510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:

K120563

B. Purpose for Submission:

To obtain 510(k) SE Determination for the KeyPath MRSA/SA Blood Culture Test – BT for use with BACTEC Standard/10 Aerobic/F (SA) and BACTEC Standard Anaerobic/F blood culture bottles (SN). This expands the intended use of this device beyond that of the previously cleared device (K102342).

C. Measurand:

Bacteriophage amplification to identify the presence of *S. aureus* and assess the phenotypic response of the target organism to cefoxitin, an indicator of oxacillin (a methicillin analog) resistance.

D. Type of Test:

Qualitative lateral flow identification and antimicrobial susceptibility test using bacteriophage amplification growth based detection.

E. Applicant:

MicroPhage, Inc.

F. Proprietary and Established Names:

KeyPath MRSA/MSSA Blood Culture Test - BT

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
OUS	I	866.2050 Staphylococcal typing bacteriophage	Microbiology (83)

H. Intended Use:

1. Intended use(s):
   The KeyPath™ MRSA/MSSA Blood Culture Test – BT is a qualitative *in vitro* diagnostic test for the timely identification of *Staphylococcus aureus (S. aureus*) and determination of methicillin susceptibility (MSSA) or methicillin resistance (MRSA) directly from positive blood cultures.

   The Test uses bacteriophage amplification to identify the presence of *S. aureus* and assess the phenotypic response of the target organism to cefoxitin, an indicator of oxacillin (a methicillin analog) resistance.

   The assay is performed directly on positive blood culture specimens that are determined as Gram Positive Cocci in singles (GPC) or as Gram Positive Cocci in Clusters (GPCC) by Gram stain.

   The KeyPath™ MRSA/MSSA Blood Culture Test – BT is performed directly on positive blood culture specimens from BD BACTEC™ blood culture bottles (Plus Aerobic/F, Plus Anaerobic/F, Standard/10 Aerobic/F and Standard Anaerobic/F).

   The Test is indicated for use in conjunction with other laboratory and clinical data available to the physician as an aid in the detection of MRSA/MSSA from positive blood cultures.

   Subculturing of positive blood cultures is necessary for additional susceptibility test determinations, differentiation of mixed growth and for epidemiological typing.

2. Indication(s) for use:
   The KeyPath™ MRSA/MSSA Blood Culture Test – BT is a qualitative *in vitro* diagnostic test for the timely identification of *Staphylococcus aureus (S. aureus*) and determination of methicillin susceptibility (MSSA) or methicillin resistance (MRSA) directly from positive blood cultures.

   The Test uses bacteriophage amplification to identify the presence of *S. aureus* and assess the phenotypic response of the target organism to cefoxitin, an indicator of oxacillin (a methicillin analog) resistance.

   The assay is performed directly on positive blood culture specimens that are determined as Gram Positive Cocci in singles (GPC) or as Gram Positive Cocci in Clusters (GPCC) by Gram stain.

   The KeyPath™ MRSA/MSSA Blood Culture Test – BT is performed directly on positive blood culture specimens from BD BACTEC™ blood culture bottles (Plus Aerobic/F, Plus Anaerobic/F, Standard/10 Aerobic/F and Standard Anaerobic/F).

   The Test is indicated for use in conjunction with other laboratory and clinical data available to the physician as an aid in the detection of MRSA/MSSA from positive blood cultures.

Subculturing of positive blood cultures is necessary for additional susceptibility test determinations, differentiation of mixed growth and for epidemiological typing.

3. Special conditions for use statement(s):

   For prescription use.

4. Special instrument requirements:

   Manual readings only.

I. Device Description:

The KeyPath™ MRSA/MSSA Blood Culture Test – BT uses lytic bacteriophage, specific for *Staphylococcus aureus,* as an amplification technology for detection of *S. aureus* and determination of methicillin resistance or susceptibility in positive blood cultures. To detect *S. aureus* the blood culture sample is inoculated into a reaction tube (ID). The bacteriophage infect the *S. aureus* (if present), replicate within the host (culminating in bacterial lysis) and over the incubation period, produce several cycles of bacteriophage amplification. In a separate Reaction Tube (RS), the KeyPath™ Test uses cefoxitin (methicillin analogue) which inhibits bacteriophage amplification for susceptible organisms (MSSA) and fails to inhibit bacteriophage amplification when the organism is resistant to methicillin (MRSA). The KeyPath™ Test then uses a self-performing immunoassay (Detector) to detect the increase in concentration of bacteriophage using antibodies specific to the KeyPath™ Test bacteriophage, and calibrated such that at a known concentration, it will produce a visible signal.

To determine antibiotic susceptibility and/or resistance of the bacteria, the KeyPath™ Test uses a second sampling device and a second lane within the Detector, in parallel with the first. The only significant difference between the two sampling devices is the presence of the beta-lactam antibiotic, cefoxitin, used here to distinguish between methicillin-sensitive and methicillin-resistant *S. aureus* (MSSA and MRSA) similar to a breakpoint antimicrobial susceptibility test. Because bacteriophage amplification relies on a viable host, susceptible organisms do not support bacteriophage amplification, and no line on the Detector will be produced. Conversely, if the organism is resistant, bacteriophage amplification will occur and a visible line on the Detector will be produced. Although this test runs in parallel with the identification test, the results are interpreted serially, as the antibiotic test result is only applicable to *S. aureus*. This measure of antimicrobial susceptibility or resistance is referred to as *phenotypic*, like antimicrobial disks, as opposed to *genotypic*, which refers to the detection of a molecular marker.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   KeyPath™ MRSA/MSSA Blood Culture Test – BT

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

   K102342

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
	KeyPath™ MRSA/MSSA Blood Culture Test – BT	**KeyPath™ MRSA/MSSA Blood Culture Test – BT (k102342)**
Intended Use	The KeyPath™ MRSA/MSSA Blood Culture Test – BT is a qualitative *in vitro* diagnostic test for the timely identification of *Staphylococcus aureus (S. aureus*) and determination of methicillin susceptibility (MSSA) or methicillin resistance (MRSA) directly from positive blood cultures. The Test uses bacteriophage amplification to identify the presence of *S. aureus* and assess the phenotypic response of the target organism to cefoxitin, an indicator of oxacillin (a methicillin analog) resistance. The assay is performed directly on positive blood culture specimens that are determined as gram positive cocci in singles (GPC) or as	The KeyPath™ MRSA/MSSA Blood Culture Test – BT is a qualitative *in vitro* diagnostic test for the timely identification of *Staphylococcus aureus (S. aureus*) and determination of methicillin susceptibility (MSSA) or methicillin resistance (MRSA) directly from positive blood cultures. The Test uses bacteriophage amplification to identify the presence of *S. aureus* and assess the phenotypic response of the target organism to cefoxitin, an indicator of oxacillin (a methicillin analog) resistance. The assay is performed directly on positive blood culture specimens that are determined as gram

Similarities		
Item	Device	Predicate
	KeyPath™ MRSA/MSSA Blood Culture Test – BT	**KeyPath™ MRSA/MSSA Blood Culture Test – BT (k102342)**
	gram positive cocci in clusters (GPCC) by Gram stain. The Test is indicated for use in conjunction with other laboratory and clinical data available to the physician as an aid in the detection of MRSA/MSSA from positive blood cultures. Subculturing of positive blood cultures is necessary for additional susceptibility test determinations, differentiation of mixed growth and for epidemiological typing	positive cocci in singles (GPC) or as gram positive cocci in clusters (GPCC) by Gram stain. The Test is indicated for use in conjunction with other laboratory and clinical data available to the physician as an aid in the detection of MRSA/MSSA from positive blood cultures. Subculturing of positive blood cultures is necessary for additional susceptibility test determinations, differentiation of mixed growth and for epidemiological typing.
Single Use	Yes	Yes
Indication for Use	Professional Use	Professional Use
Interpretation of results	Visual	Visual
Patient population	Clinical patients	Clinical patients
Specimen type	Positive blood culture	Positive blood culture
Assay controls	Pos Control 1: MRSA Pos Control 2: MSSA Neg Control: NSA Internal positive procedural controls	Pos Control 1: MRSA Pos Control 2: MSSA Neg Control: NSA Internal positive procedural controls

Differences		
Item	**KeyPath™ MRSA/MSSA Blood Culture Test – BT**	**KeyPath™ MRSA/MSSA Blood Culture Test – BT (k102342)**
Intended Use	The KeyPath™ MRSA/MSSA Blood Culture Test – BT is performed directly on positive blood culture specimens from BD BACTEC™ blood culture bottles (Plus Aerobic/F, Plus Anaerobic/F, Standard /10 Aerobic/F and Standard Anaerobic/F).	The KeyPath™ MRSA/MSSA Blood Culture Test – BT is performed directly on positive blood culture specimens from BD BACTEC™ blood culture bottles (Plus Aerobic/F, Plus Anaerobic/F).

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

CLSI M100-S21 Performance Standards for Antimicrobial Susceptibility Testing: Twenty-First Informational Supplement

L. Test Principle:

The KeyPath™ MRSA/MSSA Blood Culture Test – BT (KeyPath™ Test) is a bacteriophage amplification-enabled immunoassay to identify *Staphylococcus aureus* and determine its resistance or susceptibility to cefoxitin from positive blood cultures, which have been determined to have gram positive cocci in singles (GPC) or gram positive cocci in clusters (GPCC) by Gram stain. This method utilizes the specificity of bacteriophage/bacteria interactions and their natural amplification processes to produce a surrogate signal. In the presence of *S. aureus,* bacteriophage will replicate, increasing to a detectable concentration. In the absence of *S. aureus* or the presence of bacteria other than *S. aureus,* the KeyPath™ Test bacteriophage do not replicate and remain undetectable. In addition, susceptible strains of *S. aureus* do not grow in the presence of cefoxitin and therefore do not support bacteriophage amplification, while resistant strains will grow and support bacteriophage amplification.

To perform the KeyPath™ Test, a sample of the positive blood culture is added to each

of the two provided reaction tubes, each comprised of KeyPath™ Test bacteriophage and proprietary reagents that enhance the growth of *S. aureus* and suppress other organisms. One Reaction Tube (Blue) is used for *S. aureus* identification. The second Reaction Tube (Red) is used for resistance/susceptibility testing. Following incubation, a small amount of the sample from each Tube is pipetted onto corresponding sample wells on the Detector. If the specimen contains *S. aureus* a pink-to-dark red/ purple Test Line (T) will appear in the Blue ID Read Window of the Detector.

If the sample is positive for *S. aureus,* Resistance/Susceptibility is then determined by reading the Red RS Read Window. Resistance (MRSA) is determined by the development of a visible pink-to-dark red/purple line at the Test Line (T) in the Red RS Read Window, while Susceptibility (MSSA) is determined by the absence of a visible colored line at the Test Line (T) in the Red RS Read Window.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Not applicable for the added intended use of this device.

b. Linearity/assay reportable range:

Not applicable

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

Not applicable for the added intended use of this device.

d. Detection limit:

Not applicable for the added intended use of this devise.

e. Analytical specificity:

Not applicable for the added intended use of this device.

f. Assay cut-off:

Not applicable

g. Media Interference Studies

A media interference study was performed using both 10 µL (recommended test volume) and 20 µL (twice the recommended volume) of blood culture matrix inoculum. No interference with the expected identification or susceptibility results with the Standard/10 Aerobic/F (SA) and Standard Anaerobic/F (SN) blood culture bottles was observed, therefore demonstrating that the SA and SN blood culture matrix does not act as an interferent in the KeyPath™ MRSA/MSSA Blood Culture Test – BT.

Summary data for SA bottle interference

		KP Test Result		
Condition	**Type**	**MRSA**	**MSSA**	**NSA**
Negative Control	None	0	0	20
Control	MRSA	20	0	0
	MSSA	0	20	0
	NSA	0	0	40
Test	MRSA	20	0	0
	MSSA	0	20	0
	NSA	0	0	40

Summary data for SN bottle interference

		KP Test Result		
Condition	**Type**	**MRSA**	**MSSA**	**NSA**
Negative Control	None	0	0	20
Control	MRSA	20	0	0
	MSSA	0	20	0
	NSA	0	0	40
Test	MRSA	20	0	0
	MSSA	0	20	0
	NSA	0	0	40

h. Validation studies:

A panel of clinical isolates obtained during the BACTEC trial MP2009-B (K102342) was tested using the BACTEC Standard/10/Aerobic/F (SA) and Standard Anaerobic/F (SN) blood culture bottles and the KeyPath™ MRSA/MSSA Blood Culture Test – BT. The panel consisted of 22 methicillin resistant *S. aureus* (MRSA), 23 methicillin susceptible *S. aureus* (MSSA) and 35 non-*S.aureus* (NSA) isolates from unique patients. BACTEC™ SA and SN bottles were charged with blood from healthy volunteers per IRB-approved study protocol MP2007A. Bottles were inoculated with approximately 100 CFU of organism from fresh overnight cultures, and tests were performed as indicated in the package insert.

Results obtained in the validation studies substantiate the expanded use of the device. Results achieved performance criteria of at least 95% positive percent agreement and 95% negative percent agreement for both identification and susceptibility results for both the SA and SN bottles.

S. aureus detection	***Bottles tested in this study***		***Bottles tested in K102342***	
	SA	***SN***	***Plus A***	***Plus N***
Positive agreement N, %, (95% CI)	45/45, 100% (92-100%)	44/45, 98% (88-100%)	232/255, 91% (87-94%)	100/107, 93% (87-97%)
Negative agreement N, %, (95% CI)	35/35, 100% (90-100%)	30/30, 100% (88-100%)	546/557, 98% (96-99%)	189/189, 100% (96-100%)

Methicillin-resistance within S. aureus	***Bottles tested in this study***		***Bottles tested in K102342***	
	SA	***SN***	***Plus A***	***Plus N***
Positive agreement N, %, (95% CI)	21/22, 95% (77-100%)	20/21, 95% (76-100%)	122/123, 99% (96-100%)	52/53, 98% (90-100%)
Negative agreement N, %, (95% CI)	22/23, 96% (78-100%)	22/23, 96% (78-100%)	107/108, 99% (95-100%)	46/46, 100% (92-100%)

2. Comparison studies:

   a. *Method comparison with predicate device:*

      Isolates used in the validation study were tested using the KeyPath™ MRSA/MSSA Blood Culture Test – BT in original studies for device clearance (K102342). Results obtained in the validation studies for the expanded use of the devise were identical to those previously obtained.

   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

5. Expected values/Reference range:

Not applicable

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

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