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

A. 510(k) Number:
k031984

B. Analyte:
Ticarcillin 1 – 128 µg/mL Gram - Negative AST

C. Type of Test:
Antimicrobial Susceptibility Test (Quantitative) colorimetric oxidation-reduction, growth-based

D. Applicant:
Becton, Dickinson & Company

E. Proprietary and Established Names:
BD Phoenix™ Automated Microbiology System – Ticarcillin Gram - Negative

F. 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

G. 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 ticarcillin at
    concentrations of 1 – 128 µg/mL to the gram negative susceptibility panel.

3. Special condition for use statement(s):
    Results for *Proteus vulgaris/penneri* 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™ 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 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**
1.	Isolated colonies from culture used	Isolated colonies from culture used
2.	Inoculum density equated to 0.5 McFarland standard	Inoculum density equated to 0.5 McFarland standard
3.	Results are determined from serial twofold dilutions of antimicrobial agents	Results are determined from serial twofold dilutions of antimicrobial agents
4.	Report results as minimum inhibitory concentration (MIC) and categorical interpretation (SIR)	Report results as minimum inhibitory concentration (MIC) and categorical interpretation (SIR)
5.	<16 hours	<16 hours
Differences		
Item	**Device**	**Predicate**
1.	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-S13) "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 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.

L. Performance Characteristics (if/when applicable):
1. Analytical performance:
   a. *Precision/Reproducibility:*
   Reproducibility within sites was determined using the QC isolates for >95% reproducibility. Between sites was performed at three sites for >95% reproducibility on twelve isolates.

b. *Linearity/assay reportable range:*
Not applicable

c. *Traceability (controls, calibrators, or method):*
The recommended QC isolate was tested a sufficient number of times with acceptable results with the reference method. The Phoenix results demonstrate that the system can produce QC results in the recommended range.

QC Table

ORGANISM	conc. µg/mL	Reference		Phoenix™	
E. coli ATCC 25922 Expected range: 4-16 µg/mL	4	63			
	8	181		375	
	16	139		6	
	32	2		4	
	64			1	
	>128			1	
P. aeruginosa ATCC 27853 Expected Range: 8-32 µg/mL	8	1		1	
	16	313		151	
	32	61		221	
	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 NCCLS recommended broth dilution reference panel was prepared according to the NCCLS recommendation. Clinical testing was performed at six sites. The testing included both fresh clinical isolates and stock isolates along with a challenge set with known results. The test device had a growth rate of 99.0%.

   The NCCLS recommended breakpoints for ticarcillin are different from FDA's. This is particularly true for the organism, *P. aeruginosa.* It is for this reason that *P. aeruginosa* will be presented in a table independently of *Enterobacteriaceae* and Non-*Enterobacteriaceae*. A third table with combined results from all three groups will be included as well. The following charts are based on NCCLS interpretive criteria.

GN Accuracy MIC Summary for Enterobacteriaceae and Other Non-Enterobacteriaceae
Excluding *Pseudomonas aeruginosa*
Interpretation: ≤16 (S); 32 – 64 (I); ≥128(R)

	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA N	CA %	#R	min	maj	vmj
Clinical	1717	1622	94.5	728	664	91.2	1600	93.2	743	102	11	4
Challenge	60	59	98.3	15	14	93.3	58	96.7	36	2	0	0
Combined	1777	1681	94.6	743	678	91.3	1658	93.3	779	104	11	4

GN Accuracy MIC Summary for Pseudomonas aeruginosa
Interpretation: ≤64 (S); ≥128(R)

	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA N	CA %	#R	min	maj	vmj
Clinical	508	468	92.1	418	380	90.9	456	89.8	138	NA	40	12
Challenge	9	8	88.9	5	4	80.0	8	88.9	5	NA	0	1
Combined	517	476	92.1	423	384	90.8	464	89.7	143	NA	40	13

NA – No intermediate range therefore no minor errors possible
There were 40 maj errors and 24 of the maj errors were in essential agreement.
Out of the 13 vmj errors encountered, 11 were in essential agreement.

GN Accuracy MIC Summary for Enterobacteriaceae, P. aeruginosa and Other Non-Enterobacteriaceae

	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA N	CA %	#R	Min	maj	vmj
Clinical	2225	2090	93.9	1146	1044	91.1	2056	92.4	881	102	51	16
Challenge	69	67	97.1	20	18	90.0	66	95.7	41	2	0	1
Combined	2294	2157	94.0	1166	1062	91.1	2122	92.5	922	104	51	17

EA-Essential Agreement   **maj-**major discrepancies
CA-Category Agreement   **vmj-**very major discrepancies
R-resistant isolates   **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 agrees exactly with the reference panel result interpretation.

The following table represents data analysis using FDA interpretations.

GN Accuracy MIC Summary for Enterobacteriaceae, P. aeruginosa and Other Non-Enterobacteriaceae

Interpretation: ≤64 (S); ≥128(R)

	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA N	CA %	#R	min	maj	vmj
Clinical	2225	2090	93.9	1146	1044	91.1	2121	95.3	881	NA	68	36
Challenge	69	67	97.1	20	18	90.0	67	97.1	41	NA	1	1
Combined	2294	2157	94.0	1166	1062	91.1	2188	95.4	922	NA	69	37

NA – No intermediate range therefore no minor errors possible

Using the FDA's recommended breakpoints, there are 37 vmj errors and 69 maj errors. It is also important to point out that 25 of the vmj errors are within essential agreement and 34 of the maj errors are within essential agreement. The vmj% of 4.0 (37/922) and maj% of 5.0 (69/1372) are both higher than as recommended in the guidance document but these recommendations are based on errors that would include a minor error range. Since this antibiotic has only a Sensitive (S) and a Resistant (R) result all errors are either vmj or maj with no minor errors possible. However, if those errors that are in EA are removed, its vmj rate would be 1.3% (12/922) and maj rate is 2.6% (35/1372), both of which are 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:
Enterobacteriaceae and Other Non – *Enterobacteriaceae*:
≤16 (S); 32 – 64 (I); ≥128(R)
Ps. aeruginosa: ≤64 (S); ≥128(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:

This demonstrates acceptable performance as described in the FDA guidance document, "Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems; Guidance for Industry and FDA" and therefore the testing of ticarcillin on the BD Phoenix™ Automated Microbiology System is substantially equivalent to other commercial devices such as bioMerieux Vitek® AST panels.