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

## I Background Information:

### A 510(k) Number

K191168

### B Applicant

Microbiologics, Inc.

### C Proprietary and Established Names

Cepheid Xpert SA Nasal Complete 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 SA Nasal Complete Control Panel for use with the Cepheid Xpert SA Nasal Complete Assay on the GeneXpert Dx System.

### B Measurand:
Nucleic acid quality control material from inactivated Methicillin-Resistant *Staphylococcus aureus* (MRSA, positive control 1), *Staphylococcus aureus* (SA, positive control 2) and *Staphylococcus epidermidis* (negative control).

### C Type of Test:
The Cepheid Xpert SA Nasal Complete 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 *Staphylococcus aureus* (MRSA) and

*Staphylococcus aureus* (SA) performed with the Cepheid Xpert SA Nasal Complete Assay on the GeneXpert Dx System.

## III Intended Use/Indications for Use:

### A Intended Use(s):

See Indications for Use below.

### B Indication(s) for Use:

The Cepheid Xpert SA Nasal Complete 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* (MRSA) and *Staphylococcus aureus* (SA) performed with the Cepheid Xpert SA Nasal Complete Assay on the GeneXpert Dx System. The controls comprise cultured and inactivated Methicillin-Resistant *Staphylococcus aureus* as the positive control 1; *Staphylococcus aureus* as the positive control 2; *Staphylococcus epidermidis* as the negative control.

The Cepheid Xpert SA Nasal Complete Control Panel is not intended to replace manufacturer controls provided with the Cepheid Xpert SA Nasal Complete 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 SA Nasal Complete Assay.

### D Special Instrument Requirements:

The Cepheid Xpert SA Nasal Complete Control Panel is intended for use on the GeneXpert Dx System.

## IV Device/System Characteristics:

### A Device Description:

The Cepheid Xpert SA Nasal Complete Control Panel is used to monitor the DNA extraction, amplification and detection processes of the Cepheid Xpert SA Nasal Complete Assay. The Cepheid Xpert SA Nasal Complete Control Panel contains cultured microorganisms inactivated by heat treatments. Each Cepheid Xpert SA Nasal Complete Control Panel consists of 6 individually packaged Methicillin-Resistant *Staphylococcus aureus* (MRSA) positive control swabs (positive control 1); 6 individually wrapped methicillin-susceptible *Staphylococcus aureus* (MSSA) positive controls swabs (positive control 2); and 6 individually wrapped methicillin-susceptible *Staphylococcus epidermidis* (MSSE) negative control swabs. Each positive control 1 swab contains MRSA at a target level that is designed to provide reproducible performance above the limit of detection to produce positive results for each of the genes targeted by the Cepheid Xpert SA Nasal Complete Assay: Staphylococcal protein A gene *spa* (SPA), methicillin resistance gene *mecA* (mec), and the Staphylococcal cassette chromosome (SCC). Each positive control 2 swab contains MSSA at a target level designed to provide reproducible performance

above the limit of detection of the *spa* gene target of the Cepheid Xpert SA Nasal Complete Assay. The negative control swab contains MSSE which is not targeted/detected by the Cepheid Xpert SA Nasal Complete Assay. Each swab is individually wrapped with a desiccant in a heat-sealed foil pouch.

**B Principle of Operation:**
The Cepheid Xpert SA Nasal Complete Control Panel is intended for use as external assayed quality control material for use in monitoring the DNA extraction, amplification and detection processes associated with the Cepheid Xpert SA Nasal Complete Assay on the GeneXpert Dx 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):** | **K191168** | **K182472** |
|---|---|---|
| Device Trade Name | Cepheid Xpert SA Nasal Complete 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) and *Staphylococcus aureus* (SA) performed with the Cepheid Xpert SA Nasal Complete Assay on the GeneXpert Dx System. The controls comprise cultured and inactivated Methicillin-Resistant *Staphylococcus aureus* as the positive control 1; *Staphylococcus aureus* as the positive control 2; *Staphylococcus epidermidis* as the negative control.<br><br>The Cepheid Xpert SA Nasal | 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.<br><br>The Cepheid Xpert GBS LB |

| | | |
|---|---|---|
| | Complete Control Panel is not intended to replace manufacturer controls provided with the Cepheid Xpert SA Nasal Complete Assay. | 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 1: (MRSA) Methicillin-resistant *Staphylococcus aureus*<br>• Positive Control 2: (SA) *Staphylococcus aureus*<br>• Negative Control: *Staphylococcus epidermidis* | • Positive Control: *Streptococcus agalactiae*<br>• Negative Control: *Lactobacillus acidophilus* |
| Assay Compatibility | Cepheid Xpert SA Nasal Complete Assay (K100822) | 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 SA Nasal Complete Control Panel using the Cepheid Xpert SA Nasal Complete Assay on the GeneXpert Dx System. Testing was done at three different locations over five days. At each location, two operators each tested three different lots of control material for a total of at least 90 test results each for the positive control 1, positive control 2 and the negative control swabs (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 1 and two positive control 2 swabs produced "NO RESULT" because insufficient data were collected to determine the sample status. After re-

testing using new control swabs, all positive control swabs produced the expected positive results. Fourteen "INVALID" results due to failure of the Sample Processing Control, one "ERROR" due to system failure and one report of "NO RESULT" were observed with the negative control. After re-testing of new control swabs, all negative control swabs produced the expected negative results.

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

| **Positive Control 1 (Methicillin-Resistant *Staphylococcus aureus*)** | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Test location** | **Total Tests Performed** | **INVALID** | **NO RESULT[1]** | **ERROR** | **Correct Result** | **Incorrect Result** | **Percent Correct[2]** |
| 1 | 30 | 0 | 0 | 0 | 30 | 0 | 100% |
| 2 | 30 | 0 | 0 | 0 | 30 | 0 | 100% |
| 3 | 31 | 0 | 1 | 0 | 30 | 0 | 100% |
| All sites | 91 | 0 | 1 | 0 | 90 | 0 | 100% |
| **Positive Control 2 (Methicillin-Susceptible *Staphylococcus aureus*)** | | | | | | | |
| **Test location** | **Total Tests Performed** | **INVALID** | **NO RESULT[1]** | **ERROR** | **Correct Result** | **Incorrect Result** | **Percent Correct[2]** |
| 1 | 30 | 0 | 0 | 0 | 30 | 0 | 100% |
| 2 | 30 | 0 | 0 | 0 | 30 | 0 | 100% |
| 3 | 32 | 0 | 2 | 0 | 30 | 0 | 100% |
| All sites | 92 | 0 | 2 | 0 | 90 | 0 | 100% |
| **Negative Control (Methicillin-Susceptible *Staphylococcus epidermidis*)** | | | | | | | |
| **Test location** | **Total Tests Performed** | **INVALID[3]** | **NO RESULT[1]** | **ERROR[4]** | **Correct Result** | **Incorrect Result** | **Percent Correct[2]** |
| 1 | 38 | 8 | 0 | 0 | 30 | 0 | 100% |
| 2 | 33 | 2 | 0 | 1 | 30 | 0 | 100% |
| 3 | 35 | 4 | 1 | 0 | 30 | 0 | 100% |
| All sites | 106 | 14 | 1 | 1 | 90 | 0 | 100% |

[1]Number of NO RESULT responses observed; in each case new controls were tested, as indicated in the test protocol, and the expected results were obtained.
[2]Data from test runs that produced any type of error response were not included in the Percent Correct analysis.
[3]Number of INVALID responses observed; in each case new controls were tested, as indicated in the test protocol, and the expected results were obtained.
[4]Number of ERROR responses observed; a new control was tested, as indicated in the test protocol, and the expected results were obtained.

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

| | **Mean Ct (%CV)** | | | | |
|---|---|---|---|---|---|
| **Test location** | **Positive Control 1** | | | **Positive Control 2** | **Negative Control** |
| | **SPA** | **mec** | **SCC** | **SPA** | **SPC** |
| 1 | 27.0 (2.7) | 27.3 (2.6) | 28.5 (2.3) | 26.8 (2.7) | 32.0 (4.2) |
| 2 | 28.1 (2.3) | 28.4 (2.0) | 29.6 (1.9) | 27.8 (2.5) | 31.8 (3.5) |
| 3 | 27.8 (2.2) | 28.1 (2.1) | 29.3 (2.1) | 27.4 (2.8) | 32.1 (4.4) |
| All sites | 27.6 (3.0) | 27.9 (2.8) | 29.1 (2.7) | 27.3 (3.0) | 32.0 (4.0) |

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

The reproducibility of the Cepheid Xpert SA Nasal Complete 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 each Positive and Negative Control from the Cepheid Xpert SA Nasal Complete Control Panel. The two types of positive controls and the negative control were placed at elevated temperatures of 43˚C, 53˚C and 63˚C. The positive controls were tested in replicates of four at each of the four time points (Day 0, Day 14, Day 28 and Day 42). The negative controls were tested in duplicate at two time points (Day 0 and Day 42). The data provided no evidence of product degradation under the conditions tested. A shelf-life claim of 9 months at 2-25°C is acceptable. This shelf-life claim could be modified based on the results of the Real-Time Stability Study.

   2. A Real-Time Stability, Shelf-Life Study is in process. Under a 10-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 SA Nasal Complete 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 SA Nasal Complete Control Panel is a qualitative control expected to produce the results described in **Table 4** when tested with the Cepheid Xpert SA Nasal Complete assay using the GeneXpert Dx System.

**Table 4: Expected values**

| Control | Analyte | Expected Assay Result | Interpretation |
|---|---|---|---|
| Positive Control 1 | Methicillin-Resistant *S. aureus* (MRSA) | MRSA POSITIVE; SA POSITIVE | MRSA target DNA detected; SA target DNA detected. All MRSA targets (*spa*, *mecA* and SCC*mec*) have a Ct within the valid range and endpoint above the threshold setting. |
| Positive Control 2 | Methicillin-Susceptible *S. aureus* | MRSA NEGATIVE; SA POSITIVE | MRSA target DNA not detected; SA target DNA detected. SA target *(spa)* has a Ct within the valid range and endpoint above the threshold setting. Target DNA for SCC*mec* and/or *mecA* is not detected. |

| Control | Analyte | Expected Assay Result | Interpretation |
|---|---|---|---|
| Negative Control | Methicillin-Susceptible *S. epidermidis* | MRSA NEGATIVE; SA NEGATIVE | SA target DNA not detected. SA target (*spa*) DNA is not detected. Target DNA for *mecA* and/or SCC*mec* may or may not be 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.