GeneXpert®
Powered By CEPHEID INNOVATION

Xpert® MRSA NxG

REF **GXMRSA-NXG-CE-10**

REF **GXMRSA-NXG-CE-120**

Instructions For Use

CE IVD

Cepheid®

In Vitro Diagnostic Medical Device

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The purchase of this product includes a limited, non-transferable license under U.S. Patent No. 7,449,289 and its international counterparts owned by GeneOhm Sciences Canada, Inc (a subsidiary of Becton, Dickinson and Company), to use such product for human IVD use with a GeneXpert® instrument. No right under said patents is conveyed, expressly, by implication, or by estoppel, to use this product for any other purpose.

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

Xpert® MRSA NxG

For *In Vitro* Diagnostic Use Only.

1 Proprietary Name

Xpert® MRSA NxG

2 Common or Usual Name

Xpert MRSA NxG test

3 Intended Use

The Xpert MRSA NxG test, performed on the GeneXpert® Instrument Systems, is a qualitative *in vitro* diagnostic test intended for the detection of methicillin-resistant *Staphylococcus aureus* (MRSA) DNA directly from nasal swabs in patients at risk for nasal colonization. The test utilizes automated real-time polymerase chain reaction (PCR) for the amplification of MRSA-specific DNA targets and fluorogenic target-specific hybridization probes for the real-time detection of the amplified DNA. The Xpert MRSA NxG test is intended to aid in the prevention and control of MRSA infections in healthcare settings. The Xpert MRSA NxG test is not intended to diagnose, guide, or monitor treatment for MRSA infections, or provide results of susceptibility to methicillin. A negative result does not preclude MRSA nasal colonization. Concomitant cultures are necessary 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 that causes both community and healthcare-associated infections. It is a major healthcare-associated pathogen that can cause a variety of diseases including bacteremia, pneumonia, osteomyelitis, acute endocarditis, toxic shock syndrome, food poisoning, myocarditis, scalded skin syndrome, carbuncles, boils, and abscesses. [1]

In the early 1950s, acquisition and spread of beta-lactamase-encoding plasmids thwarted the effectiveness of penicillin for treating *S. aureus* (SA) infections. In 1959, methicillin, a semi-synthetic penicillin, was introduced. However, by 1960, methicillin-resistant SA (MRSA) strains were identified. Resistance is now known to be conferred when SA acquires a Staphylococcal cassette chromosome (SCC) *mec* gene complex containing either *mecA* or *mecC*. MRSA causes infections in both healthcare and community settings, resulting in significant morbidity and mortality. Attributable mortality of 33% has been reported for MRSA bacteremia. Control strategies and policies to limit the spread of these infections have been developed and implemented in a variety of healthcare settings. Controlling MRSA is a primary focus of most hospital infection prevention programs. [1 – 5] Currently, the standard method for detecting MRSA is culture, which can require several days to generate a definitive result. A study among patients in Veterans Administration Hospitals in the United States showed a significant impact on reducing healthcare-associated MRSA infections by using universal screening of patients for MRSA nasal colonization on admission as part of a bundle of infection control measures. [6]

5 Principle of the Procedure

The Xpert MRSA NxG test is performed on the GeneXpert Instrument Systems. The GeneXpert Instrument Systems automate and integrate sample preparation, nucleic acid extraction and amplification, and detection of the target sequence in simple or complex samples using real-time PCR tests. The systems consist of an instrument, computer, and preloaded software for running tests and viewing the results. The systems require the use of single-use disposable cartridges that hold

the PCR reagents and host the PCR process. Because the cartridges are self-contained, cross-contamination between samples is minimized. For a full description of the systems, see the *GeneXpert Dx System Operator Manual* or the *GeneXpert Infinity System Operator Manual*.

The Xpert MRSA NxG test includes reagents for the detection of MRSA. A Sample Processing Control (SPC) and a Probe Check Control (PCC) are also included in the cartridge. The SPC is present to control for adequate processing of the sample and to monitor the presence of inhibitors in the PCR reaction. The PCC verifies reagent rehydration, PCR tube filling in the cartridge, probe integrity, and dye stability.

The primers and probes in the Xpert MRSA NxG test detect proprietary sequences for methicillin/oxacillin resistance (*mecA* and *mecC* genes), and SCC*mec*, which is inserted into the SA chromosome at the *attB* site.

An Early Assay Termination function provides positive results if target DNA reaches a predetermined threshold before the full 40 PCR cycles have been completed. When MRSA target levels (*mecA/mecC and* SCC*mec*) are high enough to generate very early Cts, the SPC amplification curve will be not seen and its results will not be reported.

6 Reagents and Instruments

6.1 Materials Provided

The Xpert MRSA NxG test kit (GXMRSA-NXG-CE-10 or GXMRSA-NXG-CE-120) contains sufficient reagents to process 10 or 120 samples, respectively. The kits contain the following:

Xpert MRSA NxG 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
• Reagent 1	3.0 mL per cartridge	3.0 mL per cartridge
• Reagent 2 (Sodium Hydroxide)	3.5 mL per cartridge	3.5 mL per cartridge
Xpert MRSA NxG Elution Reagent	**10 x 2.0 mL per vial**	**120 X 2.0 mL per vial**
(Guanidinium Thiocyanate)		
CD	**1 per kit**	**1 per kit**
• Assay Definition Files (ADF)		
• Instructions to import ADF into software		
• Instructions for Use (Package Insert)		

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

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

6.2 Storage and Handling

- Store the Xpert MRSA NxG 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.
- The Elution Reagent is a colorless liquid. Do not use the Elution Reagent if it has become discolored.

6.3 Materials Required but Not Provided

- GeneXpert Dx System or GeneXpert Infinity System (catalog number varies by configuration): GeneXpert Instrument, computer with proprietary GeneXpert Software Version 4.3 or higher, barcode scanner, and operator manual.
- Printer: If a printer is required, contact Cepheid Technical Support to arrange for the purchase of a recommended printer.
- Vortex mixer
- Swabs for specimen collection, such as the swabs supplied in the Cepheid Sample Collection Device (Part No. 900-0370 Dual Rayon Swab in Liquid Stuart Medium) or the Copan Dual Rayon Swab and Transport Systems (139C LQ STUART) or Liquid Amies Elution Swab (ESwab) Collection and Transport System (Copan 480C, Copan 480CE or BD ESwab Collection Kit Part No. 220245).
- Pipet for transfer of an ESwab™ specimen, such as the Poly-Pipets 300 µL disposable, sterile exact volume transfer pipet (Part No. 300-8533) or equivalent.
- Disposable, sterile transfer pipettes for the transfer of Xpert MRSA NxG Elution Reagent.
- Sterile gauze

6.4 Materials Available but Not Provided

- NATtrol™ MRSA negative control, ZeptoMetrix Corporation catalog number NATMSSE-6MC (inactivated methicillin-susceptible *Staphylococcus epidermidis*)
- NATtrol MRSA positive control, ZeptoMetrix Corporation catalog number NATMRSA-6MC (inactivated methicillin-resistant *Staphylococcus aureus*)

7 Warnings and Precautions

- For *in vitro* diagnostic use.
- Treat all biological specimens, including used cartridges and reagents, 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[7] and the Clinical and Laboratory Standards Institute.[8]
- Follow your institution's safety procedures for working with chemicals and handling biological samples.
- Do not substitute Xpert MRSA NxG test reagents with other reagents.
- Do not open the Xpert MRSA NxG test cartridge lid until you are ready to add the sample.
- 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 invalid results.
- Do not place a sample ID label on the cartridge lid or on the bar code label.
- Each single-use Xpert MRSA NxG test cartridge is used to process one test. Do not reuse spent cartridges.
- Do not use a cartridge that has a damaged reaction tube.
- Wear clean lab coats and gloves. Change gloves between processing each sample.
- In the event of contamination of the work area or equipment with samples or controls, thoroughly clean the contaminated area with a solution of 1:10 dilution of household chlorine bleach and then repeat the cleaning of the work area with 70% ethanol. Wipe work surfaces 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 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.
- 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 Package Insert instructions and the *GeneXpert System Operator Manual* are necessary to avoid erroneous results.

- Performing the Xpert MRSA NxG test outside the recommended ranges for time and temperature may produce erroneous or invalid results. Assays not performed within the specified ranges should be repeated.

8 Chemical Hazards[9,10]

- 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 Specimen Collection, Transport and Storage

9.1 Specimen Collection

Follow your institution's guidelines for collecting nasal swab specimens using a recommended collection and transport device (see Section 6.3) and/or using the following instructions:

- When using the *dual rayon swabs*, keep both swabs attached to the red cap at all times. Holding the swab cap with both swabs attached, sample each nare one at a time. Place the dual swab specimens into the transport tube containing the Liquid Stuart Medium.

or

- When using the *ESwab*, collect the nasal specimen by sampling both nares one at a time with the same swab. Place the swab into the transport tube containing the Liquid Amies Transport Medium.

9.2 Specimen Transport and Storage

Maintain proper transport and storage conditions of the swab specimen prior to use to ensure the integrity of the specimen. Specimen stability under shipping and storage conditions other than those recommended below Table 1 has not been evaluated with the Xpert MRSA NxG test.

Table 1. Specimen Transport and Storage Conditions

Specimen Collection Device	Specimen Transport and Storage Temperature (°C)	Specimen Storage Time
Rayon (Dual Cepheid) or ESwab	15–30°C	Up to 24 hours
	2–8°C	Up to 7 days

10 Procedure

10.1 Preparing the Cartridge

Important **Place the cartridge into the GeneXpert instrument within 30 minutes of adding the Elution Reagent to the cartridge.**

1. Remove a cartridge and Elution Reagent vial from the Xpert MRSA NxG test kit.
2. Add the sample into the cartridge:

   Dual Swabs

   a) Remove the swabs from the transport container. Use only one of the swabs for the assay testing. The second swab may be used for repeat testing and should be stored according to Table 1.

   b) Insert the swab into the vial containing the Elution Reagent and break the swab off at the score mark on the swab shaft.

Note Wrap sterile gauze (not provided) around both the stem of the swab and the mouth of the Elution Reagent vial when breaking the swab to minimize risk of contamination.

   OR

   ESwab

   a) Mix the Liquid Amies transport medium containing the swab sample by vortexing at high speed for 5 seconds to release the sample from the swab tip and evenly disperse in the liquid transport medium.

   b) Using the exact volume transfer pipette (not provided), transfer 300 µL of the liquid sample into the Elution Reagent vial.

3. Close the Elution Reagent vial cap and vortex at high speed for 10 seconds.
4. Open the cartridge lid. Using a transfer pipette (not provided), transfer the entire contents of the Elution Reagent vial to the Sample Chamber of the Xpert MRSA NxG test cartridge. See Figure 1.

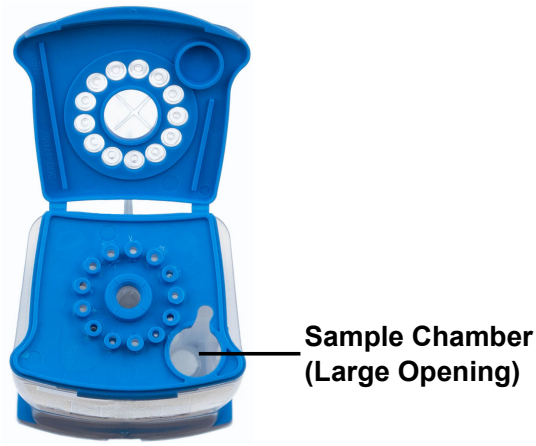

Figure 1. Cartridge (Top View)

5. Close the cartridge lid and start the test.

10.2 Starting the Test

Important **If you are running a *GeneXpert Dx system*, before you start the test, make sure that the system is running GeneXpert Dx software version 4.7b or higher and that the correct assay definition file is imported into the software.**

Important **If you are running a *GeneXpert Infinity system*, before you start the test, make sure that the system is running Xpertise software version 6.4b or higher and that 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 Dx System Operator Manual* or the *GeneXpert Infinity System Operator Manual*, depending on the model that is being used.

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

1. Turn on the GeneXpert instrument:
   - If using the *GeneXpert Dx instrument*, first turn on the GeneXpert Dx instrument, and then turn on the computer. The GeneXpert software will launch automatically. If it does not, double-click the GeneXpert Dx software shortcut icon on the Windows® desktop.

     or
   - If using the *GeneXpert Infinity instrument*, power up the instrument. The Xpertise software will launch automatically. If it does not, double-click the Xpertise software shortcut icon on the Windows® desktop.
2. Log on to the GeneXpert Instrument System software using your username and password.
3. In the **GeneXpert System** window, click **Create Test** (GeneXpert Dx) or **Orders** and **Order Test** (Infinity). The **Create Test** window opens. The **Scan Patient ID barcode** dialog box opens.
4. Scan or type in the Patient ID. 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 and all the reports. The **Scan Sample ID barcode** dialog box opens.
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 and all the reports. The **Scan Cartridge Barcode** dialog box opens.
6. Scan the barcode on the 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 cartridge does not scan, then repeat the test with a new cartridge. If you have scanned the cartridge barcode in the software and the assay definition file is not available, a screen will appear indicating the assay definition file is not loaded on the system. If this screen appears, contact Cepheid Technical Support.

7. Click **Start Test** (GeneXpert Dx) or **Submit** (Infinity). In the dialog box that appears, type your password, if required.

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. Then remove the cartridge.
   d) Dispose of the used cartridges in the appropriate specimen waste containers according to your institution's standard practices.

11 Viewing and Printing Results

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

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

12 Built-In Quality Controls

Each test includes a Sample Processing Control and a Probe Check Control.

- **Sample Processing Control (SPC)—**Ensures the sample was processed correctly. The SPC verifies that lysis of bacteria has occurred if the organisms are present and verifies that sample processing is adequate. Additionally, this control detects sample-associated inhibition of the real-time PCR assay, ensures the PCR conditions (temperature and time) are appropriate for the amplification reaction, and that the PCR reagents are functional. The SPC should be positive in a negative sample and can be negative or positive in a positive sample. The SPC passes if it meets the validated acceptance criteria.
- **Probe Check Control (PCC)—**Before the start of the PCR, the GeneXpert System measures the fluorescence signal from the probes to monitor bead rehydration, reaction tube filling, probe integrity, and dye stability. Probe Check passes if it meets the assigned acceptance criteria.
- **External Controls—** External controls described in Section 6.4 are available but not provided and may be used in accordance with local, state, and federal accrediting organizations, as applicable.

To run a control using the Xpert MRSA NxG test:

1. Vortex the NATtrol control for 5-10 seconds.
2. Pipette 100 µL of NATtrol control into 2 mL of Elution Reagent.
3. Vortex the Elution Reagent vial for 5-10 seconds.
4. Use a transfer pipette (not provided) to transfer the entire contents from the Elution Reagent vial into the Sample Chamber of the cartridge.
5. Close the cartridge lid and start the test following instructions in Starting the Test.

13 Interpretation of Results

The results are interpreted by the GeneXpert System from measured fluorescent signals and embedded calculation algorithms and will be shown in the **View Results** window. Possible results are shown in the table below.

Table 2. Xpert MRSA NxG Test Results and Interpretation

Result	Interpretation
MRSA DETECTED See Figure 2.	MRSA DNA is detected. ● MRSA DETECTED: MRSA targets, mec (*mecA/mecC*) and SCCmec, have a cycle threshold (Ct) within the valid range. ● SPC – NA (not applicable); the SPC signal is not part of the results interpretation algorithm if MRSA is detected since SPC signal may be suppressed due to competition with mec (*mecA/mecC*) and SCCmec. ● Probe Check – PASS; all probe check results pass.
MRSA NOT DETECTED See Figure 3. See Figure 4. See Figure 5.	MRSA DNA is not detected ● MRSA NOT DETECTED: Scenarios ● Target DNA for SCC mec is not detected and target DNA for mec (mecA/mecC) is not detected-Figure 3 ● Target DNA for SCC mec is not detected and target DNA for mec (mecA/mecC) is detected-Figure 4 ● Target DNA for SCC mec is detected and target DNA for mec (mecA/ mecC) is not detected-Figure 5 ● SPC: PASS; SPC has a Ct within the valid range and both target DNA mec (mecA/mecC) and SCC mec are not detected. Or, if either the mec (mecA/mecC) or SCC mec exhibit a valid Ct value, SPC result is ignored. ● Probe Chec — PASS; all probe check results pass.
INVALID See Figure 6.	Presence or absence of MRSA target DNA (mecA/mecC or SCC mec) cannot be determined. Use the instructions in Section 15 to repeat the test. ● Target DNA for SCC mec is not detected and target DNA for mec (mecA/mecC) is not detected. ● SPC: FAIL; SPC Ct is not within the valid range. ● PCC: PASS; all probe check results pass.
ERROR	Presence or absence of MRSA target DNA (mecA/mecC or SCC mec) cannot be determined. Use the instructions in Section 15 to repeat the test. ● mec (mecA/mecC): NO RESULT ● SCC mec: NO RESULT ● SPC NO RESULT ● PCC: FAIL*; one or more of the probe check results failed. * If the probe check passed, the error was caused by a system component failure.
NO RESULT	Presence or absence of MRSA target DNA (mecA /mecC or SCC mec) cannot be determined. Use the instructions in Section 15. A **NO RESULT** indicates insufficient data were collected. For example, the operator stopped a test that was in progress or a power failure occurred. ● mec (mecA/mecC): NO RESULT ● SCC mec: NO RESULT ● SPC: NO RESULT ● PCC: N/A (not applicable). An error caused by the maximum pressure limit exceeding the acceptable range terminates the run prior to probe check.

Note The screens shown in Figure 2 , Figure 3, Figure 4 , Figure 5 , and Figure 6 are examples from a GeneXpert Dx System running GeneXpert Dx software.

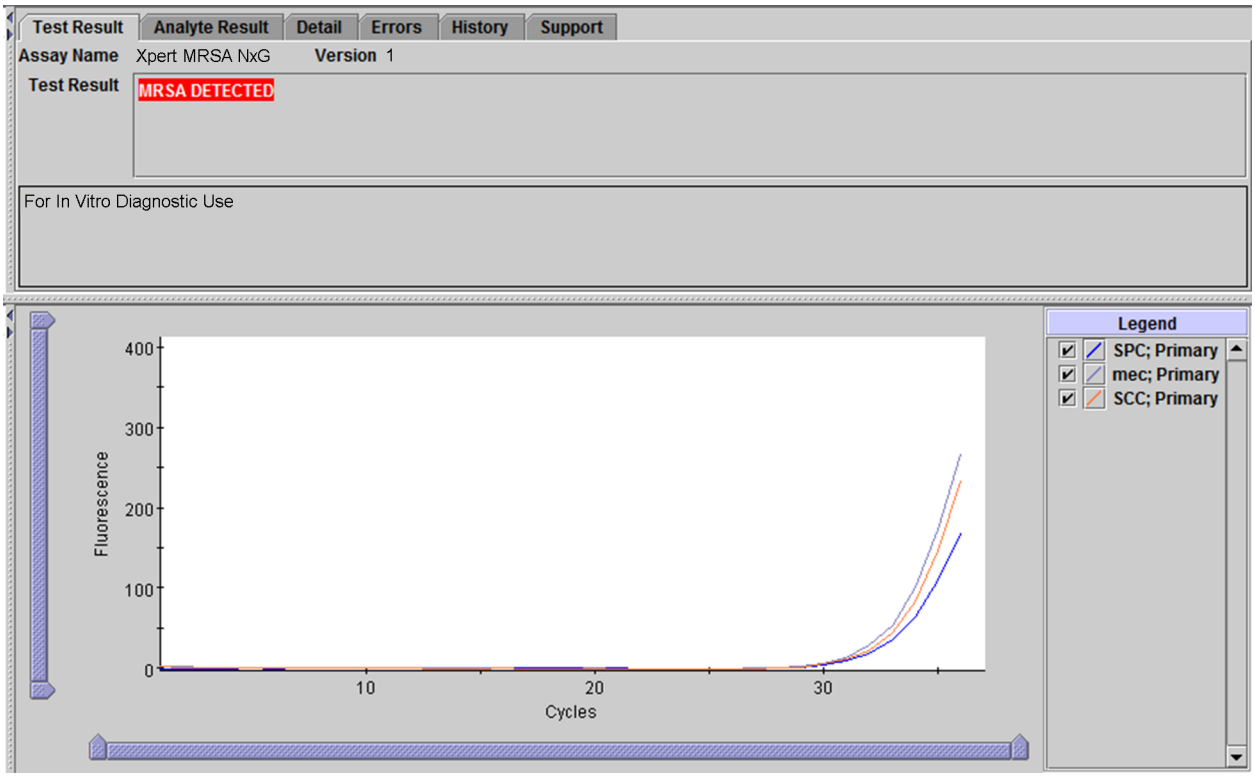

Figure 2. An Example of a MRSA DETECTED Result

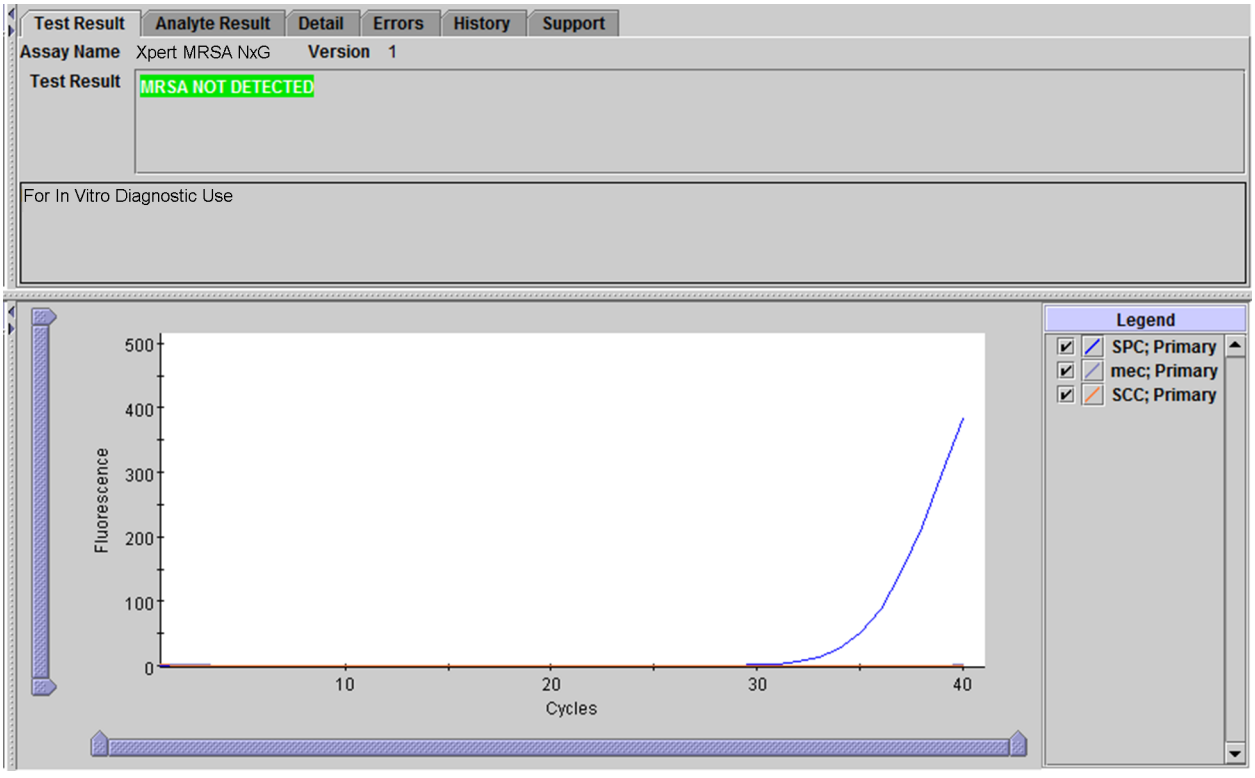

Figure 3. An Example of a MRSA NOT DETECTED Result

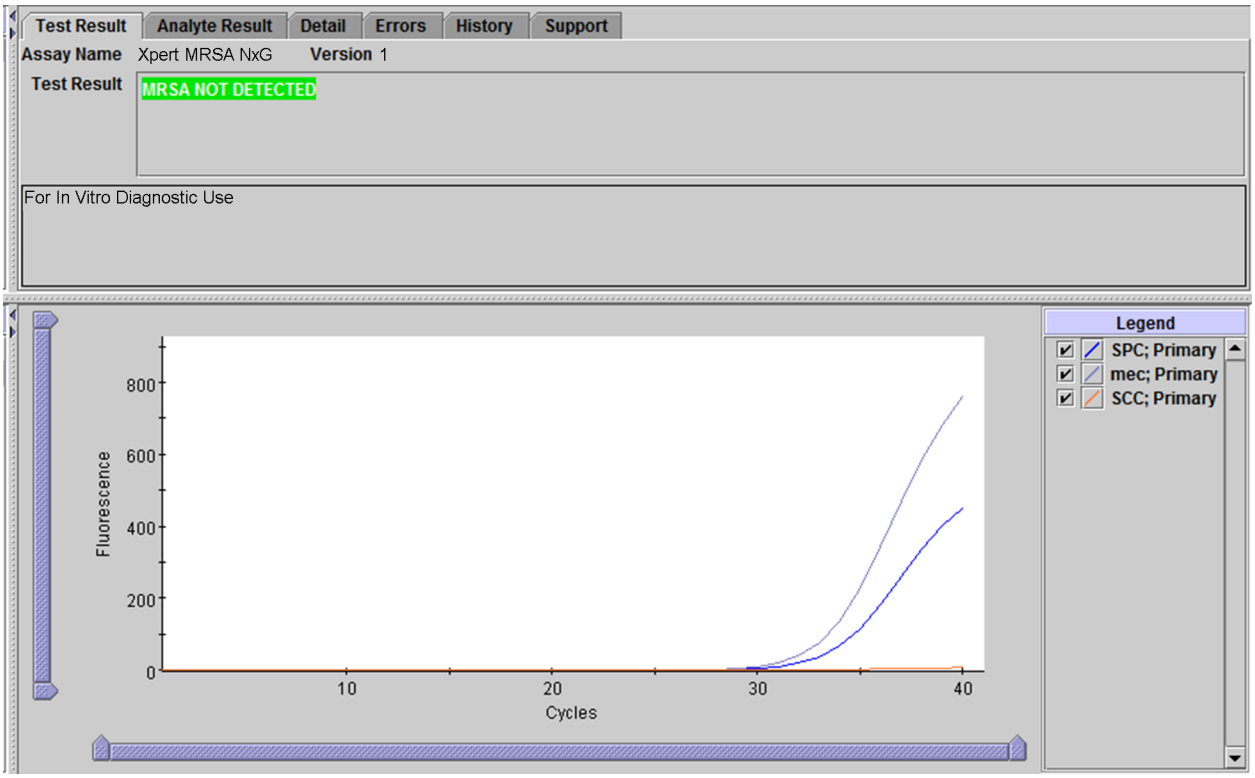

Figure 4. An Example of a MRSA NOT DETECTED Result

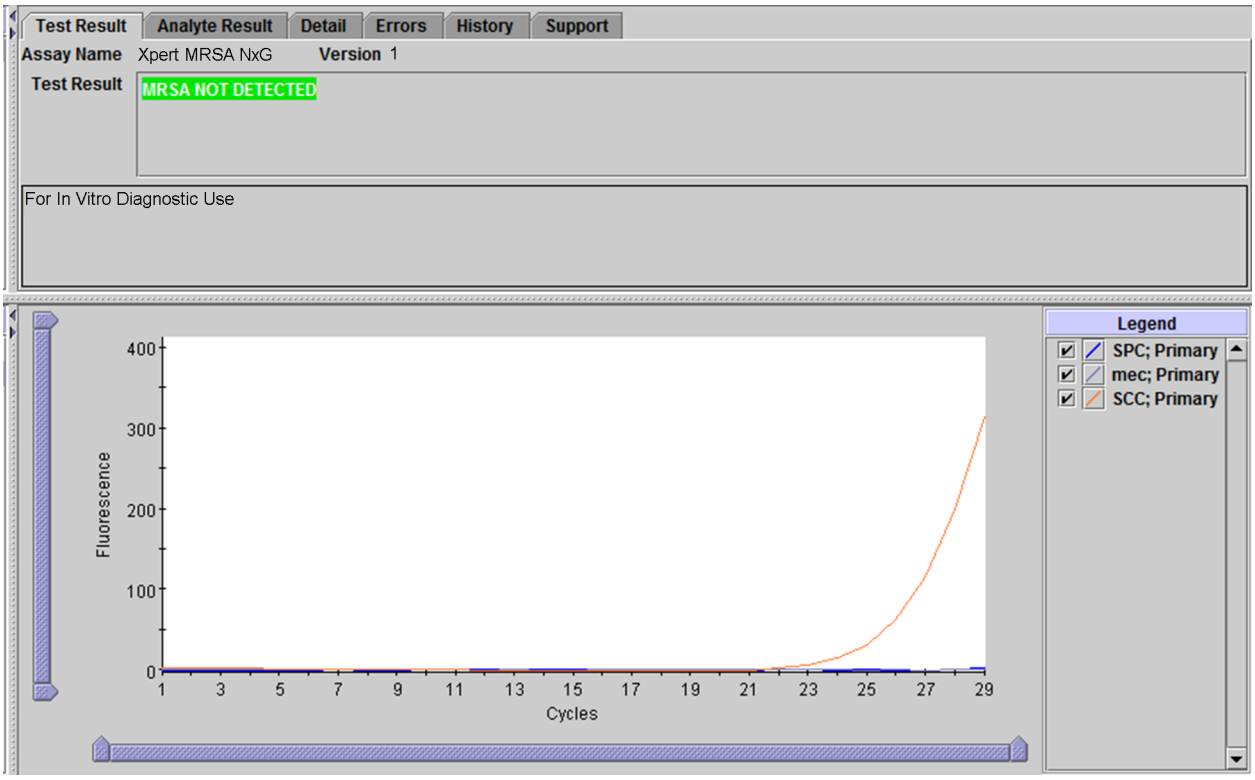

Figure 5. An Example of a MRSA NOT DETECTED Result

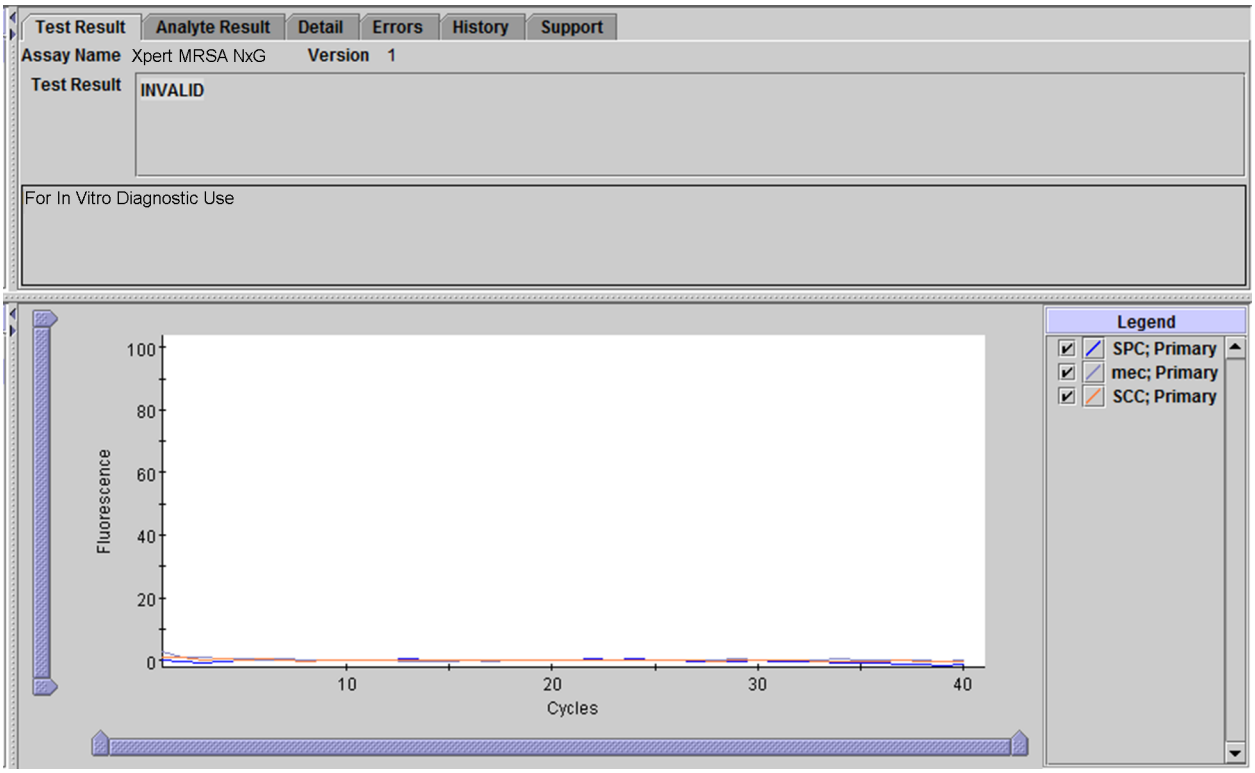

Figure 6. An Example of an INVALID Result

14 Reasons to Repeat the Test

The specimen should be retested if any of the following results are obtained from the first test. Repeat the test according to the instructions in Section 15, Retest Procedure.

- 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 Probe Check control may have failed or the maximum pressure limits were exceeded.
- A **NO RESULT** indicates that insufficient data were collected. For example, the operator stopped a test that was in progress or a power failure occurred.
- If an External Control fails to perform as expected, repeat external control test and/or contact Cepheid Technical Support for assistance.

15 Retest Procedure

Repeat the test using a new cartridge (do not re-use the cartridge) and new Elution Reagent vial.

1. Remove the cartridge and Elution Reagent vial from the Xpert MRSA NxG test kit.
2. Add the sample into the cartridge:

   Dual Swabs

   a) Remove the left-over swab from the transport container.

   b) Insert the swab into the vial containing the Elution Reagent and break the swab off at the score mark on the swab shaft.

Note Wrap sterile gauze (not provided) around both the stem of the swab and the mouth of the Elution Reagent vial when breaking the swab to minimize risk of contamination.

OR

ESwab

a) Mix the left-over Liquid Amies transport medium containing the swab sample by vortexing at high speed for 5 seconds to evenly disperse in the liquid transport medium.
b) Using a transfer pipette (not provided), transfer 300 µL of the liquid sample into the Elution Reagent vial.

3. Close the Elution Reagent vial cap and vortex at high speeds for 10 seconds.
4. Open the cartridge lid. Using a transfer pipette (not provided), transfer the entire contents of the Elution Reagent vial to the Sample Chamber of the Xpert MRSA NxG test cartridge. See Figure 1.
5. Close the cartridge lid and start the test.

16 Limitations

- Careful compliance with the instructions in this IFU and in Cepheid Sample Collection Device IFUs (Cepheid Sample Collection Device, Copan Dual Rayon Swab and Transport Systems, Liquid Amies Elution Swab (ESwab) Collection and Transport System) is necessary to avoid erroneous results.
- The Xpert MRSA NxG test performance has not been evaluated in patients less than two years of age.
- The Xpert MRSA NxG test is not intended to diagnose, guide or monitor treatment for MRSA infections, or determine susceptibility to methicillin.
- As with many diagnostic tests, results from the Xpert MRSA NxG test 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 infections.
- A positive test result does not necessarily indicate the presence of viable organisms. It is, however, presumptive for the presence of MRSA.
- A negative test result does not exclude the possibility of nasal colonization because test results 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.
- Concomitant cultures are necessary to recover organisms for epidemiology typing or for further susceptibility testing.
- The Xpert MRSA NxG test provides qualitative results. No correlation can be drawn between the magnitude of the Ct value and the number of cells in an infected sample.
- Mutations or nucleotide polymorphisms in primer or probe binding regions may affect detection of new or unknown MRSA variants resulting in a false negative result.
- An Xpert MRSA NxG test positive result does not necessarily indicate intervention eradication failure since nonviable DNA may persist. A negative result following a previously positive test result may or may not indicate eradication success.
- Because the detection of MRSA is dependent on the quantity of DNA present in the sample, reliable results are dependent on proper specimen collection, handling, and storage.
- The Xpert MRSA NxG test may generate a false positive MRSA (**MRSA DETECTED**) result when testing a nasal specimen with a mixture of organisms containing both methicillin-resistant coagulase-negative Staphylococcus and an empty cassette SA.
- The Xpert MRSA NxG test may generate a false negative result (**MRSA NOT DETECTED**) in the event of a co-colonization that contains both methicillin-resistant *Staphylococcus aureus* (MRSA) and an empty cassette *Staphylococcus aureus* (SA). This may occur in rare cases when the titer of an empty cassette SA organism is substantially higher than that of the MRSA organism.
- Test interference may be observed in the presence of Nasonex (≥ 50% v/v), Flonase (≥ 50% v/v), and Beconase (≥ 40% v/v).

17 Expected Values

The overall MRSA prevalence by the Xpert MRSA NxG test, observed in nasal swab specimens collected in two separate Xpert MRSA NxG test clinical studies using Rayon swabs and ESwabs, is presented in the table below.

Table 3. Overall Prevalence of MRSA Observed in Clinical Testing

Specimen Collection Device	Overall MRSA Prevalence Observed by the Xpert MRSA NxG Test by Collection Device
Cepheid Sample Collection Device (Rayon Swab)	12.8% (141/1103)
Liquid Amies Elution Swab (ESwab) Collection and Transport System	12.9% (109/846)

18 Clinical Performance

Performance characteristics of the Xpert MRSA NxG test were determined in two separate prospective, multi-site investigational studies using nasal specimens collected from individuals at risk for nasal colonization of methicillin-resistant S. aureus (MRSA). In the first study, eight investigational sites within the US and outside of the US tested the Xpert MRSA NxG test with nasal swabs collected using the Cepheid Sample Collection Device (Rayon Swab). In the second study, six investigational sites within the US tested the Xpert MRSA NxG test with nasal swabs collected using the Liquid Amies Elution Swab (ESwab) Collection and Transport System. Not more than one specimen per subject was included in the studies and analyses.

The Xpert MRSA NxG test results were compared to reference culture and susceptibility results.

The comparative reference method consisted of both a direct culture on MRSA selective chromogenic medium and enriched culture. Enrichment of the specimen was performed in Trypticase Soy Broth (TSB) with 6.5% Sodium Chloride followed by subculture of the TSB 6.5% NaCl on to Blood Agar (BA) and MRSA selective chromogenic medium. Identification of presumptive S. aureus colonies from BA and MRSA colonies from the selective chromogenic medium plates was confirmed with Gram stain, and catalase and coagulase testing. MRSA was confirmed by susceptibility testing with a Cefoxitin disk (30µg). The reference method result was considered positive for MRSA if the presence of MRSA was confirmed in either direct culture or enriched culture.

Results Obtained with the Xpert MRSA NxG Test in Comparison to the Reference Method using the Rayon Swab

A total of 1103 eligible Rayon swab specimens were tested by the Xpert MRSA NxG test and by the reference method. Relative to the reference method, the Xpert MRSA NxG test demonstrated a sensitivity and specificity of 91.0% and 96.9%, respectively (Table 4). For the population tested, the MRSA positive predictive value (PPV) was 78.7% and the negative predictive value (NPV) was 98.9%.

Table 4. Xpert MRSA NxG Test with Rayon Swab vs. Reference Method

	Reference Method			
Xpert MRSA NxG	MRSA	Positive	Negative	Total
	Positive	111	30[a]	141
	Negative	11[b]	951	962
	Total	122	981	1103
			Sensitivity:	91.0% (95% CI: 84.6-94.9)
			Specificity:	96.9% (95% CI: 95.7-97.8)
			PPV:	78.7% (95% CI: 71.3-84.7)
			NPV:	98.9% (95% CI: 98.0-99.4)

[a] 30/30 specimens with Xpert MRSA NxG false positive results were also MRSA culture negative upon repeat subculture of the enrichment broth.

[b] 11/11 specimens with Xpert MRSA NxG false negative results were MRSA culture positive upon repeat subculture of the enrichment broth.

Results Obtained with the Xpert MRSA NxG test in Comparison to the Reference Method using the ESwab

A total of 846 eligible ESwab specimens were tested by the Xpert MRSA NxG test and by the reference method. Relative to the reference method, the Xpert MRSA NxG test demonstrated a sensitivity and specificity of 92.9% and 97.6%, respectively (Table 5). For the population tested, the MRSA positive predictive value (PPV) was 83.5% and the negative predictive value (NPV) was 99.1%.

Table 5. Xpert MRSA NxG Test with ESwab vs. Reference Method

	Reference Method			
Xpert MRSA NxG	MRSA	Positive	Negative	Total
	Positive	91	18[a]	109
	Negative	7[b]	730	737
	Total	98	748	846
			Sensitivity:	92.9% (95% CI: 86.0-96.5)
			Specificity:	97.6% (95% CI: 96.2-98.5)
			PPV:	83.5% (95% CI: 75.4-89.3)
			NPV:	99.1% (95% CI: 98.1-99.5)

[a] 17/18 specimens with Xpert MRSA NxG false positive results were also MRSA culture negative after repeat of subculture of the enrichment broth.
[b] 6/7 specimens with Xpert MRSA NxG false negative results were MRSA culture positive after repeat subculture of the enrichment broth.

Results Obtained with the Xpert MRSA NxG test in Comparison to the Reference Method for the Rayon Swab and ESwab Combined

Table 6 shows the sensitivity and specificity analyses of the combined Xpert MRSA NxG test results with Rayon Swab and ESwab relative to the reference method.

Table 6. Xpert MRSA NxG test with Rayon Swab and ESwab Combined vs. Reference Method

	Reference Method[a]			
Xpert MRSA NxG	MRSA	Positive	Negative	Total
	Positive	202	48	250
	Negative	18	1681	1699
	Total	220	1729	1949
			Sensitivity:	91.8% (95% CI: 87.4–94.8)
			Specificity:	97.2% (95% CI: 96.3–97.9)
			PPV:	80.8% (95% CI: 75.5–85.2)
			NPV:	98.9% (95% CI: 98.3–99.3)

[a] Using the data from Table 4 and Table 5, the Fisher's Exact Test (p-value = 0.81 for sensitivity and p-value = 0.46 for specificity) demonstrated that the data are poolable across collection devices (Rayon Swab and ESwab).

19 Analytical Performance

19.1 Analytical Sensitivity (Limit of Detection)

Studies were performed to determine the analytical sensitivity or Limit of Detection (LoD) of the Xpert MRSA NxG test using two different collection kits (the Cepheid Sample Collection Device P/N 900-0370 or Copan P/N 139CFA, referred to as the "rayon swab" and the ESwab collection kit, Copan P/N 480C or Becton Dickinson P/N 220245 referred to as the "ESwab" refer to Section 6.3). The LoD is the lowest concentration of sample (reported as CFU/swab or CFU/mL in Elution Reagent) that can be reproducibly distinguished from negative samples 95% of the time with 95% confidence. This study determined the lowest concentration of methicillin-resistant *Staphylococcus aureus* (MRSA) cells diluted into simulated nasal matrix that can be detected using the Xpert MRSA NxG test. The simulated nasal matrix consisted of 5% (w/v) porcine mucin and 1% (v/v) human whole blood in a 1X Phosphate Buffered Saline (PBS) solution with 15% (v/v) glycerol.

The analytical sensitivity of the Xpert MRSA NxG test was assessed following the guidance in Clinical and Laboratory Standards Institute (CLSI) document EP17-A2 using two lots of reagents tested across three testing days with thirteen (13) individual MRSA strains and the two types of swabs (rayon swab and ESwab). The 13 individual strains represent SCC*mec* types I, II, III, IV, IVa, V, VI, VII, VIII, IX, X and XI. These strains in the LoD study represent the most common healthcare-acquired (USA100) and most common community-acquired (USA400) MRSA strains that are characterized by pulsed-field gel electrophoresis (PFGE). Strains that contained heterogeneous subpopulations with respect to their oxacillin resistance phenotype were also included in the study.

The LoD was established by testing five concentration levels with two reagent lots. The LoD and 95% confidence interval (CI) were then estimated for each lot using logistic regression analysis. The logistic regression analysis does not rely on a single concentration but utilizes the logit function to incorporate the information from all levels tested in the model. The point estimates were calculated using a method of maximum likelihood estimates (MLE) of the logistic regression model parameters. The maximum estimated LoD observed per strain from the logistic regression analysis was used to establish the LoD claim. The LoD point estimates and 95% upper and lower confidence intervals for each MRSA SCC*mec* type tested are summarized in the tables below.

The results of this study indicate that the Xpert MRSA NxG test will produce a positive MRSA result 95% of the time with 95% confidence for a nasal swab (Rayon) containing 302 CFU (see table below).

Table 7. 95% Confidence Intervals for Analytical LoD — MRSA (Rayon Swab)

MRSA Strain	PFGE ID[a]	LoD Estimate (Logistic Regression) (CFU/Swab)			LoD Estimate In Elution Reagent (CFU/mL)
		Lower 95% CI	LoD Point Estimate	Upper 95% CI	
Type I	USA500	72	**91**	136	**46**
Type II	USA100	127	**161**	236	**81**
Type III	unknown	50	**64**	96	**32**
Type IVa	USA400	46	**58**	84	**29**
Type IV (Fin 7)	unknown	256	**302**	392	**151**
Type IVa	USA300	143	**182**	282	**91**
Type V	USA1000	85	**102**	138	**51**
Type VI	USA800	32	**42**	64	**21**
Type VII	unknown	95	**128**	235	**64**
Type VIII	unknown	139	**163**	233	**82**
Type IX	unknown	142	**169**	227	**85**
Type X	unknown	86	**97**	119	**49**

MRSA Strain	PFGE ID[a]	LoD Estimate (Logistic Regression) (CFU/Swab)			LoD Estimate In Elution Reagent (CFU/mL)
		Lower 95% CI	LoD Point Estimate	Upper 95% CI	
Type XI (*mecC*)	unknown	219	**266**	358	**133**

[a] PFGE = Pulsed-field gel electrophoresis

The results of this study indicate that the Xpert MRSA NxG test will produce a positive MRSA result 95% of the time with 95% confidence for a nasal swab (ESwab) containing 812 CFU (see table below).

Table 8. 95% Confidence Intervals for Analytical LoD — MRSA (ESwab)

MRSA Strain	PFGE ID [a]	LoD Estimate (Logistic Regression) (CFU/Swab)			LoD Estimate In Elution Reagent (CFU/mL)
		Lower 95% CI	LoD Point Estimate	Upper 95% CI	
Type I	USA500	285	**343**	469	**45**
Type II	USA100	184	**218**	293	**28**
Type III	unknown	215	**254**	338	**33**
Type IVa	USA400	134	**167**	245	**22**
Type IV (Fin 7)	unknown	656	**812**	1145	**106**
Type IVa	USA300	470	**563**	733	**73**
Type V	USA1000	378	**465**	671	**61**
Type VI	USA800	71	**89**	128	**12**
Type VII	unknown	201	**245**	338	**32**
Type VIII	unknown	520	**631**	851	**82**
Type IX	unknown	311	**377**	533	**49**
Type X	unknown	149	**166**	215	**22**
Type XI (*mecC*)	unknown	597	**734**	998	**96**

[a] PFGE = Pulsed-field gel electrophoresis

19.2 Analytical Reactivity (Inclusivity)

One hundred and ninety-six methicillin-resistant *Staphylococcus aureus* strains were tested in this study. The strains tested represented Cooper and Feil Groups 1A, 1B, and 2, SCCmec types and subtypes (I, IA, II, III, IIIA, III-Hg, IV, IVa, IVb, IVc, IVd, V, VI, VII, VIII, IX, X and XI), - sequence types (STs), *spa*-types, PFGE types, and clonal complexes (CC). Known USA100, USA200, USA300, USA400, USA500, USA600, USA700, USA800, USA1000, USA1100, IBERIAN strains, heteroresistant strains, and novel *mecC* strain $MRSA_{LGA251}$ were also included in this study. A “challenge panel” of 59 well characterized MRSA strains that have Minimum Inhibitory Concentrations (MIC) for cefoxitin/oxacillin that span the measurable dynamic range were also included in this study. Oxacillin MIC values for these 59 strains ranged from 0.5 to >32 µg/mL.

All 196 MRSA strains were correctly reported as **MRSA DETECTED** using the Xpert MRSA NxG test.

19.3 Analytical Specificity (Cross-Reactivity)

The analytical specificity of the Xpert MRSA NxG test was evaluated by testing a panel of one hundred and fifty-two potentially cross-reactive microorganisms that are methicillin-susceptible *Staphylococcus aureus* (MSSA), organisms phylogenetically related to *Staphylococcus aureus* (SA), and members of the nasal commensal microflora (e.g., other

bacteria, viruses, and yeast) with the potential to cross-react with the Xpert MRSA NxG test. The one hundred and fifty two organisms tested were identified as either gram-positive (104), gram-negative (25), yeast (3), viruses (17), or Gram reaction indeterminate (3). Of these organisms, eighty-four were characterized as follows: twenty-three (23) were methicillin-susceptible, coagulase-negative *Staphylococcus* (MSCoNS), five (5) were methicillin-resistant, coagulase-negative *Staphylococcus* (MRCoNS), forty-seven (47) were methicillin-susceptible *Staphylococcus aureus* (MSSA), including two (2) empty cassette MSSA, and seven (7) borderline oxacillin-resistant *Staphylococcus aureus* (BORSA) strains. Human cells were also tested in the study.

Evaluation of BORSA Strains

The seven well-characterized borderline oxacillin-resistant *Staphylococcus aureus* (BORSA) strains that were tested included one "empty cassette" MSSA strain. Methicillin-resistant *Staphylococcus aureus* is resistant to all ß-lactam drugs (with the exception of ceftaroline) through the alternative penicillin-binding protein PBP2a encoded by *mecA* or *mecC*. BORSA strains do not carry *mecA/mecC* gene, but exhibit an oxacillin minimum inhibitory concentration (MIC) ≥ 2 and ≤ 8 µg/mL. It is especially valuable to distinguish MRSA from BORSA to aid in implementing appropriate management and isolation precaution options for patients infected with methicillin-susceptible strains of *S. aureus*. BORSA strains tested with Xpert MRSA NxG test were reported as **MRSA NOT DETECTED**.

All potentially cross-reactive microorganisms were tested in triplicate in Elution Reagent containing simulated nasal matrix at $>10^6$ CFU/mL for bacteria and $>10^5$ $TCID_{50}$/mL for viruses. Human cells were tested at 10^5 cells/mL.

All microorganisms and the human cells were reported as **MRSA NOT DETECTED** by the Xpert MRSA NxG test. For the panel of one hundred and fifty-two potentially cross-reactive microorganisms and human cells evaluated in the study, the analytical specificity of the Xpert MRSA NxG test was 100%.

In silico analysis indicates that the Xpert MRSA NxG test may produce positive results with strains of *Staphylococcus argenteus*, a recently described species of *Staphylococcus* that is closely related to *S. aureus*, that carry an SCC*mec* cassette and *mecA* or *mecC*.[11]

19.4 Microbial Interference

A study was conducted to assess the inhibitory effects of commensal microorganisms in nasal swab specimens on the performance of the Xpert MRSA NxG test. A panel of nine (9) bacterial strains, reported to be present in 10% or more of nasal cavities of healthy subjects[12, 13], were evaluated using the Xpert MRSA NxG test (see table below).

Table 9. Commensal Bacterial Strains Tested in Microbial Interference

Strain	Strain ID
Staphylococcus aureus (MSSA)	15280
Staphylococcus epidermidis (MSSE)	ATCC 35984
Corynebacterium bovis	ATCC 7715
Streptococcus mutans	ATCC 25175
Proteus vulgaris	ATCC 29905
Haemophilus influenzae	ATCC 9007
Neisseria meningitidis	ATCC 700111
Moraxella catarrhalis	ATCC 43628
Streptococcus pneumoniae	ATCC 6303

The nine commensal bacteria were spiked into the simulated nasal matrix at approximately 1.0 x 10^6 CFU/ mL in Elution Reagent and tested in the presence of MRSA (cross-reactivity) or in the absence of MRSA (interference). Two MRSA strains (see table below) were used in this study and these strains prepared at approximately 3X LoD and tested in replicates of four. None of the potentially interfering microorganisms evaluated in the study were found to cross-react or interfere with the detection of any of the MRSA strains using the Xpert MRSA NxG test.

Table 10. MRSA Strains

Target	Strain ID
MRSA (*mecA*)	MRSA Type II (NRSA70,N315)
MRSA (*mecC*)	MRSA Type XI LGA251

19.5 Potentially Interfering Substances

Nineteen substances that may be present in nasal swab specimens with the potential to interfere with the performance of the Xpert MRSA NxG test were evaluated. The potentially interfering substances included mucous, human blood, nasal sprays or drops, nasal gels, nasal corticosteroids, FluMist, oral nasal anesthetics or analgesics, nasal antibiotics, antibacterials and antivirals. The substances, active ingredients, and concentrations tested are listed in the table below. All interfering substances, with the exception of mucin, were initially tested at 50% (v/v) in a simulated nasal matrix for Negative (simulated matrix only) and MRSA-positive samples. Mucin was tested at 7% (w/v) in simulated nasal matrix for Negative (simulated matrix only) and MRSA-positive samples.

Buffer Controls (negative and positive) without interfering substances were included.

Positive samples were tested per interfering substance with two clinical MRSA strains, SCC*mec* Type II (*mecA*) and SCC*mec* Type XI ($mecC_{LGA251}$), spiked at approximately 3X analytical LoD in simulated nasal matrix.

Replicates of eight positive and negative samples with each interfering substance were evaluated in this study. Negative samples in the presence of potentially interfering substance were tested to determine the impact on the performance of the sample processing control (SPC).

The effect of each potentially interfering substance on positive and negative samples was assessed by comparing the target cycle threshold (Ct) values generated in the presence of the potentially interfering substance to the Ct values of the buffer controls in the absence of the potentially interfering substance.

The positive and negative samples for 16 potentially interfering substances were correctly identified. Potentially inhibitory effects were observed in positive samples tested with Nasonex 50% (v/v), Flonase 50% (v/v), and Beconase at 40% (v/v) and 50% (v/v) due to delay in Ct values; however, none of the substances reported false negative test results. No interference was observed in positive samples tested with Nasonex 40% (v/v), Flonase 40% (v/v), and Beconase at 30% (v/v). This is addressed in Section 16.

Table 11. Potentially Interfering Nasal Substances Tested

Substance	Active Ingredient	Concentration Tested
Mucous (Mucin)	Porcine mucin representing densely glycosylated proteins (mucous)	7% (w/v)
Blood	Blood (Human)	50% (v/v)
Aneferin Decongestant Spray	0.05% Oxymetazoline Hydrochloride	50% (v/v)
Azelastin Antihistamine Spray	0.1% Azelastine Hydrochloride	50% (v/v)
NasalCrom Allergy Symptom Controller	5.2 mg Cromolyn Sodium	50% (v/v)
Neo-Synephrine Decongestant Spray	0.5% Phenylephrine Hydrochloride	50% (v/v)
Saline Nasal Moisturizing Spray	0.65% Sodium Chloride	50% (v/v)
Zicam Nasal Gel (Upper Respiratory Allergy Symptom Relief)	4x, 12x, 30x Luffa operculata 12x, 30x Galphimia glauca 12x, 30x, 200x Histaminum hydrochloricum 12x, 30x, 200x Sulphur	50% (v/v)

Substance	Active Ingredient	Concentration Tested
Nasonex (Nasal Allergy Symptom Medication, inhaled nasal steroid)	0.05% Mometasone Furoate Monohydrate	40% (v/v), 50% (v/v)[a]
Flonase	0.05% Fluticasone Propionate	40% (v/v), 50% (v/v)[a]
FluMist	Live intranasal influenza virus vaccine	50% (v/v)
Finafta Multioral	7.5% Benzocaine	50% (v/v)
TobraDex	0.3% Tobramycin, 0.1% Dexamethasone	50% (v/v)
Bactroban	2% Mupirocin	50% (v/v)
Relenza	5 mg Zanamivir	50% (v/v)
Beconase® AQ	0.05% or $3.6x10^{-5}$g Beclomethasone	30% (v/v), 40% (v/v)[a] 50% (v/v)[a]
Nasacort® AQ	0.06% or $4.4x10^{-5}$g Triamcinolone acetonide	50% (v/v)
Rhinocort aqua®	0.06% or $4.4x10^{-5}$g Budesonide	50% (v/v)
Flunisolide Nasal Solution USP, 0.025%	0.03% or $1.9x10^{-5}$g Flunisolide	50% (v/v)

[a] Potential inhibitory effect observed for the concentration tested due to delay in Ct values.

19.6 Carry-over Contamination Study

A study was conducted to demonstrate that single-use, self-contained GeneXpert cartridges prevent carry-over contamination in negative samples tested following very high MRSA- positive samples in the same GeneXpert module. The study consisted of a negative sample processed in the same GeneXpert module immediately following a very high positive sample. The MRSA-negative samples were composed of MSSE prepared in a simulated nasal matrix at a concentration ≥1.0 x 10^7 CFU/mL in the Elution Reagent. The MRSA-positive samples were composed of MRSA in a simulated nasal matrix at a concentration ≥1 x 10^7 CFU/mL in the Elution Reagent. 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). All 40 positive samples were correctly reported as **MRSA DETECTED**. All 42 negative samples were correctly reported as **MRSA NOT DETECTED**.

20 Reproducibility

A panel of five samples with varying concentrations of MRSA was tested four times per day on six different days by two different operators, at three sites (5 samples x 4 times/day x 6 days x 2 operators x 3 sites). Three lots of Xpert MRSA NxG test cartridges were used, with each representing two days of testing. The Xpert MRSA NxG test was performed according to the Xpert MRSA NxG test procedure. Each of the 5 samples was prepared in simulated nasal matrix at the concentration levels in Table 12. Results are summarized in Table 13.

Table 12. Reproducibility Panel

Panel Sample	Concentration Level
Neg	True negative (no target)
ModPos1, MRSA Type XI (*mecC*)	Moderate positive (~2-3x LoD)
LowPos1, MRSA Type XI (*mecC*)	LOD (~1x LoD)
ModPos2, MRSA Type II (*mecA*)	Moderate positive (~2-3x LoD)
LowPos2, MRSA Type II (*mecA*)	LoD (~1x LoD)

Table 13. Summary of Reproducibility Results: % Agreement by Study Site/Operator

Sample	Site 1			Site 2			Site 3			% Total Agreement by Sample
	Op 1	Op 2	Site	Op 1	Op 2	Site	Op 1	Op 2	Site	
Neg	100% (24/24)	100% (24/24)	100% (48/48)	100% (24/24)	100% (24/24)	100% (48/48)	100% (24/24)	100% (24/24)	100% (48/48)	100% (144/144)
ModPos1	100% (24/24)	100% (24/24)	100% (48/48)	100% (24/24)	100% (24/24)	100% (48/48)	100% (24/24)	100% (24/24)	100% (48/48)	100% (144/144)
LowPos1	100% (24/24)	100% (24/24)	100% (48/48)	100% (24/24)	100% (24/24)	100% (48/48)	100% (24/24)	100% (24/24)	100% (48/48)	100% (144/144)
ModPos2	100% (24/24)	100% (24/24)	100% (48/48)	100% (24/24)	100% (24/24)	100% (48/48)	100% (24/24)	100% (24/24)	100% (48/48)	100% (144/144)
LowPos2	95.8% (23/24)	100% (24/24)	97.9% (47/48)	100% (24/24)	100% (24/24)	100% (48/48)	100% (24/24)	95.8% (23/24)	97.9 (47/48)	98.6% (142/144)

The reproducibility of the Xpert MRSA NxG test was also evaluated in terms of the fluorescence signal expressed in Ct values for each target detected. The mean, standard deviation (SD), and coefficient of variation (CV) between-sites, between-days, between-lots, between-operators and within-assay for each panel member are presented in Table 14.

Table 14. Summary of Reproducibility Data[a]

Sample	Assay Channel (Analyte)	N [b]	Mean Ct	Between-Site		Between-Day		Between-Lot		Between-Operator		Within-Assay		Total	
				SD	CV (%) [c]	SD	CV (%)[c]	SD	CV (%) [c]	SD	CV (%)[c]	SD	CV (%) [c]	SD	CV (%) [c]
Neg	SPC	144	32.3	0.0	0.0	0.0	0.0	0.3	0.9	0.3	0.8	0.8	2.3	0.8	2.6
ModPos1	*mec*	144	29.9	0.0	0.0	0.0	0.0	0.4	1.4	0.0	0.0	1.1	3.5	1.1	3.8
	SCC	144	32.6	0.0	0.0	0.0	0.0	0.5	1.5	0.0	0.0	1.0	3.0	1.1	3.3
LowPos1	*mec*	144	31.7	0.0	0.0	0.0	0.0	0.4	1.4	0.0	0.0	1.0	3.2	1.1	3.5
	SCC	144	34.3	0.0	0.0	0.0	0.0	0.5	1.5	0.0	0.0	0.9	2.7	1.1	3.1
ModPos2	*mec*	144	31.2	0.0	0.0	0.3	0.9	0.2	0.5	0.0	0.0	0.9	3.0	1.0	3.1
	SCC	144	32.8	0.0	0.0	0.3	0.8	0.3	1.0	0.0	0.0	0.9	2.7	1.0	3.0
LowPos2	*mec*	144	32.7	0.0	0.0	0.4	1.1	0.0	0.0	0.2	0.6	1.0	3.0	1.1	3.2
	SCC	144	34.4	0.0	0.0	0.4	1.1	0.0	0.0	0.1	0.3	1.0	3.0	1.1	3.3

[a] There were a total of 12 indeterminate results over the course of the study (11 reported as “Error” and 1 as “Invalid”). All 12 produced valid test results upon repeat.

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

[c] (%) is contribution of variance of component to overall CV.

21 References

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23 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

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

24 Table of Symbols

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

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25 Revision History

Section	Description of Change
Table of Symbols	Added CH REP and Importer symbols and definitions to Table of Symbols. Added CH REP and Importer information with Switzerland address.
Revision History	Updated revision history table.