GeneXpert
Powered By CEPHEID INNOVATION

Xpert® SA Nasal Complete

REF **GXSACOMP-CE-10**

Cepheid®

In Vitro Diagnostic Medical Device IVD CE

301-0189, Rev. H May 2023

Trademark, Patents and Copyright Statements

See Section 22 Revision History for a description of changes.

Xpert® SA Nasal Complete

For *In Vitro* Diagnostic Use Only

1. Proprietary Name

Xpert® SA Nasal Complete

2. Common or Usual Name

Xpert SA Nasal Complete Assay

3. Intended Use

The Cepheid Xpert SA Nasal Complete Assay performed in the GeneXpert® Dx System is a qualitative in vitro diagnostic test designed for rapid and simultaneous detection of *Staphylococcus aureus* (SA) and methicillin-resistant *Staphylococcus aureus* (MRSA) from nasal swabs in patients at risk for nasal colonization, including pre-surgical patients. The test utilizes automated real-time polymerase chain reaction (PCR) to detect MRSA/SA DNA. The Xpert SA Nasal Complete Assay is intended to aid in the prevention and control of MRSA/SA infections in healthcare settings. The Xpert SA Nasal Complete Assay is not intended to guide or monitor treatment for MRSA/SA infections. Concomitant cultures are necessary only to recover organisms for epidemiological typing or for further susceptibility testing.

4. Summary and Explanation

Staphylococcus aureus (SA) is a well documented human opportunistic pathogen and a major nosocomial pathogen that causes a range of diseases. Some of the more serious infections produced by *S. aureus* are bacteremia, pneumonia, osteomyelitis, acute endocarditis, toxic shock syndrome, food poisoning, myocarditis, pericarditis, cerebritis, meningitis, chorioamnionitis, scalded skin syndrome, and abscesses of the muscle, urogenital tract, central nervous system, and various intra-abdominal organs[1].

In the early 1950s, acquisition and spread of beta-lactamase-producing plasmids thwarted the effectiveness of penicillin for treating *S. aureus* infections. In 1959, methicillin, synthetic penicillin, was introduced. However, by 1960, methicillin-resistant *S. aureus* strains were identified. This was determined to be the result of *S. aureus* acquiring the *mecA* gene. In the U.S. today, MRSA is responsible for approximately 25% of nosocomial infections and reports of community-acquired MRSA are increasing, resulting in significant morbidity and mortality. Attributable mortalities of 33% and 16% have been reported for MRSA and methicillin-sensitive *S. aureus* (SA) bacteremias, respectively. There are also rising cost concerns for MRSA infections. In attempts to limit the spread of these infections, control strategies and policies are being developed and implemented in healthcare settings. Controlling MRSA is a primary focus of most hospital infection control programs. Historically, the standard method for detecting MRSA and SA has been culture, which is very laborious and can require several days to generate a definitive result.[2-7]

5. Principle of the Procedure

The GeneXpert Instrument Systems automate and integrate sample purification, nucleic acid amplification, and detection of the target sequence in simple or complex samples using real-time PCR and RT-PCR assays. The systems consist of an instrument, personal computer, and preloaded software for running tests and viewing the results. The systems require the use of single-use disposable cartridges that hold the PCR reagents and host the PCR process. Because the cartridges are self-contained, cross-contamination between samples is eliminated. For a full description of the systems, see the appropriate *GeneXpert Dx System Operator Manual* or *GeneXpert Infinity System Operator Manual*.

The Xpert SA Nasal Complete Assay includes reagents for the detection of MRSA and SA as well as a sample processing control (SPC) to control for adequate processing of the target bacteria and to monitor the presence of inhibitor(s) in the PCR reaction. The Probe Check Control (PCC) verifies reagent rehydration, PCR tube filling in the cartridge, probe integrity, and dye stability.

The primers and probes in the Xpert SA Nasal Complete Assay detect proprietary sequences for the staphylococcal protein A (*spa*), the gene for methicillin/oxacillin resistance (*mecA*), and the staphylococcal cassette chromosome (SCC*mec*) inserted into the SA chromosomal attB site.

6. Reagents and Instruments

6.1 Materials Provided

The Xpert SA Nasal Complete assay kit contains sufficient reagents to process 10 specimens or quality control samples. The kit contains the following:

Xpert SA Nasal Complete Assay Cartridges with Integrated Reaction Tubes	**10**
• Bead 1, Bead 2, and Bead 3 (freeze-dried)	1 per cartridge
• Reagent 1	3.0 mL per cartridge
• Reagent 2 (Sodium Hydroxide)	3.0 mL per cartridge
Xpert SA Nasal Complete Assay Elution Reagent (Guanidinium Thiocyanate)	**10 vials x 2.0 mL per kit**
CD	**1 per kit**

- Assay Definition File (ADF)
- Instructions to import ADF into GeneXpert 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 postmortem testing. During processing, there was no mixing of the material with other animal materials.

6.2 Materials Required but Not Provided

- GeneXpert Dx System (catalog number varies by configuration): GeneXpert instrument, computer with proprietary software version 4.3 or higher, hand-held barcode scanner and Operator Manual
- Printer: If a printer is needed, contact Cepheid Technical Support to arrange for the purchase of a recommended printer.
- Vortex mixer
- Cepheid Sample Collection Device (900-0370)
- Sterile Gauze
- Disposable, sterile transfer pipettes

6.3 Materials Available but Not Provided

- KWIK-STIKs™ from MicroBiologics catalog #0158MRSA (*Staphylococcus aureus subsp. aureus* ATCC 700699 (Cepheid GeneXpert)) and catalog #0360MSSA (*Staphylococcus aureus subsp. aureus* ATCC 25923 (Cepheid GeneXpert)) as positive controls, and catalog #0371MSSE (methicillin sensitive *Staphylococcus epidermidis ATCC 1228 (Cepheid GeneXpert))* as negative control.

7. Warnings and Precautions

- For *In Vitro* Diagnostic Use Only.
- 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[9] and the Clinical and Laboratory Standards Institute.[10]
- Follow your institution's safety procedures for working with chemicals and handling biological samples.
- The Xpert SA Nasal Complete assay does not provide susceptibility results. Additional time is required to culture and perform susceptibility testing.
- Do not substitute Xpert SA Nasal Complete assay reagents with other reagents.
- Do not open the Xpert SA Nasal Complete assay cartridge lid except when adding sample and reagent.
- Do not use a cartridge that has been dropped or shaken after you have added the sample and reagent.

- Do not use a cartridge that has a damaged reaction tube.
- Do not open a cartridge package until you are ready to perform testing.
- Do not use a cartridge that has leaked.
- Each single-use Xpert SA Nasal Complete assay cartridge is used to process one test. Do not reuse spent cartridges.
- 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.

8. Chemical Hazards[11,12]

- UN GHS Hazard Pictogram: 
- 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.
    - Do not eat, drink or smoke when using this product.
    - Avoid release to the environment.
    - Wear protective gloves/protective clothing/eye protection/face protection.
  - **Response**
    - IF ON SKIN: Wash with plenty of soap and water.
    - Take off contaminated clothing and wash before reuse.
    - Specific treatment, see supplemental first aid information.
    - 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.
    - IF SWALLOWED: Immediately call a POISON CENTER or doctor/physician if you feel unwell.
    - Rinse mouth
  - **Storage/Disposal**
    - Dispose of content and/or container in accordance with local, regional, national, and/or international regulations.

9. Storage and Handling

- Store the Xpert SA Nasal Complete cartridges and reagents at 2 – 28°C.
- Do not use reagents or cartridges that have passed the expiration date.
- Do not open a cartridge lid until you are ready to perform testing.
- Do not use any reagent that has become cloudy or discolored.

10. Specimen Collection, Transport and Storage

To obtain adequate specimen, follow the instructions in this section closely.

1. Open the Cepheid Collection Device by peeling back the outer packaging.
2. Moisten each swab tip with 2-3 drops of sterile physiological saline or use the swab dry.
3. Ask the patient to tilt his/her head back. Insert swabs approximately 1-2 cm into the first nostril.
4. Rotate the swabs against the inside of the nostril 15 times. Apply slight pressure with a finger on the outside of the nose to help assure good contact between the swab and the inside of the nose.
5. Using the same swabs, repeat for the second nostril, trying not to touch anything but the inside of the nose.
6. Remove the plastic transport tube. Twist off the tube cap and discard it. Place the swabs into the plastic transport tube. The swabs should go all the way into the tube until they rest on top of the sponge at the bottom of the tube. Make sure the red cap is on tightly.

Note: The swabs should stay attached to the red cap at all times.

7. Label the plastic transport tube with patient ID and send to the GeneXpert testing area.
8. Store swab specimen at room temperature (15–30 °C) if it will be processed within 24 hours, otherwise store swab at 2-8 °C. The swab specimen is stable up to 5 days when stored at 2–8 °C.

11. Procedure

11.1 Preparing the Cartridge

Important **Start the test within 15 minutes of adding the sample to the cartridge.**

To add the sample into the cartridge:

1. Remove the cartridge and Elution reagent from the package.
2. Remove the swab from the transport container.

Note Use sterile gauze to minimize risk of contamination.

3. Insert the swab into the tube containing the Elution reagent and break the swab.
4. Close the Elution vial lid and vortex at high speed for 10 seconds.
5. Open the cartridge lid. Using a sterile transfer pipette (not provided), transfer the entire contents of the Elution Reagent to the “S” chamber of the Xpert SA Nasal Complete Assay cartridge. See Figure 1.
6. Close the cartridge lid.

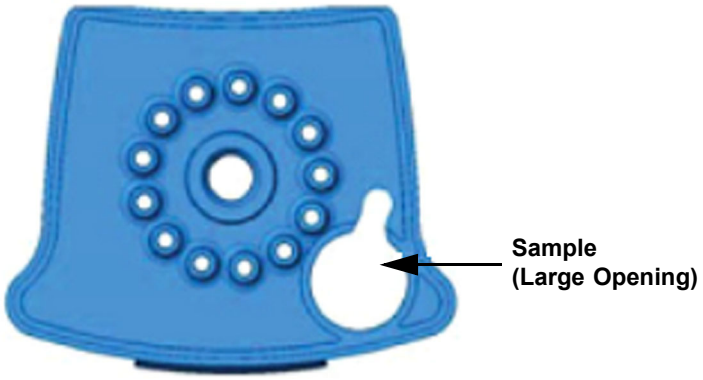

Figure 1. Xpert SA Nasal Complete Assay Cartridge (Top View)

11.2 Starting the Test

Important **Before you start the test, make sure the Xpert SA Nasal Complete assay definition file is imported into the software. This section lists the default steps to operate the GeneXpert Instrument System. For detailed instructions, see the *GeneXpert Dx System Operator Manual* or *GeneXpert Infinity System Operator Manual*.**

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 instrument and then turn on the computer. The GeneXpert 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 **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 associated with the test results and is shown in the **View Results** window.
5. Scan or type in the Sample ID. If typing the Sample ID, make sure the Sample ID is typed correctly. The Sample ID is associated with the test results and is shown in the **View Results** window.
6. Scan the barcode on the Xpert SA Nasal Complete Assay cartridge. Using the barcode information, the software automatically fills the boxes for the following fields: Select Assay, Reagent Lot ID, Cartridge SN, and Expiration Date.

Note If the barcode on the pert SA Nasal Complete Assay cartridge does not scan, then repeat the test with a new cartridge.

7. Click **Start Test** (GeneXpert Dx) or **Submit** (Infinity). In the dialog box that appears, type your password.
8. 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. The used cartridges should be disposed in the appropriate specimen waste containers according to your institution's standard practices.

11.3 Viewing and Printing Results

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

12. Quality Control

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 contains spores of *Bacillus globigii* in the form of a dry spore cake that is included in each cartridge to verify adequate processing of the Xpert SA Nasal Complete Assay sample. The SPC verifies that lysis of *Staphylococcus aureus* has occurred if the organisms are present and verifies that specimen processing is adequate. Additionally, this control detects specimen-associated inhibition of the real-time PCR assay. The SPC should be positive in a negative sample and can be negative or positive in a positive sample. The SPC passes if it meets the validated acceptance criteria.

- **Probe Check Control (PCC)** — Before the start of the PCR reaction, the GeneXpert System measures the fluorescence signal from the probes to monitor bead rehydration, reaction-tube filling, probe integrity and dye stability. The PCC passes if it meets the assigned acceptance criteria.
- **External controls** — KWIK-STIKs (MicroBioLogics, catalog # 0158 MRSA and catalog # 0360 SA as positive controls and catalog # 0371 MSSE as negative control) may be used for training, proficiency testing, and external QC of the GeneXpert System. External controls may be used in accordance with local, state, federal accrediting organizations, as applicable. Follow the MicroBioLogics external control procedure described below:

1. Tear open the pouch at notch and remove the KWIK-STIK.
2. Pinch the bottom of the ampoule in the cap to release the hydrating fluid.
3. Hold vertically and tap to facilitate flow of fluid through the shaft and into the bottom of unit containing pellet.
4. To facilitate dissolution of the lyophilized cell pellet, crush the pellet and gently pinch the bottom chamber.
5. Pull apart the KWIK-STIK to release the swab, and insert the swab into the tube containing the Elution Reagent (black cap).
6. The KWIK-STIK swab is now ready for SA Nasal Complete Assay testing.

13. Interpretation of Results

The results are interpreted automatically by the GeneXpert System from measured fluorescent signals and embedded calculation algorithms and are shown in the **View Results** window. The possible results are:

Table 1. Xpert SA Nasal Complete Results and Interpretation

Result	Interpretation
MRSA POSITIVE; SA POSITIVE (Figure 2)	MRSA target DNA sequences are detected; SA target DNA sequence is detected. • MRSA POSITIVE - All MRSA targets (*spa*, *mecA* and SCC*mec*) have a Ct within the valid range and endpoint above the threshold setting. • SPC – NA (not applicable); SPC is ignored since MRSA amplification may compete with this control. • Probe Check – PASS; all probe check results pass.
MRSA NEGATIVE; SA POSITIVE (Figure 3)	MRSA target DNA sequences are not detected; SA target DNA sequence is detected. • SA POSITIVE - Only the SA target (*spa*) has a Ct within the valid range and endpoint above the threshold setting. Target DNA for SCC*mec* is not detected and target DNA for *mecA* is or is not detected. • SPC – NA (not applicable); SPC is ignored since SA amplification may compete with this control. • Probe Check – PASS; all probe check results pass.
MRSA NEGATIVE; SA NEGATIVE (Figure 4)	SA target DNA sequence is not detected. • NEGATIVE - SA target (*spa*) DNA is not detected. Target DNA for *mecA* may or may not be detected; target DNA for SCC*mec* may or may not be 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 (Figure 5)	Presence or absence of MRSA and SA target DNA cannot be determined. SPC does not meet acceptance criteria, the sample was not properly processed, or PCR was inhibited. Repeat test according to instructions in the section below. • INVALID – Presence or absence of SA DNA cannot be determined. • SPC – FAIL; SPC target result is negative, and the SPC Ct is not within the valid range and endpoint is below the threshold setting. • Probe Check – PASS; all probe check results pass.

Table 1. Xpert SA Nasal Complete Results and Interpretation (Continued)

Result	Interpretation
ERROR	Presence or absence of MRSA and SA target DNA cannot be determined. The Probe Check Control failed, which is probably due to an improperly filled reaction tube, a probe integrity problem, or because the maximum pressure limits were exceeded. Repeat test according to instructions in the section below. • MRSA and SA targets – NO RESULT • SPC – NO RESULT. • Probe Check – FAIL*; one or more of the probe check results failed. *If the probe check passed, the error is caused by a system component failure.
NO RESULT	Presence or absence of MRSA and SA target DNA cannot be determined. Insufficient data were collected to produce a test result. For example, this can occur if the operator stopped a test that was in progress. Repeat test according to instructions in the section below. • MRSA and SA targets – NO RESULT • SPC – NO RESULT • Probe Check – not applicable

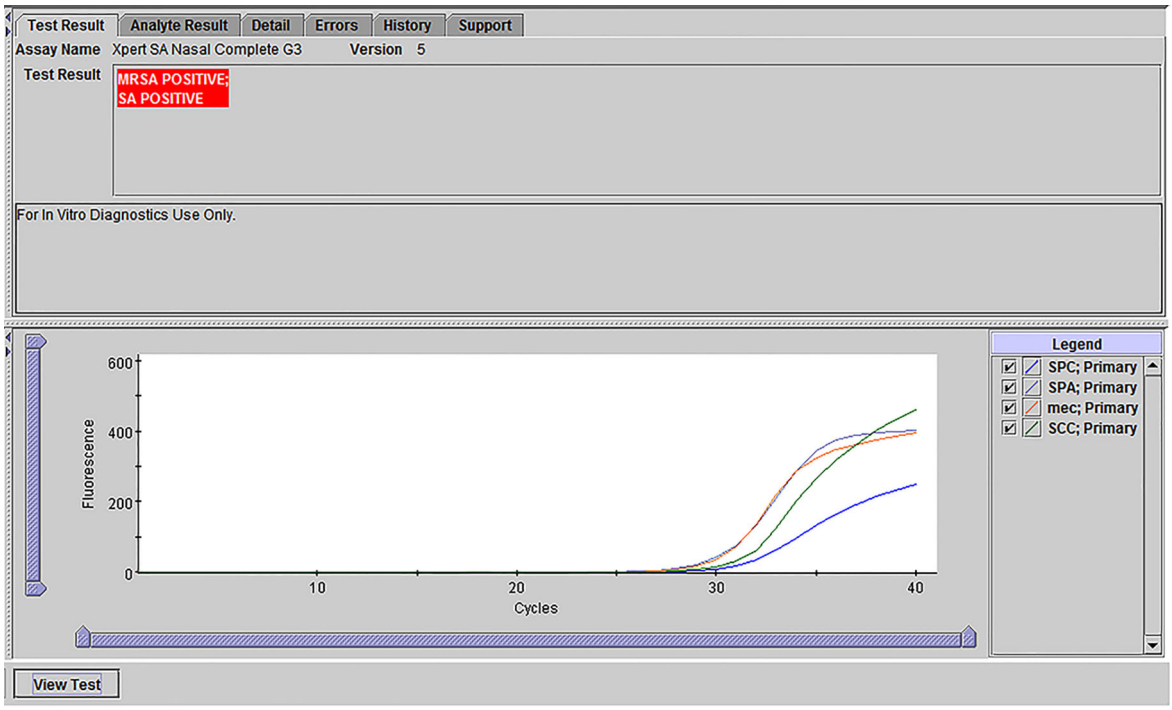

Figure 2. Example of a MRSA POSITIVE; SA POSITIVE Result

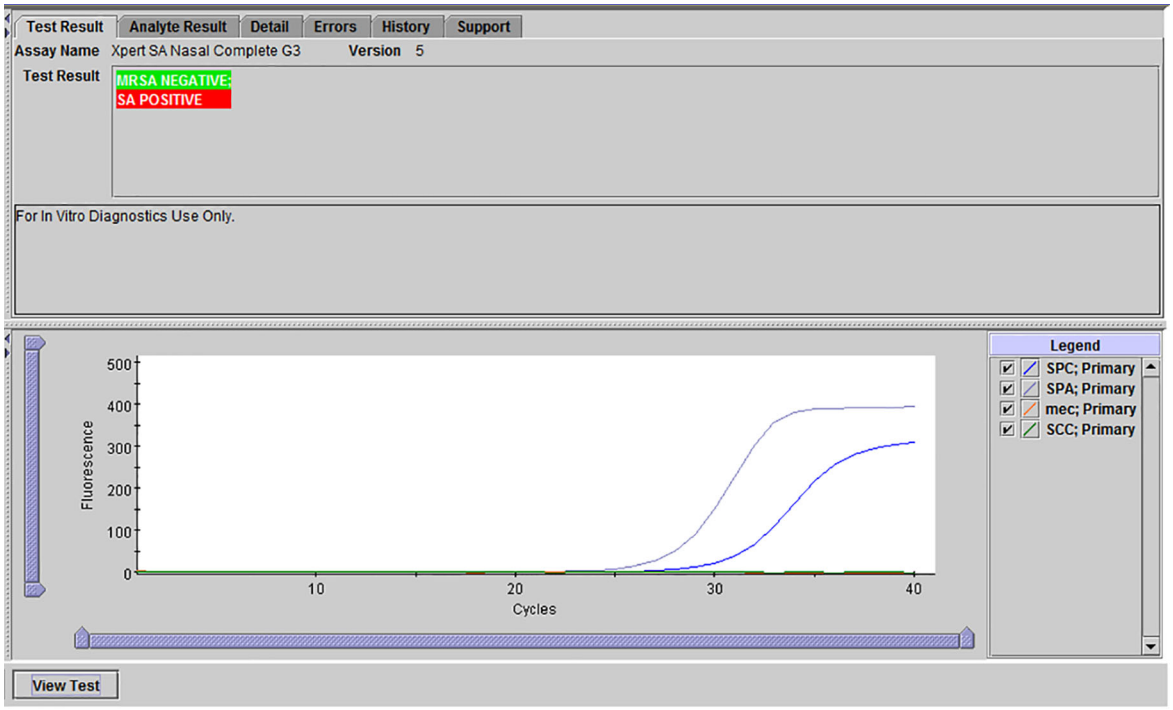

Figure 3. Example of a MRSA NEGATIVE; SA POSITIVE Result

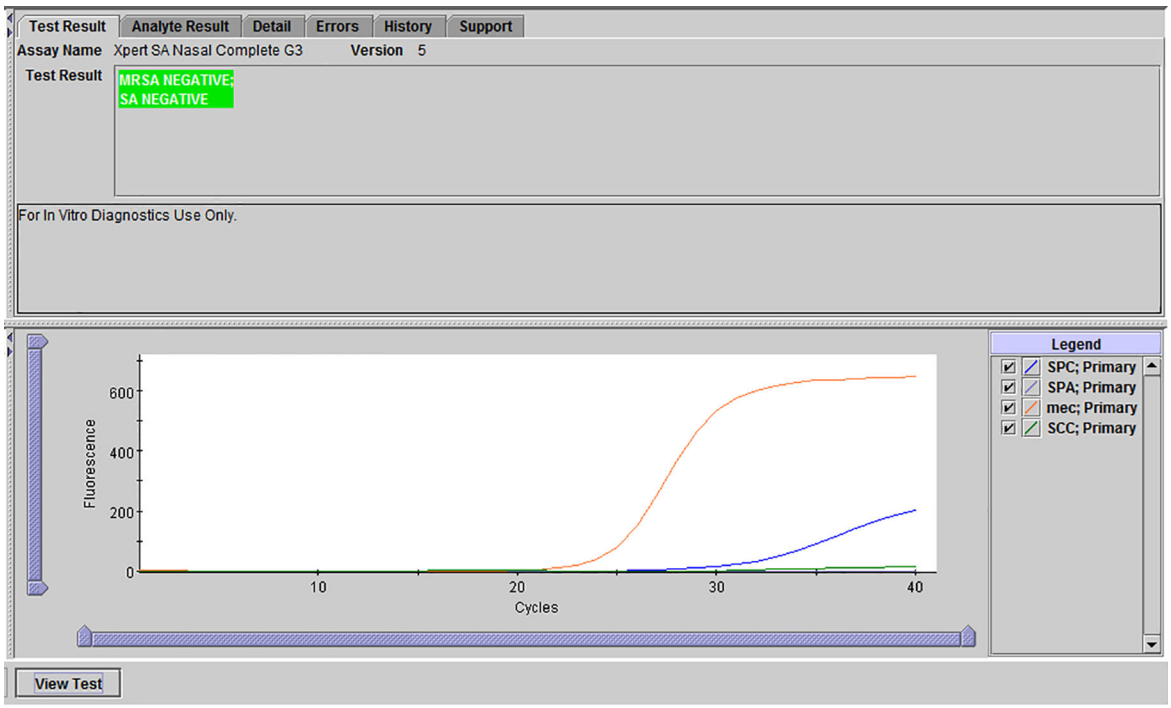

Figure 4. Example of a MRSA NEGATIVE; SA NEGATIVE Result

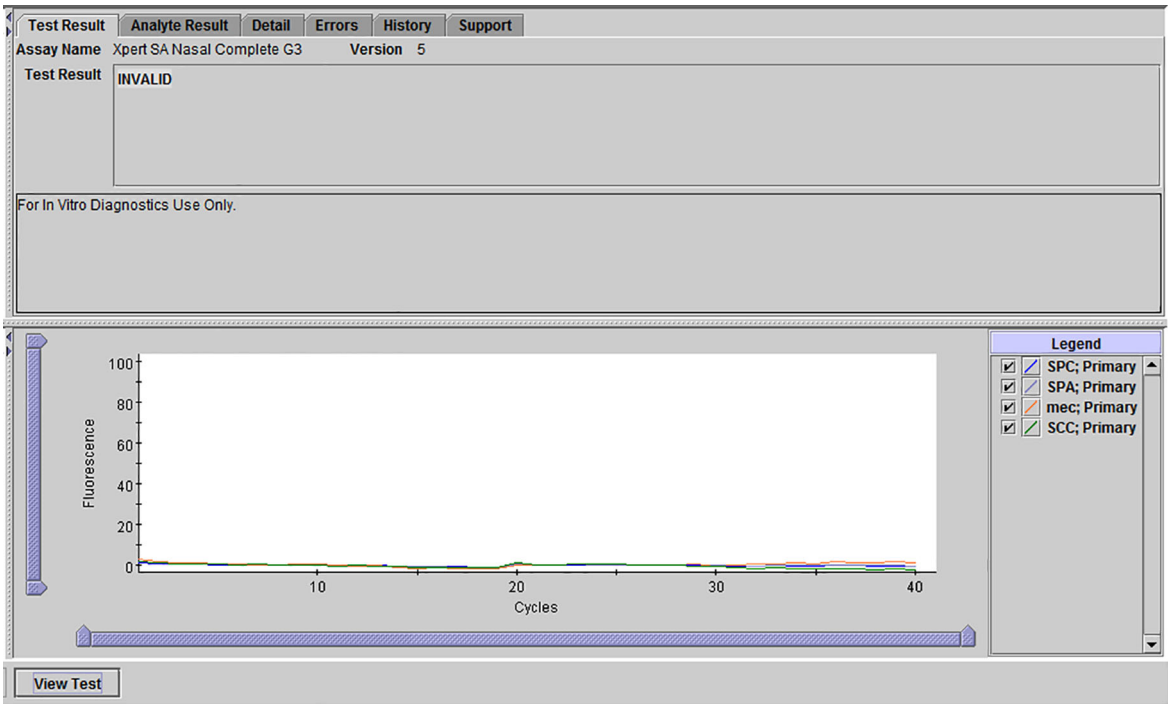

Figure 5. Example of an INVALID Result

14. Reasons to Repeat the Assay

If any of the test results mentioned below occur, repeat the test using a new sample, new cartridge (do not re-use the cartridge), and new reagents. Follow instructions for starting a new test (see the "Procedure / Preparing the Cartridge" section).

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

An **ERROR** result indicates that the assay was aborted possibly due to the reaction tube being filled improperly, a reagent probe integrity problem, or because 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.

15. Limitations

- The performance of the Xpert SA Nasal Complete Assay 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 SA Nasal Complete assay should be interpreted in conjunction with other laboratory and clinical data available to the clinician, and should be used as an adjunct to nosocomial infection control efforts to identify patients needing enhanced precautions. Results should not be used to guide or monitor treatment for MRSA or SA infections.
- 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.
- A positive test result does not necessarily indicate the presence of viable organisms. It is however, presumptive for the presence of MRSA or SA.
- The Xpert SA Nasal Complete assay positive result does not necessarily indicate intervention eradication failure since non-viable DNA may persist. A negative result following a previously positive test result may or may not indicate eradication success.
- The performance characteristics were not established for patients ≤ 21 years of age.
- Because the detection of MRSA and SA is dependent on the number of organisms present in the sample, reliable results are dependent on proper specimen collection, handling, and storage.
- Mutations or polymorphisms in primer or probe binding regions may affect detection of new or unknown MRSA variants resulting in a false negative result.

- The Xpert SA Nasal Complete assay may generate a false positive MRSA result when testing a mixed infection nasal specimen containing both methicillin-resistant coagulase-negative *Staphylococcus* and empty cassette SA.
- Xpert SA Nasal Complete assay results may sometimes be **INVALID** due to a failed SPC control, **ERROR** or **NO RESULT**, and require retesting that can lead to a delay in obtaining final results

16. Interfering Substances

A study was performed to assess potentially inhibitory effects, if any, of substance(s) encountered in nasal specimens using the Xpert SA Nasal Complete Assay. Potentially inhibitory substances may include, but are not limited to blood, nasal secretions or mucous and nasal sprays used to relieve congestion, nasal dryness or irritation. Substances were tested undiluted (except for mucous) in replicates of eight with MRSA cells spiked near the analytical Limit of Detection (~3-4x LoD). Both 10% and 5% (w/v) solutions of porcine mucin were used to simulate viscous nasal secretions or mucous. Negative samples were also tested to determine the effect on the performance of the sample processing control (SPC).

Under the conditions of this study, all negative specimens were correctly reported MRSA negative; SA negative using the Xpert SA Nasal Complete Assay. None of the potentially interfering substances had a statistically significant inhibitory effect on SPC performance in negative samples, p-value = 0.734.

All positive specimens were correctly reported MRSA positive; SA positive at levels near the analytical LoD using the Xpert SA Nasal Complete Assay. One-way ANOVA analysis indicates a slight but statistically significant Ct shift for MRSA targets *spa* (p=0.024) and *mecA* (p=0.002) in the presence of 10% mucin. However, the mean Ct differences between 10% mucin and the buffer control for *spa* and *mecA* were 0.34 and 0.63 respectively, and were not considered to be practically significant. The SCC*mec* signal was not significantly effected by 10% mucin (p=0.339).

17. Performance Characteristics

Performance characteristics of the Xpert SA Nasal Complete Assay was determined in a multi-site prospective investigation study at two US institutions by comparing the Xpert SA Nasal Complete Assay on the GeneXpert System with culture (direct and enriched). Subjects included inpatients and outpatients at risk for nasal colonization by *S. aureus*.

Double swabs were collected from each subject. One swab was tested by the Xpert SA Nasal Complete Assay at the enrolling center and the other swab was tested at a central laboratory by culture.

At the centralized laboratory, the specimen was streaked directly and after overnight enrichment in tryptic soy broth containing 6.5% NaCl to selective chromogenic agar plates with and without cefoxitin. The plates containing cefoxitin were incubated for 24-48 hours at 35 to 37°C. The plates that did not contain cefoxitin were incubated for 24 hours at 33 to 37°C. Confirmation of presumptive positive colonies was performed with catalase, a tube coagulase test and Gram stain. Oxacillin/methicillin susceptibility was tested by disk diffusion test using a 30 µg cefoxitin disk and cutoff of 21/22 mm.

Assay performance of the Xpert SA Nasal Complete Assay was calculated relative to the direct and enriched culture results.

17.1 Overall Results

A total of 744 specimens were tested for MRSA and SA by Xpert SA Nasal Complete Assay and culture. The Xpert SA Nasal Complete Assay identified 100% of the specimens positive for MRSA and 95.8% of the specimens negative for MRSA relative to the direct culture method. For the specimens tested, the MRSA positive predictive value was 74.1% and the MRSA negative predictive value was 100% (Table 2).

The Xpert SA Nasal Complete Assay identified 99.3% of the specimens positive for SA and 83.8% of the specimens negative for SA relative to the direct culture method. For the specimens tested, the SA positive predictive value was 61.3% and the SA negative predictive value was 99.8% (Table 3).

The Xpert SA Nasal Complete Assay identified 88.2% of the specimens positive for MRSA and 98.3% of the specimens negative for MRSA relative to the enriched culture method. For the specimens tested, the MRSA positive predictive value was 89.8% and the MRSA negative predictive value was 98.0% (Table 4).

The Xpert SA Nasal Complete Assay identified 92.7% of the specimens positive for SA and 91.4% of the specimens negative for SA relative to the enriched culture method. For the specimens tested, the SA positive predictive value was 81.9% and the SA negative predictive value was 96.8% (Table 5).

Table 2. MRSA — Direct Culture

		Culture +	Culture -			
Xpert SA Nasal Complete Assay	+	80	28	108	Sensitivity	100%
	-	0	636	636	Specificity	95.8%
		80	664	744		

Table 3. SA — Direct Culture

		Culture +	Culture -			
Xpert SA Nasal Complete Assay	+	152	96	248	Sensitivity	99.3%
	-	1	495	496	Specificity	83.8%
		153	591	744		

Table 4. MRSA — Enriched Culture

		Culture +	Culture -			
Xpert SA Nasal Complete Assay	+	97	11	108	Sensitivity	88.2%
	-	13	623	636	Specificity	98.3%
		110	634	744		

Table 5. SA — Enriched Culture

		Culture +	Culture -			
Xpert SA Nasal Complete Assay	+	203	45	248	Sensitivity	92.7%
	-	16	480	496	Specificity	91.4%
		219	525	744		

17.2 Analytical Specificity

Cultures from 98 American Type Culture Collection (ATCC) and 7 Network on Antimicrobial Resistance in *Staphylococcus aureus* (NARSA) strains representing species phylogenetically related to *Staphylococcus aureus* or those potentially encountered in a hospital environment, 29 strains of methicillin-sensitive coagulase negative staphylococci, and 9 strains of methicillin-resistant coagulase negative staphylococci were tested using the Xpert SA Nasal Complete Assay. The organisms tested represented 74 Gram positive, 28 Gram negative, 3 yeast, 95 aerobic and 10 anaerobic species. Two or more replicates of each isolate were tested at 1.7 - 3.2 McFarland units. Under the conditions of the study, all isolates were reported MRSA negative and SA negative, none of the isolates were detected by the Xpert SA Nasal Complete Assay. Positive and Negative controls were included in the study. The specificity was 100%.

17.3 Analytical Ubiquity (Inclusivity)

The analytical ubiquity (inclusivity) of the Xpert SA Nasal Complete Assay was determined using 25 *Staphylococcus aureus* strains supplied by the Centers for Disease Control and Prevention (CDC). These specimens are reported to be representative of MRSA and MSSA strains currently encountered in the healthcare community. All strains were tested in triplicate using 100 µL of stationary phase cell suspensions diluted 10 million-fold. The panel consists of MRSA strains representing SCC*mec* types II, IV, IVa, IVb, and IVc in addition to several unknown types. Data supplied by the CDC indicate these strains, when characterized by pulsed-field gel electrophoresis (PFGE), represent numerous USA types including USA 100, the most common hospital-acquired strain and USA 300 and 400, the most common community-acquired strains.[10]

As shown in Table 6, all MRSA strains were correctly reported MRSA positive and SA positive using the Xpert SA Nasal Complete Assay. Additionally, each MSSA strain was correctly reported MRSA negative and SA positive. Ct values represent the mean of three replicates. After CHROMagar and Xpert SA Nasal Complete Assay results were reported to the CDC, they revealed that the Xpert SA Nasal Complete Assay did not incorrectly identify specimen 95:99. Specimen 95:99 was mislabeled by the CDC. Specimen 95:99 was correctly reported MRSA negative and SA negative by the Xpert SA Nasal Complete Assay. Colony forming units per assay were determined by plate counts in duplicate.

Table 6. Analytical Ubiquity of the Xpert SA Nasal Complete Assay

Lab ID	Sender	Source	PFGE Type	SCC*mec* Type	CHROMagar MRSA Result	Xpert Result	SPC Ct	*spa*Ct	*mecA* Ct	SCC Ct	CFU per assay
94:1013	VT	Skin lesion	USA1000	IV	+	MRSA POSITIVE; SA POSITIVE	34.7	30.7	31	32.6	152
*95:99	CT	Blood	USA500	IV	-	MRSA NEGATIVE; SA NEGATIVE	34.1	0	0	0	37
96:308	NM	Stool	USA900	MSSA	-	MRSA NEGATIVE; SA POSITIVE	34	29.4	0	0	201
96:281	NC	Blood	USA200	II	+	MRSA POSITIVE; SA POSITIVE	33.4	33.6	34	35.3	101
148-99	NY	Blood	USA600	II	+	MRSA POSITIVE; SA POSITIVE	34.3	33.2	33.1	35.2	43
182-99	MN	Unknown	USA400	IVa	+	MRSA POSITIVE; SA POSITIVE	43.7	26.7	27.1	28.7	417
18626	OH	Blood	USA100	II	+	MRSA POSITIVE; SA POSITIVE	34.8	30.7	31	32.7	138
0:50	TN	Stool	USA600	not typed	+	MRSA POSITIVE; SA POSITIVE	33.6	31.2	31.4	33.2	115
0-25-4	MS	Nasal	USA700	IVa	+	MRSA POSITIVE; SA POSITIVE	35.5	29.1	29.3	30.9	178
0-25-37	MS	Skin/Soft Tissue	USA300	IVa	+	MRSA POSITIVE; SA POSITIVE	34.7	32.3	32.7	34.2	94
1-1-81	WA	Nasal	USA400	not typed	+	MRSA POSITIVE; SA POSITIVE	34.3	33	33.7	35.5	106
1-1-493	WA	Wound	USA800	IV	+	MRSA POSITIVE; SA POSITIVE	33.7	31.5	31.7	33.4	113
N7129	NHANES	Nasal	USA900	MSSA	-	MRSA NEGATIVE; SA POSITIVE	34.3	29.9	0	0	84
107-03	NV	Blood	USA200	not typed	+	MRSA POSITIVE; SA POSITIVE	34	33	33.3	34.9	99
GA201	GA-ABC	Unknown	USA100	II	+	MRSA POSITIVE; SA POSITIVE	33.6	32.3	32.4	34	95

Table 6. Analytical Ubiquity of the Xpert SA Nasal Complete Assay (Continued)

Lab ID	Sender	Source	PFGE Type	SCC*mec* Type	CHROMagar MRSA Result	Xpert Result	SPC Ct	*spa*Ct	*mecA* Ct	SCC Ct	CFU per assay
GA217	GA-ABC	Unknown	USA300	IVb	+	MRSA POSITIVE; SA POSITIVE	33.6	30.8	31.2	33	121
GA229	GA-ABC	Unknown	USA500	IV	+	MRSA POSITIVE; SA POSITIVE	37.8	31.7	31.9	33.3	81
7031	AK	Abscess	USA1100	IVa	+	MRSA POSITIVE; SA POSITIVE	34.2	30.8	31.5	32.9	73
102-04	CA	Nasal	USA1200	MSSA	-	MRSA NEGATIVE; SA POSITIVE	33.9	29.4	0	0	110
8-03	WI	Unknown	USA700	not typed	+	MRSA POSITIVE; SA POSITIVE	33.3	29	29.2	30.9	202
510-04	Uruguay	Abscess	USA1100	IVc	+	MRSA POSITIVE; SA POSITIVE	34.6	31.5	32	33.8	143
27-05	HI	Wound	USA800	IVc	+	MRSA POSITIVE; SA POSITIVE	40.7	27.8	28.1	29.8	373
CA46	CA	Blood	USA1000	IV	+	MRSA POSITIVE; SA POSITIVE	33.4	32.6	33.7	35.8	81
398-05	HI	Wound	USA1000	IVb	+	MRSA POSITIVE; SA POSITIVE	33.6	32.8	33.4	35.9	59
N4151	NHANES	Nasal	USA800	IVb	+	MRSA POSITIVE; SA POSITIVE	34	30.7	31.2	32.9	101

* Specimen 95:99: After CHROMagar and Xpert SA Nasal Complete Assay results were reported to the CDC, they revealed that the Xpert SA Nasal Complete Assay correctly identified specimen 95:99. Specimen 95:99 was mislabeled by the CDC. Specimen 95:99 was correctly reported MRSA negative and SA negative by the Xpert SA Nasal Complete Assay. The information contained in the grey columns was provided to Cepheid by CDC.

17.4 Analytical Sensitivity

Additional studies were performed to determine the 95% confidence interval for the analytical limit of detection (LoD) of this assay. The limit of detection is defined as the lowest number of colony forming units (CFU) per sample that can be reproducibly distinguished from negative samples with 95% confidence. For SA, replicates of 20 were evaluated at four concentrations (0, 50, 100, and 150 CFU/sample). For MRSA (SCC*mec* type II cells), replicates of 20 were evaluated at four concentrations (0, 25, 50, and 125 CFU/sample).

Under the conditions of the study, results indicate that the LoD point estimate for SA is 93.7 CFU/sample with the 95% confidence interval ranging from 75.5 CFU to 137.8 CFU. The estimate and confidence levels were determined using logistic regression with data (number of positives per number of tests at each level) taken at four levels (0, 50, 100, and 150 CFU/sample). Note that the analytical LoD for SA will be conservatively reported as 138 CFU/sample.

The LoD point estimate for MRSA is 43.9 CFU/sample with the 95% confidence interval ranging from 35.7 CFU to 68.3 CFU. The estimate and confidence levels were determined using logistic regression with data (number of positives per number of tests at each level) taken at four levels (0, 25, 50, and 125 CFU/sample). Note that the analytical LoD for MRSA will be conservatively reported as 70 CFU/sample.

The confidence intervals were determined using maximum likelihood estimates on the logistic model parameters using the large sample variance-covariance matrix.

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19. Cepheid Headquarters Locations

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20. Technical Assistance

Before contacting Cepheid Technical Support, collect the following information:

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

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21. Table of Symbols

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

Cepheid AB
Röntgenvägen 5
SE-171 54 Solna
Sweden

CH REP

Cepheid Switzerland GmbH
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CE IVD

22. Revision History

Description of Changes: 301-0189 Rev G to Rev H

Section	Description of Changes
Trademark, Patents and Copyright Statements	Updated per legal standard.
20	Updated company contact information.
21	Added CH REP and Importer symbols and definitions to Table of Symbols. Added CH REP and Importer information with Switzerland address.