Food and Drug Administration
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510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K191172

B Applicant

Microbiologics, Inc.

C Proprietary and Established Names

Cepheid Xpert MRSA NxG Control Panel

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
PMN	Class II	21 CFR 866.3920 - Assayed Quality Control Material For Clinical Microbiology Assays	IM - Immunology & MI - Microbiology

II Submission/Device Overview:

A Purpose for Submission:
To obtain a Substantial Equivalence determination for the Cepheid Xpert MRSA NxG Control Panel for use with the Cepheid Xpert MRSA NxG Assay on the GeneXpert Instrument System.

B Measurand:
Nucleic acid quality control material from inactivated Methicillin-Resistant *Staphylococcus aureus* (MRSA, positive control) and *Staphylococcus epidermidis* (negative control).

C Type of Test:
The Cepheid Xpert MRSA NxG Control Panel is an external assayed positive and negative quality control material to monitor the performance of *in vitro* laboratory nucleic acid testing procedures for the qualitative detection of Methicillin-Resistant *Staphylococcus aureus* (MRSA) performed with the Cepheid Xpert MRSA NxG Assay on the GeneXpert Instrument System.

III Intended Use/Indications for Use:

A Intended Use(s):
See Indications for Use below.

B Indication(s) for Use:
The Cepheid Xpert MRSA NxG Control Panel is intended for use as an external assayed positive and negative quality control to monitor the performance of in vitro laboratory nucleic acid testing procedures for the qualitative detection of Methicillin-Resistant Staphylococcus aureus performed with the Cepheid Xpert MRSA NxG Assay on the GeneXpert Instrument System. The controls comprise cultured and inactivated Methicillin-Resistant Staphylococcus aureus as the positive control and Staphylococcus epidermidis as the negative control.

The Cepheid Xpert MRSA NxG Control Panel is not intended to replace manufacturer controls provided with the Cepheid Xpert MRSA NxG Assay.

C Special Conditions for Use Statement(s):
Rx - For Prescription Use Only

For in vitro diagnostic use only.

This product is not intended to replace the manufacturer controls provided with the Cepheid Xpert MRSA NxG Assay.

D Special Instrument Requirements:
The Cepheid Xpert MRSA NxG Control Panel is intended for use on the GeneXpert Instrument System.

IV Device/System Characteristics:

A Device Description:
The Cepheid Xpert MRSA NxG Control Panel is used to monitor the DNA extraction, amplification and detection processes of the Cepheid Xpert MRSA NxG Assay. The Cepheid Xpert MRSA NxG Control Panel contains cultured microorganisms inactivated by heat treatments. Each Cepheid Xpert MRSA NxG Control Panel consists of 6 individually packaged positive control swabs and 6 individually wrapped negative control swabs. Each positive control swab contains cultured and inactivated Methicillin-Resistant *Staphylococcus aureus* (MRSA) at a target level that is designed to provide reproducible performance above the limit of detection for each of the genes targeted by the Cepheid Xpert MRSA NxG Assay: methicillin resistance gene *mecA* (mec) and the Staphylococcal cassette chromosome (SCC). Each negative control swab contains Methicillin-Susceptible *Staphylococcus epidermidis* (MSSE) that is not targeted/detected by the assay. Each swab is individually wrapped with a desiccant in a heat-sealed foil pouch.

B Principle of Operation:
The Cepheid Xpert MRSA NxG Control Panel is intended for use as external assayed quality control materials for use in monitoring the DNA extraction, amplification and detection

processes associated with the Cepheid Xpert MRSA NxG Assay on the GeneXpert Instrument System.

V Substantial Equivalence Information:

A Predicate Device Name(s):
Cepheid Xpert GBS LB Control Panel

B Predicate 510(k) Number(s):
K182472

C Comparison with Predicate(s):

Table 1. Comparison with the Predicate

Device & Predicate Device(s):	**K191172**	**K182472**
Device Trade Name	Cepheid Xpert MRSA NxG Control Panel	Cepheid Xpert GBS LB Control Panel
General Device Characteristic Similarities		
Intended Use/ Indications for Use	External assayed positive and negative quality control to monitor the performance of *in vitro* laboratory nucleic acid testing procedures for the qualitative detection of Methicillin-Resistant *Staphylococcus aureus* (MRSA) performed with the Cepheid Xpert MRSA NxG Assay on the GeneXpert Instrument System. The controls comprise cultured and inactivated Methicillin-Resistant *Staphylococcus aureus* as the positive control and *Staphylococcus epidermidis* as the negative control. The Cepheid Xpert MRSA NxG Control Panel is not intended to replace manufacturer controls provided with the Cepheid Xpert MRSA NxG Assay.	External assayed positive and negative quality control materials to monitor the performance of *in vitro* laboratory nucleic acid testing procedures for the qualitative detection of Group B *Streptococcus* (GBS) performed with the Cepheid Xpert GBS LB Assay on the GeneXpert Instrument System. The controls comprise cultured and inactivated *Streptococcus agalactiae* as the positive control and *Lactobacillus acidophilus* as the negative control. The Cepheid Xpert GBS LB Control Panel is not intended to replace the manufacturer controls provided with the device.
Composition	Inactivated microorganisms	Same
Test System	Cepheid GeneXpert System	Same
Directions for Use	Process like a patient sample	Same

Assay Steps Monitored	Extraction, amplification, and detection	Same
Physical Format	Lyophilized swab	Lyophilized swab
General Device Characteristic Differences		
Analytes	• Positive Control: (MRSA) Methicillin-resistant *Staphylococcus aureus* • Negative Control: *Staphylococcus epidermidis*	• Positive Control: *Streptococcus agalactiae* • Negative Control: *Lactobacillus acidophilus*
Assay Compatibility	Cepheid Xpert MRSA NxG Assay (K162444)	Cepheid Xpert GBS LB Assay (K121539)

VI Standards/Guidance Documents Referenced:

CLSI. *Evaluation of Stability of In Vitro Diagnostic Reagents; Approved Guideline.* CLSI Document EP25-A. Wayne, PA: Clinical and Laboratory Standards Institute; 2009.

CLSI. *Evaluation of Precision of Quantitative Measurement Procedures: Approved Guideline – Third Edition.* CLSI Document EP05-A3. Wayne, PA: Clinical and Laboratory Standards Institute; 2014.

ANSI. *Sampling Procedures and Tables for Inspection by Attributes.* ANSI/ASQ Z1.4-2003; 2013.

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

A study was performed to determine the reproducibility of the Cepheid Xpert MRSA NxG Control Panel using the Cepheid Xpert MRSA NxG Assay on the GeneXpert Instrument System. Testing was done at three different locations over five days. At each location, two operators each tested three lots of control material for a total of at least 90 test results for each control swab (3 sites x 5 days x 2 operators x ≥3 replicates = ≥90 replicates in total). Summaries of the results for both the positive and negative controls are provided in **Table 2** and **Table 3**. On initial testing one positive control and three negative controls were reported as "ERROR" due to system failure. In each case, retesting was performed with new control swabs and all positive and negative controls produced the expected results.

Table 2. Summary of results from the Reproducibility Study (qualitative)

Positive Control (Methicillin-Resistant *Staphylococcus aureus*)					
Test location	**Total Tests Performed**	**ERROR[1]**	**Correct Result[2]**	**Incorrect Result**	**Percent Correct[3]**
1	33	1	32	0	100%
2	31	0	31	0	100%
3	30	0	30	0	100%
All sites	94	1	93	0	100%

Negative Control (*Staphylococcus epidermidis*)					
Test location	**Total Tests Performed**	**ERROR[1]**	**Correct Result[2]**	**Incorrect Result**	**Percent Correct[3]**
1	33	2	31	0	100%
2	32	1	31	0	100%
3	30	0	30	0	100%
All sites	95	3	92	0	100%

[1] Number of ERROR responses observed; in each case new controls were tested and the expected results were obtained.
[2]As indicated in the test protocol, both positive and negative controls were retested in the event of an ERROR response.
[3] Data from the test runs with the ERROR response were not included in the Percent Correct analysis.

Table 3. Summary of results from the Reproducibility Study (quantitative)

	Mean Ct (%CV)		
Test location	**Positive Control**		**Negative Control**
	mec	**SCC**	**SPC**
1	28.0 (3.5)	29.5 (3.3)	32.4 (3.1)
2	29.2 (3.8)	30.8 (3.7)	32.2 (2.0)
3	29.1 (4.9)	30.6 (4.6)	32.6 (3.2)
All sites	28.7 (4.5)	30.3 (4.3)	32.4 (2.8)

SPC: Sample processing control
Ct: Cycle Threshold; %CV: Percent Coefficient of Variation;

The reproducibility of the Cepheid Xpert MRSA NxG Control Panel within and between test locations, GeneXpert Instruments, operators, and lots was determined to be acceptable.

2. Linearity:
Not applicable.

3. Analytical Specificity/Interference:
Not applicable.

4. Assay Reportable Range:
Not applicable.

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

Traceability:
Not applicable.

Stability:
1. Shelf-life was established through an Accelerated Stability Study that was performed with three lots of the Cepheid Xpert MRSA NxG Control Panel placed at elevated temperatures (43˚C, 53˚C and 63˚C). Four replicates of the positive control were tested at each of the four time points (Day 0, Day 14, Day 28 and Day 42). The negative control was tested in duplicate at two time points (Day 0 and Day 42). At each time point, each replicate of both the positive and negative controls produced the expected results with the Cepheid Xpert

MRSA NxG Assay on the GeneXpert Instrument System. Together with regression analysis of Ct values, these results were used to support assignment of 9 month expiration dating from the date of manufacture when the Cepheid Xpert MRSA NxG Control Panel is held at 2°C - 25°C.

2. A Real-Time, Shelf-Life Stability Study is in process. Under a 14-point regression design, three lots of each control will be incubated at two temperatures (2-8°C and 25°C). Regression analysis will be performed at the end of the study to evaluate performance and determine if the acceptance criteria are met. At that time, the expiration date will be updated to the time point at which all criteria are met.

3. An In-Use Stability Study was done to determine how long the positive and negative controls would remain stable after reconstitution. Controls from a single lot were rehydrated and kept at room temperature for different time periods prior to testing. All results were as expected and indicate that Cepheid Xpert MRSA NxG Control Panel swabs may be used up to five hours following rehydration.

6. Detection Limit:
   Not applicable.

7. Assay Cut-Off:
   Not applicable.

B Comparison Studies:

1. Method Comparison with Predicate Device:
   Not applicable.

2. Matrix Comparison:
   Not applicable.

C Clinical Studies:

1. Clinical Sensitivity:
   Not applicable.

2. Clinical Specificity:
   Not applicable.

3. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):
   Not applicable.

D Clinical Cut-Off:
Not applicable.

E Expected Values/Reference Range:

The Cepheid Xpert MRSA NxG Control Panel is a qualitative control expected to produce the results described in **Table 4** when tested with the Cepheid Xpert MRSA NxG Assay using the GeneXpert Instrument System.

Table 4: Expected values

Control	Analyte	Expected Assay Result	Interpretation
Positive Control	Methicillin-Resistant *S. aureus* (MRSA)	MRSA DETECTED	MRSA DNA is detected. MRSA targets, *mec* (*mecA*/*mecC*) and SCC*mec*, have a cycle threshold (Ct) within the valid range.
Negative Control	Methicillin-Susceptible *S. epidermidis*	MRSA NOT DETECTED	MRSA DNA is detected. Target DNA for SCC*mec* and/or *mec* (*mecA/mecC*) is not detected.

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

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