG
Corynebacterium sp.	3.30E+06 CFU/mL	NEG	NEG	NEG
Escherichia coli	1.00E+07 CFU/mL	NEG	NEG	NEG
Enterococcus faecalis	1.30E+06 CFU/mL	NEG	NEG	NEG
Haemophilus influenzae	1.00E+06 CFU/mL	NEG	NEG	NEG
Lactobacillus reuter	1.00E+06 CFU/mL	NEG	NEG	NEG
Legionella spp.	1.00E+06 CFU/mL	NEG	NEG	NEG
Moraxella catarrhalis	1.00E+07 CFU/mL	NEG	NEG	NEG
Mycobacterium tuberculosis (avirulent)	1.00E+06 CFU/mL	NEG	NEG	NEG
Mycoplasma pneumoniae	1.00E+06 CFU/mL	NEG	NEG	NEG
Neisseria meningitidis	2.15E+06 CFU/mL	NEG	NEG	NEG
Neisseria mucosa	1.00E+07 CFU/mL	NEG	NEG	NEG
Propionibacterium acnes	2.40E+07 CFU/mL	NEG	NEG	NEG
Pseudomonas aeruginosa	3.70E+06 CFU/mL	NEG	NEG	NEG
Staphylococcus aureus (protein A producer)	2.20E+06 CFU/mL	NEG	NEG	NEG
Staphylococcus epidermidis	3.40E+06 CFU/mL	NEG	NEG	NEG

Organism	Concentration	Result		
		Influenza A	Influenza B	RSV
Staphylococcus haemolyticus	4.00E+06 CFU/mL	NEG	NEG	NEG
Streptococcus agalactiae	3.50E+06 CFU/mL	NEG	NEG	NEG
Streptococcus pneumoniae	1.00E+06 CFU/mL	NEG	NEG	NEG
Streptococcus pyogenes	1.00E+07 CFU/mL	NEG	NEG	NEG
Streptococcus salivarius	1.00E+07 CFU/mL	NEG	NEG	NEG
Streptococcus sanguinis	3.10E+06 CFU/mL	NEG	NEG	NEG

20.3 Analytical Reactivity (Inclusivity)

The analytical reactivity of the Xpert Xpress Flu/RSV test was evaluated against multiple strains of influenza A H1N1 (seasonal pre-2009), influenza A H1N1 (pandemic 2009), influenza A H3N2 (seasonal), avian influenza A (H5N1, H5N2, H6N2, H7N2, H7N3, H2N2, H7N9, and H9N2), influenza B (representing strains from both Victoria and Yamagata lineages), and respiratory syncytial virus subgroups A and B (RSV A and RSV B) at levels near the analytical LoD. A total of 53 strains comprised of 48 influenza viruses (35 influenza A and 13 influenza B) and 5 RSV strains were tested in this study with the Xpert Xpress Flu/RSV test. Three replicates were tested for each strain. All flu and RSV strains tested positive in all three replicates, except for one Flu A H1N1 strain (A/New Jersey/8/76), which tested positive in 2 of 3 replicates at 0.1 $TCID_{50}$/mL. Results are shown in Table 17.

Predicted cross-reactivity from in silico analyses showed 100% sequence homology for additional pH1N1 strains.

Table 17. Analytical Reactivity (Inclusivity) of the Xpert Xpress Flu/RSV Test

Virus	Strain	Target Concentration	Result		
			Flu A	Flu B	RSV
No Template Control		n/a	NEG	NEG	NEG
Influenza A H1N1 (pre-2009)	A/swine/Iowa/15/30	0.1 $TCID_{50}$/mL	POS	NEG	NEG
	A/WS/33	0.1 $TCID_{50}$/mL	POS	NEG	NEG
	A/PR/8/34	0.1 $TCID_{50}$/mL	POS	NEG	NEG
	A/Mal/302/54	0.1 $TCID_{50}$/mL	POS	NEG	NEG
	A/Denver/1/57	0.1 $TCID_{50}$/mL	POS	NEG	NEG
	A/New Jersey/8/76	0.1 $TCID_{50}$/mL	POS	NEG	NEG
	A/New Caledonia/20/1999	0.1 $TCID_{50}$/mL	POS	NEG	NEG
	A/New York/55/2004	0.1 $TCID_{50}$/mL	POS	NEG	NEG
	A/Soloman Island/3/2006	0.1 $TCID_{50}$/mL	POS	NEG	NEG
	A/Taiwan/42/06	0.1 $TCID_{50}$/mL	POS	NEG	NEG
	A/Brisbane/59/2007	0.1 $TCID_{50}$/mL	POS	NEG	NEG
Influenza A H1N1 (pdm2009)	A/swine/NY/02/2009	0.1 $TCID_{50}$/mL	POS	NEG	NEG
	A/Colorado/14/2012	0.1 $TCID_{50}$/mL	POS	NEG	NEG
	A/Washington/24/2012	0.1 $TCID_{50}$/mL	POS	NEG	NEG

Virus	Strain	Target Concentration	Result		
			Flu A	Flu B	RSV
Influenza A H3N2 (Seasonal)	A/Aichi/2/68	2.0 $TCID_{50}$/mL	POS	NEG	NEG
	A/HongKong/8/68	2.0 $TCID_{50}$/mL	POS	NEG	NEG
	A/Port Chalmers/1/73	2.0 $TCID_{50}$/mL	POS	NEG	NEG
	A/Hawaii/15/2001	2.0 $TCID_{50}$/mL	POS	NEG	NEG
	A/Wisconsin/67/05	2.0 $TCID_{50}$/mL	POS	NEG	NEG
	A/Brisbane/10/2007	2.0 $TCID_{50}$/mL	POS	NEG	NEG
	A/Minnesota/11/2010 (H3N2)v	2.0 $TCID_{50}$/mL	POS	NEG	NEG
	A/Indiana/08/2011 (H3N2)v	2.0 $TCID_{50}$/mL	POS	NEG	NEG
	A/Texas/50/2012	2.0 $TCID_{50}$/mL	POS	NEG	NEG
Avian influenza A	A/duck/ Hunan/795/2002 (H5N1)	≤ 1ρg/µL[a]	POS	NEG	NEG
	A/chicken/ Hubei/327/2004 (H5N1)	≤ 1ρg/µL[a]	POS	NEG	NEG
	A/Anhui/01/2005 (H5N1)	≤ 1ρg/µL[a]	POS	NEG	NEG
	A/Japanese white eye/HongKong/ 1038/2006 (H5N1)	≤ 1ρg/µL[a]	POS	NEG	NEG
	A/mallard/WI/34/75 (H5N2)	≤ 1ρg/µL[a]	POS	NEG	NEG
	A/chicken/ CA431/00 (H6N2)	≤ 1ρg/µL[a]	POS	NEG	NEG
	A/duck/ LTC-10-82743/1943 (H7N2)	≤ 1ρg/µL[a]	POS	NEG	NEG
	A/chicken/ NJ/15086-3/94 (H7N3)	≤ 1ρg/µL[a]	POS	NEG	NEG
	A/Anhui/1/2013 (H7N9)	N/A[b]	POS	NEG	NEG
	A/Shanghai/1/2013 (H7N9)	N/A[b]	POS	NEG	NEG
	A/chicken/Korea/38349-p96323/ 1996 (H9N2)	≤ 1ρg/µL[a]	POS	NEG	NEG
	A/Mallard/ NY/6750/78 (H2N2)	≤ 1ρg/µL[a]	POS	NEG	NEG
Influenza B	B/Lee/40	1.0 $TCID_{50}$/mL	NEG	POS	NEG
	B/Allen/45	1.0 $TCID_{50}$/mL	NEG	POS	NEG
	B/GL/1739/54	1.0 $TCID_{50}$/mL	NEG	POS	NEG
	B/Maryland/1/59	1.0 $TCID_{50}$/mL	NEG	POS	NEG
	B/Panama/45/90[c]	1.0 $TCID_{50}$/mL	NEG	POS	NEG
	B/Florida/07/2004[d]	1.0 $TCID_{50}$/mL	NEG	POS	NEG

Virus	Strain	Target Concentration	Result		
			Flu A	Flu B	RSV
	B/Florida/02/06[c]	1.0 $TCID_{50}$/mL	NEG	POS	NEG
	B/Florida/04/06[d]	1.0 $TCID_{50}$/mL	NEG	POS	NEG
	B/Hong Kong/5/72	1.0 $TCID_{50}$/mL	NEG	POS	NEG
	B/Wisconsin/01/2010[d]	1.0 $TCID_{50}$/mL	NEG	POS	NEG
	B/Malaysia/2506/04[c]	1.0 $TCID_{50}$/mL	NEG	POS	NEG
	B/Taiwan/2/62	1.0 $TCID_{50}$/mL	NEG	POS	NEG
	B/Brisbane/60/2008[c]	1.0 $TCID_{50}$/mL	NEG	POS	NEG
RSV A	RSV-A/NY (Clinical unknown)	3.0 $TCID_{50}$/mL	NEG	NEG	POS
	RSV-A/WI/629-8-2/2007	3.0 $TCID_{50}$/mL	NEG	NEG	POS
	RSV-A/WI/629-11-1/2008	3.0 $TCID_{50}$/mL	NEG	NEG	POS
RSV B	RSV-B/WV14617/85	7.0 $TCID_{50}$/mL	NEG	NEG	POS
	RSV-B/CH93(18)-18	7.0 $TCID_{50}$/mL	NEG	NEG	POS

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

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

[c] Known Victoria lineage.

[d] Known Yamagata lineage.

20.4 Interfering Substances Study

In a non-clinical study, potentially interfering substances that may be present in the nasopharynx were evaluated directly relative to the performance of the Xpert Xpress Flu/RSV test. Potentially interfering substances in the 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. Negative samples (n = 8) were tested per each substance to determine the effect on the performance of the sample processing control (SPC). Positive samples (n = 8) were tested per substance with six influenza (four influenza A and two influenza B) and four RSV (two RSV A and two RSV B) strains spiked at 3X the analytical LoD determined for each strain. All results were compared to positive and negative simulated background matrix controls. The simulated background matrix consisted of 2.5% (w/v) porcine mucin, 1% (v/v) human whole blood in 0.85% sodium chloride (NaCl) formulated in 1x PBS solution with 15% glycerol, which was then diluted 1:5 in UTM. The evaluated substances are listed in Table 18 with active ingredients and concentrations tested shown. None of the substances caused interference of the assay at the concentrations tested in this study. All positive and negative replicates were identified correctly using the Xpert Xpress Flu/RSV test.

Table 18. Potentially Interfering Substances in the Xpert Xpress Flu/RSV Test

Substance/Class	Description/Active Ingredient	Concentration Tested
Control	Simulated background matrix	100% (v/v)
Beta-adrenergic bronchodilator	Albuterol Sulfate	0.83 mg/mL (equivalent to 1 dose per day)
Blood	Blood (Human)	2% (v/v)
BD™ Universal Viral Transport System	Transport Media	100% (v/v)
Remel M4®	Transport Media	100% (v/v)

Substance/Class	Description/Active Ingredient	Concentration Tested
Remel M4RT®	Transport Media	100% (v/v)
Remel M5®	Transport Media	100% (v/v)
Remel M6®	Transport Media	100% (v/v)
Throat lozenges, oral anesthetic and analgesic	Benzocaine, Menthol	1.7 mg/mL
Mucin	Purified Mucin protein (Bovine or porcine submaxillary gland)	2.5% (w/v)
Antibiotic, nasal ointment	Mupirocin	10 mg/mL
Saline Nasal Spray	Sodium Chloride (0.65%)	15% (v/v)
Anefrin Nasal Spray	Oxymetazoline, 0.05%	15% (v/v)
PHNY Nasal Drops	Phenylephrine, 0.5%	15% (v/v)
Tamiflu Anti-viral drugs	Zanamivir	7.5 mg/mL
Antibacterial, systemic	Tobramycin	4 µg/mL
Zicam Nasal Gel	Luffa opperculata, Galphimia glauca, Histaminum hydrochloricum Sulfur	15% (w/v)
Nasal corticosteroid	Fluticasone Propionate	5 µg/mL

20.5 Carry-over Contamination Study

A study was conducted to demonstrate that single-use, self-contained GeneXpert cartridges prevent carry-over contamination of negative samples if preceded by very high positive samples in the same GeneXpert module. The study consisted of a negative sample processed in the same GeneXpert module immediately following a very high influenza A sample (A/Victoria/361/2011, $2x10^7$ $TCID_{50}$/mL) or a very high RSV A sample (A/Long/MD/26, $1x10^4$ $TCID_{50}$/mL) spiked into a simulated background matrix. This testing scheme was repeated 20 times on two GeneXpert modules for a total of 82 runs resulting in 40 positive and 42 negative specimens for each virus type. All 40 positive samples were correctly reported as **Flu A POSITIVE**; **Flu B NEGATIVE**; **RSV NEGATIVE** or **Flu A NEGATIVE**; **Flu B NEGATIVE**; **RSV POSITIVE**. All 42 negative samples were correctly reported as **Flu A NEGATIVE**; **Flu B NEGATIVE**; **RSV NEGATIVE**.

20.6 Competitive Interference Study

Competitive interference of the assay caused by the presence of two targets in the Xpert Xpress Flu/RSV test was evaluated by testing individual influenza and RSV strains near the LoD in the presence of different influenza or RSV strains at a higher concentration in a simulated background matrix. The concentration of each strain at LoD ranged from 0.45 $TCID_{50}$/mL to 1.6 $TCID_{50}$/mL and the concentration of the competitive strains ranged from 10^1 $TCID_{50}$/mL to 10^4 $TCID_{50}$/mL. Analytical competitive interference was assessed using one (1) seasonal Flu A H3 strain (H3/Victoria/361/2011), one (1) Flu B strain (B/Mass/2/2012), one (1) RSV A strain (RSV-A/2/Australia/61), and one (1) RSV B strain (RSV-B/Wash/18537/62). Replicates of 20 were tested for each target strain and each competitive strain combination. The normal binomial distribution with 20 replicate samples at LoD is between 17 and 20 positive results based on the binomial distribution with N=20, p=.95 (X~Bin(20,0.95)). Therefore, sets of 20 with 16 or less positives would be rare and an indication of a competitive inhibitory effect due to high levels of a competing analyte.

With Flu A/Victoria/361/2011 at a concentration of 0.8 $TCID_{50}$/mL no competitive inhibitory effects were observed in the presence of $1x10^3$ $TCID_{50}$/mL of Flu B/Mass/2/2012; $1x10^3$ $TCID_{50}$/mL of RSV-A/2/Australia/6; or $1x10^4$ $TCID_{50}$/mL of RSV-B/Wash/18537/62.

With Flu B/Mass/2/2012 at a concentration of 0.45 $TCID_{50}$/mL competitive inhibitory effects were observed in the presence of $1x10^3$ $TCID_{50}$/mL of Flu A/Victoria/361/2011. No competitive inhibitory effects were observed in the presence of $1x10^2$ $TCID_{50}$/mL of Flu A/Victoria/361/2011; $1x10^3$ $TCID_{50}$/mL of RSV-A/2/Australia/6; or $1x10^3$ $TCID_{50}$/mL of RSV-B/Wash/18537/62.

With RSV-A/2/Australia/6 at a concentration of 1.1 $TCID_{50}$/mL competitive inhibitory effects were observed in the presence of $1x10^3$ $TCID_{50}$/mL of Flu A/Victoria/361/2011. No competitive inhibitory effects were observed in the presence of $1x10^2$ $TCID_{50}$/mL of Flu A/Victoria/361/2011; or $1x10^3$ $TCID_{50}$/mL of Flu B/Mass/2/2012.

With RSV-B/Wash/18537/62 at a concentration of 0.9 $TCID_{50}$/mL competitive inhibitory effects were observed in the presence of $1x10^2$ $TCID_{50}$/mL of Flu A/Victoria/361/2011 or $1x10^3$ $TCID_{50}$/mL of Flu B/Mass/2/2012. No competitive inhibitory effects were observed in the presence of 10 $TCID_{50}$/mL of Flu A/Victoria/361/2011; or $1x10^2$ $TCID_{50}$/mL of Flu B/Mass/2/2012. When the concentration of RSV-B/Wash/18537/62 was increased to 1.6 $TCID_{50}$/mL, no competitive inhibitory effects were observed in the presence of $1x10^2$ $TCID_{50}$/mL of Flu A/Victoria/361/2011; or $1x10^3$ $TCID_{50}$/mL of Flu B/Mass/2/2012.

Under the conditions of this study, internal competitive inhibitory effects were observed on the targets (Flu A, Flu B, and RSV) in the presence of two targets for the Xpert Xpress Flu/RSV test. The competitive inhibitory effect on the Xpert Xpress Flu/RSV targets is addressed in the Limitations section of this package insert.

21 Reproducibility

Reproducibility was established in a multi-center, blinded study using a 7-member specimen panel. Testing was performed at three sites (one internal, two external) using the GeneXpert Dx system, the Infinity-48 system, and the Infinity-80 system. Testing was conducted for 6 (not necessarily consecutive) days, with three lots of Xpert Xpress Flu/RSV cartridges and consisted of two testing days per lot. Each site had two operators, one experienced and one inexperienced, who tested each panel in duplicate twice each day. Results are summarized in Table 19.

Table 19. Summary of Reproducibility Results

Sample ID	Site 1/Infinity-80			Site 2/DX			Site 3/Infinity-48			% Total Agreement by Sample[a]
	Op 1	Op 2	Site	Op 1	Op 2	Site	Op 1	Op 2	Site	
Negative	100% (24/24)	100% (24/24)	100% (48/48)	100% (24/24)	100% (24/24)	100% (48/48)	100% (24/24)	100% (24/24)	100% (48/48)	100% (144/144)
Flu A-Low Pos	87.0% (20/23)	95.8% (23/24)	91.5% (43/47)	95.7% (22/23)	91.7% (22/24)	93.6% (44/47)	100% (23/23)	91.3% (21/23)	95.7% (44/46)	93.6% (131/140)[b]
Flu A-Mod Pos	100% (24/24)	100% (24/24)	100% (48/48)	100% (23/23)	100% (23/23)	100% (46/46)	100% (24/24)	100% (24/24)	100% (48/48)	100% (142/142)[b]
Flu B-Low Pos	95.8% (23/24)	95.8% (23/24)	95.8% (46/48)	95.8% (23/24)	95.8% (23/24)	95.8% (46/48)	95.8% (23/24)	91.7% (22/24)	93.8% (45/48)	95.1% (137/144)
Flu B-Mod Pos	100% (23/23)	100% (24/24)	100% (47/47)	100% (24/24)	100% (24/24)	100% (48/48)	100% (24/24)	100% (23/23)	100% (47/47)	100% (142/142)[b]
RSV-Low Pos	91.7% (22/24)	87.5% (21/24)	89.6% (43/48)	100% (23/23)	100% (24/24)	100% (47/47)	91.7% (22/24)	95.8% (23/24)	93.8% (45/48)	94.4% (135/143)[b]
RSV-Mod Pos	100% (24/24)	100% (23/23)	100% (47/47)	100% (23/23)	100% (24/24)	100% (47/47)	100% (24/24)	100% (24/24)	100% (48/48)	100% (142/142)[b]

[a] Agreement calculated based on expected result: Negative for Negative (targeted positivity: 0%); Positive for Low Pos (targeted positivity: 95%) and Mod Pos (targeted positivity: 100%) samples.

[b] Eleven samples 2x indeterminate [Flu A Low Pos (4); Flu A Mod Pos (2); Flu B Mod Pos (2); RSV Low Pos (1); RSV Mod Pos (2)].

The reproducibility of the Xpert Xpress Flu/RSV test was also evaluated in terms of the fluorescence signal expressed in Ct values for each target detected. The mean, standard deviation (SD), and coefficient of variation (CV) between-sites, between-days, between-lots and between-operators for each panel member are presented in Table 20.

Table 20. Summary of Reproducibility Data

Sample	Assay Channel (Analyte)	N[a]	Mean Ct	Between-Site		Between-Lot		Between-Day		Between-Operator		Within-Assay		Total	
				SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
Negative	SPC	144	32.3	0	0	0.7	2.1	0	0	0.2	0.5	0.6	1.8	0.9	2.8
Flu A-Low Pos	FluA1	131	35.3	0	0	0.4	1.0	0.6	1.7	0.1	0.2	0.9	2.6	1.2	3.3
Flu A-Mod Pos	FluA1	142	33.1	0	0	0.1	0.4	0.1	0.4	0	0	0.6	1.9	0.7	2.0
Flu B-Low Pos	FluB	137	34.6	0	0	0	0	0.4	1.3	0	0	1.4	4.1	1.5	4.3
Flu B-Mod Pos	FluB	142	32.3	0.1	0.3	0.2	0.7	0	0	0.2	0.7	0.8	2.5	0.9	2.7
RSV-Low Pos	RSV	135	36.5	0	0	0.6	1.7	0	0	0.5	1.3	0.9	2.6	1.2	3.3
RSV-Mod Pos	RSV	142	33.6	0.1	0.2	0.1	0.3	0	0	0.2	0.5	0.4	1.3	0.5	1.4

[a] Results with non-zero Ct values of 144.

22 References

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7. Clinical and Laboratory Standards Institute. Protection of Laboratory Workers from Occupationally Acquired Infections; Approved Guideline. Document M29 (refer to latest edition).
8. Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006.
9. Occupational Safety and Health Standards, Hazard Communication, Toxic and Hazard Substances (March 26, 2012) (29 C.F.R., pt. 1910, subpt. Z).

23 Cepheid Headquarters Locations

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24 Technical Assistance

Before contacting Cepheid Technical Support, collect the following information:

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

US

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

France

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

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

25 Table of Symbols

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

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IVD CE

26 Revision History

Description of Changes: 301-6580, Rev. G to Rev. H

Purpose: Updates to the Instructions for Use

Section	Description of Change
Trademark, Patents and Copyright Statements	Updated to current legal standards.
8	Updates to the Materials Required but Not Provided section.
9.2	Updates to the Warnings in the Specimen section.
25	Addition of the CH REP symbol, definition, and address. Addition of the Importer symbol, definition, and address.
26	Addition of the Revision History section and table.
Throughout	Updates to the formatting and design of the IFU.