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

A. 510(k) Number:
k062944

B. Purpose for Submission:
To remove the limitation of *Proteus vulgaris/penneri* with ceftriaxone on the Gram-Negative (GN) ID/AST or AST only Phoenix panels

C. Measurand:
Ceftriaxone at 0.5-64 µg/mL

D. Type of Test:

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

E. Applicant:
Becton, Dickinson & Company

F. Proprietary and Established Names:
BD Phoenix™ Automated Microbiology System – Ceftriaxone 0.5-64 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):
Ceftriaxone at 0.5-64 µg/mL on the GN ID/AST or AST only Phoenix panels is intended for use with the BD Phoenix Automated Microbiology System for *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*, *Enterococcus*, and *Streptococcus*.

2. Indication(s) for use:
This application is indicated for the removal of the "Do Not Report" ceftriaxone limitation for *Proteus vulgaris/penneri*.

3. Special conditions for use statement(s):
For prescription use only

4. Special instrument requirements:
Not Applicable

I. Device Description:

This submission is for AST Panel only. The ID System was not reviewed.

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^{o}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 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 CLSI documentation. Readings are taken every 20 minutes with an AST result available between 4-16 hours. This is only an autoread result; no manual readings are possible with this system.

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 *in vitro* 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
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 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. Instrumentation continuously monitors changes until sufficient growth is determined.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

The data included in this submission were acquired during the clinical studies performed at multiple sites and described in the previous submission for ceftriaxone at 0.5-64 µg/ml. The accuracy performance data using ID specific algorithm for clinical and challenge isolates of *Proteus vulgaris/penneri* and ceftriaxone are contained in this submission. The Reproducibility study was performed in the original submission and was not performed for this submission because the drug formulation has not changed. The QC testing was performed and was within the expected ranges as shown under the "Traceability, Stability…. section (c)".

a. Precision/Reproducibility:
Intersite and Intrasite testing demonstrated >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 >95% of the time. The same trend for the reference result and the ceftriaxone result demonstrated below were observed in the original clearance.

ORGANISM	**conc. (µg/mL)**	**Reference**	**BD Phoenix™**
E. coli ATCC 25922 Expected Range : 0.03-0.12 µg/mL	≤ 0.5	49	69
P. aeruginosa ATCC 27853 Expected Range : 8-64 µg/mL	≤ 0.5		
	1		
	2		
	4		
	8	25	28
	16	18	38
	32	1	1

	≥ 64		3		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.

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. A total of 78 *Proteus vulgaris/penneri* isolates were tested with acceptable EA and no maj or very maj errors. Additionally, 466 clinical strains of related appropriate groups were tested to demonstrate that there would be no difference in performance from the original studies. The following table includes the overall performance of all appropriate organisms tested with the addition of all previously cleared data for appropriate organisms.

	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA N	CA %	#R	min	maj	vmj
New data	**544**	**527**	**96.9**	**113**	**104**	**92**	**511**	**93.9**	**109**	**32**	**0**	**1**
Original data	**1872**	**1794**	**95.8**	**491**	**426**	**86.8**	**1702**	**90.9**	**376**	**163**	**4**	**3**
Total performance	**2416**	**2321**	**96.1**	**604**	**530**	**87.7**	**2213**	**91.6**	**485**	**195**	**4**	**4**

EA-Essential Agreement **vmj** – very major discrepancies
CA-Category Agreement **maj -** 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 (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:
Enterobacteriaceae ≤8 (S); 16-32 (I); ≥64(R)

N. Proposed Labeling:

The expected value range, interpretive criteria and QC for gram negative panels are included in the package insert. The labeling is sufficient and 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.