Food and Drug Administration
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Silver Spring, MD 20993-0002
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SPECIAL 510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

I Background Information:

A 510(k) Number

K190771

B Applicant

Cepheid

C Proprietary and Established Names

Xpert MRSA/SA Blood Culture, GeneXpert Dx System, GeneXpert Infinity-48s System, GeneXpert Infinity-80 System

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
NQX	Class II	21 CFR 866.1640 - Antimicrobial Susceptibility Test Powder	IM - Immunology & MI - Microbiology
OOI	Class II	21 CFR 862.2570 - Instrumentation for clinical multiplex test systems	CH - Clinical Chemistry

II Review Summary:

This 510(k) submission contains information/data on modifications made to the submitter's own CLASS II device requiring 510(k). The following items are present and acceptable

1. The name and 510(k) number of the SUBMITTER'S previously cleared device:

   Xpert MRSA/SA Blood Culture Assay

   510(k) number: K130894

2. Submitter's statement that the **INDICATIONS FOR USE/INTENDED USE** of the modified device as described in its labeling **HAS CHANGED** along with the proposed labeling which includes instructions for use, package labeling, and, if available, advertisements or promotional materials (labeling changes are permitted as long as they do not affect the intended use).

   This change was for the device name changed from "Xpert MRSA/SA Blood Culture Assay" to "Xpert MRSA/SA Blood Culture".

3. A description of the device **MODIFICATION(S)**, including clearly labeled diagrams, engineering drawings, photographs, user's and/or service manuals in sufficient detail to demonstrate that the **FUNDAMENTAL SCIENTIFIC TECHNOLOGY** of the modified device **has not changed.**

   This change was for the incorporation of enhanced algorithms (rules-based) into the Xpert MRSA/SA Blood Culture assay definition file (ADF) for determining SA positive, MRSA positive, SA negative and MRSA negative test results. This change is a post-PCR rules-based analysis. The minimum software requirement of the GeneXpert Dx software version 5.3, on which the updated ADF is locked and the rules-based, post-PCR analysis settings are supported and compatible with Infinity software version 6.8 and higher.

   The Xpert MRSA/SA Blood Culture Package Insert was updated to revise the Results and Interpretations table to reflect the revisions to assay test results reporting and to update the minimum software requirement to GeneXpert Dx software version 5.3 or GeneXpert Infinity Xpertise 6.8.

   The Xpert MRSA/SA Blood Culture Package Insert was updated to include performance characteristics with a summary of re-analyses of original data with newly released updated software modifications.

4. Comparison Information (i.e., similarities and differences) to the submitter's legally marketed predicate device including, labeling, intended use, and physical characteristics.

Device & Predicate Device(s):	Device: Xpert MRSA/SA Blood Culture (K190771)	Predicate: Xpert MRSA/SA Blood Culture Assay (K130894)
Similarities		
Intended Use/Indications For Use	The Cepheid Xpert MRSA/SA Blood Culture test, performed on the GeneXpert Instrument Systems, is a qualitative *in vitro* diagnostic test intended for the detection of *Staphylococcus aureus* (SA) and methicillin-resistant *Staphylococcus aureus* (MRSA) DNA directly from positive blood cultures. The assay utilizes automated real-time polymerase chain reaction (PCR) for the amplification of MRSA/SA	Same

	specific DNA targets and fluorogenic target-specific hybridization probes for the real-time detection of the amplified DNA. The assay is performed directly on positive blood culture samples using BD BACTEC Plus Aerobic/F, BacT/ALERT SA (Standard Aerobic) or VersaTREK REDOX 1 (aerobic) blood culture bottles that are determined as Gram Positive Cocci in Clusters (GPCC) or as Gram Positive Cocci in singles (GPC) by Gram stain. The Xpert MRSA/SA Blood Culture test is indicated for use in conjunction with other laboratory tests, such as culture, and clinical data available to the clinician as an aid in the detection of MRSA/SA from positive blood cultures. Subculturing of positive blood cultures is necessary to recover organisms for susceptibility testing or for epidemiological typing. The Cepheid Xpert MRSA/SA Blood Culture test is not intended to monitor treatment for MRSA/SA infections.	
Specimen Type	Positive Blood Culture	Same
Technological Principles	Fully automated nucleic acid amplification (DNA); real-time PCR	Same
Test Cartridge	Disposable single-use, multi-chambered fluidic cartridge	Same
Sample Preparation	Self-contained and automated after mixed specimen is added to cartridge. All other reagents are contained in the cartridge	Same
Probes	TaqMan Probes	Same
Internal Controls	Sample processing (SPC) and probe check control (PCC)	Same
DNA Target Sequence	Sequence incorporating the insertion site (*attB*) of Staphylococcal Cassette Chromosome *mec* (SCC*mec*) for detection of MRSA.	Same
DNA Target Sequence	Sequence specific to methicillin/oxacillin resistance (*mecA* gene)	Same
DNA Target Sequence	Sequence specific to *Staphylococcus*	Same

	aureus species (*spa* gene)	
Ability to identify correctly "Empty Cassette Variants"	Yes, sequence specific to *Staphylococcus aureus* species (*mecA* gene)	Same
Time to Result	Approximately 60 minutes to result	Same

Device & Predicate Device(s):	Device: Xpert MRSA/SA Blood Culture (K190771)	Predicate: Xpert MRSA/SA Blood Culture Assay (K130894)
Differences		
Trade Name	Xpert MRSA/SA Blood Culture	Xpert MRSA/SA Blood Culture Assay
Instrument System	Cepheid GeneXpert Dx Systems and GeneXpert Infinity-48s and Infinity-80 Systems	Cepheid GeneXpert Dx Systems, GeneXpert Infinity-48 System, and GeneXpert Infinity-48s and Infinity-80 Systems
Minimum software requirements	GeneXpert Dx software version 5.3 and higher, GeneXpert Infinity-48s and Infinity-80 Xpertise software version 6.8 and Higher	GeneXpert Dx software version 4.3 and higher, GeneXpert Infinity-48 Xpertise 4.3 and higher, GeneXpert Infinity-48s and Infinity-80 Xpertise software version 6.0 and higher
Assay Definition File	Rules-based algorithms incorporating delta Ct values between targets within a valid Ct range and algorithms based on the Ct value for the targets falling within a valid Ct range	Algorithms based on the Ct value for the targets falling within a valid Ct range

5. A Design Control Activities Summary which includes:

   a) Identification of Risk Analysis method(s) used to assess the impact of the modification on the device and its components, and the results of the analysis.

   A formal risk assessment was conducted for the Xpert MRSA/SA Blood Culture test and the GeneXpert Instrument Systems. This assessment included safety Failure Mode Effects and Analyses (sFMEA) and Device Hazard Analysis (DHA) with the updated ADF and software modifications. False negative results i.e., true MRSA not identified as MRSA, were considered the worst case hazard effects to the patient. It was concluded that based on the Risk Management Reviews, discussions, sFMEA and the mitigation

actions taken, the risks identified are acceptable and Xpert MRSA/SA Blood Culture is safe and effective for its intended use.

b) Based on the Risk Analysis, an identification of the verification and/or validation activities required, including methods or tests used and acceptance criteria to be applied.

To confirm assay performance was not negatively impacted by the incorporation of the new software algorithms (and corresponding changes to the ADF) for determining SA positive, MRSA positive, SA negative and MRSA negative test results, Cepheid performed the following re-analysis of original raw data:

- LoD
  - No new test runs were performed. Data acquired for MRSA and MSSA during the original LoD study were retrieved and reanalyzed using the updated ADF.
  - Testing showed that the LoD estimates were not affected.
- Inclusivity
  - No new test runs were performed. Data acquired during the original Inclusivity study were retrieved and reanalyzed using the updated ADF.
  - Testing showed that all isolates were correctly reported, and the acceptance criteria were met.
- Exclusivity
  - No new test runs were performed. Data acquired during the original Exclusivity study were retrieved and reanalyzed using the updated ADF.
  - Testing showed that none of the non-*Staphylococcus aureus* isolates were detected and the acceptance criteria were met.
- Potentially Interfering Substances
  - No new test runs were performed. Data acquired during the original Potentially Interfering Substances study were retrieved and reanalyzed using the updated ADF.
  - Testing showed no substantial changes to the Ct values from the original report except for two tests with triglycerides and bilirubin that changed from correct test results (MRSA NEGATIVE; SA POSITIVE) to incorrect test results (MRSA POSITIVE; SA POSITIVE) attributed to a contaminant introduced during the original testing as *mecA* contamination was also observed in a MSSA negative control.
- Precision
  - No new test runs were performed. Data acquired during the original Precision study were retrieved and reanalyzed using the updated ADF.
  - Testing showed 95.2% of the results were identical. The majority of the exceptions were high negative samples that changed from MRSA NEGATIVE to MRSA POSITIVE due to the original ADF requiring three targets to be positive MRSA call, and the updated ADF requiring two of the three targets to be positive for a positive MRSA call.
- Reproducibility
  - No new test results were performed. Data acquired during the original Reproducibility study were retrieved and reanalyzed using the updated ADF.
  - Testing showed 97.5% of the results were identical. The majority of the exceptions were high negative samples that changed from MRSA NEGATIVE to MRSA POSITIVE due to the original ADF requiring three

targets to be positive MRSA call, and the updated ADF requiring two of the three targets to be positive for a positive MRSA call.

- Clinical Performance
  - No new tests were performed. Data acquired during the original Clinical Performance study were retrieved and reanalyzed using the updated ADF.
  - Testing showed similar performance and acceptance criteria were met. See Table 1 below for comparison between the original and updated analyses.

Table 1. Xpert MRSA/SA Blood Culture Performance Comparison

Target	Original		Updated	
	PPA (n/N, 95% CI)	**NPA (n/N, 95% CI)**	**PPA (n/N, 95% CI)**	**NPA (n/N, 95% CI)**
MRSA	98.1% (103/105, 93.3-99.8)	99.6% (684/687, 98.7-99.9)	99.0% (104/105, 94.8-100.0)	99.0% (680/687, 97.9-99.5)
SA	99.6% (235/236, 97.7-99.9)	99.5% (553/556, 98.4-99.9)	100.0% (236/236, 98.4-100.0)	99.3% (552/556, 98.2-99.8)

The firm provided a summary of the results from the verification and validation studies. The results demonstrated that requirements were met and any test failures have been reviewed and determined to be due to software defects that can be prevented or corrected if they are encountered.

The labeling for this modified subject device has been reviewed to verify that the indication/intended use for the device is unaffected by the modification. In addition, the submitter's description of the particular modification(s) and the comparative information between the modified and unmodified devices demonstrate that the fundamental scientific technology has not changed. The submitter has provided the design control information as specified in The New 510(k) Paradigm and on this basis, I recommend the device be determined substantially equivalent to the previously cleared (or their preamendment) device.