

Xpert[®] Xpress Strep A

REF XPRSTREPA-10

REF XPRSTREPA-120

For Information Only - Not a Controlled Copy

Instructions For Use

CLIA Complexity: Waived

IVD

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See Section 29, Revision History for a description of changes.

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Xpert[®] Xpress Strep A

For *In Vitro* Diagnostic Use



For use with throat swab specimens.

CLIA Complexity: Waived

A Certificate of Waiver is required to perform this test in a CLIA Waived setting. To obtain CLIA waiver information and a Certificate of Waiver, please contact your state health department. Additional CLIA waiver information is available at the Centers for Medicare and Medicaid website at www.cms.hhs.gov/CLIA.

Failure to follow the instructions or modification to the test system instructions will result in the test no longer meeting the requirements for waived classification.

1 Proprietary Name

Xpert[®] Xpress Strep A

2 Common or Usual Name

Xpert Xpress Strep A

3 Intended Use

The Xpert Xpress Strep A test, performed on the GeneXpert[®] Xpress System, is a rapid, qualitative *in vitro* diagnostic test for the detection of *Streptococcus pyogenes* (Group A β -hemolytic *Streptococcus*, Strep A) in throat swab specimens from patients with signs and symptoms of pharyngitis. The Xpert Xpress Strep A test can be used as an aid in the diagnosis of Group A Streptococcal pharyngitis. The test is not intended to monitor treatment for Group A *Streptococcus* infections.

The Xpert Xpress Strep A test utilizes an automated real-time polymerase chain reaction (PCR) to detect *Streptococcus pyogenes* DNA.

4 Summary and Explanation

Group A streptococci are gram-positive, beta-hemolytic bacterial pathogens that commonly cause infections in the throat (pharyngitis or “strep throat”) or on skin (cellulitis and impetigo), and can cause a wide range of other infections (e.g., sepsis, pneumonia, and meningitis). Pharyngitis may also be caused by other bacteria including *Neisseria gonorrhoeae* and *Corynebacterium diphtheriae*, for which specific culture methods are required. If left untreated, mild infections can lead to more serious infections. The most severe but least common forms of invasive Group A streptococcal disease are necrotizing fasciitis and streptococcal toxic shock syndrome (STSS). Approximately 9,000 to 11,500 cases of invasive Group A streptococcal (GAS) disease occur annually in the United States, resulting in 1,000 to 1,800 deaths, although several million cases of strep throat and impetigo occur each year.¹ Treating an infected person with an appropriate

antibiotic generally prevents the spread of the infection and reduces the risk of post-infectious complications, such as rheumatic fever and acute glomerular nephritis.²

The Xpert Xpress Strep A test is a rapid PCR test for the qualitative detection of Group A streptococci from throat swab specimens without the need for culture confirmation of negative Xpert Xpress Strep A results. For negative samples, the time to result is 24 minutes. For positive samples, the time to result can be as early as 18 minutes.

5 Principle of the Procedure

The Xpert Xpress Strep A test is an automated *in vitro* diagnostic test for qualitative detection of *Streptococcus pyogenes* DNA. The test is performed on the Cepheid GeneXpert Xpress System. With this platform, an untrained operator can run the test by performing three simple steps: 1) transfer liquid sample to the cartridge with a transfer pipette, 2) run the test on the GeneXpert Xpress System, and 3) read the results.

The GeneXpert Xpress System automates and integrates sample preparation, nucleic acid extraction, amplification, and detection of the target sequences in samples by using real-time PCR.

The GeneXpert Xpress System consists of an instrument, computer, and preloaded software for running tests and viewing the results. The system requires the use of single-use disposable GeneXpert cartridges that hold the PCR reagents and host the PCR processes. Because the cartridges are self-contained, the risk of cross-contamination between samples is minimized. For a full description of the system, refer to the *GeneXpert Xpress System User's Guide*.

The Xpert Xpress Strep A test includes reagents for the detection of Group A streptococcal bacterial DNA from throat swab specimens from patients with signs and symptoms of pharyngitis. 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 that reagent rehydration, PCR tube filling, and all reaction components, including probes and dyes, are present and functional in the cartridge.

An Early Assay Termination function provides positive results if the signal from the target DNA reaches a predetermined threshold before the full 43 PCR cycles have been completed. When the Strep A target level is high enough to generate very early Cts (≤ 30 Cts), the SPC amplification curve will be not seen and its results will not be reported as the SPC Ct may not reach the expected cycle threshold in high Strep A titer specimens.

6 Reagents and Instruments

6.1 Materials Provided

The Xpert Xpress Strep A kit (XPRSTREPA-10) contains sufficient reagents to process 10 specimens or quality control samples and the Xpert Xpress Strep A kit (XPRSTREPA-120) contains sufficient reagents to process 120 specimens or quality control samples.

Each kit contains the following:

Xpert Xpress Strep A Cartridges with Integrated Reaction Tubes	10 per kit	120 per kit
Bead 1, Bead 2, and Bead 3 (freeze-dried)	1 of each per cartridge	1 of each per cartridge
Lysis Reagent (Guanidinium Thiocyanate)	1.5 mL per cartridge	1.5 mL per cartridge
Sodium Hydroxide	1.5 mL per cartridge	1.5 mL per cartridge
Elution Reagent	2.0 mL per cartridge	2.0 mL per cartridge
Disposable Transfer Pipettes	12 per kit	144 per kit
Instructions for Use (Package Insert)	1 per kit	1 per kit
CLIA Complexity: Waived (For use with the GeneXpert Xpress System only)		
Quick Reference Instructions	1 per kit	1 per kit
CLIA Complexity: Waived (For use with the GeneXpert Xpress System-Tablet Configuration only)		
Quick Reference Instructions	1 per kit	1 per kit
CLIA Complexity: Waived (For use with the GeneXpert Xpress System-Hub Configuration only)		
CD	1 per kit	1 per kit
<ul style="list-style-type: none"> • Assay Definition File (ADF) • Instructions to import ADF into GeneXpert software • Instructions for Use (Package Insert) (For use with the GeneXpert Dx and Infinity Systems only) 		

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 Strep A cartridges at 2–28 °C until the expiration date provided on the label.
- Do not open the 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 is wet or has leaked.

8 Materials Required but Not Provided

- Copan Liquid Amies Elution Swab (ESwab™) Collection and Transport System, Copan catalog number 480CFA with 50 kits per shelf pack; purple non-capture cap collection kit.
- GeneXpert Xpress System (Tablet configuration): GeneXpert Xpress II and IV Instruments with proprietary GeneXpert Xpress Software Version 5.x, tablet computer device with touchscreen, barcode scanner, external CD drive, wireless printer, *Getting Started Guide*, and *GeneXpert Xpress System User's Guide*.
- GeneXpert Xpress System (Hub configuration): GeneXpert Xpress IV Instrument with proprietary GeneXpert Xpress Software Version 6.0 or higher, GeneXpert Hub with integrated computer, touchscreen monitor and barcode scanner, external CD drive, *Getting Started Guide*, and *GeneXpert Xpress System User's Guide*.

9 Materials Available but Not Provided

- NATtrol™ Strep A negative control, ZeptoMetrix Corporation catalog number NATSDG-6MC (inactivated *Streptococcus dysgalactiae* cells)
- NATtrol Strep A positive control, ZeptoMetrix Corporation catalog number NATSPY-6MC (inactivated *Streptococcus pyogenes* cells)

10 Warnings and Precautions

10.1 General

- For *in vitro* diagnostic use.
- For prescription use only.
- Treat all biological specimens, including used cartridges, as if capable of transmitting infectious agents. All biological specimens should be handled using standard precautions. Guidelines for specimen handling are available from the U.S. Centers for Disease Control and Prevention³ and the Clinical and Laboratory Standards Institute⁴.
- Follow safety procedures set by your institution for working with chemicals and handling biological samples.
- Performance characteristics of this test have been established with the specimen type listed in the Intended Use section only. The performance of this test with other specimen types or samples has not been evaluated.
- Reliable results are dependent on adequate specimen collection, transport, storage and processing. Incorrect test results may occur from improper specimen collection, handling or storage, technical error, sample mix-up or because the number of organisms in the specimen is below the limit of detection of the test. Careful compliance with the Instructions for Use and the

GeneXpert Xpress System Operator Manual are necessary to avoid erroneous results.

- Performing the Xpert Xpress Strep A test outside the recommended storage temperature ranges and time may produce erroneous or indeterminate results (i.e., **NO RESULT – REPEAT TEST** or **INSTRUMENT ERROR**).

10.2 Specimen

- For collection and transport of throat swab specimens, use the ESwab collection kit.
- Throat swab specimens must be collected and tested before the printed expiration date on the ESwab collection kit label.
- Maintain proper storage conditions during specimen transport to ensure the integrity of the specimen (see Section 12). Specimen stability under shipping conditions other than those recommended has not been evaluated.
- Do not freeze ESwab specimens.
- Proper sample collection, storage, and transport are essential for correct results.

10.3 Test/Reagent

- Do not open the Xpert Xpress Strep A 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 indeterminate results.
- Do not place the sample ID label on the cartridge lid or on the barcode label of the cartridge.
- Do not use a cartridge with a damaged barcode label.
- Do not use a cartridge that has a damaged reaction tube.
- It is recommended that the Xpert Xpress Strep A cartridges be at room temperature (20–30°C) when used for testing.
- Each single-use Xpert Xpress Strep A 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 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 repeat the cleaning of the work area with 70% denatured ethanol. Wipe work surfaces and allow to dry completely before proceeding.
- Biological specimens, transfer devices, and used cartridges should be considered capable of transmitting infectious agents requiring standard precautions. Follow your institution's environmental waste procedures for proper disposal of used cartridges and unused reagents. These materials may exhibit characteristics of chemical hazardous waste requiring specific disposal. If country or regional regulations do not provide clear direction on proper disposal, biological specimens and used cartridges should be disposed per WHO [World Health Organization] medical waste handling and disposal guidelines.

11 Chemical Hazards^{5,6}

Sodium Hydroxide

- Signal Word: WARNING ⚠

Lysis Reagent

- Contains Guanidinium Thiocyanate
- Signal Word: WARNING ⚠
- **UN GHS Hazard Statements:**
 - Harmful if swallowed.
 - Causes skin irritation.
 - Causes serious eye irritation.
- **UN GHS Precautionary Statements:**
 - **Prevention**
 - Wash thoroughly after handling.
 - Wear protective gloves/protective clothing/eye protection/face protection.
 - **Response**
 - IF ON SKIN: Wash with plenty of soap and water.
 - Specific treatment, see supplemental first aid information.
 - Take off contaminated clothing and wash before reuse.
 - 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 ensure the integrity of the specimen and performance of the test. Inadequate specimen collection, improper specimen handling and/or transport may yield a false result; therefore, specimen collection requires specific training and guidance due to the importance of specimen quality for accurate test results. The Xpert Xpress Strep A test is validated for use only with throat swab specimens. Follow your institution's guidelines for collecting swab specimens using a recommended collection and transport device (see Section 8) and/or follow the instructions below.

12.1 Swab Collection Procedure

1. Use the ESwab Collection and Transport System (Copan catalog number 480CFA). Remove the swab from the wrapper.
2. Swab the posterior pharynx, tonsils, and other inflamed areas. Avoid touching the tongue, cheeks, and teeth with the swab when collecting specimens.
3. Uncap the ESwab transport tube.
4. Place the specimen containing swab into the ESwab transport tube and break the swab at the indicated score line.
5. Cap the ESwab transport tube.

Note Do not place multiple swabs in the same ESwab transport tube.

Note To reduce the potential for false negative results, do not collect throat swab specimens immediately after patients have used antiseptic mouthwash.

12.2 Specimen Transport and Storage

Specimen stability under shipping and storage conditions other than those listed in Table 1 have not been evaluated with the Xpert Xpress Strep A test.

Table 1. Specimen Transport and Storage Conditions

Specimen Collection Device	Specimen Transport and Storage Temperature (°C)	Specimen Storage Time
ESwab (Copan 480CFA)	15–30 °C	Up to 48 hours
	2–8 °C	Up to 6 days

13 Starting the System

1. Put on a clean pair of gloves.
2. Determine which system configuration you have (see Figure 1).

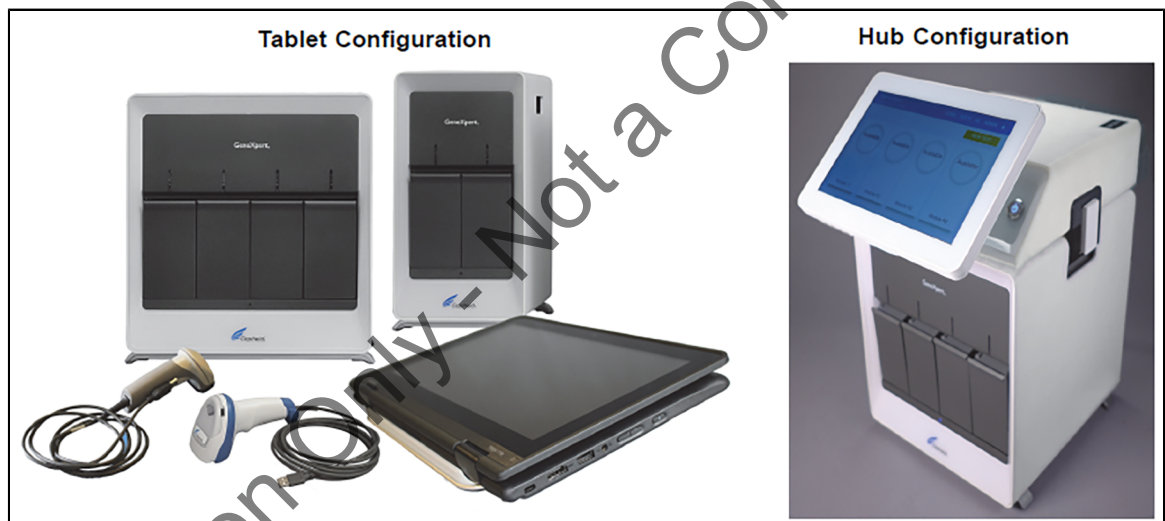


Figure 1. Tablet and Hub System Configurations

- For the *Tablet* configuration, see Section 13.1, Starting the Tablet Configuration.
- For the *Hub* configuration, see Section 13.2, Starting the Hub Configuration.

13.1 Starting the Tablet Configuration

Before you start the test, make sure that:

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

This section lists the basic steps for running the test. For detailed instructions, see the *GeneXpert Xpress System User's Guide*.

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

1. Turn on the GeneXpert Xpress instrument (GeneXpert Xpress II or GeneXpert Xpress IV).
2. Turn on the tablet computer:
 - *Windows*® 7: The **Windows 7 account** screen displays. Touch the **Cepheid-Admin** icon to continue.
 - *Windows*® 10: The **Windows Lock** screen displays. Swipe up to continue.
The **Windows Password** screen displays.
3. Touch **Password** to display the **keyboard**, then type your password.
4. Touch the **arrow** button at the right of the password entry area.
The GeneXpert Xpress Software starts.

13.2 Starting the Hub Configuration

Before you start the test, make sure that:

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

This section lists the basic steps for running the test. For detailed instructions, see the *GeneXpert Xpress System User's Guide*.

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

1. Turn on the GeneXpert Xpress instrument.
2. Turn on the Hub computer. The **Windows Lock** screen displays.
3. Swipe up to continue. The **Windows Password** screen displays.
4. Touch **Password** to display the **keyboard**, then type your Windows password.
5. Touch the **arrow** button at the right of the password entry area. The GeneXpert Xpress Software starts, and a **login** screen displays.
6. If enabled, you may log in by scanning a barcode on your institutional ID, using the barcode scanner (located behind the right side of the touchscreen). Then proceed to Step 9. Otherwise, follow the steps below to login manually.
7. Enter your User Name and Password (the virtual keyboard displays once you touch the entry fields).
8. Touch the **X** in the upper right of the virtual keyboard. The keyboard disappears, and the **LOGIN** button displays at the bottom of the screen. Touch the **LOGIN** button to continue.
9. The **Database Maintenance Reminder** screen and the **Archive Tests Reminder** dialog boxes may display, depending on your system configuration. For more information, see the *GeneXpert Xpress System User's Guide*.

13.3 Determining Your Software Version

When your Xpress opening screen displays, determine your software version and the procedure to follow (see Figure 2).

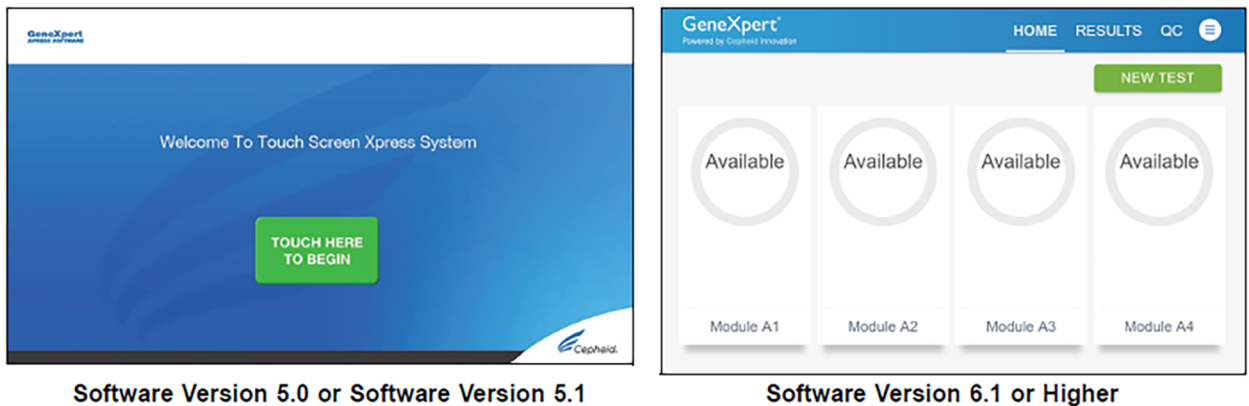


Figure 2. Xpress Opening Screens and Software Versions

- For Software Version 5.0 or Software Version 5.1, see Section 14.
- For Software Version 6.1 or higher, see Section 16.

14 GeneXpert Xpress Software Version 5.0 or Software Version 5.1

1. On the **Welcome** screen, touch the **TOUCH HERE TO BEGIN** button (see Figure 3).

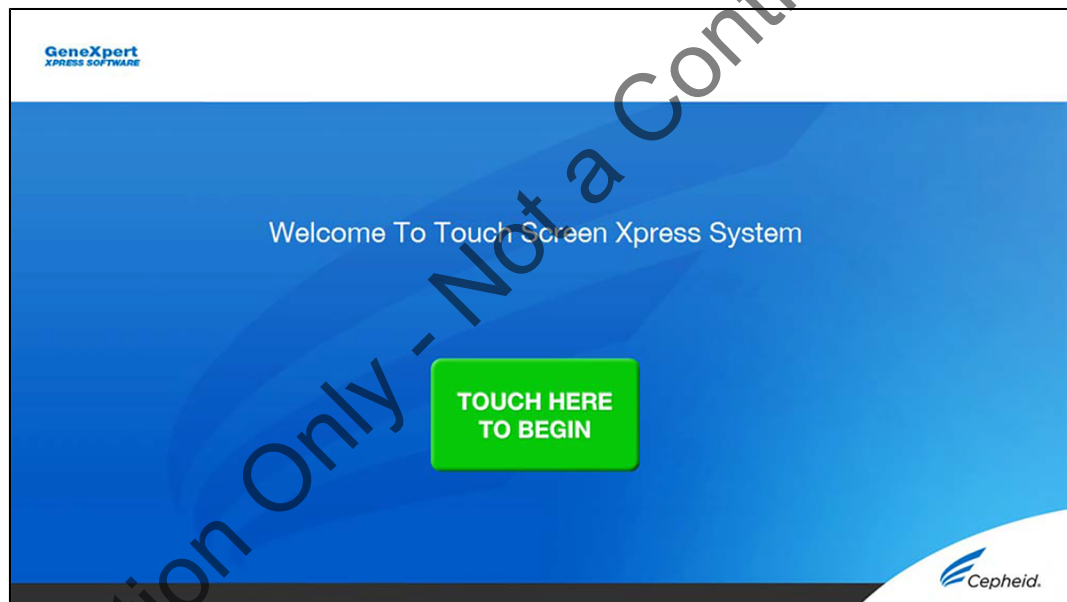


Figure 3. Welcome Screen

2. The **VIEW PREVIOUS TESTS** button displays. The **RUN NEW TEST** button displays on the **Home** screen within 3 minutes.

Note If the **Home** screen does not display **RUN NEW TEST**, the instrument was not powered up or is no longer powered on. Exit the software using the **EXIT** button. The GeneXpert Xpress instrument must first be turned on then turn on the computer. Click the **software icon** to launch software and enter the password.

14.1 Starting a Test

Note Instructions showing how to prepare the sample and the cartridge are shown on-screen in a video and are also described in the *Quick Reference Instructions* (QRI).

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

1. Put on a new pair of gloves if performing a new test.

2. Touch the **RUN NEW TEST** button on the **Home** screen (see Figure 4) to run a patient specimen or an external control.

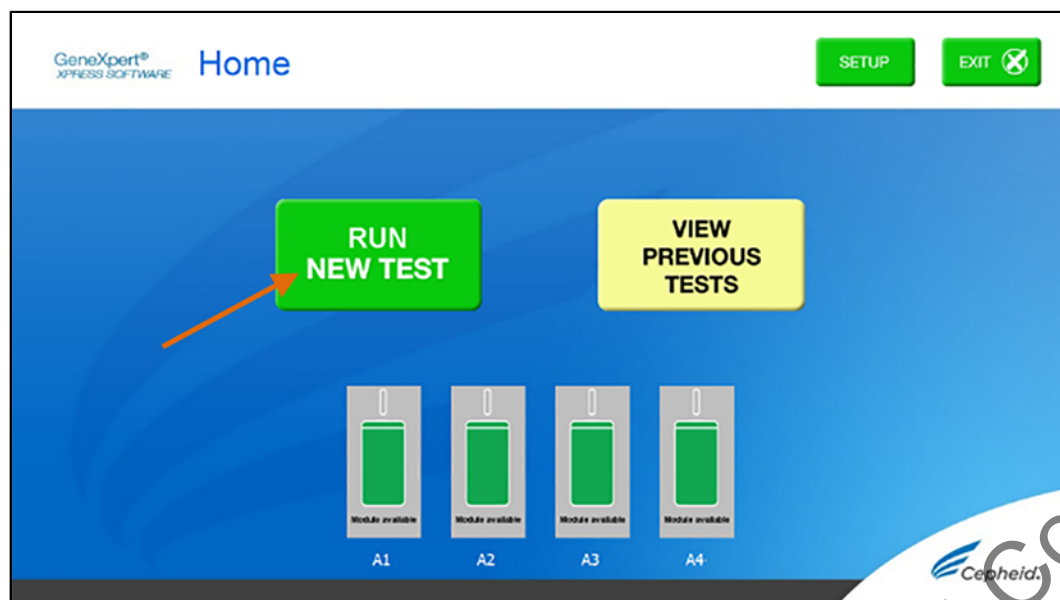


Figure 4. RUN NEW TEST button on Home Screen (GeneXpert Xpress IV screen shown)

3. Check that the specimen transport medium tube cap is closed.
4. If there is a Patient/Sample ID barcode, touch the **YES** button, then scan the Patient/Sample ID with the scanner. If there is no Patient/Sample ID barcode, touch the **NO** button, then manually enter the Patient/Sample ID and touch the **OK** button. For external control, type **Positive Control** or **Negative Control**.
5. Confirm the Patient/Sample ID. Touch **YES** if the Patient/Sample ID is correct.

14.2 Preparing the Specimen and Cartridge

The recommended environmental operating conditions for Xpert Xpress Strep A are 15–30°C, 20–80% relative humidity.

1. Remove a cartridge and a transfer pipette from the cartridge kit box.
2. Scan the barcode on the cartridge with the scanner.
3. Confirm that the name on the cartridge is Xpert Xpress Strep A (shown in Figure 5) and touch **YES** if the displayed information is correct. If applicable, enter your user name and password.

In the following steps, cartridges should be kept upright when handling or scanning. Do not rotate or tip the cartridge, because damage to the contents or injury to personnel may occur.

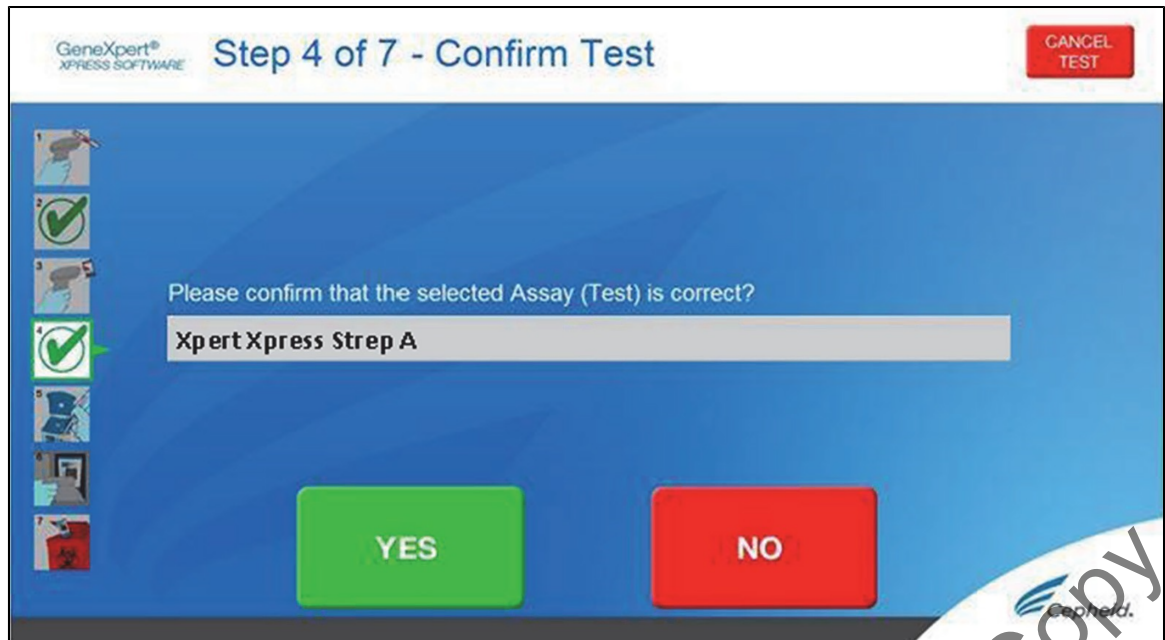


Figure 5. Confirm Screen Test

4. Watch the video before continuing. The video will repeat. Touch the **CONTINUE** button to exit video. The **Load Cartridge** screen appears.

Note The pipette received in the kit may not be identical to the one shown in the video. If the pipette received is different than the one shown in the video, please follow the written instructions in this document or in the QRI.

5. Mix specimen by vigorously shaking the specimen transport tube (ESwab tube) for 5 seconds. Open the cap on the specimen transport tube.
6. Open the cartridge lid by lifting the front of the cartridge lid.
7. Remove the transfer pipette from the wrapper. Follow the steps below in Option 1 or Option 2 according to the transfer pipette type included in the kit.

Note Do not place unwrapped pipette on the workbench.

Pipette Option 1:

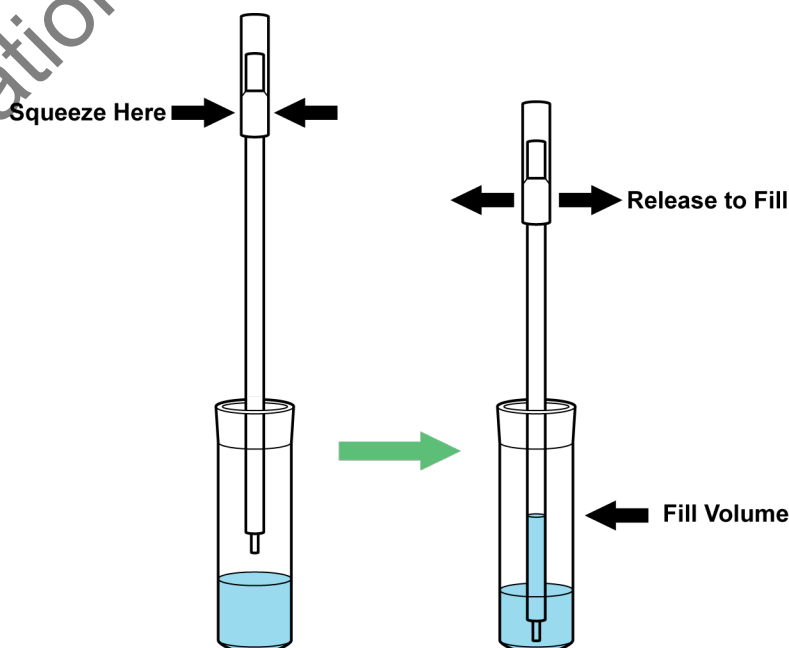


Figure 6. Transfer Pipette

1. Squeeze the bulb of the transfer pipette **completely** and place the pipette tip in the specimen transport tube containing the patient specimen (see Figure 6).
2. Release the bulb of the pipette to fill the pipette with the patient specimen. Check that the pipette does not contain bubbles.

3. To transfer the patient specimen to the cartridge, squeeze the bulb of the transfer pipette completely again to empty the contents of the pipette into the large opening (Sample Chamber) in the cartridge shown in Figure 7.



Figure 7. Cartridge (Top View)

Take care to dispense the **entire** volume of liquid into the sample chamber.

Note False negative or indeterminate results may occur if insufficient sample is added to the cartridge.

4. Close the cartridge lid.
5. Dispose of the used pipette in an appropriate waste container.

Pipette Option 2:

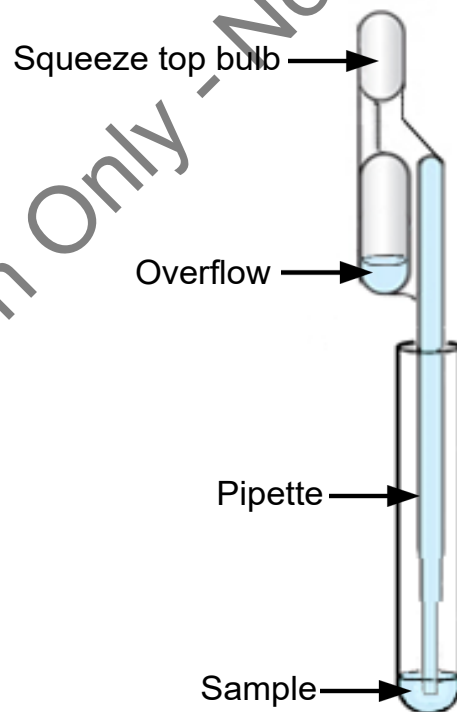


Figure 8. Transfer Pipette

1. Squeeze the top bulb of the transfer pipette **completely** and place the pipette tip in the specimen transport tube containing the patient specimen (see Figure 8).
2. Release the bulb of the pipette to fill the pipette with the patient specimen. Check that the pipette does not contain bubbles.
3. To transfer the patient specimen to the cartridge, squeeze the top bulb of the transfer pipette completely again to empty the contents of the pipette into the large opening (Sample Chamber) in the cartridge shown in Figure 9. It is okay to have excess specimen left in the overflow reservoir of the pipette (Figure 8).

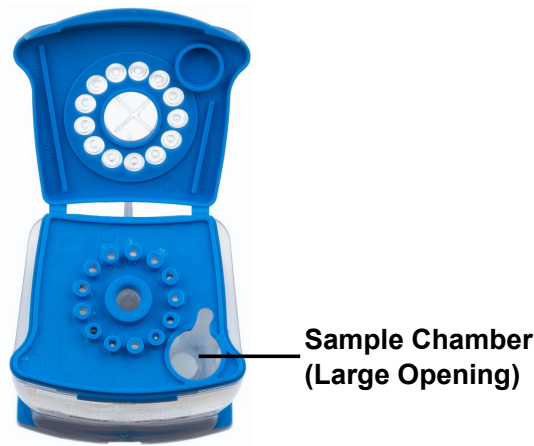


Figure 9. Cartridge (Top View)

Note Take care to dispense the **entire** volume of liquid in the pipette into the sample chamber. False negative or indeterminate results may occur if insufficient sample is added to the cartridge.

4. Close the cartridge lid.
5. Dispose of the used pipette in an appropriate waste container.

14.3 Loading the Cartridge

1. Pull open the module door with the flashing green light.
2. Load the cartridge with the barcode facing the operator onto the cartridge bay platform. Do not try to insert the cartridge past the cartridge bay platform.
3. Close the door until it clicks.
The green light stops flashing, and the test starts. The **Test in Progress** screen displays. When the test is completed (green light goes out), the door automatically unlocks and the **Remove Cartridge** screen displays.
4. Follow the on-screen instructions to remove the cartridge and to reset the module for a new test.
5. Touch **CONTINUE** to view the result of the test.
6. To print results, touch the **PRINT RESULT** button.
7. Remove cartridge. Dispose of the used cartridge and gloves according to your institution's standard practices.
8. To log out, touch the **SIGN OUT** button.

Note Do not turn off or unplug the instruments while a test is in progress. Turning off or unplugging the GeneXpert Xpress instrument or computer stops the test.

Note If the barcode on the cartridge does not scan or scanning the barcode results in an error message stating that the cartridge is expired, then repeat the test with a new cartridge.

Note If you have scanned the cartridge barcode in the Xpress software and the assay definition file is not available, a screen displays indicating that the assay definition file is not loaded or that the product code was not found on the system. If this screen displays, contact Cepheid Technical Support.

14.4 Time to Result

Time to result is 24 minutes. A strongly positive sample will have a time to result as early as 18 minutes.

14.5 Starting a New Test

1. Put on a clean pair of gloves.
2. Touch the **HOME** button to return to the **Home** screen.
3. Start a new test following the steps in Section 14.1, Starting a Test. Or for starting a test while a test is running or a new test with another user, see Section 14.6, Starting a New Test While a Test is Running.

14.6 Starting a New Test While a Test is Running

1. Put on a clean pair of gloves if performing a new test.
2. Touch the **HOME** button to go to the **Home** screen.
3. Touch the **SIGN OUT** button to log out the previous user, if applicable.
4. Start a new test following the steps in Section 14.1, Starting a Test.

15 Viewing Tests in Progress, Completed Tests, and Past Tests

15.1 Viewing Tests in Progress

1. Touch the **HOME** button to view the status of tests in progress.
2. Touch the **Test in progress touch for status** button.
The time remaining to complete the testing displays on the progress bar at the bottom of the **Test in Progress** screen.

15.2 Viewing Completed Tests

1. When a test is completed, touch the **Test complete, touch to continue** button.
The **Remove Cartridge** screen displays.
2. Follow the on-screen instructions to remove the cartridge.
3. Touch the **CONTINUE** button to view the result of the test.

15.3 Viewing Results of Past Tests

1. Touch the **VIEW PREVIOUS TESTS** button on the **Home** screen shown in Figure 10.

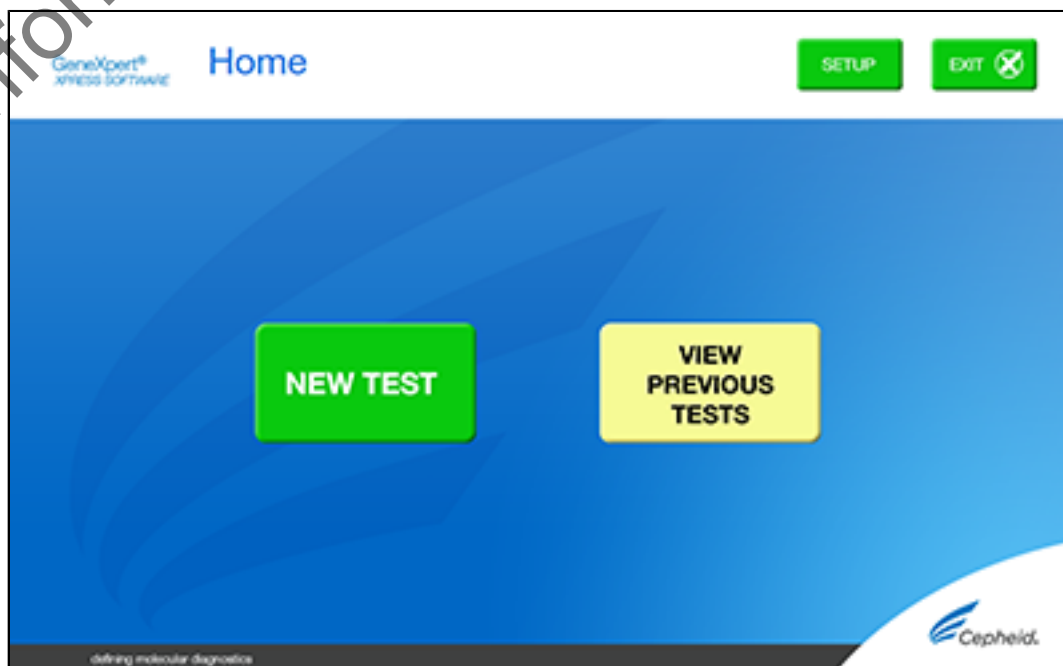


Figure 10. VIEW PREVIOUS TESTS button on Home Screen

2. Select the test by either touching the test name or using the **arrows** to select the test.
3. Touch the **SELECT** button shown in Figure 11 to view results.
4. To print results, touch the **PRINT RESULT** button.

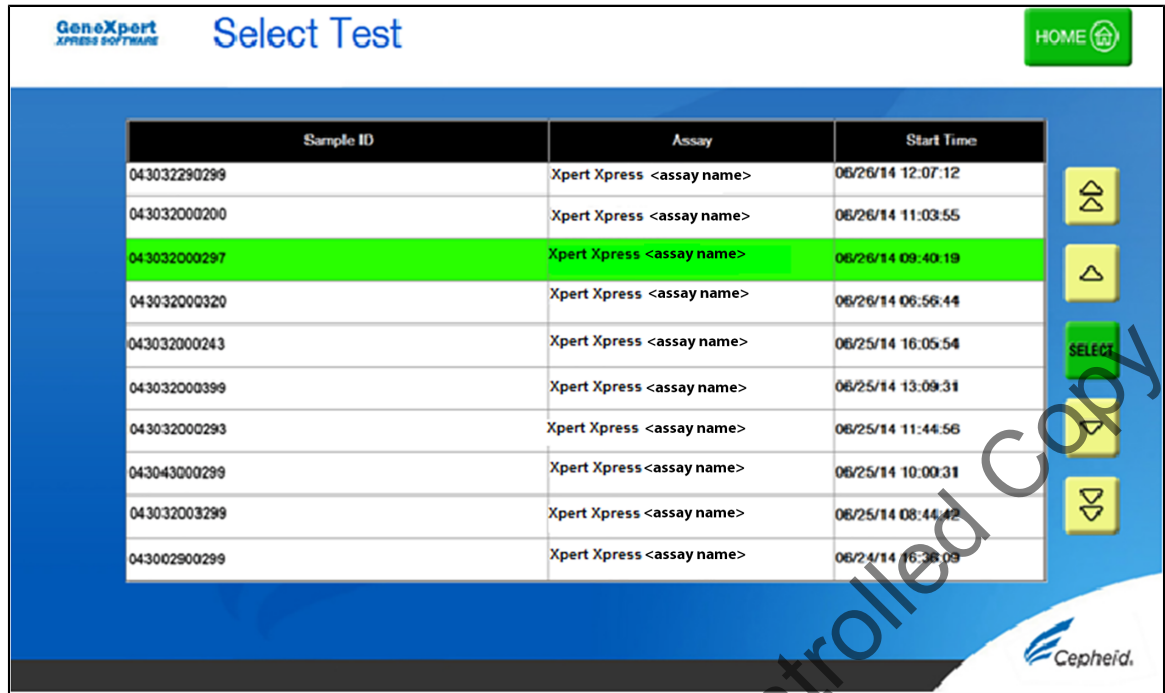


Figure 11. SELECT button

16 GeneXpert Xpress Software Version 6.1 or Higher

16.1 Starting a Test

Note Instructions showing how to prepare the sample and the cartridge are shown on-screen in videos and in the following procedure.

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

1. Put on a new pair of gloves if performing a new test.
2. Touch the **NEW TEST** button on the **Home** screen (see Figure 12).



Figure 12. Home Screen

3. Check that the specimen transport medium tube cap is closed.
If Patient Information is configured by an administrator, then the **Patient Information** screen displays (see Figure 13). If Patient Information is not configured, the **Sample ID** screen displays.
4. Skip to Preparing the Specimen and Cartridge if the **Sample ID** screen displays.



Figure 13. Patient Information Screen

5. Scan patient ID barcode or manually enter the Patient ID.
6. Touch **CONTINUE**. The Confirm **Patient Information** screen displays.

7. Verify the Patient ID and touch **CONFIRM**. The **Sample ID** screen displays.

16.2 Preparing the Specimen and Cartridge

The recommended environmental operating conditions for Xpert Xpress Strep A are 15–30°C, 20–80% relative humidity.

1. Remove a cartridge and a transfer pipette from the cartridge kit box.
2. Check that the transport medium tube cap is closed. Scan Sample ID barcode or manually enter the Sample ID for patient specimen.
3. Touch **CONTINUE**. The **Confirm Sample ID** screen displays.
4. Verify the Sample ID and touch **CONFIRM**. The **Scan Cartridge Barcode** screen displays (see Figure 14).

Note In the following steps, keep the cartridges upright when handling or scanning. Do not rotate or tip the cartridge, because damage to the contents or injury to personnel may occur.

Note If the barcode on the Xpert Xpress Strep A cartridge does not scan or scanning the barcode results in an error message stating that the cartridge is expired, then repeat the test with a new cartridge.

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

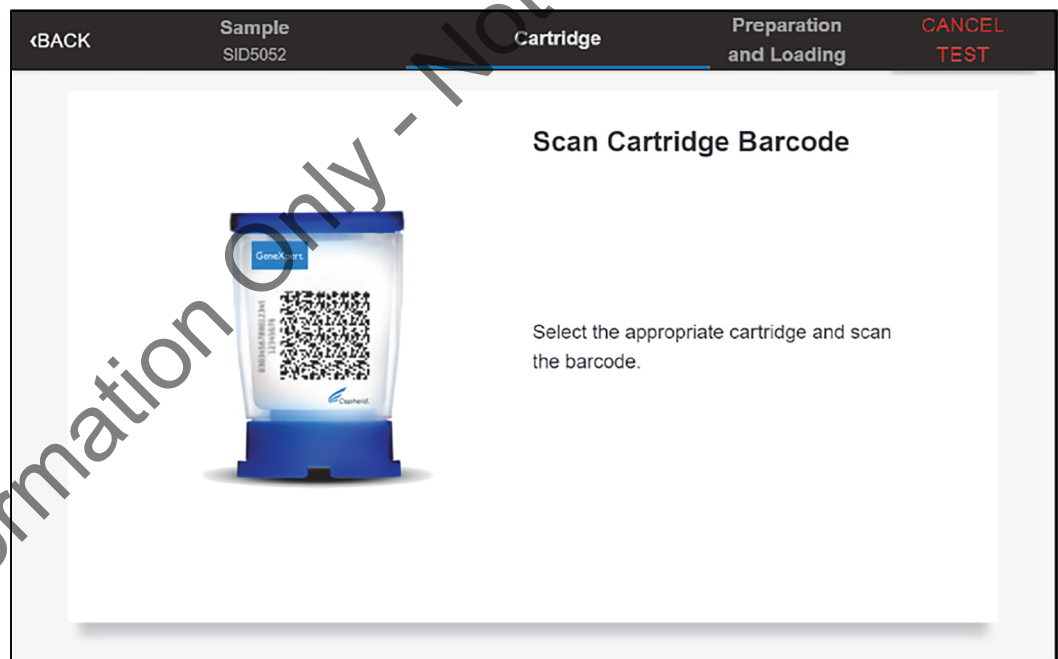


Figure 14. Scan Cartridge Barcode Screen

5. Select the appropriate cartridge with the sample and scan the cartridge barcode. After scanning, the **Confirm Test Information** screen displays (see Figure 15).

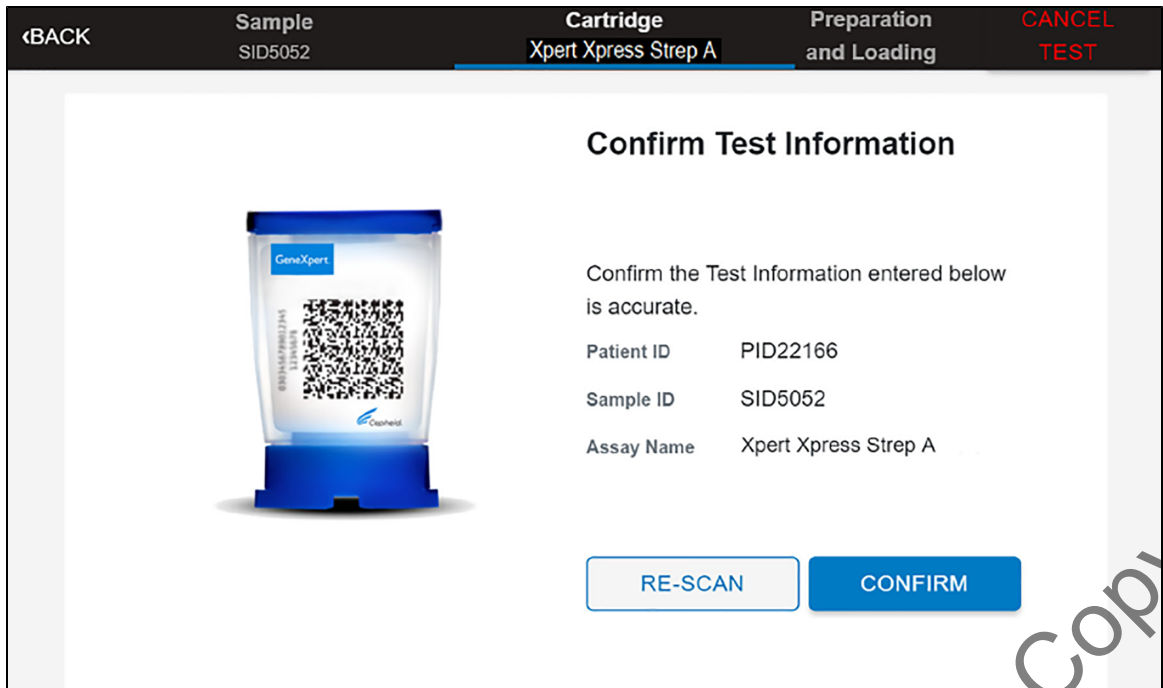


Figure 15. Confirm Test Information Screen

6. Verify that the correct cartridge has been scanned and that the test name matches the name of the test on the cartridge.
7. Touch **CONFIRM** if the displayed information is correct.
8. Depending on your configuration, the **Enter Credentials to Continue** screen may display (see Figure 16). If enabled, you may log in by scanning your institutional ID. Otherwise, manually enter your User Name and Password and touch **LOGIN** to continue.

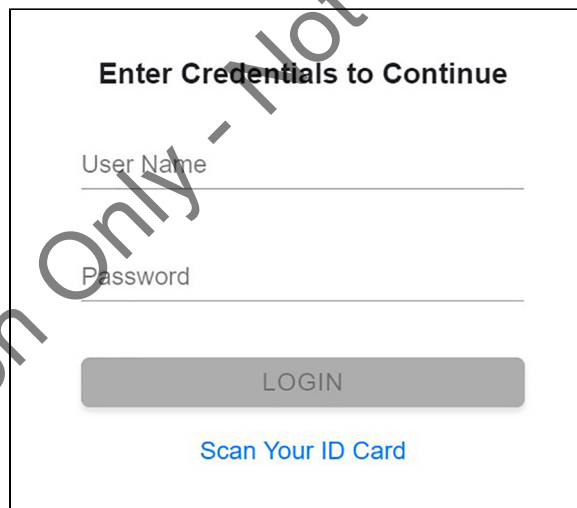


Figure 16. Enter Credentials to Continue Screen

9. The **Cartridge Preparation** screen displays (see Figure 17).



Figure 17. Cartridge Preparation Screen

10. A video clip shows the cartridge preparation steps. Prepare the cartridge according to the directions below, which are also shown in the video. Once complete, the video restarts from the beginning automatically. Touch the **CONTINUE** button to exit video.

Note The pipette received in the kit may not be identical to the one shown in the video. If the pipette received is different than the one shown in the video, please follow the written instructions in this document or in the QRI.

11. Verify the specimen ID on the patient specimen.
12. Confirm the name on the cartridge is Xpert Xpress Strep A. Specimen and cartridge are ready for use.
13. Mix specimen by vigorously shaking the specimen transport tube (ESwab tube) for 5 seconds. Open the cap on the specimen transport tube.
14. Open the cartridge lid by lifting the front of the cartridge lid.
15. Remove the transfer pipette from the wrapper. Follow the steps below in Option 1 or Option 2 according to the transfer pipette type included in the kit.

Note Do not place unwrapped pipette on the workbench.

Pipette Option 1:

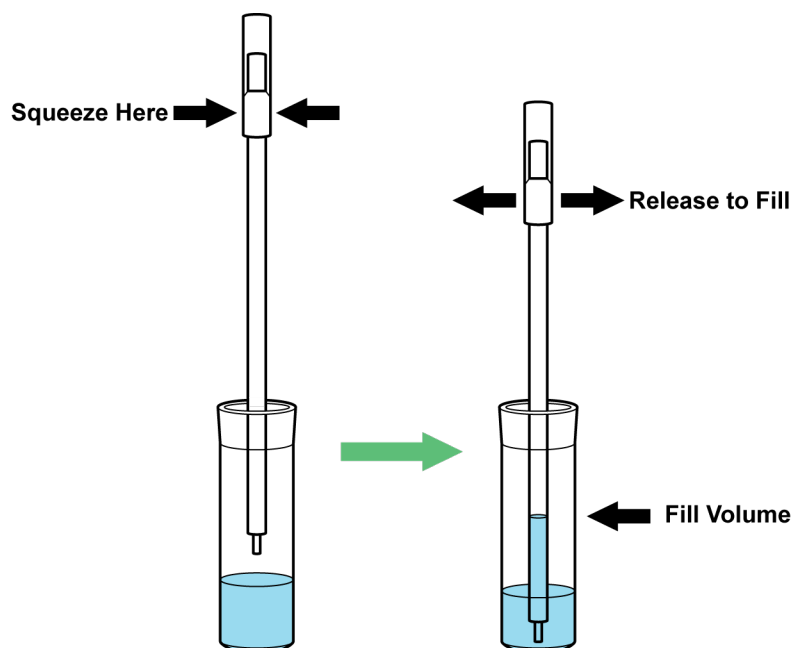


Figure 18. Transfer Pipette

1. Squeeze the bulb of the transfer pipette **completely** and place the pipette tip in the specimen transport tube containing the patient specimen (see Figure 18).
2. Release the bulb of the pipette to fill the pipette with the patient specimen. Check that the pipette does not contain bubbles.
3. To transfer the patient specimen to the cartridge, squeeze the bulb of the transfer pipette completely again to empty the contents of the pipette into the large opening (Sample Chamber) in the cartridge shown in Figure 19.

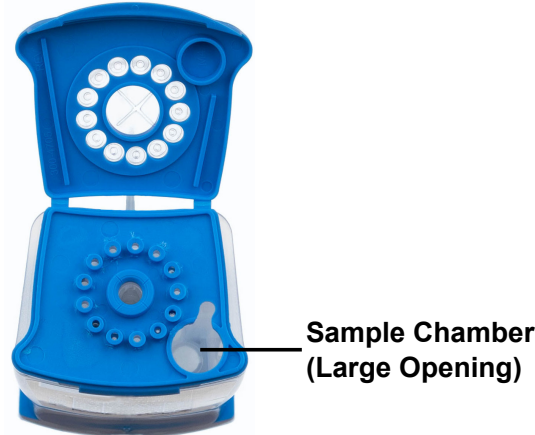


Figure 19. Cartridge (Top View)

Note Take care to dispense the **entire** volume of liquid into the sample chamber. False negative or indeterminate results may occur if insufficient sample is added to the cartridge.

4. Close the cartridge lid.
5. Dispose of the used pipette in an appropriate waste container.

Pipette Option 2:

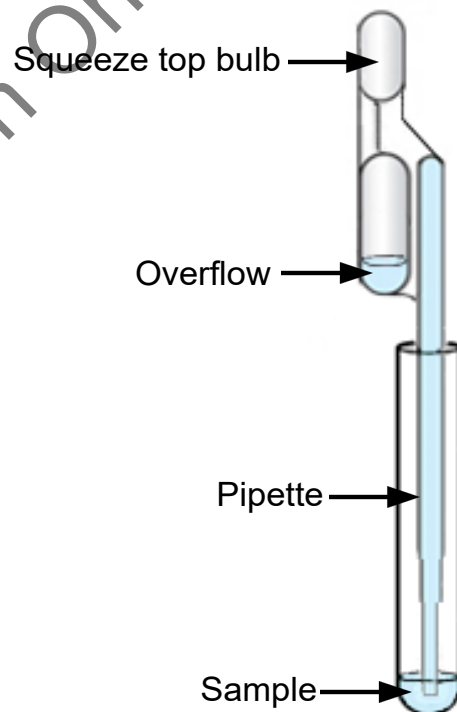


Figure 20. Transfer Pipette

1. Squeeze the top bulb of the transfer pipette **completely** and place the pipette tip in the specimen transport tube containing the patient specimen (see Figure 20).
2. Release the bulb of the pipette to fill the pipette with the patient specimen. Check that the pipette does not contain bubbles.

- To transfer the patient specimen to the cartridge, squeeze the top bulb of the transfer pipette completely again to empty the contents of the pipette into the large opening (Sample Chamber) in the cartridge shown in Figure 21. It is okay to have excess specimen left in the overflow reservoir of the pipette (Figure 20).

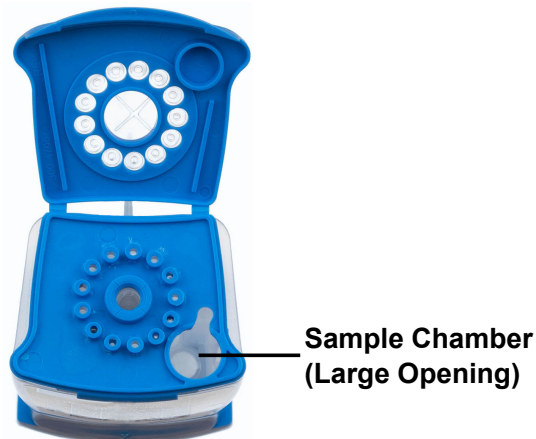


Figure 21. Cartridge (Top View)

Note Take care to dispense the **entire** volume of liquid in the pipette into the sample chamber. False negative or indeterminate results may occur if insufficient sample is added to the cartridge.

- Close the cartridge lid.
- Dispose of the used pipette in an appropriate waste container.

16.3 Loading the Cartridge

- Touch the **CONTINUE** button on the **Cartridge Preparation** screen. The **Load Cartridge into Module** screen displays (see Figure 22).
- Open the module door with the flashing green light.



Figure 22. Load Cartridge into Module Screen

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

Note While a test is running, you can start another test. See Section 16.4, Start a New Test While a Test is Running.

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

When the test is done, the green light goes out and the door automatically unlocks. The screen text changes to **Test Completed**. The **Test Completed** screen provides the results for the test just completed.

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

6. Open the module door, remove the used cartridge, and properly dispose of the cartridge according to your institution's policy.
7. Touch **HOME** to go back to the **Home** screen.
8. To log out, touch the **User Menu** icon, then select **Logout**.

16.4 Starting a New Test while a Test is Running

You can start a new test while another test is in progress.

1. Touch the **HOME** button on the **Test Running** screen.
2. For a new user log in, touch the **User Menu** icon to log in.
3. Repeat the steps in Section 16.1, Preparing the Specimen, and Section 16.3.
4. After a second test has started, touch the **HOME** button.

The status of both tests displays. The **Home** screen displays the module(s) in use with a circular graphic indicator around each test and Patient Identification below the module graphic (see Figure 23).

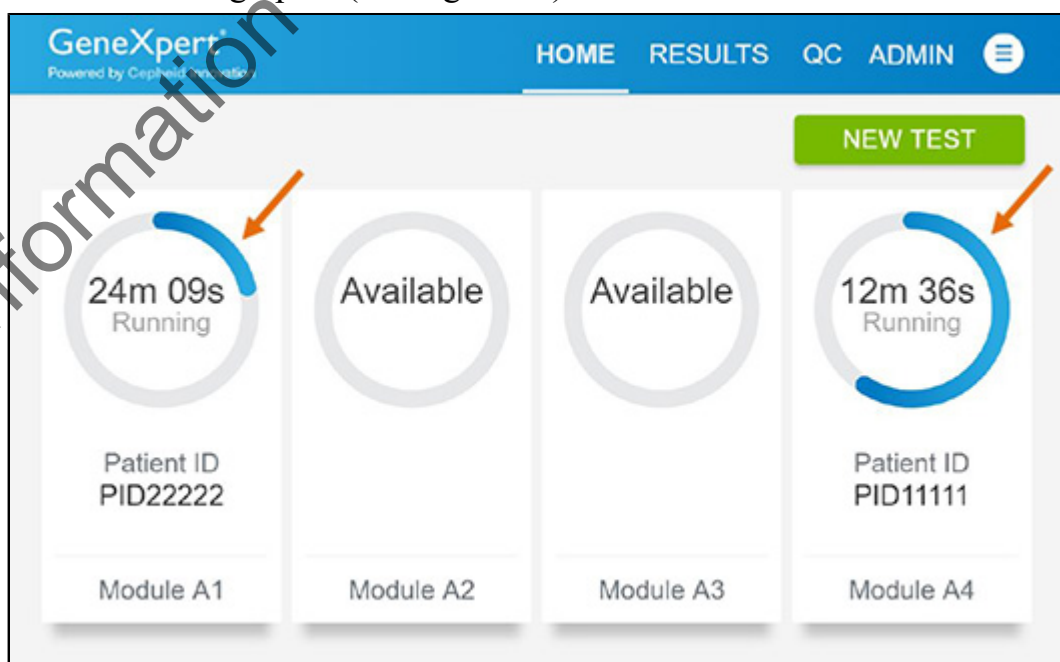


Figure 23. Home Screen showing Two Tests Running

After a test has completed, the module icon text changes to **Complete** (see Figure 24).

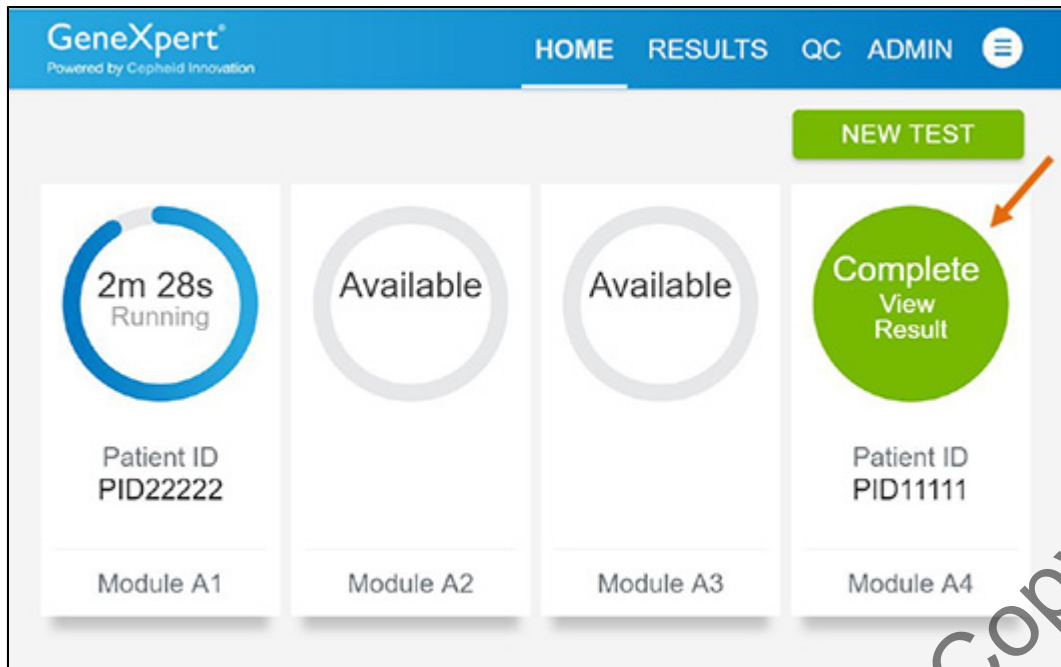


Figure 24. Home Screen with One of Two Tests Completed

5. Touch **Complete View Result** to view test results.

16.5 Viewing Test Results

1. Touch the **RESULTS** button located on the panel at the top of the screen. The Results screen displays (see Figure 25).

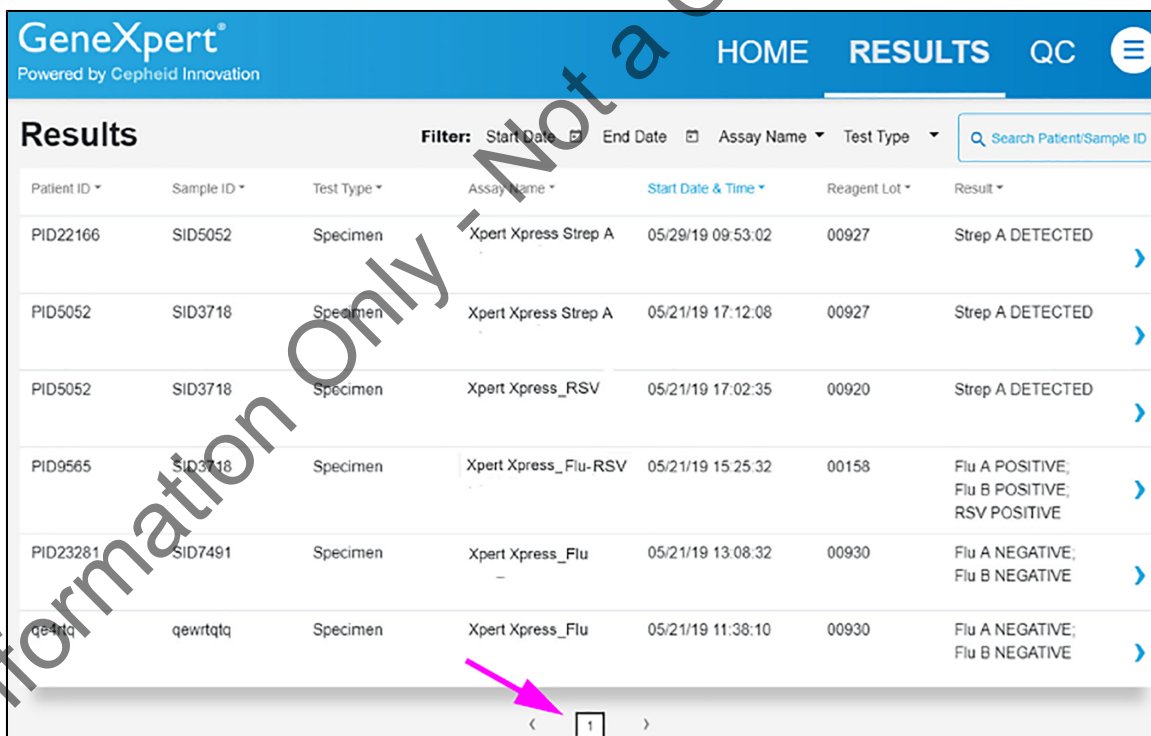


Figure 25. Results Screen

Test results are, by default, in order of the date and time that the test was run. Navigate through the test result pages by touching the numbered buttons or arrows at the bottom of the screen.

2. Touch the desired result to open the **Test Result** screen (see Figure 26).

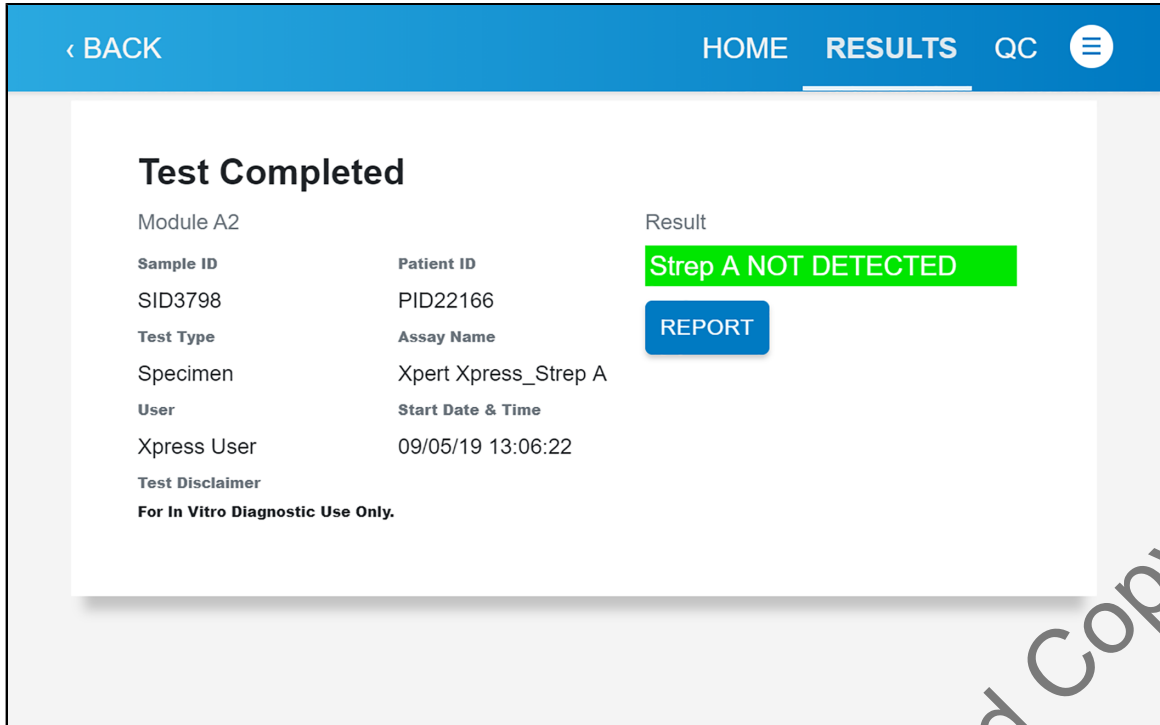


Figure 26. Test Result Screen (Example)

17 Quality Control

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

- **Sample Processing Control (SPC):** Ensures that the sample was processed correctly. The SPC verifies that sample processing is adequate. Additionally, this control detects sample-associated inhibition of the real-time PCR test, 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 assigned acceptance criteria.
- **Probe Check Control (PCC):** Before the start of the PCR reaction, the GeneXpert Xpress 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 assigned acceptance criteria.

17.1 Testing Quality Control Samples (External Controls)

Note If the QC Lockout feature is enabled, follow the QC Lockout instructions detailed in the *GeneXpert Xpress System User's Guide*.

Test the Negative and Positive External Controls:

Note Cepheid recommends that external controls be tested at the frequency noted below.

- Each time a new lot of Xpert Xpress Strep A reagents is received.
- Each time a new shipment of Xpert Xpress Strep A reagents is received even if it is the same lot previously received.
- Each time a new operator is performing the test (i.e., operator who has not performed the test before).
- When problems (storage, operator, instrument, or other) are suspected or identified.
- If otherwise required by your institution's standard QC procedures.

1. Put on a clean pair of gloves.
2. Have a new Xpert Xpress Strep A cartridge, a control tube, and a transfer pipette ready.
3. For GeneXpert Xpress Software *Version 5.x*:
 - a) On the **Home** screen, touch **RUN NEW TEST** (see Figure 4).
 - b) Touch **NO** for the sample barcode on the **Sample ID** screen if there is no Sample ID barcode.
 - c) Touch the **Sample ID** field to display the **keyboard**.
 - d) Type **negative control** for the Negative Control or **positive control** for the Positive Control.
 - e) Touch the **OK** button.
 - f) Proceed to step 4.

For GeneXpert Xpress Software *Version 6.0 or Higher*:

- a) On the **Home** screen, touch **QC** (see Figure 12).
The **Quality Control** screen displays (see Figure 27).



Figure 27. Quality Control Screen

- b) Touch **RUN QC POSITIVE TEST**, **RUN QC NEGATIVE TEST**, or **RUN PROFICIENCY TEST**.
The **Sample ID** screen displays.
 - c) Manually enter **negative control** for the Negative Control or **positive control** for the Positive Control, or scan the sample ID barcode if available.
 - d) Touch **CONTINUE**.
4. Scan the barcode on the cartridge with the scanner. Touch **YES** to verify the information displayed is correct.
 5. If applicable, enter your user name and password.
 6. Watch the video before continuing. The video will repeat. Touch the **CONTINUE** button to exit video.
 7. Mix control by vigorously shaking the control tube for 5 seconds. Open the cap on the control tube.
 8. Open the cartridge lid by lifting the front of the cartridge lid.
 9. Remove the transfer pipette from the wrapper.
 10. Squeeze the bulb of the transfer pipette **completely** and place the pipette tip in the control tube (see Figure 6 or Figure 8).
 11. Release the bulb of the pipette to fill the pipette with the sample from the control tube. Check that the pipette does not contain bubbles.

12. To transfer the control sample to the cartridge, squeeze the bulb of the pipette **completely** to empty the pipette into the large opening (Sample Chamber) in the cartridge (see Figure 7).

Note Dispense the **entire** volume of liquid into the sample chamber. False negative or indeterminate results may occur if insufficient sample is added to the cartridge.

13. Close the cartridge lid.
14. Dispose of the used pipette in an appropriate waste container.
15. Open the module door with the flashing green light.
16. Load the cartridge with the barcode facing the operator onto the cartridge bay platform. Do not try to insert the cartridge past the cartridge bay platform.
17. Close the door until it clicks.
The flashing green light stops flashing. The **Test in Progress** screen displays. The **Remove Cartridge** screen displays (Software Version 5.x) or the screen text changes to **Test Completed** (Software Version 6.0 or higher).
18. Open the module door, remove the used cartridge, and properly dispose of the cartridge according to your institution's hazardous waste disposal policies.
19. Touch **CONTINUE** (Software Version 5.x) or **REPORT** (Software Version 6.0 or higher) to view the result of the test.
20. Repeat the above steps with the second control tube before testing patient samples.

Note Do not turn off or unplug the instruments while a test is in progress. Turning off or unplugging the GeneXpert Xpress instrument or computer will stop the test.

Note If the barcode on the Xpert Xpress Strep A cartridge does not scan or scanning the barcode results in an error message stating the cartridge is expired, then repeat the test with a new cartridge.

Note If you have scanned the cartridge barcode in the Xpress software and the assay definition file is not available, a screen displays indicating the assay definition file is not loaded or that the product code was not found on the system. Contact Cepheid Technical Support.

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

18 Interpretation of Results

The results are interpreted automatically by the GeneXpert Xpress System and are clearly shown in the **View Results** window. The possible results and interpretations are shown in Table 2.

Table 2. Xpert Xpress Strep A Results and Interpretations

Results	Interpretation
Strep A NOT DETECTED	Strep A target DNA is not detected.
Strep A DETECTED	Strep A target DNA is detected.
NO RESULT- REPEAT TEST	If the result is NO RESULT- REPEAT TEST , then retest with a new cartridge. If the retest is NO RESULT- REPEAT TEST , contact Cepheid Technical Support at (888) 838-3222.
INSTRUMENT ERROR	Result is an instrument error. Touch CLEAR ERROR and follow the on-screen instructions. When the Home screen displays, repeat the test using a new cartridge.

19 Retests

19.1 Reasons to Repeat the Test

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

- An **INSTRUMENT ERROR** result could be due to, but not limited to, the maximum pressure limits were exceeded.
- A **NO RESULT- REPEAT TEST** indicates that insufficient data were collected. For example, Probe Check control failed or a power failure occurred.

19.2 Retest Procedure

To retest an **INSTRUMENT ERROR** or **NO RESULT- REPEAT TEST** result (indeterminate result), use a new cartridge (do not re-use the cartridge).

Do not perform more than one retest of the original sample.

Use the leftover sample from the original swab transport medium tube.

1. Put on a clean pair of gloves. Obtain a new Xpert Xpress Strep A cartridge and a new transfer pipette.
2. Mix the specimen by vigorously shaking the transport medium tube (ESwab tube) for 5 seconds.
3. Open the cartridge lid. Using a clean transfer pipette (supplied), transfer specimen (one draw) to the sample chamber with the large opening in the cartridge.
4. Close the cartridge lid.
5. Start the test according to instructions in Section 14.1 (Software Version 5.x) or Section 16.1 (Software Version 6.0 or Higher).

20 Limitations

- Additional follow-up testing by culture is required if the Xpert Xpress Strep A test result is negative and clinical symptoms persist, or there is an outbreak of acute rheumatic fever (ARF).
- The performance of the Xpert Xpress Strep A test was evaluated using the procedures provided in this package insert only. Modifications to these procedures may alter the performance of the test.
- Careful compliance with the instructions in this package insert and in the Copan Liquid Amies Elution Swab (ESwab) Collection and Transport System package insert is necessary to avoid erroneous results.
- The Xpert Xpress Strep A test has been validated only with Copan Liquid Amies Elution Swab (ESwab) Collection Kit (Copan catalog number 480CFA).
- Because the detection of *Streptococcus pyogenes* is dependent on the organism's DNA present in the sample, reliable results are dependent on proper sample collection, handling, and storage.
- The Xpert Xpress Strep A test provides qualitative results and does not provide the quantitative value of the organism detected in the specimen.
- Mutations or nucleotide polymorphisms in primer or probe binding regions may affect detection of new or unknown *Streptococcus pyogenes* strains resulting in a false negative result.
- A negative test result does not exclude the possibility of infection because the test result may be affected by improper specimen collection, technical error, sample mix-up, or because the number of organisms in the sample is below the limit of detection of the test.
- As with many diagnostic tests, negative results from the Xpert Xpress Strep A test do not preclude a Strep A infection and should not be used as the sole basis for treatment or other patient management decisions. The Xpert Xpress Strep A test does not differentiate asymptomatic carriers of Group A streptococci from those exhibiting streptococcal infection. The results from the Xpert Xpress Strep A test should be interpreted in conjunction with other laboratory and clinical data available to the clinician.
- This test has not been evaluated for patients without signs and symptoms of pharyngitis.
- This test cannot rule out pharyngitis caused by other bacterial or viral pathogens besides Group A streptococci.
- Cross-reactivity with organisms other than those listed in the Exclusivity Table 10 may lead to erroneous results.
- The analyte target (bacterial nucleic acid) may persist in vivo, independent of pathogen viability. Detection of the analyte target does not imply that the corresponding pathogen is infectious, or is the causative agent of the clinical symptoms.

21 Expected Values

In a multi-center clinical study for Xpert Xpress Strep A, 618 throat swab specimens were analyzed. Of the 618 specimens, 329 (53.2%) were collected from female subjects and 289 (46.8%) from male subjects. The distribution by age range, along with the number and percentage of cases positive for Strep A, as determined by Xpert Xpress Strep A, are shown in Table 3.

Table 3. Number and Percent of Specimens by Age Range

Age Range	N	% of Total	Number of Positives	Positivity
0-1 year	6	1.0%	1	16.7%
2-5 years	91	14.7%	31	34.1%
6-12 years	336	54.4%	129	38.4%
13-21 years	150	24.3%	18	12.0%
22-65 years	34	5.5%	5	14.7%
>65 years	1	0.2%	0	0%
Total	618	100%^a	184	29.8%

^a Total=100.1% due to rounding

22 Performance Characteristics

22.1 Clinical Performance at CLIA Waived Sites

A prospective, multi-center investigational study was conducted to evaluate the clinical performance of Xpert Xpress Strep A. An initial throat swab was collected for the standard of care method and a second throat swab was collected from consented subjects for testing by Xpert Xpress Strep A and reference method. The specimens were collected using ESwabs (flocked swab in Liquid Amies medium) from patients presenting with signs and symptoms of pharyngitis. The Xpert Xpress Strep A test was evaluated at nine clinical sites from geographically diverse regions within the United States between January 2017 and May 2017.

Six hundred sixty-six (666) specimens were initially enrolled in the study. Of these, 43 were excluded from the analysis due to failure to comply with the inclusion criteria (11), delay in shipment (27), reference method indeterminate (4) or incorrect specimen type (1).

Among the 623 specimens included in the analysis, 94.7% (590/623, 95% CI: 92.7–96.2) were successful on the initial test and 99.2% (618/623, 95% CI: 98.1–99.7) upon retest.

The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of Xpert Xpress Strep A were established relative to culture and latex agglutination for Strep A typing. The overall performance of Xpert Xpress Strep A is presented in Table 4. Discordant results between Xpert Xpress Strep A and culture were investigated using an alternative PCR/bidirectional sequencing assay; the results of which are footnoted in Table 4.

Table 4. Performance of Xpert Xpress Strep A vs. Reference Method

	Reference Method			Total
	Positive	Negative	Total	
Xpert Xpress Strep A	Positive	157	27 ^a	184
	Negative	1 ^b	433	434
	Total	158	460	618 ^c

Sensitivity	99.4% (95%CI: 96.5-99.9)
Specificity	94.1% (95%CI: 91.6-95.9)
PPV	85.3% (95%CI: 79.5-89.7)
NPV	99.8% (95%CI: 98.7-100.0)
Accuracy	95.5% (95%CI: 93.5-96.8)
Prevalence	25.6% (95%CI: 22.3-29.1)

- a Results from alternative PCR with bidirectional sequencing: 10 of 27 were Strep A Positive; 13 of 27 were Strep A Negative; 4 of 27 were inconclusive.
- b Results from alternative PCR with bidirectional sequencing: 1 of 1 was Strep A Negative.
- c On initial testing, 33/623 specimens (5.3%, 95% CI: 3.8–7.3) produced indeterminate results; 31/33 were retested, of which 28 produced valid results that were included in the analysis of performance for a final indeterminate rate of 5/623 (0.8%, 95% CI: 0.3–1.9).

22.2 Reproducibility

A four member reproducibility panel with varying concentrations of *Streptococcus pyogenes* was tested two times per day on five different days by three different operators at three sites (4 specimens x 2 times/day x 5 days x 3 operators x 3 sites). Three lots of Xpert Xpress Strep A cartridges were used. The samples were prepared in simulated throat swab matrix at the different concentration levels and are presented in Table 5. Results of the reproducibility study are summarized in Table 6 by study site/operator.

Table 5. Reproducibility Panel

Strain	Panel Member
Not applicable	Negative
ATCC BAA-946 (<i>Streptococcus pyogenes</i>)	High Negative (~0.05X LoD)
ATCC BAA-946 (<i>Streptococcus pyogenes</i>)	Low Positive (~1XLoD)
ATCC BAA-946 (<i>Streptococcus pyogenes</i>)	Moderate Positive (~3X LoD)

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

Sample	Site 1				Site 2				Site 3				% Total Agreement by Sample ^a b
	Op 1	Op 2	Op 3	Site	Op 1	Op 2	Op 3	Site	Op 1	Op 2	Op 3	Site	
Neg	100% (10/10)	100% (10/10)	100% (10/10)	100% (30/30)	100% (10/10)	100% (10/10)	100% (10/10)	100% (30/30)	100% (10/10)	100% (10/10)	100% (10/10)	100% (30/30)	100% (90/90)
Strep A High Neg	70% (7/10)	100% (10/10)	100% (10/10)	90% (27/30)	80% (8/10)	100% (10/10)	100% (10/10)	93% (28/30)	90% (9/10)	100% (10/10)	80% (8/10)	90% (27/30)	91% (82/90)
Strep A Low Pos	100% (10/10)	100% (10/10)	90% (9/10)	97% (29/30)	100% (10/10)	90% (9/10)	100% (10/10)	97% (29/30)	100% (10/10)	100% (10/10)	90% (9/10)	97% (29/30)	97% (87/90)

Sample	Site 1				Site 2				Site 3				% Total Agreement by Sample ^a b
	Op 1	Op 2	Op 3	Site	Op 1	Op 2	Op 3	Site	Op 1	Op 2	Op 3	Site	
Strep A Mod Pos	100% (10/10)	100% (10/10)	100% (10/10)	100% (30/30)	100% (10/10)	100% (10/10)	100% (10/10)	100% (30/30)	100% (10/10)	100% (10/10)	100% (10/10)	100% (30/30)	100% (90/90)

^a Agreement based on expected result: Neg and High Neg=expected negative; Low Pos and Mod Pos=expected positive

^b Thirteen (13) indeterminate results were obtained over the course of the study for an initial indeterminate rate of 3.6% (13/360). In all cases, the expected results were obtained upon retesting.

The reproducibility of Xpert Xpress Strep A 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-lots, between-days, between-operators and within-assay for each panel member are presented in Table 7.

Table 7. 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
Neg	SPC	90	33.5	0.3	0.9	1.0	3.0	0.3	0.9	0	0	1.5	4.5	1.9	5.5
Strep A High Neg	SPC	82	33.6	0.4	1.2	1.1	3.2	0	0	0	0	1.3	3.9	1.7	5.2
Strep A Low Pos	SA ^b	87	38.6	0	0	0.4	0.9	0	0	0	0	1.3	3.4	1.3	3.5
Strep A Mod Pos	SA ^b	90	37.2	0	0	0.1	0.3	0.2	0.5	0.2	0.5	0.9	2.4	1.0	2.6

^a Results with non-zero Ct values out of 90.

^b SA= Strep A

23 Analytical Performance

23.1 Analytical Sensitivity (Limit of Detection)

Studies were performed to determine the analytical sensitivity or Limit of Detection (LoD) of the Xpert Xpress Strep A using the ESwab collection kit. The limit of detection is the lowest concentration of sample (reported as CFU/mL in ESwab transport medium or CFU/test) that can be reproducibly distinguished from negative samples 95% of the time, or the lowest concentration of organisms at which 19 of 20 replicates were positive. This study determined the lowest concentration of *Streptococcus pyogenes* cells diluted into pooled clinical throat swab matrix that can be detected using the Xpert Xpress Strep A.

The analytical sensitivity of the Xpert Xpress Strep A was performed using two lots of reagents tested across three testing days with two *Streptococcus pyogenes* strains: ATCC BAA-946 and ATCC 19615.

The claimed LoD for each Strep A strain tested is summarized in Table 8.

Table 8. Strep A LoD

Strep A Strain	emm type	LoD (CFU/ mL in ESwab transport medium)	LoD (CFU/test)
ATCC BAA-946	6	9	3
ATCC 19615	80	18	6

23.2 Analytical Reactivity (Inclusivity)

Twenty-four *Streptococcus pyogenes* strains were tested at 3X LoD using the Xpert Xpress Strep A in replicates of three. The strains tested included representative isolates of emm types 1, 3, 4, 6, 11, 12, 18, 22, 25, 27, 38, 75, 77, 89, 94, 95. The list of strains tested in ESwab medium containing simulated throat swab matrix is shown in Table 9. All 24 strains were correctly reported as **Strep A DETECTED** with the Xpert Xpress Strep A.

Table 9. Analytical Reactivity (Inclusivity) of Xpert Xpress Strep A

Strep A Strain ID	emm type	Strain
ATCC 12202	1	NCTC 8370
ATCC 12344	1	T1
ATCC 700294	1	SF370
ATCC 12383	3	D58X
ATCC 12384	3	C203
ATCC 12385	4	J17A4
ATCC 12203	6	NCTC 8709
ATCC 12352	11	T11
ATCC BAA-1065	12	MGAS 2096
ATCC BAA-1315	12	MGAS9429
ATCC 12357	18	J17C
ATCC 10403	22	T22
ATCC 12204	25	A25
ATCC 8135	27	T27
ATCC 12365	38	C107
ATCC 12370	38	C94
ATCC 700497	75	CDC-SS-1147
ATCC 700499	77	CDC-SS-1149
ATCC 700949	89	CDC-SS-1397
ATCC BAA-355	94	N/A
ATCC BAA-356	95	N/A

Strep A Strain ID	emm type	Strain
ATCC 14289	M protein deficient <i>S.pyogenes</i>	C203 S
ATCC 49399	emm type not available	QC A62
ATCC 51339	emm type not available	1805

23.3 Analytical Specificity (Exclusivity)

The analytical specificity of the Xpert Xpress Strep A was evaluated by testing a panel of 70 potentially cross-reactive microorganisms, including species that are phylogenetically related to *Streptococcus pyogenes* and members of the throat commensal microflora (e.g., other bacteria, viruses, and yeast). The 70 organisms tested were identified as either Gram-positive (27), Gram-negative (33), or Gram-indeterminate (3), yeast (1), and viruses (6). *Streptococcus* Group B, *Streptococcus* Group C, and *Streptococcus* Group G strains were also included in this study. All strains were tested in triplicate in ESwab transport medium containing simulated throat swab matrix at $\geq 10^6$ CFU/mL for bacteria and yeast and $\geq 10^5$ TCID₅₀/mL for viruses. All three replicates of all 70 organisms were reported as **Strep A NOT DETECTED** by the Xpert Xpress Strep A (Table 10). The analytical specificity of the Xpert Xpress Strep A was 100%.

Table 10. Analytical Specificity of Xpert Xpress Strep A

Organism	Results
<i>Acinetobacter baumannii</i>	Strep A NOT DETECTED
<i>Arcanobacterium haemolyticum</i>	Strep A NOT DETECTED
Adenovirus, Type 1	Strep A NOT DETECTED
Adenovirus, Type 7	Strep A NOT DETECTED
<i>Bacillus cereus</i>	Strep A NOT DETECTED
<i>Bordetella bronchiseptica</i>	Strep A NOT DETECTED
<i>Bordetella parapertussis</i>	Strep A NOT DETECTED
<i>Bordetella pertussis</i>	Strep A NOT DETECTED
<i>Burkholderia cepacia</i>	Strep A NOT DETECTED
<i>Campylobacter rectus</i>	Strep A NOT DETECTED
<i>Candida albicans</i>	Strep A NOT DETECTED
<i>Corynebacterium diphtheriae</i>	Strep A NOT DETECTED
<i>Corynebacterium pseudodiphtheriticum</i>	Strep A NOT DETECTED
Cytomegalovirus AD-169	Strep A NOT DETECTED
<i>Enterococcus faecalis</i>	Strep A NOT DETECTED
<i>Enterococcus faecium</i>	Strep A NOT DETECTED
Epstein-Barr Virus 4	Strep A NOT DETECTED
<i>Escherichia coli</i>	Strep A NOT DETECTED

Organism	Results
<i>Fusobacterium necrophorum</i>	Strep A NOT DETECTED
<i>Haemophilus influenzae</i> type A	Strep A NOT DETECTED
<i>Haemophilus parahaemolyticus</i>	Strep A NOT DETECTED
<i>Haemophilus parainfluenzae</i>	Strep A NOT DETECTED
<i>Hepatitis B Virus</i>	Strep A NOT DETECTED
<i>Herpes Simplex Virus</i>	Strep A NOT DETECTED
<i>Klebsiella pneumoniae</i>	Strep A NOT DETECTED
<i>Lactobacillus acidophilus</i>	Strep A NOT DETECTED
<i>Lactococcus lactis</i> subsp. <i>lactis</i>	Strep A NOT DETECTED
<i>Legionella jordanis</i>	Strep A NOT DETECTED
<i>Legionella micdadei</i>	Strep A NOT DETECTED
<i>Legionella pneumophila</i>	Strep A NOT DETECTED
<i>Listeria monocytogenes</i>	Strep A NOT DETECTED
<i>Moraxella catarrhalis</i> (two strains)	Strep A NOT DETECTED
<i>Moraxella lacunata</i>	Strep A NOT DETECTED
<i>Mycoplasma pneumoniae</i>	Strep A NOT DETECTED
<i>Neisseria gonorrhoeae</i>	Strep A NOT DETECTED
<i>Neisseria lactamica</i>	Strep A NOT DETECTED
<i>Neisseria meningitidis</i>	Strep A NOT DETECTED
<i>Neisseria mucosa</i>	Strep A NOT DETECTED
<i>Neisseria sicca</i>	Strep A NOT DETECTED
<i>Neisseria subflava</i>	Strep A NOT DETECTED
<i>Peptostreptococcus micros</i>	Strep A NOT DETECTED
<i>Prevotella (Bacteroides) oralis</i>	Strep A NOT DETECTED
<i>Proteus mirabilis</i>	Strep A NOT DETECTED
<i>Proteus vulgaris</i>	Strep A NOT DETECTED
<i>Pseudomonas aeruginosa</i>	Strep A NOT DETECTED
<i>Pseudomonas fluorescens</i>	Strep A NOT DETECTED
<i>Serratia marcescens</i>	Strep A NOT DETECTED
<i>Staphylococcus aureus</i>	Strep A NOT DETECTED
<i>Staphylococcus epidermidis</i>	Strep A NOT DETECTED
<i>Staphylococcus haemolyticus</i>	Strep A NOT DETECTED
<i>Stenotrophomonas maltophilia</i>	Strep A NOT DETECTED
<i>Streptococcus agalactiae</i>	Strep A NOT DETECTED
<i>Streptococcus anginosus</i>	Strep A NOT DETECTED
<i>Streptococcus bovis</i>	Strep A NOT DETECTED
<i>Streptococcus canis</i>	Strep A NOT DETECTED

Organism	Results
<i>Streptococcus constellatus</i>	Strep A NOT DETECTED
<i>Streptococcus dysgalactiae</i>	Strep A NOT DETECTED
<i>Streptococcus equi</i>	Strep A NOT DETECTED
<i>Streptococcus gallolyticus</i>	Strep A NOT DETECTED
<i>Streptococcus intermedius</i>	Strep A NOT DETECTED
<i>Streptococcus mitis</i>	Strep A NOT DETECTED
<i>Streptococcus mutans</i>	Strep A NOT DETECTED
<i>Streptococcus oralis</i>	Strep A NOT DETECTED
<i>Streptococcus pneumoniae</i>	Strep A NOT DETECTED
<i>Streptococcus salivarius</i>	Strep A NOT DETECTED
<i>Streptococcus sanguinus</i>	Strep A NOT DETECTED
<i>Treponema denticola</i>	Strep A NOT DETECTED
<i>Veillonella parvula</i>	Strep A NOT DETECTED
<i>Yersinia enterocolitica</i>	Strep A NOT DETECTED

23.4 Carry-over Contamination

A study was conducted to demonstrate that single-use, self-contained GeneXpert cartridges prevent specimen and amplicon carry-over contamination from very high titer positive samples (*S. pyogenes*) into successively run negative samples when processed in the same GeneXpert module. The study consisted of a negative sample processed in the same GeneXpert module immediately after processing a very high titer positive sample at a concentration $\geq 1 \times 10^6$ CFU/mL in ESwab transport medium containing simulated throat swab matrix. The testing scheme was repeated 40 times between 2 GeneXpert instruments (one module per instrument) for a total of 41 runs per instrument (20 high positive samples per instrument and 21 negative samples per instrument). There was no evidence of any carry-over contamination. All 42 negative samples were correctly reported as **Strep A NOT DETECTED**. All 40 positive samples were correctly reported as **Strep A DETECTED**.

23.5 Potentially Interfering Substances

Ten potentially interfering substances that may be present in clinical throat specimens with the potential to interfere with the performance of the Xpert Xpress Strep A were evaluated. The potentially interfering substances included blood, mucus, human saliva, sugar-containing cold and flu remedies, cough medicine, antiseptic, salt-modifying remedies, pH-modifying remedies, antacids, and foods or drinks that increase salivary viscosity. The substances, active ingredients, and concentrations tested are listed in Table 11. Medically and/or physiologically relevant concentrations of potential interferents were tested in simulated throat swab matrix in the presence and absence of Strep A at 3X LoD.

There was no test interference in the presence of the substances at the concentrations tested in this study. All positive and negative samples were correctly identified using the Xpert Xpress Strep A.

Table 11. Potential Interfering Substances Tested

Substance/Class	Description/Active Ingredient	Concentration Tested
Saliva	100% Human Saliva	6.5% (v/v)
Mucin	Bound sialic acid, 0.5-1.5%	2.5% (w/v)
Blood	Whole human blood	5.0% (v/v)
Antiseptic	0.092% Eucalyptol, 0.042% menthol, 0.060% methyl salicylate, 0.064% thymol	6.5% (v/v) ^a
Cough Medicine	Dextromethorphan HBr USP 10 mg, Guaifenesin USP 200 mg	5 mg/mL
Sugar-containing cold and flu remedies	Acetaminophen 650 mg, Dextromethorphan HBr 20 mg, Doxylamine Succinate 12.5 mg, Phenylephrine HCl 10 mg	6.5% (v/v)
Salt-modifying remedies	Sodium Chloride (0.65%)	6.5% (v/v)
Foods/drinks that increase salivary viscosity	Milk	6.5% (v/v)
pH Modifying Remedies	100% Orange juice	6.5% (v/v)
Antacids	Aluminum Hydroxide 400 mg (equivalent to dried gel, USP) – antacid, Magnesium Hydroxide 400 mg – antacid, Simethicone 40 mg – antigas	6.5% (v/v)

^a Although all samples were reported appropriately as positive or negative, reduced fluorescent signal for the *S. pyogenes* target was observed in the presence of antiseptic mouthwash at 6.5% v/v.

23.6 Microbial Interference

An interfering microorganism study was performed to assess the inhibitory effects of commensal microorganisms in throat swab samples on the performance of the Xpert Xpress Strep A. Twenty-seven microorganisms were tested for potential interference with Strep A detection (Table 12). The microorganisms were tested at $\geq 10^6$ CFU/mL in the presence of Strep A at 3X LoD concentration in ESwab

medium containing simulated throat swab matrix. The results showed that the presence of the tested microorganisms did not interfere with the detection of Strep A target DNA.

Table 12. Commensal Microorganisms Tested

Organism		
<i>Acinetobacter baumannii</i>	<i>Staphylococcus epidermidis</i>	<i>Streptococcus intermedius</i>
<i>Candida albicans</i>	<i>Streptococcus agalactiae</i>	<i>Streptococcus mitis</i>
<i>Enterococcus faecalis</i>	<i>Streptococcus anginosus</i>	<i>Streptococcus mutans</i>
<i>Fusobacterium necrophorum</i>	<i>Streptococcus bovis</i>	<i>Streptococcus oralis</i>
<i>Haemophilus influenzae</i> type A	<i>Streptococcus canis</i>	<i>Streptococcus pneumoniae</i>
<i>Lactobacillus acidophilus</i>	<i>Streptococcus constellatus</i>	<i>Streptococcus salivarius</i>
<i>Neisseria lactamica</i> ^a	<i>Streptococcus dysgalactiae</i>	<i>Streptococcus sanguinus</i>
<i>Peptostreptococcus micros</i>	<i>Streptococcus equi</i>	<i>Treponema denticola</i>
<i>Prevotella (Bacteroides) oralis</i>	<i>Streptococcus gallolyticus</i>	<i>Veillonella parvula</i>

^a Although all samples were reported appropriately as positive, reduced fluorescent signal was observed for the *S. pyogenes* target in the presence of high concentrations of *N. lactamica*.

24 CLIA Waiver Studies

The accuracy of Xpert Xpress Strep A was evaluated when it was used by operators who had no laboratory experience and who were representative of CLIA waived testing sites (intended users). The study was conducted at 9 CLIA waived sites with 21 intended users participating. No training on the use of the test was provided to the operators. Testing included 618 prospectively collected throat swab specimens, described above in Section 22. The performance of Xpert Xpress Strep A was established relative to culture and the results are shown in Section 22, Table 4.

Near the Cutoff Study

A study was conducted to evaluate the performance of Xpert Xpress Strep A with weakly reactive samples when used by untrained users. Randomized blind-coded panels, containing weak negative (~0.05X LoD) and weak positive (~1X LoD or assay cutoff) Strep A specimens, were tested with Xpert Xpress Strep A by nine untrained users at 3 sites (90 tests in total per sample type). The panel testing was conducted over a minimum of five days at each site. The performance of Xpert Xpress Strep A with samples near the assay cutoff was acceptable when used by untrained users.

Table 13 below shows the performance of the test with samples near the cutoff of the assay for Strep A in the hands of untrained users.

Table 13. Performance of Xpert Xpress Strep A with Samples Near the Cutoff of the Assay for Strep A by Untrained Intended Operators

Sample Type	Untrained Operators	
	Percent Detection	95% Confidence Interval
Weak Positive (~1X LoD)	97% (87/90)	90.7–98.9
Weak Negative (~0.05X LoD)	9% (8/90)	4.6–16.6

25 References

- Centers for Disease Control and Prevention, National Center for Immunization and Respiratory Diseases, Division of Bacterial Diseases. ABCs Report: group A Streptococcus, 2003. December 27, 2004. Available at: <https://www.cdc.gov/abcs/reports-findings/survreports/gas03.html>. Accessed May 3, 2017.
- Centers for Disease Control and Prevention, National Center for Immunization and Respiratory Diseases, Division of Bacterial Diseases. Scarlet Fever: A Group A Streptococcal Infection. January 20, 2015. Available at: <http://www.cdc.gov/features/scarletfever/>. Accessed October 22, 2015.
- Centers for Disease Control and Prevention. Biosafety in Microbiological and Biomedical laboratories (refer to latest edition). <http://www.cdc.gov/biosafety/publications/>
- Clinical and Laboratory Standards Institute. Protection of Laboratory Workers from Occupationally Acquired Infections; Approved Guideline. Document M29 (refer to latest edition).
- REGULATION (EC) No 1272/2008 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 16 December 2008 on the classification labeling and packaging of substances and mixtures amending and repealing, List of Precautionary Statements, Directives 67/548/EEC and 1999/45/EC (amending Regulation (EC) No 1907/2007).
- Occupational Safety and Health Standards, Hazard Communication, Toxic and Hazard Substances (March 26, 2012) (29 C.F.R., pt. 1910, subpt. Z).

26 Cepheid Headquarters Locations

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27 Technical Assistance

Before Contacting Us

Collect the following information before contacting Cepheid Technical Support:

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

United States Technical Support
















Telephone: + 1 888 838 3222
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Contact information for all Cepheid Technical Support offices is available on our website: www.cepheid.com/en/support/contact-us.

28 Table of Symbols

Symbol	Meaning
	Catalog number
	<i>In vitro</i> diagnostic medical device
	Do not reuse
	Batch code
	Consult instructions for use
	Caution
	Manufacturer
	Country of manufacture
	Contains sufficient for <i>n</i> tests
	Control
	Expiration date
	Temperature limitation
	Biological risks
	Warning
	For prescription use only



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29 Revision History

Description of Changes: 302-2294, Rev. B to Rev. C

Purpose: To add a new pipette procedure and make continuous improvement updates

Section	Description of Change
Throughout	Added general formatting updates, standard improvements, and wording and grammar corrections.
Trademarks	Updated to current Cepheid standards.
Preparing the Specimen and Cartridge	Updated both Preparing the Specimen and Cartridge sections to include steps for two types of pipettes.
Revision History	Added revision history section and table

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