GeneXpert®
Powered By CEPHEID INNOVATION

Xpert® MRSA

REF GXMRSA-100N-10

REF GXMRSA-120

Cepheid®

In Vitro Diagnostic Medical Device

IVD CE

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Xpert® MRSA

For *In Vitro* Diagnostic Use Only.

1 Proprietary Name

Xpert® MRSA

2 Common or Usual Name

Xpert MRSA Assay

3 Intended Use

The Cepheid Xpert MRSA Assay performed in the GeneXpert® Dx System (Xpert MRSA) is a qualitative *in vitro* diagnostic test designed for rapid detection of methicillin-resistant *Staphylococcus aureus* (MRSA) from nasal swabs in patients at risk for nasal colonization. The test utilizes automated real-time polymerase chain reaction (PCR) to detect MRSA DNA. The Xpert MRSA Assay is intended to aid in the prevention and control of MRSA infections in healthcare settings. The Xpert MRSA Assay is not intended to diagnose MRSA nor to guide or monitor treatment for MRSA 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 major nosocomial pathogen that causes a range of diseases including endocarditis, osteomyelitis, toxic shock syndrome, food poisoning, carbuncles and boils. 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, a synthetic penicillin, was introduced. 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 US today, MRSA is responsible for approximately 25% of nosocomial infections and reports of community-acquired MRSA are increasing, resulting in significant morbidity and mortality. In an attempt 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. Currently, the standard surveillance method for detecting MRSA is culture, which is very laborious and time intensive.[1,2,3,4,5] A rapid and more sensitive method for surveillance of MRSA will represent a definite advantage for infection control programs.

5 Principle of the Procedure

The GeneXpert Dx System automates and integrates 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 system consists of an instrument, personal computer, and preloaded software for running tests on collected samples and viewing the results. The system requires the use of single-use disposable GeneXpert 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 system, see the *GeneXpert Dx System Operator Manual*.

Xpert MRSA Assay includes reagents for the detection of MRSA 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 fluorophore stability.

The primers and probes in the Xpert MRSA assay detect a proprietary sequence for the presence of a cassette inserted into the *S. aureus* chromosome.

6 Reagents and Instruments

6.1 Material Provided

The Xpert MRSA(GXMRSA-100N-10) kit contains sufficient reagents to process 10 specimens or quality control samples. The Xpert MRSA (GXMRSA-120 and GXMRSA-CE-120) kits contain sufficient reagents to process 120 specimens or quality control samples.

The kits contain the following items:

	10	120
Xpert MRSA Assay Cartridges with integrated reaction tubes		
• Bead 1,Bead 2, and Bead 3 (freeze-dried) ~6000 non-infectious sample preparation control spores	1 of each per cartridge	1 of each per cartridge
• Reagent 1 (Sodium Hydroxide)	3.0 mL per cartridge	3.0 mL per cartridge
• Reagent 2	3.0 mL per cartridge	3.0 mL per cartridge
Xpert MRSA Reagent Pouch	1	1
Elution Reagent (Guanidinium thiocyanate)	10 × 1.5 mL per vial	120 × 1.5 mL per vial
CD	1	1
• 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 postmortem testing. During processing, there was no mixing of the material with other animal materials.

6.2 Storage and Handling

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

6.3 Materials Required but Not Provided

- GeneXpert Dx System (catalog number varies by configuration): GeneXpert instrument, computer, barcode wand reader, and Operator Manual
- Printer If a printer is required, contact Cepheid Sales Representative to arrange for the purchase of a recommended printer.
- Cepheid Sample Collection Device (part number 900-0370)
- Vortex mixer
- Disposable, sterile transfer pipettes
- Sterile gauze

6.4 Materials Available but Not Provided

KWIK-STIK™ from MicroBiologics catalog # 0158 MRSA as positive control and #0371 MSSE (methicillin-sensitive *Staphylococcus epidermis*) as negative control.

7 Warnings and Precautions

- 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[6] and the Clinical and Laboratory Standards Institute.[7]
- Follow your institution's safety procedures for working with chemicals and handling biological samples.
- Biological specimens, transfer devices, and used cartridges should be considered capable of transmitting infectious agents requiring standard precautions. Follow your institution's environmental waste procedures for proper disposal of used cartridges and unused reagents. These materials may exhibit characteristics of chemical hazardous waste requiring specific national or regional disposal procedures. If national or regional regulations do not provide clear direction on proper disposal, biological specimens and used cartridges should be disposed per WHO [World Health Organization] medical waste handling and disposal guidelines. Consult your institution's environmental waste personnel on proper disposal of used cartridges and unused reagents.
- The Xpert MRSA Assay does not provide susceptibility results. Additional time is required to culture and perform susceptibility testing.
- Do not substitute Xpert MRSA reagents with other reagents.
- Do not open the Xpert MRSA cartridge lid except when adding sample.
- Do not use a cartridge that has been dropped or shaken after you have added the sample.
- Do not use a cartridge that has a damaged reaction tube.
- Each single-use Xpert MRSA cartridge is used to process one test. Do not reuse spent cartridges.
- Store the Xpert MRSA kit at 2–28 °C

8 Chemical Hazards[8,9]

- 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 hands 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.
    - Specific treatment, see supplemental first aid information.
    - Take off contaminated clothing and wash before reuse.
    - If skin irritation occurs: Get medical advice/attention.
    - IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
    - If eye irritation persists: Get medical advice/attention.
    - 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 and Transport

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

1. Open the Cepheid Collection Device by peeling back the outer packaging.
2. Ask the patient to tilt his/her head back. Insert dry swabs approximately 1–2 cm into each nostril.
3. Rotate the swabs against the inside of the nostril for 3 seconds. 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.
4. Using the same swabs, repeat for the second nostril, trying not to touch anything but the inside of the nose.
5. 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. The swabs should stay attached to the red cap at all times.
6. Label the plastic transport tube with patient ID and send to the laboratory.
7. 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.

10 Procedure

10.1 Preparing the Cartridge

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

Note Use only one of the swabs. The second swab is required for repeat testing.

To add the sample into the cartridge (Xpert MRSA):

1. Remove the cartridge and Elution Reagent from the kit.
2. Remove the swabs from the transport container and then remove one swab from the red cap.
3. Insert the swab into the tube containing the Elution Reagent.
4. Use sterile gauze to minimize risks of contamination.
5. Hold the swab by the stem near the rim of the tube, lift the swab a few millimeters from the bottom of the tube and push the stem against the edge of the tube to break it. Make sure the swab is short enough to allow the cap to close tightly.
6. Close the cap and vortex at high speed for 10 seconds.
7. Open the cartridge lid. Using a sterile transfer pipette, transfer the entire contents of the Elution Reagent to the sample chamber (Figure 1) in the GeneXpert cartridge.
8. Close the cartridge lid.

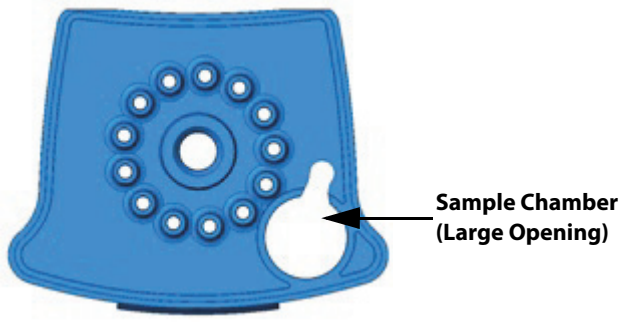

Figure 1. Xpert MRSA Cartridge (Top View).

10.2 Starting the Test

Important **Before you start the test, make sure the Xpert MRSA assay definition is imported into the GeneXpert software.**

This section lists the basic steps of running the test. For detailed instructions, see the *GeneXpert Dx System Operator Manual.*

1. Turn on the computer, and then turn on the GeneXpert Dx instrument.
2. On the Windows® desktop, double-click the GeneXpert Dx shortcut icon.
3. Log on to the GeneXpert Dx System software using your user name and password.
4. In the GeneXpert Dx System window, click **Create Test.** The Scan Cartridge Barcode dialog box appears.
5. Scan the barcode on the Xpert MRSA cartridge. The Create Test window appears. Using the barcode information, the software automatically fills the boxes for the following fields: Select Assay, Reagent Lot ID, Cartridge SN, and Expiration Date.

CONTROL

6. In the Sample ID box, scan or type the sample ID. Make sure you type the correct sample ID. The sample ID is associated with the test results and is shown in the View Results window and all the reports.
7. Click **Start Test**. In the dialog box that appears, type your password.
8. Open the instrument module door with the blinking green light and load the cartridge.
9. Close the door. The test starts and the green light stops blinking. When the test is finished, the light turns off.
10. Wait until the system releases the door lock before opening the module door and removing the cartridge.
11. Dispose of the used cartridges in the appropriate specimen waste containers according to your institution's standard practices.

10.3 Viewing and Printing Results

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

11 Quality Control

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

Sample Processing Control (SPC)—Ensures the sample was correctly processed. 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 MRSA. The SPC verifies that lysis of MRSA 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 Dx System measures the fluorescence signal from the probes to monitor bead rehydration, reaction-tube filling, probe integrity and fluorophore stability. Probe Check passes if it meets the assigned acceptance criteria.

External Controls—KWIK-STIK™ (MicroBioLogics, catalog # 0158 MRSA as positive control and # 0371 MSSE as negative control) may be used for training, proficiency testing and external QC of the GeneXpert Dx 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 shaft into 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.
6. The KWIK-STIK swab is now ready for Xpert MRSA testing.

12 Interpretation of Results

The results are interpolated by the GeneXpert Dx System from measured fluorescent signals and embedded calculation algorithms and will be shown in the View Results window. Possible results are:

Result	Interpretation
MRSA POSITIVE	MRSA target DNA is detected (presumptive positive for MRSA colonization). • MRSA—POSITIVE: MRSA target has a Ct within the valid range and endpoint above the minimum 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	MRSA target DNA is not detected (presumed not colonized with MRSA), SPC meets acceptance criteria. • MRSA—NEGATIVE: MRSA target DNA is not detected. • SPC—PASS: SPC has a Ct within the valid range and endpoint above the endpoint minimum setting. • Probe Check—PASS: All probe check results pass.
INVALID	Presence or absence of MRSA cannot be determined, repeat test with extra swab. SPC does not meet acceptance criteria, the sample was not properly processed, or PCR is inhibited. • MRSA—INVALID: Presence or absence of MRSA DNA cannot be determined. • SPC—FAIL: MRSA target result is negative and the SPC Ct is not within valid range and endpoint below minimum setting. • Probe Check—PASS: All probe check results pass.
ERROR	Presence or absence of MRSA cannot be determined, repeat test with extra swab. 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. • MRSA—NO RESULT • SPC—NO RESULT • Probe Check—FAIL*; all or one of the probe check results fail. * If the Probe Check passed, the error is caused by a system component failure.
NO RESULT	Presence or absence of MRSA cannot be determined, repeat test with extra swab. Insufficient data were collected to produce a test result (for example, the operator stopped a test that was in progress). • MRSA—NO RESULT • SPC—NO RESULT • Probe Check—NA (not applicable)

Figure 2. Example of a MRSA POSITIVE Result

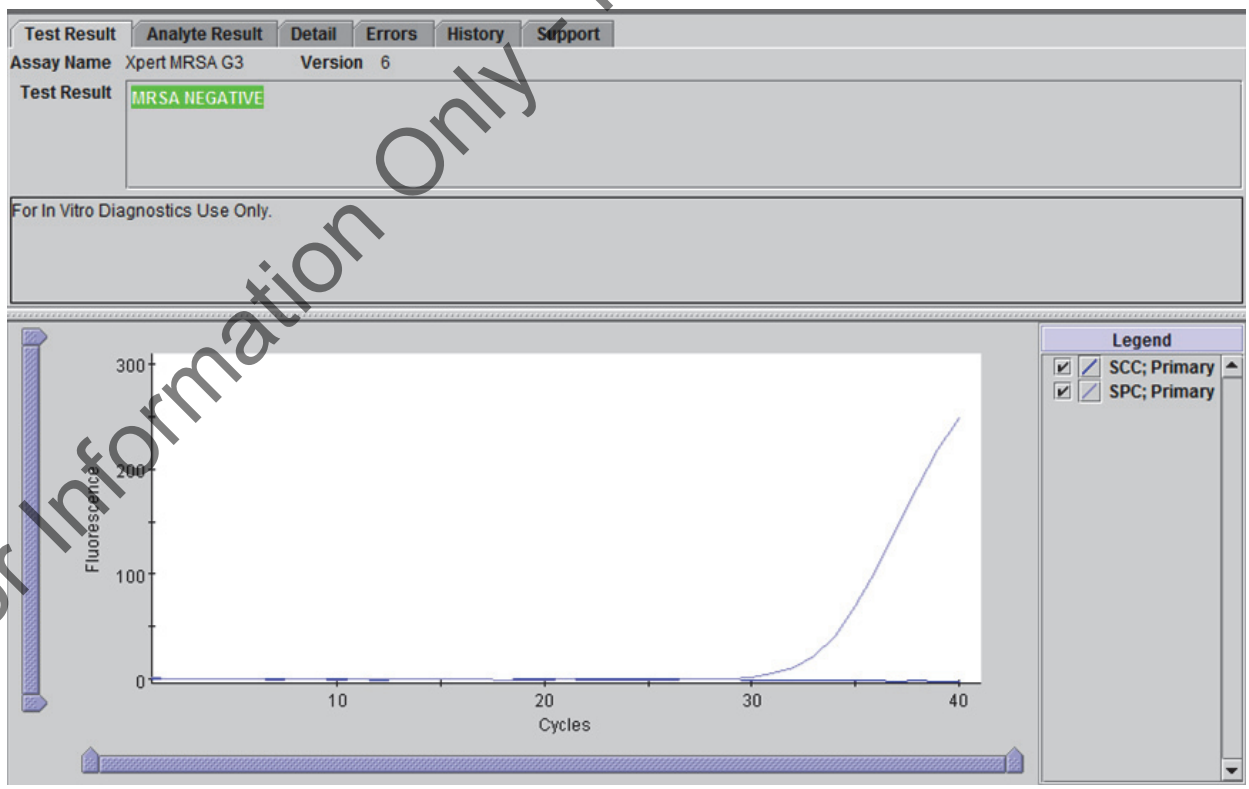

Figure 3. Example of a MRSA NEGATIVE Result

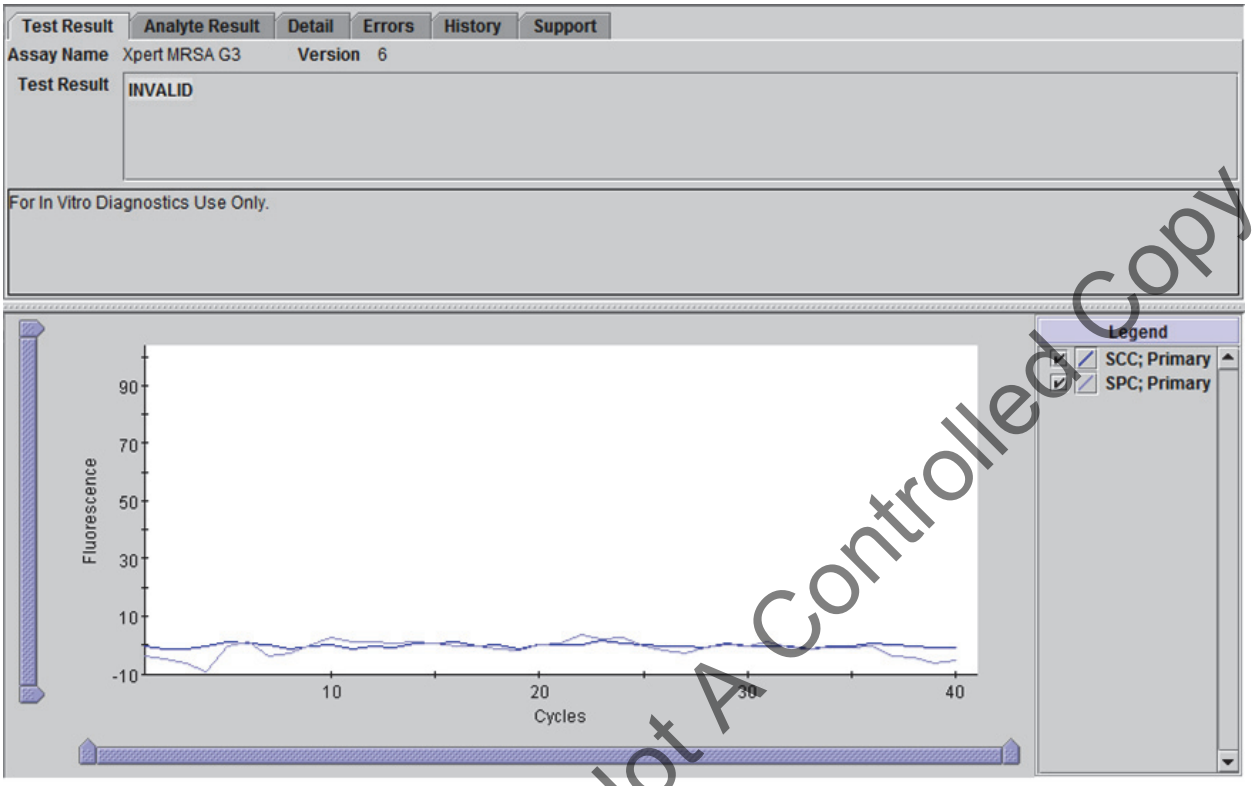

Figure 4. Example of a MRSA INVALID Result

13 Reasons to Repeat the Assay

Repeat the test using a new cartridge and new Elution Reagent (do not re-use the cartridge) or initiate alternate procedures if one of the following test results occurs:

- An **INVALID** result indicates that the controls SPC failed. The sample was not properly processed or PCR is inhibited.
- An **ERROR** result indicates that the Probe Check control failed and the assay was aborted possibly due to the reaction tube being filled improperly, a reagent probe integrity problem was detected, 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.

14 Limitations

- The performance of the Xpert MRSA 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 MRSA Assay should be interpreted in conjunction with other laboratory and clinical data available to the clinician.
- Xpert MRSA Assay performance has not been evaluated in patients less than two years of age.
- Nasal swab specimens from neonatal patients having high levels of *mecA* gene-containing coagulase negative staphylococci may yield false positive results due to the presence of an SCC*mec* sequence.
- Erroneous test results might occur from improper specimen collection, not following the recommended sample collection procedure, handling or storage, technical error, sample mix-up, or because the number of organisms in the specimen is not detected by the test. Careful compliance to the instructions in this insert is necessary to avoid erroneous results.
- Because the detection of MRSA is dependent on the number of organisms present in the sample, reliable results are dependent on proper specimen collection, handling, and storage.
- Rerunning the Xpert MRSA when results are **INVALID**, **ERROR**, and **NO RESULT** should depend on practices and policies within each facility. Alternate procedures (e.g. culture using selective agar plates with or without overnight incubation in a selective enrichment broth) should be available. For culturing, remaining swab specimens should be placed in appropriate transport systems and cultured within 4 days.

- A positive test result does not necessarily indicate the presence of viable organism. It is however, presumptive for the presence of MRSA.
- Testing with Xpert MRSA assay should be used as an adjunct to other methods available.
- Test results might also be affected by concurrent antibiotic therapy. Therefore, therapeutic success or failure cannot be assessed using this test because DNA might persist following antimicrobial therapy.
- Mutations or polymorphisms in primer or probe binding regions may affect detection of new or unknown MRSA variants resulting in a false negative result.

15 Interfering Substances

Potentially interfering substances evaluated include blood, mucus and nasal sprays used to relieve decongestion, nasal dryness or irritation. The presence of these substances did not significantly inhibit PCR and did not give invalid or erroneous results.

In the investigational study for Xpert MRSA Assay, potential interfering substances (blood, mucus or both) were reported on 45 of 1077 (4.2%) nasal swab specimens. Of the 31 specimens that gave an equivocal result on initial testing, three specimens had mucus and one specimen had blood on the swab. Three of the four specimens gave a result on retesting while one that contained mucus remained indeterminate.

16 Expected Values

In the Xpert MRSA clinical study, a total of 1077 nasal specimens were collected from 1077 subjects at 7 enrolling sites across the United States. The study population was grouped into subjects in nursing homes or extended stay facilities, hospitalized over 3 days, hospitalized for 3 days or less, out patient clinic and staff or others. The number and percentage of positive and negative cases relative to the reference culture method are calculated and presented in the table below.

Table 1. Expected Values for MRSA in Different Population Studies

Group	Positive n (%)	Negative n (%)	Total (%)[a]
Nursing homes, long term and extended stay facilities	62 (25.5)	181 (74.5)	243 (22.6)
Hospitalized >3 days	61 (23.0)	204 (77.0)	265 (24.7)
Hospitalized =3 days	29 (13.1)	193 (86.9)	222 (20.7)
Out patient clinic	46 (17.7)	214 (82.3)	260 (24.2)
Staff and others	11 (12.9)	74 (87.1)	85 (7.9)
Total	**209 (19.4)**	**866 (80.6)**	**1075**

a. Two culture positive hospitalized subjects had unknown admission dates.

17 Performance Characteristics

17.1 Clinical Performance

Performance characteristics of the Xpert MRSA Assay were determined in a multi-site prospective investigation study at seven institutions by comparing the MRSA assay on the GeneXpert System (Xpert MRSA Assay) with a second FDA-cleared nucleic acid amplification test (NAAT), and enriched culture, the most sensitive culture method. Subjects included individuals and medical staff at risk for nasal colonization. Each subject was enrolled in the study only one time. Subjects who had received systemic or topical-nasal antibiotics in the period 48 hours to one week prior to study enrollment, under 2 years of age, had contraindication to nasal swab collection were excluded from the study. Only those subjects meeting the inclusion and exclusion criteria were enrolled.

Nasal swabs were collected from each subject. One swab was tested by the Xpert MRSA Assay and another swab by the second FDA-cleared NAAT test. The two types of NAAT tests were performed at each participating institution and an additional swab was sent to a centralized laboratory for culture testing.

At the centralized laboratory, the swab was directly streaked on to a selective chromogenic agar plate with cefoxitin and the plate was incubated for 24–48 hours at 35 ±2 °C. The swab was transferred to trypticase soy broth (TSB) with 6.5% sodium chloride and incubated for 18–24 hours at 35 ±2 °C. If the direct streak was negative at 24 hours, the enriched TSB was streaked onto another chromogenic agar plate with cefoxitin and incubated for 24–48 hours at 35 ±2 °C. Confirmation of presumptive positives colonies from either culture method was performed with a tube coagulase test and Gram stain.

Assay performance of the Xpert MRSA Assay and the second FDA-cleared NAAT test were calculated relative to the central laboratory culture results (reference culture).

17.2 Overall Results

A total of 1077 eligible subjects (one specimen per patient) were tested for MRSA by Xpert MRSA, and a 2nd FDA-cleared NAAT test and culture. The Xpert MRSA identified 86.3% of the specimens positive for MRSA and 94.9% of the specimens negative for MRSA relative to the reference culture method. For the subjects tested, the positive predictive value was 80.5% and the negative predictive value was 96.6%.

Table 2. Xpert MRSA Compared to Reference Culture Method

		Culture				
		+	-			
Xpert MRSA	+	182	44	226	Positive Agreement:	86.3%
	-	29	819	848	Negative Agreement:	94.9%
		211	863	1074[a]	PPV[b]:	80.5%
					NPV[c]:	96.6%

a. Three specimens did not give Xpert results on two attempts.
b. Positive predictive value
c. Negative predictive value

When compared to the direct culture method (swabs directly streaked on selective chromogenic agar plates with cefoxitin without TSB enrichment and incubated for 24–48 hours at 35 ±2 °C), Xpert MRSA identified 94.3% of the specimens positive for MRSA and 93.2% of the specimens negative for MRSA; the positive predictive value was 73.0% and the negative predictive value was 98.8%.

Table 3. Xpert MRSA Compared to Direct Culture Method

		Direct Culture				
		+	-			
Xpert MRSA	+	165	61	226	**Positive Agreement:**	94.3%
	-	10	838	848	**Negative Agreement:**	93.2%
		175	899	1074	PPV[a]:	73.0%
					NPV[b]:	98.8%

a. Positive predictive value
b. Negative predictive value

The following tables show the performance of Xpert MRSA and MRSA prevalence at each clinical site compared to the reference culture and direct culture methods.

Table 4. Performance of Xpert MRSA by Site Compared to Reference Culture Method

Site	MRSA prevalence[a]	Positive Agreement (n) (95% CI)[b]	Negative Agreement (n) (95% CI)[c]	No. of indeterminate results
1	20.2% (78/387)	87.2% (n=78) (77.7-93.7%)	93.9% (n=309) (90.6-96.3%)	10
2	5.2% (3/58)	100.0% (n=3) (29.2-100.0%)	98.2% (n=55) (90.3-100.0%)	3
3	44.4% (12/27)	91.7% (n=12) (61.5-99.8%)	100.0% (n=15) (78.2-100.0%)	3
4	12.3% (20/162)	80.0% (n=20) (56.3-94.3%)	97.2% (n=142) (92.9-99.2%)	9
5	20.5% (46/224)	89.1% (n=46) (76.4-96.4%)	94.9% (n=178) (90.6-97.7%)	1
6	22.3% (42/188)	81.0% (n=42) (65.9-91.4%)	93.2% (n=146) (87.8-96.7%)	6
7	35.7% (10/28)	90.0% (n=10) (55.5-99.8%)	94.4% (n=18) (72.7-99.9%)	2
Total	**19.6% (211/1074)**	**86.3% (n=211) (80.9-90.6%)**	**94.9% (n=863) (93.2-96.3%)**	**34**

a. Determined from results by reference culture method
b. Number of positive determined by reference culture method
c. Number of negative determined by reference culture method

Table 5. Performance of Xpert MRSA by Site—Comparison to Direct Culture Method

Site	Positive Agreement	Negative Agreement
1	95.4% (87.1-99.0%)	92.2% (88.8-94.9%)
2	100.0% (29.2-100.0%)	98.2% (90.3-100.0%)
3	91.7% (61.5-99.8%)	100.0% (78.2-100.0%)
4	81.3% (54.4-96.0%)	95.2% (90.4-98.1%)
5	94.9% (82.7-99.4%)	93.0% (88.3-96.2%)
6	97.1% (84.7-99.9%)	92.9% (87.6-96.4%)
7	100.0% (54.1-100.0%)	81.8% (59.7-94.8%)
Total	**94.3% (89.7-97.2%)**	**93.2% (91.4-94.8%)**

Performances of Xpert MRSA, the 2nd FDA-cleared NAAT and direct culture method from individual sites relative to the reference culture method are presented in the tables below.

Table 6. Results from Xpert MRSA, Direct Culture Method and Second FDA-cleared NAAT Test with Specimens Positive for MRSA by Reference Culture Method

	Positive Agreement (95% CI)		
Site	**Xpert MRSA**	**2nd NAAT**	**Direct Culture[a]**
1	87.2% (77.7-93.7%)	80.8% (70.3-88.8%)	83.3% (73.2-90.8%)
2	100.0% (29.2-100.0%)	100.0% (29.2-100.0%)	100.0% (29.2-100.0%)
3	91.7% (61.5.-99.8%)	83.3% (51.6-97.9%)	100.0% (73.5-100.0%)
4	80.0% (56.3-94.3%)	78.9% (54.4-93.9%)	80.0% (56.3-94.3%)
5	89.1% (76.4-96.4%)	89.1% (76.4-96.4%)	84.8% (71.1-93.7%)
6	81.0% (65.9-91.4%)	78.6% (63.2-89.7%)	81.0% (65.9-91.4%)
7	90.0% (55.5-99.7%)	100.0% (69.2-100.0%)	60.0% (26.2-87.8%)
Total	**86.3% (80.9-90.6%)**	**83.3% (77.6-88.1%)**	**82.9% (77.2-87.8%)**

a. Swabs directly streaked on selective chromogenic agar plates with cefoxitin and incubated for 24-48 hours at 35 ±2 °C.

Table 7. Results from Xpert MRSA, Direct Culture Method and Second FDA-cleared NAAT Test with Specimens Negative for MRSA by Reference Culture Method

	Negative Agreement (95% CI)		
Site	**Xpert MRSA**	**2nd NAAT**	**Direct Culture[a]**
1	93.9% (90.6-96.3%)	92.2% (88.7-95.0%)	100.0% (98.8-100.0%)
2	98.2% (90.3-100.0%)	98.2% (90.3-100.0%)	100.0% (93.6-100.0%)
3	100.0% (78.2-100.0%)	100.0% (79.4-100.0%)	100.0% (79.4-100.0%)
4	97.2% (92.9-99.2%)	97.9% (93.9-99.6%)	100.0% (97.5-100.0%)
5	94.9% (90.6-97.7%)	93.8% (89.2-96.9%)	100.0% (97.9-100.0%)
6	93.2% (87.8-96.7%)	94.5% (89.5-97.6%)	100.0% (97.5-100.0%)
7	94.4% (72.7-99.9%)	94.4% (72.7-99.9%)	100.0% (81.5-100.0%)
Total	**94.9% (93.2-96.3%)**	**94.4% (92.7-95.9%)**	**100.0% (99.6-100.0%)**

a. Swabs directly streaked on selective chromogenic agar plates with cefoxitin and incubated for 24-48 hours at 35 ±2 °C.

18 Analytical Specificity

Cultures from 51 American Type Culture Collection (ATCC) and Network on Antimicrobial Resistance in *Staphylococcus aureus* (NARSA) strains representing species phylogenetically related to *S. aureus* and members of the nasal commensal flora, 32 strains of methicillin-sensitive coagulase negative staphylococci, and 12 strains of methicillin-resistant coagulase negative staphylococci were tested. Three replicates of each isolate were tested at =1 × 10^6 CFU/swab. None of these isolates were detected by the assay. The specificity was 100%.

19 Analytical Sensitivity

The analytical sensitivity of the Xpert MRSA was determined using 6 strains of MRSA representing the six SCC*mec* types and subtypes (I, II, III, IV, IVa and V). Cultures of these strains were quantified then diluted to values spanning the range of 10 to 1000 colony forming units (CFU) per swab. All dilutions were tested in replicates of 4. Limit of detection obtained for each type or subtype tested shows the lowest number of CFU/swab at which all 4 replicates were reported positive. All of the strains representing the SCC*mec* cassette types I - V were detected by the Xpert MRSA Assay.

Table 8. Detection of SCC*mec* Types

SCCmec	(CFU/swab)
type I	10
type II	10
type III	10
type V	10
type IV	50
type IVa	100

Additional studies using type II cells 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 MRSA colony forming units (CFU) per swab that can be reproducibly distinguished from negative samples with 95% confidence. Results indicate that the Xpert MRSA will produce a positive result with 95% confidence for a swab containing 80 CFU.

20 Reproducibility

A panel of specimens with varying concentrations of MRSA and methicillin sensitive *Staphylococcus epidermidis* (negative) were tested in triplicate on 10 different days at each of the three sites (4 specimens × 3 times /day × 10 days × 3 sites). One lot of Xpert MRSA kit was used at each of the 3 testing sites. Xpert MRSA assays were performed according to the Xpert MRSA procedure.

Table 9. Summary of Reproducibility Results

Specimen ID	MRSA in CFU/ swab	MSSE CFU/ swab	Site 1	Site 2	Site 3	Total Agreement	% Total Agreement
Negative	0	2.6×10^6	30/30	30/30	30/31[a]	90/91	98.9%
Weak positive	117	2.6×10^6	30/30	30/30	27/29 [a]	87/89	97.8%
Positive	800	2.6×10^6	30/30	30/30	30/30	90/90	100.0%
Strong positive	2.6×10^4	2.6×10^6	30/30	30/30	30/30	90/90	100.0%
Total Agreement			120/120	120/120	117/120	357/360	99.2%
% Agreement			100.0%	100.0%	97.5%		

a. Xpert MRSA assay was inadvertently performed on one additional negative specimen and one less weak positive specimen

21 References

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23 Technical Assistance

Before contacting Cepheid Technical Support, collect the following information:

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

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24 Table of Symbols

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

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IVD CE