510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:

K190223

B. Purpose for Submission:

To obtain a substantial equivalence determination for the Cepheid Xpert CT/NG Control Panel for use with the Cepheid Xpert CT/NG Assay on the GeneXpert Instrument System.

C. Measurand:

Nucleic acids from inactivated *Chlamydia trachomatis* and *Neisseria gonorrhoeae* (positive control) and from human epithelial cells (negative control).

D. Type of Test:

The Cepheid Xpert CT/NG Control Panel is an external assayed quality control material (positive and negative) designed to monitor the performance of *in vitro* laboratory nucleic acid testing procedures for the qualitative detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* in genitourinary specimens when used with the Cepheid Xpert CT/NG assay on the Cepheid Xpert Instrument System.

E. Applicant:

Microbiologics, Inc.

F. Proprietary and Established Names:

Trade Name: Cepheid Xpert CT/NG Control Panel

G. Regulatory Information:

1. Regulation section:

   21 CFR 866.3920, Assayed quality control material for clinical microbiology assays

2. Classification:

   Class II (Special Controls)

3. Product code:

PMN Assayed external control material for microbiology nucleic acid amplification assays

4. Panel:

(83) Microbiology

H. Intended Use:

1. Intended use:

The Cepheid Xpert CT/NG 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 *Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (NG) performed with the Cepheid Xpert CT/NG assay on the GeneXpert Instrument System. The controls consist of cultured and inactivated *Chlamydia trachomatis* and *Neisseria gonorrhoeae* as the positive control and human cells as the negative control.

The Cepheid Xpert CT/NG Control Panel is not intended to replace manufacturer controls provided with the device.

2. Indication(s) for use:

Same as Intended Use.

3. Special conditions for use statement(s):

For *in vitro* diagnostic use only.

For prescription use only.

3. Special instrument requirements:

Cepheid Xpert Instrument System

I. Device Description:

The Cepheid Xpert CT/NG Control Panel is a quality control material provided to the customer as six individually packaged positive and negative swabs. Each positive swab consists of inactivated *Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (NG) microorganisms. Each negative swab consists of human epithelial cells. The positive swabs were prepared with cultured, inactivated and quantified stocks of CT and NG. The negative swabs were prepared from human cells derived from a cultured cell line, certified for sterility, and quantified in cells/mL.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Cepheid Xpert GBS LB Control Panel

2. Predicate 510(k) number(s):

   K182472

3. Comparison with predicate:

	K190223	**K182472 (Predicate)**
Device Trade Name	**Cepheid Xpert CT/NG Control Panel**	**Cepheid Xpert GBS LB Control Panel**
Similarities		
Intended Use	The Cepheid Xpert CT/NG 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 *Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (NG) performed with the Cepheid Xpert CT/NG assay on the GeneXpert Instrument System. The controls consist of cultured and inactivated *Chlamydia trachomatis* and *Neisseria gonorrhoeae* as the positive control and human cells as the negative control. The Cepheid Xpert CT/NG Control Panel is not intended to replace manufacturer controls provided with the device.	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.
Physical Format	Swabs	Swabs
Composition	Inactivated microorganisms	Inactivated microorganisms
Test System	Cepheid GeneXpert System	Cepheid GeneXpert System
Directions for Use	Process like patient sample	Process like patient sample
Assay Steps Monitored	Extraction, amplification, and detection	Extraction, amplification, and detection
Number of Targets Monitored in One Assay	Multiple	Multiple

Differences		
Assay Compatibility	Cepheid Xpert CT/NG Assay	Cepheid Xpert GBS LB Assay
Positive Control	*Chlamydia trachomatis* *Neisseria gonorrhoeae*	*Streptococcus agalactiae*
Negative Control	Human epithelial cells	*Lactobacillus acidophilus*

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

Evaluation of Stability of In Vitro Diagnostic Reagents; Approved Guideline. CLSI Document EP25-A. Wayne, PA: Clinical and Laboratory Standards Institute; 2009.
Evaluation of Precision of Quantitative Measurement Methods: Approved Guideline. CLSI Document EP05-A3, 2014.

L. Test Principle:

Not applicable; this is control material to monitor performance of an *in vitro* diagnostic test. The test principle defaults to the Cepheid Xpert CT/NG assay, K121710.

M. Performance Characteristics:

1. Analytical performance:

a. Reproducibility:

The Cepheid Xpert CT/NG Control Panel was evaluated at three testing sites with two operators at each site (total of six operators). Three lots of the control material were tested with the Cepheid Xpert CT/NG assay on the Cepheid Xpert Instrument, over five days. Each positive and negative control was tested in three replicates on each day. There were seven ERROR results (assay aborted due to instrument or reagent problem) and one INVALID result (failure of the internal control/s). Those samples were retested using a new control swab according to the Instructions for Use. All testing utilized the Xpert Vaginal/Endocervical Swab Specimen Collection kit. The Cepheid Xpert CT/NG Assay detects one target for CT) and two different targets for NG (NG2 and NG4). Both NG targets need to be positive for the Xpert CT/NG Assay to return a positive NG result.

The qualitative results from the reproducibility study are summarized below.

Positive Control

Target	% Agreement with Expected Results, by Test Site			
	Site 1 [1,3]	Site 2[2,3]	Site 3	Overall
C. trachomatis	31/31 (100%)	31/31 (100%)	30/30 (100%)	92/92 (100%)
***N. gonorrhoeae* (NG2)**	31/31 (100%)	31/31 (100%)	30/30 (100%)	92/92 (100%)
***N. gonorrhoeae* (NG4)**	31/31 (100%)	31/31 (100%)	30/30 (100%)	92/92 (100%)
SPC	31/31 (100%)	31/31 (100%)	30/30 (100%)	92/92 (100%)

SPC: Sample Processing Control

[1]Three ERROR results were observed; in all cases a new control was retested and the expected results were obtained.

[2]Two ERROR results and one INVALID result were obtained; in all cases a new control was retested and the expected results were obtained.

[3] More than 30 measurements were taken as extra positive controls were ran during re-tests of negative controls.

Negative Control

Target	% Agreement with Expected Results, by Test Site			
	Site 1[1,2,3]*	Site 2[1,2,3]	Site 3	Overall
SAC	33/33 (100%)	34/34 (100%)	30/30 (100%)	97/97 (100%)
SPC	33/33 (100%)	34/34 (100%)	30/30 (100%)	97/97 (100%)

SAC: Sample Adequacy Control;

SPC: Sample Processing Control

[1]Two ERROR results were observed; in all cases a new control was retested and the expected results were obtained.

[2]One Negative Control at site 1 and two Negative Control at Site 2 generated a positive result for NG2 target, however, the qualitative results were negative in each case because the Xpert CT/NG Assay requires both NG2 and NG4 targets to be positive in order to return a positive result for NG. In accordance with the assay protocol, the work area was cleaned and the controls were retested.

[3]More than 30 measurements were taken as extra positive controls were ran during re-tests of negative controls.

The calculated average Ct score values and the associated standard deviation (SD) and percent coefficient of variation (% CV) across the three testing sites obtained in the reproducibility study are shown below.

Positive Control

Target	N	Mean (Ct)	SD	%CV
C. trachomatis	92	31.8	1.204	3.78
***N. gonorrhoeae* NG2**	92	32.1	1.290	4.02
***N. gonorrhoeae* NG4**	92	31.4	1.223	3.89
SPC	92	31.5	0.219	0.70

SPC: Sample Processing Control

Negative Control

Target	N	Mean (Ct)	SD	%CV
Human Epithelial Cells (SAC)	97	27.9	0.988	3.54
SPC	97	31.5	0.233	0.74

SAC: Sample Adequacy Control
SPC: Sample Processing Control

b. Linearity/assay reportable range:

Not applicable

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

Traceability:

Not applicable

Stability:

1. Shelf life stability of the Cepheid Xpert CT/NG Control Panel was initially evaluated through an accelerated study with three lots of the controls. The product was placed into chambers at elevated temperatures: 43˚C, 53˚C and 63˚C. Each lot was tested in 4 replicates at each of the following time points: Day 0, Day 14, Day 28, and Day 42. The stability of the product was evaluated by calculating the change (delta) in mean Ct value at each time point for the three microbial targets (CT, NG2 and NG4) from the mean Ct value obtained at Day 0. Both Positive and Negative Controls were tested.

   For Positive Control, the change in Ct score for all targets, across the three lots, ranged from 2.2% to 9.3% when stored at 43°C, from 1.6% to 9.7% when stored at 53°C, and from 2.9% to 14.4% when stored at 63°C. All valid tests generated expected (positive) results for all analytes.

   For Negative Control, the change in Ct score for the human epithelial cells target, across the three lots, ranged from 2.2% to 6.0% when stored at 43°C, from 3.7% to 6.8% when stored at 53°C, and from 3.3% to 12.8% when stored at 63°C. All valid tests generated expected (negative) results.

   The data from the accelerated stability study with three lots of the product is summarized below.

Positive Control

		43°C			53°C			63°C		
	Day	**Mean (Ct)**	**Delta (Ct)**	**% Change**	**Mean (Ct)**	**Delta (Ct)**	**% Change**	**Mean (Ct)**	**Delta (Ct)**	**% Change**
Lot 1										
CT	0	**30.6**			**30.6**			**30.6**		
	14	31.6	1.1	3.4	31.6	1.1	3.4	32.0	1.4	4.5
	28	31.8	1.2	4.0	31.1	0.5	1.6	32.2	1.6	5.3
	42	31.5	0.9	3.1	32.8	2.2	7.1	32.1	1.6	5.1
NG2	0	**30.4**			**30.4**			**30.4**		
	14	31.3	0.9	3.0	31.7	1.3	4.1	31.9	1.5	5.0
	28	31.8	1.4	4.4	31.3	0.9	2.9	31.8	1.4	4.7
	42	31.4	1.0	3.2	32.4	2.0	6.5	31.7	1.3	4.2
NG4	0	**30.0**			**30.0**			**30.0**		
	14	30.9	0.9	2.9	31.2	1.2	4.0	31.7	1.7	5.6
	28	31.4	1.4	4.7	30.9	0.9	2.9	31.2	1.3	4.2
	42	30.8	0.8	2.8	31.8	1.8	5.9	31.5	1.5	5.0
Lot 2										
CT	0	**31.2**			**31.2**			**31.2**		
	14	32.1	0.9	3.0	33.5	2.4	7.5	33.3	2.1	6.7
	28	33.5	2.4	7.5	32.2	1.0	3.2	33.5	2.3	7.5
	42	33.1	1.9	6.0	33.3	2.1	6.8	34.5	3.3	10.7
NG2	0	**31.1**			**31.1**			**31.08**		
	14	32.4	1.3	4.3	33.7	2.6	8.3	33.05	2.0	6.4
	28	34.0	2.9	9.3	32.8	1.7	5.4	34.08	3.0	9.7
	42	33.1	2.0	6.5	34.1	3.0	9.7	35.23	4.2	13.4
NG4	0	**30.8**			**30.8**			**30.8**		
	14	31.9	1.1	3.6	33.3	2.5	8.0	32.5	1.7	5.5
	28	33.1	2.3	7.5	32.8	2.0	6.3	33.4	2.6	8.3
	42	32.3	1.5	4.8	33.4	2.6	8.4	35.2	4.4	14.4
Lot 3										
CT	0	**31.1**			**31.1**			**31.1**		
	14	31.9	0.8	2.7	32.3	1.2	3.9	32.0	0.9	3.0
	28	32.0	0.9	3.0	32.5	1.4	4.4	32.7	1.7	5.3
	42	32.5	1.4	4.5	32.1	1.0	3.2	33.3	2.2	7.0
NG2	0	**31.2**			**31.2**			**31.2**		
	14	31.9	0.7	2.2	32.4	1.2	3.9	32.3	1.1	3.5
	28	32.5	1.3	4.2	32.7	1.5	4.6	32.8	1.6	5.0
	42	32.3	1.1	3.5	32.5	1.3	4.0	33.4	2.2	7.1
NG4	0	**30.7**			**30.7**			**30.7**		
	14	31.7	1.0	3.3	32.0	1.3	4.2	31.6	0.9	2.9

	28	31.8	1.2	3.7	32.5	1.9	6.0	32.5	1.9	6.0
	42	31.9	1.2	4.0	31.8	1.1	3.7	32.5	1.8	5.8

Negative Control (SAC)

		43°C			53°C			63°C		
	Day	**Mean (Ct)**	**Delta (Ct)**	**% Change**	**Mean (Ct)**	**Delta (Ct)**	**% Change**	**Mean (Ct)**	**Delta (Ct)**	**% Change**
Lot 1	0	**27.2**			**27.2**			**27.2**		
	14	28.4	1.2	4.5	28.2	1.0	3.7	29.1	1.9	6.9
	28	28.7	1.6	5.7	28.5	1.3	4.7	29.6	2.4	8.9
	42	28.8	1.6	6.0	28.2	1.1	3.9	30.1	2.9	10.8
Lot 2	0	**26.6**			**26.6**			**26.6**		
	14	27.2	0.6	2.2	27.9	1.3	4.9	28.4	1.8	6.8
	28	27.5	0.9	3.2	28.2	1.6	5.8	28.9	2.2	8.4
	42	27.5	0.9	3.2	28.4	1.8	6.8	30.0	3.4	12.8
Lot 3	0	**26.6**			**26.6**			**26.6**		
	14	27.5	0.9	3.3	28.2	1.6	5.8	27.5	0.9	3.3
	28	27.2	0.6	2.2	28.1	1.5	5.5	28.8	2.2	8.1
	42	27.5	0.9	3.4	27.9	1.3	4.8	28.7	2.0	7.6

2. Real time shelf stability data was submitted for 5 months of storage at 2-8°C and at 25°C. One lot of the product was tested in 4 replicates prior to placing the product in the controlled temperature chambers (T=0). After 5 months (T=1), Positive and Negative Controls were tested with the Cepheid Xpert CT/NG Assay. The stability was assessed by calculating the mean Ct of the 4 replicates at each time point. The difference (**Δ**) of the average Ct means between the two time points, across all the measured targets (i.e., CT, NG2, NG4 and SAC), ranged from 0 to 0.7, indicating no loss of DNA after 5 months of storage at 2-8°C and at 25°C. The summary of the data collected after 5 months of storage is shown below.

Real Time Stability after 5 months of Storage

		2-8°C		25°C	
Target	**Mean T=0**	**Mean T=1**	**Δ Ct**	**Mean T-1**	**Δ Ct**
CT	30.6	30.8	0.2	30.7	0.1
NG2	30.4	34.4	0.0	30.5	0.1
NG4	30.0	30.4	0.4	30.7	0.7
SAC (Negative Control)	27.2	27.5	0.3	27.6	0.4

3. An in-use stability of the hydrated Control swabs (i.e., placed in the Transport Reagent Tube from the Xpert Vaginal/Endocervical Specimen Collection kit) was evaluated at room temperature (21°C) over the period of 6 hours. The controls

were tested in three replicates immediately after hydration (t=0), and then again at 4 hours, and at 6 hours. All samples produced expected results after 4 and 6 hours, with minimal variation. The summary of the data collected over 6 hours is shown below.

In-Use Stability Study Using Swab Specimen Collection Kit

	Target	N	Mean (Ct)	SD	%CV
Positive Control	***C. trachomatis***	9	30.9	0.357	1.16
	***N. gonorrhoeae* NG2**	9	30.4	0.186	0.61
	***N. gonorrhoeae* NG4**	9	30.1	0.331	1.10
Negative Control	**Human Epithelial Cells**	9	27.2	0.194	0.72

4. A similar study was performed with control swabs hydrated in the Transport Reagent Tube from the Xpert Urine Specimen Collection Kit. Due to the low fluid volume in the Transport Reagent Tube from the Xpert Urine Specimen Collection Kit, it is necessary for the user to add 1.5 mL of nuclease-free water to properly hydrate the swab. This is part of the Cepheid Xpert CT/NG Control Panel instructions for use.

In-Use Stability Study Using Urine Specimen Collection Kit

	Target	N	Mean (Ct)	SD	%CV
Positive Control	***C. trachomatis***	9	32.9	0.537	1.63
	***N. gonorrhoeae* NG2**	9	32.3	0.464	1.44
	***N. gonorrhoeae* NG4**	9	32.1	0.675	2.10
Negative Control	**Human Epithelial Cells**	9	28.3	0.450	1.59

5. Shipping Stability

   The Cepheid CT/NG Controls are packaged in sealed foil pouches with desiccants to prevent effects of high humidity. However, the product may be exposed and affected by high temperatures. The product is shipped by FedEx for delivery in two days, however, delays may be encountered. The effect of exposure to high temperatures was evaluated at 43°C after 14 days (the worst-case delay scenario) in the accelerated stability study described above. The observed change in Ct values (a measure of product deterioration) was less than 5%, ranging from 2.2% to 4.3% for the positive control (for all the microbial targets), and from 2.2% to 4.5% for the negative control (human cells target), across three lots of the product.

Expected Values:

The Cepheid CT/NG Control Panel consists of qualitative positive and negative controls. The following are the expected assay results.

Control	Expected Assay Result	Interpretation
Positive Control	CT Detected NG Detected	CT target and NG target DNA sequences are detected.
Negative Control	CT Not Detected NG Not Detected	Neither CT nor NG target DNA sequences are detected.

d. Detection limit:

Not applicable.

e. Analytical Specificity:

Not applicable.

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

Not applicable.

b. *Matrix comparison:*

Not applicable.

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable.

b. Clinical specificity:

Not applicable.

c. Other clinical supportive data (when a. and b. are not applicable):

Not applicable.

4. Clinical cut-off**:**

   Not applicable.

N. Proposed Labeling:

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

O. Conclusion:

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