510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:

K190086

B. Purpose for Submission:

To obtain a substantial equivalence determination for the Cepheid Xpert Respiratory Control Panel for use with the Cepheid Xpert Xpress Flu/RSV Assay on the GeneXpert Instrument System.

C. Measurand:

Nucleic acids from inactivated Influenza A (H1N1) virus, Influenza A (H3N2) virus, Influenza B virus, and Respiratory Syncytial Virus A.

D. Type of Test:

The Cepheid Xpert Respiratory 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 Influenza A (H1N1) virus, Influenza A (H3N2) virus, Influenza B virus, and Respiratory Syncytial Virus A when used with the Cepheid Xpert Xpress Flu/RSV assay on the Cepheid Xpert Instrument System.

E. Applicant:

Microbiologics, Inc.

F. Proprietary and Established Names:

Trade Name: Cepheid Xpert Respiratory 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 Respiratory 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 Influenza A (H1N1) virus, Influenza A (H3N2) virus, Influenza B virus and Respiratory Syncytial Virus A performed with the Cepheid Xpert Xpress Flu/RSV assay on the GeneXpert Instrument System. The controls comprise cultured and inactivated Influenza A (H1N1) virus, Influenza A (H3N2) virus, Influenza B virus and Respiratory Syncytial Virus A as the positive control and Coxsackie virus B1 as the negative control.

The Cepheid Xpert Respiratory 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:

The Cepheid Xpert Respiratory Control Panel is intended for use on the Gene Xpert Instrument System.

I. Device Description:

The Cepheid Xpert Respiratory Control Panel is a quality control material provided to the customer as six individually packaged positive control swabs. Each positive control swab contains cultured and inactivated Influenza A (H1N1) virus, Influenza A (H3N2) virus, Influenza B virus and Respiratory syncytial virus A. The kit also includes six individually packaged negative controls swabs of cultured and inactivated Coxsackie virus B1.

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:

Characteristic	Cepheid Xpert Respiratory Control Panel	Cepheid Xpert GBS LB Control Panel (K182472)
Intended Use	The Cepheid Xpert Respiratory 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 Influenza A (H1N1) virus, Influenza A (H3N2) virus, Influenza B virus and Respiratory Syncytial Virus A performed with the Cepheid Xpert Xpress Flu/RSV assay on the GeneXpert Instrument System. The controls comprise cultured and inactivated Influenza A (H1N1) virus, Influenza A (H3N2) virus, Influenza B virus and Respiratory Syncytial Virus A as the positive control and Coxsackie virus B1 as the negative control The Cepheid Xpert Respiratory 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, detection

Differences		
Assay Compatibility	Cepheid Xpert Xpress Flu/RSV Assay	Cepheid Xpert GBS LB Assay
Positive Control Analytes	Influenza A (H1N1) virus, Influenza A (H3N2) virus, Influenza B virus and Respiratory Syncytial Virus A	*Streptococcus agalactiae*
Negative Control	Coxsackie virus B1	*Lactobacillus acidophilus*

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

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

L. Test Principle:

Not applicable; this is control material to monitor performance of an *in vitro* diagnostic test.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Reproducibility:

The reproducibility of results obtained with the Cepheid Xpert Respiratory Control Panel was evaluated in a study performed at three testing sites over five days, with two operators per site. Three lots of the control material were tested with the Cepheid Xpert Xpress Flu/RSV Assay on three Cepheid GeneXpert Systems.

The qualitative results from the reproducibility study are summarized below.

Analyte	Agreement (%) with Expected Results by Test Site			
	Site 1	Site 2	Site 3[1]	Overall
Influenza A (H1N1)	30/30 (100%)	30/30 (100%)	30/30 (100%)	90/90 (100%)
Influenza A (H3N2)	30/30 (100%)	30/30 (100%)	30/30 (100%)	90/90 (100%)
Influenza B	30/30 (100%)	30/30 (100%)	30/30 (100%)	90/90 (100%)
Respiratory Syncytial Virus A	30/30 (100%)	30/30 (100%)	30/30 (100%)	30/30 (100%)

1 One No RESULT was observed; a new control was retested and the expected results were obtained.

Analyte	Agreement (%) with Expected Results by Test Site			
	Site 1	Site 2	Site 3	Overall
Coxsackie virus B1	30/30 (100%)	30/30 (100%)	31/31 (100%)	91/91 (100%)

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

	Influenza A (H1N1)	Influenza A (H3N2)	Influenza B	Respiratory Syncytial Virus A	SPC
N	90	90	90	90	90
Mean	29.9	32.1	32.1	30.1	29.6
%CV	2.8	2.4	4.2	2.7	1.7

SPC: Sample Processing Control

	Coxsackie virus B1	SPC
N	91	91
Mean	0	29.5
%CV	N/A	1.7

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. Accelerated stability study

Shelf life stability 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 four microbial targets (Flu A1, Flu A2, Flu B and RSV) 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 -0.8 to 1.8 when stored at 43°C, from -0.4 to 2.4 when stored at 53°C, and from -0.8 to 3.1 when stored at 63°C. All valid tests generated expected (positive) results for all analytes.
For Negative Control all valid tests generated expected (negative) results.

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

Flu A1		Lot 1			Lot 2[1]			Lot 3		
		43°C	53°C	63°C	43°C	53°C	63°C	43°C	53°C	63°C
	Day	Ct score	Ct score	Ct score	Ct score	Ct score	Ct score	Ct score	Ct score	Ct score
Mean	0	30.1	30.1	30.1	29.8	29.8	29.8	29.6	29.6	29.6
Mean Change in Ct score	14	0.1	0.5	-0.1	0.4	1.8	1.1	1.1	1.2	1.2
	28	0.3	0.1	0.3	1.6	2.2	2.0	1.2	1.8	2.0
	42	0.5	0.7	1.4	1.8	2.2	2.9	1.3	1.6	1.6

1 Lot #2 was used in the study despite that it failed QC release criteria

Flu A2		Lot 1			Lot 2[1]			Lot 3		
		43°C	53°C	63°C	43°C	53°C	63°C	43°C	53°C	63°C
	Day	Ct score	Ct score	Ct score	Ct score	Ct score	Ct score	Ct score	Ct score	Ct score
Mean	0	32.2	32.2	32.2	32.2	32.2	32.2	32.0	32.0	32.0
Mean Change in Ct score	14	0.1	0.8	0.0	0.3	1.6	1.0	0.9	1.2	1.3
	28	0.2	0.3	0.7	1.5	2.2	2.1	1.4	1.8	1.8
	42	0.7	1.0	1.5	1.8	2.3	2.6	1.4	1.5	1.6

1 Lot #2 was used in the study despite that it failed QC release criteria

Flu B		Lot 1			Lot 2[1]			Lot 3		
		43°C	53°C	63°C	43°C	53°C	63°C	43°C	53°C	63°C
	Day	Ct score	Ct score	Ct score	Ct score	Ct score	Ct score	Ct score	Ct score	Ct score
Mean	0	32.5	32.5	32.5	33.3	33.3	33.3	31.8	31.8	31.8
Mean Change in Ct score	14	0.0	0.1	-0.2	-0.1	1.7	0.6	1.3	1.2	1.2
	28	0.2	0.1	0.3	2.0	2.0	1.8	1.3	1.9	2.0
	42	0.7	0.4	1.6	1.5	2.4	3.1	1.7	1.6	2.2

1 Lot #2 was used in the study despite that it failed QC release criteria

RSV		Lot 1			Lot 2[1]			Lot 3		
		43°C	53°C	63°C	43°C	53°C	63°C	43°C	53°C	63°C
	Day	Ct score	Ct score	Ct score	Ct score	Ct score	Ct score	Ct score	Ct score	Ct score
Mean	0	29.7	29.7	29.7	29.9	29.9	29.9	30.0	30.0	30.0
Mean Change in Ct score	14	0.0	-0.4	-0.8	-0.8	1.1	-0.8	-0.1	0.3	0.5
	28	0.3	0.8	0.3	0.8	0.6	1.0	-0.1	1.0	0.7
	42	0.8	0.7	1.9	0.8	1.5	1.3	1.6	-0.2	0.2

1 Lot #2 was used in the study despite that it failed QC release criteria

2. *Real-time stability study*

Real-time shelf life stability study with three lots of the controls is in progress. Data for 2 and 3 months of storage at 4˚C and 25˚C ware submitted. The product was placed into chambers at two temperatures: 4˚C and 25˚C. Each lot was tested in 4 replicates at each of the following time points: Day 0, 2 months, and 3 months. The stability of the product was

evaluated by calculating the change (delta) in mean Ct value at each time point for the four microbial targets (Flu A1, Flu A2, Flu B and RSV) 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 -0.3 to 2.3 when stored at 4°C, and from 0.4 to 1.5 when stored at 25°C. All valid tests generated expected (positive) results for all analytes.

For Negative Control all valid tests generated expected (negative) results.

The data from the real time stability study with three lots of the product are summarized below.

Flu A1		**Lot 1**		**Lot 2**		**Lot 3**	
		4°C	25°C	4°C	25°C	4°C	25°C
	Month	Ct score	Ct score	Ct score	Ct score	Ct score	Ct score
Mean	0	27.9	27.9	29.8	29.8	29.3	29.3
Mean Change in Ct score	2	-0.3	0.7	0.1	0.7	1.9	1.4
	3	1.2	0.6	0.5	1.0	1.2	0.5

Flu A2		**Lot 1**		**Lot 2**		**Lot 3**	
		4°C	25°C	4°C	25°C	4°C	25°C
	Month	Ct score	Ct score	Ct score	Ct score	Ct score	Ct score
Mean	0	30.2	30.2	32.2	32.2	31.8	31.8
Mean Change in Ct score	2	-0.2	0.8	0.1	0.8	1.7	1.5
	3	1.3	0.6	0.4	0.8	1.3	0.5

Flu B		**Lot 1**		**Lot 2**		**Lot 3**	
		4°C	25°C	4°C	25°C	4°C	25°C
	Month	Ct score	Ct score	Ct score	Ct score	Ct score	Ct score
Mean	0	30.7	30.7	30.1	30.1	29.6	29.6
Mean Change in Ct score	2	0.0	1.2	0.1	0.8	0.4	1.5
	3	1.5	0.8	0.5	0.9	1.2	0.5

RSV		**Lot 1**		**Lot 2**		**Lot 3**	
		4°C	25°C	4°C	25°C	4°C	25°C
	Month	Ct score	Ct score	Ct score	Ct score	Ct score	Ct score
Mean	0	30.6	30.6	28.2	28.2	27.8	27.8
Mean Change in Ct score	2	0.2	0.5	0.4	0.6	2.3	1.3
	3	0.7	0.8	0.3	1.1	0.6	0.4

3. In use stability study

An in-use stability of the hydrated control swabs (i.e., placed in the Transport Reagent Tube from the Cepheid Xpert Xpress Flu/RSV Assay Kit) was evaluated at room temperature (20°C) over 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 positive and negative samples produced expected results after 4 and 6 hours. The summary of the data collected over 6 hours is shown below.

Target	Mean Ct	SD	%CV
Flu A1	30.1	0.4	1.4
Flu A2	32.2	0.3	1.0
Flu B	32.9	0.2	0.5
RSV	29.7	0.5	1.7

4. Shipping stability

The Cepheid Xpert Respiratory 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 2 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 score for all targets, across the three lots, ranged from -0.8 to 1.8. For Negative Control all valid tests generated expected (negative) results upon the storage at 43°C for 14 days.

Human Factors/Operator Errors

The Cepheid Xpert Respiratory Control Panel tested with the Cepheid Xpert Xpress Flu/RSV assay may be used in CLIA waived settings, therefore the controls were evaluated to determine the risk of erroneous results due to incorrect volume of the sample added to the cartridge and deviations from the recommended sample mixing conditions. Both Positive and Negative Controls were tested. All valid tests generated expected results.

Expected Values:

The Cepheid Xpert Respiratory Control Panel is a qualitative positive and negative controls. The following are the expected assay results.

Control	Expected Assay Result	Interpretation
Positive Control	Flu A Positive Flu B Positive RSV Positive	Flu A, Flu B, and RSV target RNA sequences are detected
Negative Control	Flu A Negative Flu B Negative RSV Negative	Neither Flu A, Flu B, nor RSV target RNA 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.

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.