

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE**

A. 510(k) Number:

k061327

B. Purpose for Submission:

To add additional organism groups to the antibiotics amoxicillin-clavulanate, ampicillin-sulbactam, and ticarcillin on the BD Phoenix™ gram-negative ID/AST or AST panel only

C. Measurand:

Amoxicillin-clavulanate 0.5/0.25 – 32/16 µg/mL

Ampicillin-sulbactam 0.5/0.25 – 32/16 µg/mL

Ticarcillin 1 – 128 µg/mL

D. Type of Test:

Antimicrobial Susceptibility Test (AST) (Qualitative) colorimetric oxidation-reduction, growth-based

E. Applicant:

Becton, Dickinson & Company

F. Proprietary and Established Names:

BD Phoenix™ Automated Microbiology System – Amoxicillin-clavulanate (0.5/0.25 – 32/16 µg/mL), Ampicillin-sulbactam (0.5/0.25 – 32/16 µg/mL), Ticarcillin (1 – 128 µg/mL)

G. Regulatory Information:

1. Regulation section:

21 CFR 866.1645 Fully Automated Short-Term Incubation Cycle Antimicrobial Susceptibility System

2. Classification:

II

3. Product code:

LON System, Test, Automated, Antimicrobial Susceptibility, Short Incubation

4. Panel:

83 Microbiology

H. Intended Use:

1. Intended use(s):

Amoxicillin-clavulanate at 0.5/0.25 – 32/16 µg/mL, Ampicillin-sulbactam at 0.5/0.25 – 32/16 µg/mL, Ticarcillin at 1 – 128 µg/mL on the Phoenix™ Gram Negative ID/AST or AST only panel is intended for use with the BD Phoenix Automated Microbiology System for the quantitative determination of antimicrobial susceptibility by minimal inhibitory concentration of gram-negative aerobic and facultative anaerobic bacteria belonging to the family *Enterobacteriaceae* and non – *Enterobacteriaceae*.

The BD Phoenix™ Automated Microbiology System is intended for the *in vitro* quantitative determination of antimicrobial susceptibility by minimal inhibitory concentration (MIC) of most gram-negative aerobic and facultative anaerobic bacteria isolates from pure culture for *Enterobacteriaceae* and non – *Enterobacteriaceae* and most Gram-positive bacteria isolates from pure culture belonging to the genera *Staphylococcus* and *Enterococcus*.

2. Indication(s) for use:

This device is indicated for additional organism groups and amoxicillin-clavulanate at 0.5/0.25 – 32/16 µg/mL, ampicillin-sulbactam at 0.5/0.25 – 32/16 µg/mL, ticarcillin at 1 – 128 µg/mL on the Phoenix™ Gram Negative ID/AST or AST only panel.

3. Special conditions for use statement(s):

For prescription use only

Results for *Acinetobacter species* and *Proteus species* with ampicillin-sulbactam has been excluded in the BD Phoenix™ therefore no results will be reported. An alternate method should be performed when this combination is identified.

Results for *Proteus vulgaris/penneri* with ticarcillin has been excluded in the BD Phoenix™ therefore no results will be reported. An alternate method should be performed when this combination is identified.

4. Special instrument requirements:

Not Applicable

I. Device Description:

The BD Phoenix™ Automated Microbiology System includes instrumentation and software, sealed and self-inoculating molded polystyrene trays with 136 micro-wells containing dried reagents, and specific inoculum broth formulations for ID and AST Indicator. The organism to be tested must be a pure culture and be preliminarily identified as gram positive or gram negative. Colonies are then suspended in broth, and equated to a 0.5 McFarland with the recommendation to use the BD CrystalSpec™ Nephelometer. A further dilution is made into an AST broth, which contains an AST

indicator, prior to inoculating the panel. The AST broth is a cation-adjusted formulation of Mueller-Hinton broth containing 0.01% Tween 80. After adding the indicator solution to the AST inoculum the color is blue and after inoculation and incubation changes to pink then to colorless as reduction in the panel well proceeds. Inoculated panels are barcode scanned and loaded into the BD Phoenix™ Automated Microbiology System instrument where the panels are continuously incubated at 35°C. The AST has a final inoculum of 5×10^5 CFU/ml. The instrument incubates, reads and records the results of the biochemical substrates and antimicrobial agents and interprets the reactions to give an ID of the isolate and MIC value and category interpretation of the antimicrobial agents. Organisms growing in the presence of a given antimicrobial agent reduce the indicator, signaling organism growth and resistance to the antimicrobial agent. Organisms killed or inhibited by a given antimicrobial do not cause reduction of the indicator and therefore do not produce a color change. Additional interpretation is done using software driven “EXPERT” System using rules derived from the NCCLS documentation.

Readings are taken every 20 minutes with an ID result available between 2-12 hours and an AST result available between 4-16 hours. This is only an autoread result; there are no manual readings possible.

J. Substantial Equivalence Information:

1. Predicate device name(s):
VITEK® System
2. Predicate 510(k) number(s):
N50510
3. Comparison with predicate:

Similarities		
Item	Device	Predicate
1. Intended Use	Intended for the <i>in vitro</i> rapid identification (ID) and quantitative determination of antimicrobial susceptibility by minimal inhibitory concentration (MIC) of most bacteria.	Same
2. Isolates	Isolated colonies from culture used	Isolated colonies from culture used
3. Result Reported	Report results as minimum inhibitory concentration (MIC) and categorical interpretation (SIR)	Report results as minimum inhibitory concentration (MIC) and categorical interpretation (SIR)
4. Incubation Time	<16 hours	<16 hours

Similarities		
Item	Device	Predicate
5. Type of Test	Automated	Automated

Differences		
Item	Device	Predicate
1. Results achieved	Results are determined from serial twofold dilutions of antimicrobial agents	Results are determined from extrapolation of doubling dilutions
2. Sample Preparation	Inoculum density equated to 0.5 McFarland standard	Inoculum density equated to 1.0 McFarland standard
3. Technology	Automated growth based enhanced by use of a redox indicator (colorimetric oxidation-reduction) to detect organism growth.	Automated growth based with detection using an attenuation of light measured by an optical scanner.

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

“Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test Systems; Guidance for Industry and FDA”; CLSI M7 (M100-S16) “Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard.”

L. Test Principle:

The system employs conventional, colorimetric, fluorogenic and chromogenic substrates to identify the genus and species of the isolate. The AST portion of the BD Phoenix™ Automated Microbiology System is a broth based microdilution method that utilizes a redox indicator (colorimetric oxidation-reduction) to enhance detection of organism growth. The MIC is determined by comparing growth in wells containing serial two-fold dilutions of an antibiotic to the growth in “growth control wells” which contains no antibiotic.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Ten isolates were evaluated for site to site and inter site reproducibility demonstrating >95% reproducibility. The ten isolate study described in the guidance document was used (10 organisms tested 3 times on 3 days at 3 sites).

b. Linearity/assay reportable range:

Not applicable

- c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*
Quality Control was performed on every test occasion with the following results. BD Phoenix™ produced acceptable QC results as compared to the reference method results >95% of the time.

Amoxicillin-Clavulanate Gram Negative Quality Control Table

ORGANISM	conc. (µg/mL)	Reference		BD Phoenix™	
<i>E. coli</i> ATCC 25922 Expected Range: 2/1 – 8/4 µg/mL	2		2		
	4		239	7	
	8		143	375	
	16			2	
	>32		1	3	
<i>E. coli</i> ATCC 35218 Expected Range : 4/2 – 16/8 µg/mL	4		1		
	8		375	380	
	16		6	2	
	32			1	
	>32		5	9	

Ampicillin-Sulbactam Gram Negative Quality Control Table

ORGANISM	conc. (µg/mL)	Reference		BD Phoenix™	
<i>E. coli</i> ATCC 25922 Expected Range: 2/1 – 8/4 µg/mL	2		32	7	
	4		165	189	
	8		2	2	
	16		1	5	
	>32			2	
<i>E. coli</i> ATCC 35218 Expected Range: 8/4 – 32/16 µg/mL	8			8	
	16		149	188	
	32		50	4	
	>32			2	

Ticarcillin Gram Negative Quality Control Table

ORGANISM	conc. (µg/mL)	Reference		BD Phoenix™	
<i>E. coli</i> ATCC 25922 Expected Range: 4 – 16 µg/mL	4		63		
	8		181	375	
	16		139	6	
	32		2	4	
	64			1	
	>128			1	

<i>P. aeruginosa</i>	8		1		1
ATCC 27853	16		313		151
Expected Range:	32		61		221
8 – 32 µg/mL	64		9		2
	128				2
	>128				8

Inoculum density control: The organism suspension density of the ID broth was equivalent to a 0.5 McFarland standard using the BBL™ CrystalSpec™ Nephelometer which was verified each day of testing. Internal data was used to demonstrate that the use of the BBL™ CrystalSpec™ Nephelometer would produce reproducible results. Five different instruments were used.

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:*

The broth dilution reference panel was prepared according to the CLSI recommendation and used to compare with the BD Phoenix™ results. Clinical testing was performed at several sites. The testing included both fresh clinical isolates and stock isolates along with a challenge set with known results. Performance charts below include all data, original and the additional organisms for fresh and challenge organisms.

Gram Negative (GN) Accuracy Summary Clinical and Challenge with Additional Organisms Included

Amoxicillin-Clavulanate	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA N	CA %	#R	min	maj	vmj
Combined (Original Data and Additional Org)	2249	2174	96.7	1439	1382	96.0	2044	90.9	991	162	26	17

Gram Negative (GN) Accuracy Summary Clinical and Challenge with Additional Organisms Included

Ampicillin-Sulbactam	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA N	CA %	#R	min	maj	vmj
Combined (Original Data and Additional Org)	1305	1269	97.2	850	827	97.3	1142	87.5	649	155	6	2

Gram Negative (GN) Accuracy Summary Clinical and Challenge with Additional Organisms Included

Ticarcillin	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA N	CA %	#R	min	maj	vmj
Combined (Original Data and Additional Org)	2882	2728	94.7	1270	1156	91.0	2673	92.7	1424	139	53	17

EA-Essential Agreement
CA-Category Agreement
R-resistant isolates

maj-major discrepancies
vmj-very major discrepancies
min- minor discrepancies

Essential agreement (EA) is when the BD Phoenix™ panels agree with the reference test panel results exactly or within one doubling dilution of the reference method. Category agreement (CA) is when the BD Phoenix™ panel result interpretation (SIR) agrees exactly with the reference panel result interpretation. Evaluable EA is when the MIC result is on scale for both the BD Phoenix™ and the reference and have on-scale EA.

- 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:

Amoxicillin - clavulanate

Enterobacteriaceae ≤8/4(S), 16/8 (I), ≥32/16

Ampicillin – sulbactam

Enterobacteriaceae $\leq 8/4$ (S), 16/8 (I), $\geq 32/16$ (R)

Ticarcillin

Enterobacteriaceae ≤ 16 (S), 32 – 64 (I), ≥ 128 (R)

Pseudomonas aeruginosa ≤ 64 (S), ≥ 128 (R)

Non – *Enterobacteriaceae* ≤ 16 (S), 32 – 64 (I), ≥ 128 (R)

N. Proposed Labeling:

The interpretive criteria and QC will be included in the package insert.

O. Conclusion:

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

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