

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

A. 510(k) Number:

K042932

B. Purpose for Submission:

To add piperacillin-tazobactam to the Gram-Negative ID/AST or AST only Phoenix™ panels

C. Measurand:

Piperacillin-tazobactam at concentrations between 0.5/4 to 128/4 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 – piperacillin-tazobactam- 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 piperacillin-tazobactam at concentrations between 0.5/4 – 128/4 ug/mL

3. Special conditions for use statement(s):

Prescription Use

Results for the Piperacillin-tazobactam and the family *Enterobacteriaceae* should only be reported for isolates that have never been frozen and are <60 days old. Results should not be reported for this family if isolates have been frozen or are ≥ 60 days old because these isolates may show variability when tested *in vitro* and therefore may produce erroneous results.

Results for *Stenotrophomonas maltophilia* 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 5×10^5 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 with rules derived from the NCCLS 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 <i>in vitro</i> 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 inhibitory concentration (MIC) and categorical interpretation (SIR)	Report results as 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 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:*

Twenty three 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):*

NCCLS 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
<i>E. coli</i> ATCC 25922 (range 1/4- 4/4 ug/ml)	≤ 0.5/4		
	1/4	141	182
	2/4	67	31
	4/4		1
<i>P aeruginosa</i> ATCC 27853 (range 1/4-8/4 ug/ml)	1		
	2	51	4
	4	134	206
	8	22	3
	16	1	
<i>E. coli</i> ATCC 35218 (range 0.5/4-2/4 ug/ml)	≤ 0.5	16	
	1	179	194
	2	11	11
	4		1
	8	1	2
	16		1

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 NCCLS recommended broth dilution reference panel was prepared according to the NCCLS recommendation and used to compare with the Phoenix™ results. Clinical testing was performed at four sites. The testing included both fresh clinical isolates and stock isolates. Only *Pseudomonas aeruginosa* had a challenge set tested for comparison to an expected result since the *Enterobacteriaceae* group is only intended for fresh and recent isolates. A comparison was provided to the reference method with the following agreement.

The interpretive criteria for *P. aeruginosa* has no intermediate category so all discrepant results are either a very major error or a major error. This is true even if the result is in EA. The evaluation of *P. aeruginosa* alone is as follows:

	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA N	CA %	#R	min	maj	vmj
Clinical	267	247	92.5	220	201	91.4	251	94.0	61	NA	11	5
Challenge	187	182	97.3	177	173	97.7	187	100	4	NA	0	0
Total	454	429	94.5	397	374	94.2	438	96.5	65	NA	11	5

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

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

There are no minor errors in these calculations because there is no intermediate category. Four of the 5 very major errors are in EA but since there is no intermediate category instead of these 4 as minor errors they are reported as very major errors. For statistical calculations this would result in a true very major rate of 1 very major error out of 65 resistant which is acceptable.

This table demonstrates the performance of *Enterobacteriaceae* that are fresh and recent and with all non-enterobacteriaceae except for *P. aeruginosa* which is presented separately.

	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA N	CA %	#R	min	maj	vmj
Total	1092	1012	92.7	807	742	91.9	1029	94.2	94	52	8	3

To assess the overall performance all organism are combined.

	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA N	CA %	#R	min	maj	vmj
Total	1546	1441	93.2	1204	1116	92.7	1467	94.9	159	52	19	8

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

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vmj-very major discrepancies
min- minor discrepancies

The overall performance is acceptable for the EA, CA, and major errors. When the very major errors that are within EA are removed (4 *P. aeruginosa*)

the overall very major rate of 4 very major errors out of 159 resistant organisms 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 NCCLS and will appear in the Package Insert and software. Interpretative criteria used for the evaluation and that will appear in the Package Insert are as follows:

Enterobacteriaceae; $\leq 16/4$ (S), $32/4-64/4$ (I), $\geq 128/4$ (R)

Pseudomonas aeruginosa; $\leq 64/4$ (S), $\geq 128/4$ (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.