510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
DEVICE AND INSTRUMENT TEMPLATE

A. 510(k) Number:
k070462

B. Purpose for Submission:
New 510k

C. Measurand:
Sequence incorporating the insertion site (*attBsc*) of *Staphylococcal* chromosome cassette *mec* (SCC*mec*)

D. Type of Test:
Nucleic Acid Amplification Test, DNA, Methicillin-resistant *Staphylococcus aureus* (MRSA), qualitative

E. Applicant:
Cepheid

F. Proprietary and Established Names:
Xpert MRSA

G. Regulatory Information:

1. Regulation section:
   21 CFR 866. 1640 Antimicrobial susceptibility test powder

2. Classification:
   Class II

3. Product Code:
   NQX

4. Panel:
   83 Microbiology

H. Intended Use:

1. Intended use(s):
   The Cepheid Xpert MRSA Assay performed on 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. Concomittant cultures are necessary only to recover organisms for epidemiological typing for further susceptibility testing.

2. Indication(s) for Use:
   The Cepheid Xpert MRSA Assay is indicated for the rapid detection of methicillin-resistant *Staphylococcus aureus* (MRSA) from nasal swabs in patients at risk for nasal colonization.

3. Special condition for use statement(s):
   Prescription Use

4. Special instrument Requirements:
   Gene Xpert® Dx System

I. Device Description:

The Xpert methicillin-resistant *Staphylococcus aureus* (MRSA) Assay system performs real-time, multiplex polymerase chain reaction (PCR) for detection of DNA after an initial sample processing step. In this platform, additional sample preparation, amplification, and real-time detection are all fully automated and completely integrated. The assay is performed on a GeneXpert® Dx System, which consists of the GeneXpert instrument, personal computer, hand-held barcode scanner, and disposable fluidic cartridges that are designed to complete sample preparation and real-time PCR for detection of MRSA in about 75 minutes. Each instrument contains 1 to 4 randomly accessible modules that are capable of performing separate sample preparation and real-time PCR tests. Each module contains a syringe drive for dispensing fluids, an ultrasonic horn for lysing cells or spores, and I-CORE® thermocycler for performing real-time PCR and detection.

The patented single-use cartridge contain: (1) eleven chambers for holding sample, reagents, or other materials, (2) a valve body composed of a plunger and syringe barrel, (3) a rotary valve system for controlling the movement of fluids between chambers, (4) an area for capturing, concentrating, washing, and lysing spores/cells, (5) dry real-time PCR reagents, and (6) an integrated PCR reaction tube that can be automatically filled by the instrument. To eliminate test-to-test contamination, all fluids including amplicons, are contained within the disposable cartridge. The instrument never comes into contact with any fluids within the cartridge. Each disposable cartridge is intended to test one sample. Cartridges are not re-usable.

The Xpert MRSA Assay includes self-contained reagents, including primers and probes for the simultaneous detection of the target MRSA. Each assay includes a system control (Probe Check Control) and an internal control (Sample Processing Control). The Probe Check Control (PCC) verifies bead rehydration, PCR tube filling in the cartridge,

probe integrity, and dye stability. The Sample Processing Control (SPC) is present as a spore cake in a bead form at a specific concentration of organisms per bead. It is located in one of the chambers in the Xpert MRSA assay cartridge and is reconstituted by the eluted specimen before processing. During sample processing, the SPC is co-processed through all automated steps of the sample preparation procedure, including treatment, filtration/concentration, washing, ultrasonic lysis, and lysate recovery. It verifies adequate processing of the target MRSA bacteria and to monitor the presence of inhibitor(s) in the PCR assay to avoid false–negative results.

A nasal specimen is collected using the Cepheid Sample Collection Device and transported to the GeneXpert Dx System area. The swab is placed in a tube containing 1.5 mL elution buffer. Following a brief vortexing, the eluted material and two other reagents are transferred to different chambers of the cartridge. The GeneXpert Dx System completes sample preparation by mixing the eluted sample with the sample preparation control and treatment reagents, capturing the bacterial cells on a filter, lysing the cells using glass beads and an ultrasonic horn, and then eluting the released DNA. The DNA solution is then mixed with dry PCR reagents and transferred into the PCR reaction tube for real-time PCR and detection.

Figure 1. Xpert MRSA cartridge (top view).

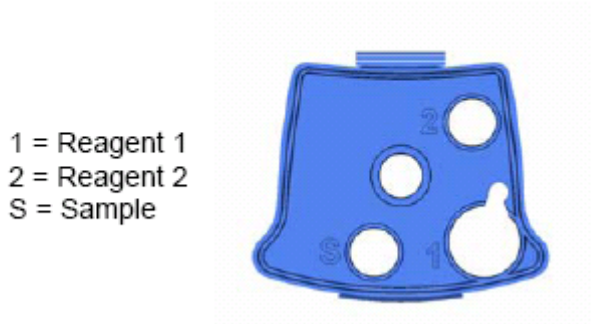


Figure 11-2: Xpert MRSA Assay

Figure 11-3: GeneXpert Dx System

J. Substantial Equivalence Information:

1. Predicate device name(s):
   IDI MRSA™ Assay

2. Predicate K number(s):
   k033415

3. Comparison with predicate:

DEVICE		PREDICATE
A. Similarities		
Technological Principles	Nucleic Acid Amplification (DNA) real-time PCR	Nucleic Acid Amplification (DNA) real-time PCR
Intended Use	Rapid detection of MRSA	Rapid detection of MRSA
DNA Target Sequence	Sequence incorporating the insertion site (*attBsc*) of *Staphylococcal* Chromosome Cassette *mec* (SCC *mec*)	Sequence incorporating the insertion site (*attBsc*) of *Staphylococcal* Chromosome Cassette *mec* (SCC *mec*)
Samples	Direct from nasal swabs	Direct from nasal swabs
Sample Collection/Transport Storage	Copan Liquid Stuarts Room temperature for 24 hours; 2-8°C for up to 5 days	Copan Liquid Stuarts Room temperature for 24 hours; 2-8°C for up to 5 days
Thermal cycling	Automated	Automated
B. Differences		
Probes	Taqman® Probes	Molecular beacons
Assay platform	Cepheid GeneXpert DX System	Cepheid SmartCycler System
Fluidics	Self-contained and automated after swab elution and two single-dose reagent additions (see Sample Preparation and Assay Reagents)	Multiple manual steps including pipetting, fluid transfers, vortexing, centrifugation, and sample heating (see Sample Preparation and Assay Reagents)
Criteria for Ct determination	Primary growth curve	2nd derivative analysis

Time to result	75 minutes total	60 to 75 minutes total
Internal Assay Controls	Sample Processing Control; Probe Check Control (all optical channels)	Internal control Site check (1 optical channel)
External Controls	Available but not provided -Positive control -Negative control	Provided: -Positive control -Negative control

K. Standard/Guidance Document Referenced (if applicable):

Not Applicable

L. Test Principle:

The primers and probes in the Xpert MRSA Assay detect the presence of the *staphylococcal* cassette chromosome (SCC) inserted into the SA chromosomal *attB* site. Nasal swabs are collected and transported to the GeneXpert® System area. The swab is placed in a tube containing 1.5 mL elution buffer. Following a brief vortexing, the eluted material and two other liquid reagents are transferred to different chambers of the cartridge.

The user initiates a test from the system user interface, the instrument signals the user where to place the cartridge by flashing a green light, and the cartridge is placed into the indicated module in the GeneXpert® Dx System instrument. The instrument moves the sample and reagents to and from different chambers within the Xpert MRSA Assay cartridge. The GeneXpert® Dx System performs sample preparation by mixing the eluted sample with the sample preparation control and treatment reagents, capturing the bacterial cells on a filter, lysing the cells using glass beads and ultrasonic horn, then eluting the released DNA. The DNA solution is then mixed with dry PCR reagents and transferred into the PCR tube for real-time PCR and detection. The Xpert MRSA Assay completes sample preparation and real-time PCR in approximately 75 minutes. Internal controls in Xpert MRSA Assay check key automated steps.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Reproducibility was determined by testing 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 x 3 times/day x 10 days x 3 sites). One lot of Xpert MRSA kit was used at each of the 3 testing sites.

Table 6 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%		

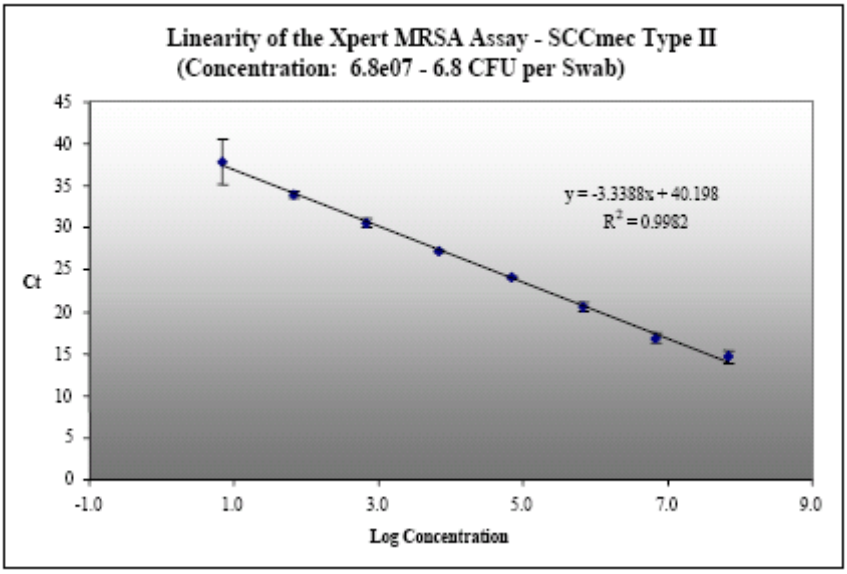
[A] Xpert MRSA assay was inadvertently performed on one additional negative specimen and one less weak positive specimen.

b. Linearity/assay reportable range:

Linearity was evaluated using two strains of MRSA (type II and type III) cells serially diluted over 8 orders of magnitude (6.8e7 CFU/swab to 0.68 CFU/swab).

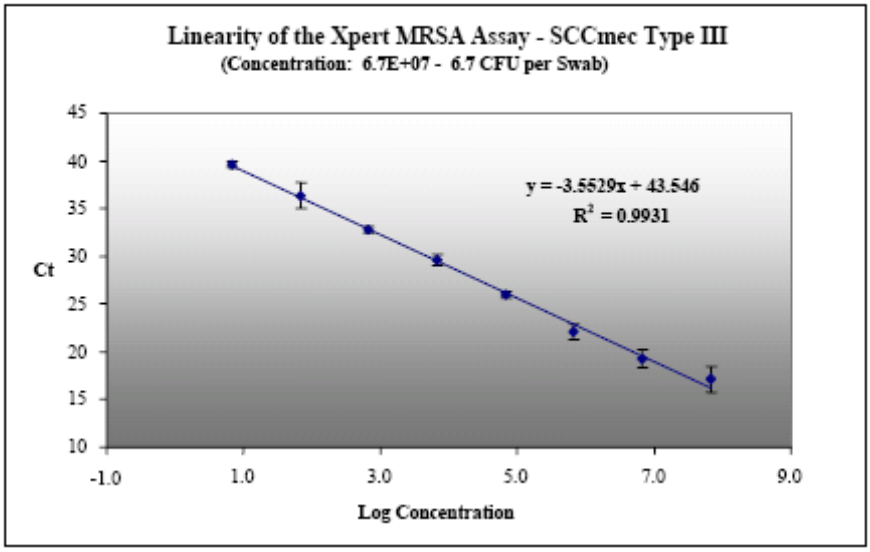
The type II MRSA cells responded linearly ($r^2 = 0.9982$) with respect to SCC*mec* detection as a function of MRSA cell input over 7 orders of magnitude (Figure 18-2). The Xpert MRSA Assay was linear to 6.8 CFU/swab.

Figure 18-2: Linearity of the Xpert MRSA Assay- SCCmec type II



The type III MRSA cells responded linearly ($r^2 = 0.9931$) with respect to SCC*mec* detection as a function of MRSA cell input over 7 orders of magnitude (Figure 18-3). The Xpert MRSA Assay was linear to 6.7 CFU/swab.

Figure 18-3: Linearity of the Xpert MRSA Assay- SCCmec type III



c. Traceability (controls, calibrators, or method):

External controls were run at each study site prior to start of clinical testing as proficiency samples. External controls used are *Staphylococcus epidermidis* and Methicillin-resistant *Staphylococcus aureus*. Summary of results are shown below.

Table 2 Summary Results for Xpert MRSA Proficiency/External Control Specimens

Site No.	Number of operators	No. of Valid Results	No. of Invalid Results	No. of Correctly Classified Valid Tests/ Total Valid Tests (%)
14	5	20	2[A]	20/20 (100)
17	4	16	0	16/16 (100)
18	2	8	1[B]	8/8 (100)
19	2	12	0	11/12[D] (91.6)
20	3	12	0	12/12 (100)
21	2	8	0	8/8 (100)
22	2	8	1[C]	8/8 (100)
Total	20	84	4	83/84 (98.8)

[A] MRSA high-Error = 1; NEG (MSSE high)-MRSA INVALID = 1

[B] MRSA high-Error = 1

[C] MRSA high-Error = 1

[D] NEG (SA low) misclassified as positive

The labeling includes a recommendation that "external controls may be used in accordance with local, state, federal accrediting organizations, as applicable".

In addition to the recommended external controls, the Xpert MRSA assay also includes the Probe Check Control and Sample Processing Control which were previously addressed under the Device Description Section.

d. Detection limit (functional sensitivity):

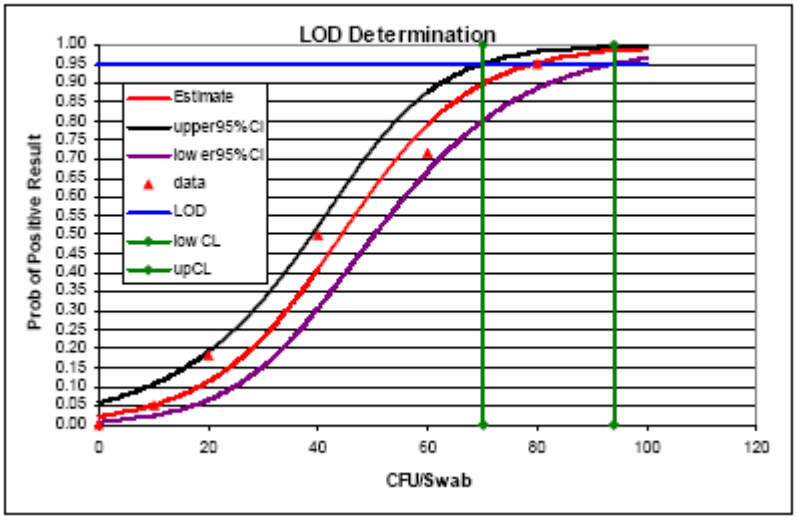
The analytical sensitivity was determined using 6 strains of MRSA representing the six SCC*mec* types and subtypes (I, II, III, IV, IVa, and V). Cultures of these strains were quantified then diluted from 10 to 1000 colony forming units (CFU) per swab and tested in replicates of 4. Limit of detection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

Table 5 Detection of Each SCC*mec* Types

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

An additional limit of detection or analytical sensitivity study was performed using MRSA *SCCmec* type II cells. Replicates of at least 20 each were evaluated at seven concentrations. A cycle threshold (Ct) was established to determine positivity or negativity for the target. Results of the study are shown in the table below, which indicates that the Xpert MRSA will produce a positive result with 95% confidence for a swab containing 80 CFU.

Figure 18-1: Limit of Detection Determination of the Xpert MRSA Assay (type II cells)



e. Analytical specificity:

The analytical specificity was determined using 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*. Each isolate was tested in three replicates at $\geq 1 \times 10^6$ CFU/swab. None of these isolates were detected by the assay.

Potentially interfering substances evaluated include blood, mucus, and nasal sprays 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 investigation 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. Results are summarized in the table below.

Table 18-7: Percent Inhibition of SCC (TxRed EPF) by Potentially Interfering Substances using the Xpert MRSA Assay

Interfering Substance	50 CFU/swab	125 CFU/swab
TET Buffer (control)	0 %	0 %
Nasal Sprays		
Saline	7 %	9 %
Neo-Synephrine	13 %	0 %
Anefrin	0 %	1 %
Zicam	11 %	0 %
Human Blood	24 %	17 %
Mucin 10% (w/v)	21 %	0 %

Carry-Over Contamination study consisted of a negative sample (no MRSA cells spiked onto swabs) processed in the same Gene Xpert module immediately following a very high positive sample ($1x10^7$ MRSA cells spiked onto swabs). This was repeated 20 times between 2 Gene Xpert modules for a total of 40 runs. The study demonstrated no evidence of carry-over contamination.

f. Assay cut-off:

Receiver operator characteristics (ROC) analysis was performed using the clinical data to verify the 36 cycle threshold (Ct) cut-off used in the clinical study. This cut-off is supported by data analysis as the optimal cut-off for the Xpert MRSA Assay.

2. Comparison studies:

a. Method comparison with predicate device:

Clinical trial using nasal swab specimens was performed at seven institutions by comparing the Xpert MRSA Assay with a second FDA-cleared nucleic acid amplification test (NAAT), and an enriched culture. 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 2nd 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 fro 24-48 hours at 35±2°C. Confirmation of presumptive positive colonies from either culture method was performed with a tube coagulase test and Gram stain.

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.

Table 2A Xpert MRSA Compared to Reference Culture Method

Xpert MRSA vs. Reference culture method						
		Culture				
		+	-			
	+	182	44	226	**Positive Agreement:**	86.3%
Xpert MRSA	-	29	819	848	**Negative Agreement:**	94.9%
		211	863	1074*	PPV[1:]	80.5%
					NPV[2:]	96.6%
* 3 specimens did not give Xpert results on 2 attempts						

[1] Positive predictive value

[2] 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±2ºC), Xpert MRSA identified 94.3% of the specimens positive for MRSA and 93.2% of the specimens negative for MRSA.

Table 2B Xpert MRSA Compared to Direct Culture Method

Xpert MRSA vs. Direct culture						
		Direct Culture				
		+	-			
Xpert MRSA	+	165	61	226	**Positive Agreement:**	94.3%
	-	10	838	848	**Negative Agreement:**	93.2%
		175	899	1074	PPV[1:]	73.0%
					NPV[2:]	98.8%

* 3 specimens did not give Xpert results on 2 attempts

[1] Positive predictive value

[2] 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 3A Performance of Xpert MRSA by Site Compared to Reference Culture Method

Site	MRSA prevalence[1]	Positive Agreement (n^2) (95% CI)	Negative Agreement (n^3) (95% CI)	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%)	10
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%)	32

[1]Determined from results by reference culture method
[2]Number of positive determined by reference culture method
[3]Number of negative determined by reference culture method

Table 3B Performance of Xpert MRSA by Site - Comparison to Direct Culture Method

Site	Positive Agreemente	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 4A Results from Xpert MRSA, Direct Culture Method and 2nd FDA-cleared NAAT Test with Specimens Positive for MRSA by Reference Culture Method

	Positive Agreement (95% CI)		
Site	Xpert MRSA	2nd NAAT	Direct Culture[1]
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%)

Table 4B Results from Xpert MRSA, Direct Culture Method and 2nd FDA-cleared NAAT Test with Specimens Negative for MRSA by Reference Culture Method

	Negative Agreement (95% CI)		
Site	Xpert MRSA	2nd NAAT	Direct Culture[1]
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%)

[1]Swabs directly streak on selective chromogenic agar plates with cefoxitin and incubate for 24-48 hours at 35±2ºC.

b. Matrix comparison:

Not applicable

3. Clinical studies:

a. Clinical sensitivity:

Not applicable

b. Clinical specificity:

Not applicable

4 Clinical cut-off:

Not applicable

5. Expected values/Reference range:

A total of 1077 nasal specimens were collected from 1077 patients 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 Study Populations

Group	Positive n (%)	Negative n (%)	Total[†] (%)
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

[†]Two culture positive hospitalized subjects had unknown admission dates

N. Instrument Name:

GeneXpert Dx system

O. System Descriptions:

1. Modes of Operation:

The GeneXpert Dx system operates in random access mode and up to four single use cartridges may be run simultaneously. Up to four GeneXpert Dx Systems may be linked together, resulting in a total of up to 16 samples processed per run.

2. Software:

FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types: Yes _√_ or No _____

The GeneXpert Dx system is the same instrument that is used with the FDA cleared Cepheid GBS Assay. The software used on the GeneXpert Dx system for use with the Xpert MRSA Assay is also the same as the Xpert GBS assay

except that the software use for Xpert MRSA Assay is Version 1.6 and software for Xpert GBS was Version 1.2.

Version 1.6 includes changes for compatibility with the Xpert MRSA Assay, compatibility with Cepheid's future assays, and improvements for usability. Thermal control, optical control, and data handling for version 1.6 are equivalent to that in version 1.2. Equivalency testing for version 1.2 assays was performed in version 1.6 software to ensure that the changes did not affect normal GeneXpert functionality. The Xpert MRSA Assay has been verified and validated using the Version 1.6 software.

3. Sample Identification:

The software assigns access by predefined user types. The user interface software is designed with a mouse driven graphical user interface. To perform a test, the user clicks on the Create Test icon, scans the cartridge barcode, enters the sample ID barcode, and loads the cartridge into the module to start the test. An estimated time-to-completion is provided at the beginning of the test. A test result is provided when the test is completed.

4. Specimen Sampling and Handling:

GeneXpert Dx System Hardware Components for Automated Sample Processing

Module Hardware Components	Function
Valve Drive	Rotates the cartridge valve body to address the different cartridge chambers.
Syringe Pump drive	Dispenses fluids to and from the different cartridge chambers.
Ultrasonic horn	Lyses the bacterial cells and sample prep control.
I-CORE® module	Performs PCR amplification and detection. As the user inserts the cartridge into the system, the reaction tube component of the cartridge is inserted into the I-CORE module. After sample preparation within the cartridge, the sample and reagent mixture is transferred from the cartridge chamber into the reaction tube. During the amplification process, the I-CORE heater heats up and the fan cools down the reaction tube contents. Two optical blocks positioned within the I-CORE excite the dye molecules that make up the probes and detect the fluorescence emitted. The system uses calibration and data analysis algorithms to determine a relative fluorescence value for each reporter dye after each thermal cycle.
Hand-held Barcode Scanner	Scans cartridge barcode and optional Patient or Sample ID barcode into the GeneXpert Dx System.

5. Assay Types:

The GeneXpert Dx Instrument accepts the Xpert MRSA Assay-specific cartridges that are loaded into the instrument, concentrates bacterial cells, lyses the samples in the cartridges, releases the nucleic acid, amplifies the target sequences, and detects the presence of target and controls.

6. Reaction Types:

   Not applicable

7. Calibration:

   Optical and thermal calibration of the GeneXpert Dx System is performed at the time of manufacture prior to installation and once yearly or after 1000 runs per module. The user does not calibrate or perform any serviceable functions on the instrument. The normalization function compensates for any optical degradation between calibrations.

8. Quality Control:
   Before the start of the PCR reaction, the GeneXpert Dx system is programmed to perform a probe check on the amplification mixture. The Probe Check Control (PCC) verifies bead rehydration, PCR tube filling in the cartridge, probe integrity, and dye stability. The PCC is considered to PASS if it meets the validated acceptance criteria. If the PCC fails in the MRSA target or Sample Processing Control (SPC), an error is reported and the test will not continue.

   The SPC verifies adequate processing of the target MRSA bacteria. The SPC PASSES if it meets the validated acceptance criteria. The SPC verifies that lysis of MRSA has occurred if the bacteria is present and verifies that specimen processing is adequate. It also monitors the integrity of the PCR assay, including sample inhibition.

   External controls may be obtained commercially and may be used in accordance with local, state, or federal accrediting organizations as applicable.

P. Other Supportive Instrument Performance Characteristics Data Not Covered in the Performance Characteristics Section Above

Not applicable

Q. Labeling

The labeling is sufficient and satisfies the requirements of 21 CFR Part 809.10.

R. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.