

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

A. 510(k) Number:

k032675

B. Analyte:

Cefepime at 0.5-64 ug/mL -AST

C. Type of Test:

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

D. Applicant:

Becton, Dickinson and Company

E. Proprietary and Established Names:

BD Phoenix™ Automated Microbiology System – Cefepime 0.5-64 ug/mL.

F. Regulatory Information:

1. Regulation section:
CFR 866.1645 Short Term Antimicrobial Susceptibility Test System
2. Classification:
Class II
3. Product Code:
LON Automated short incubation AST system
4. Panel:
83 Microbiology

G. Intended Use:

1. Intended use(s):
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 cefepime at concentrations of 0.5-64 ug/mL to gram negative ID/AST or AST BD Phoenix™ panels.
3. Special condition for use statement(s):
Prescription Use Only

Results for *Proteus species* have 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

H. Device Description:

The BD Phoenix™ 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 5×10^5 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 a 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

I. Substantial Equivalence Information:

1. Predicate device name(s):
Vitek® System
2. Predicate K number(s):
N50510
3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Specimen	Isolated colonies from culture used	Isolated colonies from culture used
Incubation	<16 hours	< 16 hours
Panels	Dried antibiotics	Dried antibiotics
Differences		
Item	Device	Predicate
Results	Results based on readings from serial dilutions of antibiotics	Results based on extrapolation of several concentrations of an antibiotic
Inoculum	Inoculum density to 0.5 McFarland standard	Inoculum density to 1 McFarland standard
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.

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

“Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems; Guidance for Industry and FDA”, NCCLS M7 (M100-S14)
 “Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard.”

K. 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 Phoenix™ 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.

L. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Inter-site and intra-site reproducibility was performed on 21 isolates 3 times at each of the three sites. The overall reproducibility was acceptable at $\geq 95\%$.

b. *Linearity/assay reportable range:*

Not applicable

c. *Traceability (controls, calibrators, or method):*

NCCLS recommended Quality Control strains were tested with acceptable results. The Phoenix results demonstrate that the system can produce QC results in the recommended range, although there is a trend for a one well more resistant result for both QC strains of *Pseudomonas aeruginosa*. This was also observed with the clinical isolates.

Organism	Concentration	Reference results	Phoenix™ results
<i>E. coli</i> ATCC 25922 (range ≤ 0.5 ug/mL)	≤ 0.5	190	196
	1		
	2		
	4		
<i>P aeruginosa</i> ATCC 27853 (range 1-8 ug/mL)	≤ 0.5		
	1	123	3
	2	64	178
	4	2	16
	8		
	16		
<i>P aeruginosa</i> ATCC 35032	≤ 0.5		
	1		
	2	1	
	4	158	65
	8	32	132
	16		3
	>16		

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.

The growth rate was >90%.

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 NCCLS recommended broth reference panel prepared according to the recommendations in the NCCLS M7 Approved Standard was used to compare the Phoenix™ results. Clinical testing was performed at four sites. The testing included both fresh clinical isolates and stock isolates. Two different challenge sets of selected organisms were tested to acquire more resistant isolates. There was a 0.6% no growth rate in the study. A comparison was provided to the reference method with the following agreement.

	total	EA	% EA	Total evalu-able	EA of evalu-able	% EA	CA	% CA	#R	min	maj	vmj
Combined	1683	1602	95.2	562	499	88.8	1567	93.1	175	102	8	6

EA-Essential Agreement

CA-Category Agreement

R-resistant isolates

maj-major discrepancies

vmj-very major discrepancies

min- minor discrepancies

Evaluable(EA) results are those that fall within the test range of the reference method and could also be on-scale with the new device if within the plus/minus one well variability. EA is when there is agreement between the reference method and the Phoenix™ within plus or minus one serial two-fold dilution of antibiotic. CA is when the interpretation of the reference method agrees exactly with the interpretation of the Phoenix™ result.

There was trending below the diagonal resulting in a Phoenix result of more resistant which is the same trend as seen in the QC data set. The %EA, CA and reproducibility are all acceptable when compared to the reference method as described in the FDA guidance document, “Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems; Guidance for Industry and FDA”.

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:
 ≤ 8 (S), 16 (I), ≥ 32 (R)
The expected value range, interpretative criteria and QC are the same as recommended in NCCLS. All values will be included in the package insert.

M. Conclusion:

Data analysis when analyzed as recommended in the “Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems; Guidance for Industry and FDA” demonstrates that the Phoenix™ System is substantially equivalent to the Vitek® System.