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

I Background Information:

A 510(k) Number

K190463

B Applicant

Microbiologics, Inc.

C Proprietary and Established Names

Cepheid Xpert C. difficile/Epi 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 C. difficile/Epi Control Panel.

B Measurand:

Quality control panel comprised of inactivated microorganisms.

C Type of Test:

External assayed quality control material used to monitor the performance of the Cepheid Xpert C. difficile/Epi assay (K110203) for the detection of *Clostridium (Clostridioides) difficile* toxin B gene sequences and the presumptive identification of 027/NAP1/B1 strains of *C. difficile* in liquid or unformed stool specimens.

III Intended Use/Indications for Use:

A Intended Use(s):

The Cepheid Xpert C. difficile/Epi Control Panel is intended for use as external assayed positive and negative quality controls to monitor the performance of in vitro laboratory nucleic acid testing procedures for the qualitative detection of Clostridioides (Clostridium) difficile performed with the Cepheid Xpert C. difficile/Epi assay on the GeneXpert Dx System. The controls comprise cultured and inactivated Clostridioides (Clostridium) difficile 027-NAP1-B1 as the positive control and Clostridium sordellii as the negative control.

The Cepheid Xpert C. difficile/Epi Control Panel is not intended to replace manufacturer controls provided with the device.

B Indication(s) for Use:

Same as Intended Use

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

For in vitro diagnostic use.

The Cepheid Xpert C. difficile/Epi Control Panel is not intended to replace manufacturer controls provided with the device

D Special Instrument Requirements:

Cepheid GeneXpert Dx System

IV Device/System Characteristics:

A Device Description:

The Cepheid Xpert C. difficile/Epi Control Panel comprises lyophilized Positive and Negative Control swabs that are individually packaged in foil pouches containing dessicant. The Positive Control swabs are formulated with a heat-inactivated 027/NAP1/B1 strain of *Clostridium* (*Clostridioides*) *difficile* that carries each of the targets detected by the Cepheid Xpert C. difficile/Epi Assay (i.e., the toxin B [*tcdB*] and binary toxin genes and a single base deletion in the *tcdC* gene). The Negative Control Swab contains a heat-inactivated strain of *Clostridium sordellii* that lacks the toxin B, binary toxin and *tcdC* targets.

B Principle of Operation:

The Cepheid Xpert C. difficile/Epi Control Panel is intended for use as assayed quality control material to monitor the DNA extraction, amplification and detection processes associated with

the Cepheid Xpert C. difficile/Epi Assay (K110203) performed on the Cepheid GeneXpert 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):

Device & Predicate Device(s):	K190463	K182472
Device Trade Name	**Cepheid Xpert C. difficile/Epi Control Panel**	**Cepheid Xpert GBS LB Control Panel**
General Device Characteristic Similarities		
Intended Use/Indications For Use	The Cepheid Xpert C. difficile/Epi Control Panel is intended for use as external assayed positive and negative quality controls to monitor the performance of *in vitro* laboratory nucleic acid testing procedures for the qualitative detection of *Clostridioides (Clostridium) difficile* performed with the Cepheid Xpert C. difficile/Epi assay on the GeneXpert Dx System. The controls comprise cultured and inactivated *Clostridioides (Clostridium) difficile* 027-NAP1-B1 as the positive control and *Clostridium sordellii* as the negative control.	The Cepheid Xpert GBS LB Control Panel is intended for use as 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

Device & Predicate Device(s):	K190463	K182472
	The Cepheid Xpert C. difficile/Epi Control Panel is not intended to replace manufacturer controls provided with the device.	manufacturer controls provided with the device.
Control Format	Lyophilized swab	Same
Control Composition	Cultured and inactivated organisms	Same
General Device Characteristic Differences		
Positive Control	*Clostridioides (Clostridium) difficile* 027/NAP1/B1	*Streptococcus agalactiae*
Negative Control	*Clostridium sordellii*	*Lactobacillus acidophilus*
Measurand	*tcdB* gene Binary toxin gene *tcdC* deletion	3' untranslated region of the *cfb* gene
Assay Compatibility	Cepheid Xpert C. difficile/Epi Assay	Cepheid Xpert GBS LB Assay
Instrument System	GeneXpert Dx System	GeneXpert Instrument Systems GeneXpert Dx GeneXpert Infinity-48 GeneXpert Infinity-80

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.

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

The reproducibility of results obtained with the Cepheid Xpert C. difficile/Epi Control Panel was evaluated in a study performed at three sites over five days, with two operators per site. Each operator tested at least three Positive and three Negative Control Swabs on each day of the study according to the instructions for use (3 sites x 5 days x 2 operators x ≥3 replicates = ≥90 replicates per control in total). Three lots of Positive and Negative Controls were included in the study, the results of which are summarized in **Tables 1** and **2**. Repeat testing was performed for three controls (1 Positive; 2 Negative) that were associated with run failures due to instrument or reagent error. After repeat testing, all Positive and Negative Control swabs produced the expected results. The reproducibility of the Cepheid Xpert C. difficile/Epi Control Panel within and between sites/GeneXpert Dx Systems, operators and within and between lots was determined to be acceptable.

Table 1. Summary of qualitative Cepheid Xpert C. difficile/Epi Control Panel results from the Reproducibility Study

Site	Expected Result/Number Tested (%)	
	Positive Control	Negative
1	30/30 (100)	30/30 (100)
2	31/31 (100) [1, 2]	31/31 (100) [1, 2]
3	30/30 (100)	30/30 (100)
All Sites Combined	91/91 (100)	91/91 (100)

[1] One Positive and two Negative Controls at Site 2 were reported as "ERROR" due to instrument or reagent failure. The expected results were obtained upon retesting with new reagents and controls.
[2] One additional replicate of the Positive and Negative Controls was tested at Site 2

Table 2. Summary of cycle threshold and endpoint fluorescence values obtained in the Reproducibility Study with the Cepheid Xpert C. difficile/Epi Control Panel

Site	Mean (%CV)							
	tcdB		Binary Toxin		*tcdC*		Process Control [1]	
	Ct	EP	Ct	EP	Ct	EP	Ct	EP
1	29.5 (2.6)	250 (6.0)	29.0 (2.5)	645 (3.0)	28.8 (2.5)	392 (8.4)	32.7 (2.1)	375 (11.0)
2	29.7 (2.2)	255 (6.7)	29.2 (2.1)	649 (5.6)	29.1 (2.1)	387 (12.5)	32.3 (1.6)	430 (12.2)
3	29.3 (1.5)	246 (2.9)	28.7 (1.6)	651 (2.6)	28.6 (1.6)	397 (7.9)	32.5 (2.0)	400 (11.4)
All Sites	29.5 (2.2)	250 (5.6)	28.9 (2.2)	648 (4.0)	28.8 (2.2)	392 (9.8)	32.5 (2.0)	402 (12.8)

Ct: Cycle Threshold; %CV: Percent Coefficient of Variation; EP: relative endpoint fluorescence
[1] The values shown are only for testing performed with Negative Controls

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):

Reagent Stability
Reagent shelf-life was established in an Accelerated Stability Study that was performed with three lots of Cepheid Xpert C. difficile/Epi Control Panels that were placed at 43, 53 or 63°C for up to 42 days. All qualitative control results were as expected and there was no evidence of product degradation under the conditions tested. The results of this study were used to support a claimed shelf-life of 18 months at 2-25°C, which will be verified by conducting a Real-time Stability Study.

In Use Stability
The stability of Cepheid Xpert C. difficile/Epi Control Panel members after expression in Cepheid Xpert C. difficile/Epi Sample Reagent was evaluated by holding rehydrated controls at ambient temperature for different lengths of time prior to testing. The results of the study support use of the Cepheid Xpert C. difficile/Epi Control Panel within 5 hours of reconstitution in Sample Reagent when held at 20°C.

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 C. difficile/Epi Control Panel does not have assigned values and the panel members are reported as positive or negative for each of the target analytes, as appropriate. Performance was evaluated through testing at three sites using three different GeneXpert Dx Instruments and three lots of controls (refer to **Section VII A(1)**).

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.