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

A. 510(k) Number:

K043389

B. Purpose for Submission:

To add ampicillin-sulbactam to the Gram-Negative ID/AST or AST only Phoenix™ panels

C. Measurand:

Ampicillin-sulbactam at concentrations between 0.5/0.25 to 32/16 ug/mL

D. Type of Test:

Antimicrobial Susceptibility Test (Quantitative and qualitative) colorimetric oxidation-reduction, growth-based

E. Applicant:

Becton, Dickinson & Company

F. Proprietary and Established Names:

BD Phoenix™ Automated Microbiology System – ampicillin-sulbactam- Gram Negative

G. Regulatory Information:

1. Regulation section:
   21 CFR 866.1645 Fully Automated Short-Term Incubation Cycle Antimicrobial
2. Classification:
   Class II
3. Product Code:
   LON

4. Panel: 83 Microbiology

H. Intended Use:

1. Intended use(s):
    BD Phoenix™ Automated Microbiology System:
    The BD Phoenix™ Automated Microbiology System is intended for
    in vitro 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 and gram-positive bacteria belonging to the genera
    Staphylococcus and *Enterococcus*.

    The BD Phoenix™ GN Panel: The BD Phoenix™ Automated Microbiology
    System is intended for the *in vitro* rapid identification (ID) and quantitative
    determination of antimicrobial susceptibility by minimal inhibitory
    concentration (MIC) of gram-negative aerobic and facultative anaerobic
    bacteria belonging to the family *Enterobacteriaceae* and non-
    Enterobacteriaceae.

2. Indication(s) for use:

    This submission is for the addition of the antibiotic ampicillin-sulbactam at
    concentrations between 0.5/0.25 – 32/16 ug/mL for *Enterobacteriaceae* testing.

3. Special conditions for use statement(s):

    Prescription Use

    Results for *Proteus spp.* and *Acinetobacter spp.* have been excluded in the BD
    Phoenix™ therefore no results will be reported. An alternate method should be
    performed with these combinations.

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 goes to pink 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 x 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 antimicrobic agent reduce the indicator, signaling organism growth and resistance to the antimicrobic agent. Organisms killed or inhibited by a given antimicrobic do not cause reduction of the indicator and therefore do not produce a color change. Additional interpretation is done using software driven "EXPERT" System with rules derived from the CLSI (Clinical and Laboratory Standards Institute) standards.

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
Intended use	Intended for the *in vitro* rapid identification (ID) and quantitative determination of antimicrobial susceptibility by minimal inhibitory concentration (MIC) of gram-negative aerobic and facultative anaerobic bacteria.	same
Isolates	Isolated colonies from culture used	Isolated colonies from culture used
Results	Report results as minimum	Report results as

Similarities		
Item	Device	Predicate
	inhibitory concentration (MIC) and categorical interpretation (SIR)	minimum inhibitory concentration (MIC) and categorical interpretation (SIR)
Incubation conditions	<16 hours	<16 hours

Differences		
Item	Device	Predicate
Inoculum preparation	Inoculum density equated to 0.5 McFarland standard	Inoculum density equated to 1.0 McFarland standard
Reading algorithm	Results are determined from serial twofold dilutions of antimicrobial agents	Results are determined from extrapolation of specific dilutions
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 (AST) Systems; Guidance for Industry and FDA"; NCCLS/CLSI M7 (M100-S14) "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 contain no antibiotic.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Fifteen strains with on-scale results were tested at each of three clinical sites in triplicate on three separate days with results that were reproducible at $\geq$ 95%.

b. Linearity/assay reportable range:

Not Applicable

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

CLSI recommended Quality Control strains were tested (see table below). The full panel was tested each day of testing for both the reference test and the Phoenix™. The table reflects the numbers with the MIC at each concentration. The expected range is stated. The Phoenix results demonstrate that the system can produce QC results in the recommended range. The modes were the same for the Phoenix™ and the reference test result. The Quality Control failure rate is acceptable.

Organism (expected range)	Concentration	Reference results	Phoenix™ results
E. coli ATCC 25922 (range 2/1- 8/4 ug/ml)	$\leq$ 0.5/4		
	1		
	2	32	7
	4	165	189
	8	2	2
	16	1	5
	32		
	>32		2
E. coli ATCC 35218 (range 8/4-32/16 ug/mL)	$\leq$ 0.5		
	1		
	2		
	4		
	8		8
	16	149	188
	32	50	4
	>32		2

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.

The overall growth rate was greater than 95%.

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 CLSI recommended broth dilution reference panel was prepared according to the CLSI recommendation and used to compare with the Phoenix™ results. Clinical testing was performed at four sites. The testing included clinical isolates comprised of fresh, recent and stock isolates.

A comparison was provided to the reference method with the following agreement for the *Enterobacteriaceae* excluding *Proteus spp.* This table demonstrates the performance of all *Enterobacteriaceae* tested:

	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA N`	CA %	#R	min	maj	vmj
Clinical	988	960	97.7	702	686	97.7	870	88.1	428	112	5	1
Challenge	64	64	100	33	33	100	59	92.2	36	5	0	0
Total	1052	1024	97.3	735	719	97.8	929	88.3	464	117	5	1

EA-Essential Agreement **maj-**major discrepancies
CA-Category Agreement **vmj-**very major discrepancies
R-resistant isolates **min-** minor discrepancies

The maj, vmj, EA and EA of evaluable are acceptable. The CA is low due to mostly minor errors. Of the 117 minor errors, 97 are within EA but not CA.

Given the high EA, the lower than expected CA are mainly due to minor errors which is acceptable.

    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:

    The interpretative criteria and the recommended Quality Control Ranges are the same as the FDA and CLSI.

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

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.