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

A. 510(k) Number:
K051138

B. Purpose for Submission:
Addition of the antibiotic ceftriaxone to the Phoenix™ SMIC/ID and SMIC Panels

C. Measurand:
Ceftriaxone 0.0625 – 4 µg/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 – Ceftriaxone (strep) 0.0625 – 4 µg/mL

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 the *in vitro* quantitative determination of antimicrobial susceptibility by minimal inhibitory concentration (MIC) of most gram-negative aerobic and facultative anaerobic bacteria belonging to the family *Enterobacteriaceae* and non - E*nterobacteriaceae* and gram-positive bacteria belonging to the genera *Staphylococcus, Enterococcus* and *Streptococcus*.

The BD Phoenix™ SMIC/ID and SMIC Panel is intended for the *in vitro* rapid identification (ID) of bacteria from pure culture belonging to the genera *Streptococcus.* The BD Phoenix™ SMIC/ID and SMIC panels are also intended for the quantitative determination of antimicrobial susceptibility by minimal inhibitory concentration (MIC) of most bacteria isolates from pure culture belonging to the genera *Streptococcus* when used with the BD Phoenix™ Automated Microbiology System.

2. Indication(s) for use:
   This submission is for the addition of the antibiotic ceftriaxone at concentrations of 0.0625 – 4 µg/mL to the Phoenix™ SMIC/ID and SMIC *Streptococcus* Panels.

3. Special condition for use statement(s):
   Prescription Use Only

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-S 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-S broth, which contains an AST- S indicator, prior to inoculating the panel. The AST-S broth is a non-blood, cation-adjusted broth containing purified water, Tween 80, pancreatic digest of casein, peptones and other additional supplements for optimization of streptococcal growth. After adding the indicator solution to the AST – S inoculum, the color is blue, and after inoculation and incubation, it changes to pink then 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 resulting 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 Clinical and Laboratory Standards Institute (CLSI).

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 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 most 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
Type of Test	Automated	Automated

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 doubling 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"; CLSI M7 (M100-S15) "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-one isolates were evaluated for site to site and inter site reproducibility demonstrating >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 method):

CLSI recommended Quality Control strain was tested at the concentrations listed (see table below). The mode for the reference method is different from the mode for the test device, but both are still in the expected range. The Phoenix™ results demonstrate that the system can produce QC results in the recommended range.

Quality Control Table

Organism	**Concentration µg/mL**	**Reference results**	**Phoenix™ results**
S. pneumoniae ATCC 49619 Expected range 0.03 – 0.12 µg/mL	<= 0.0625	122	54
	0.125	1	69
	0.25		
	0.5		
	1		
	2		
	4		
	>4		

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. Additional testing on 5 streptococcal strains was performed to demonstrate acceptable performance for streptococcal species.

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 with 2-5% lysed horse blood 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 both fresh clinical isolates and stock isolates along with a challenge set with known results. An additional collection of clinical isolates was tested to provide more resistant and on scale results. A comparison of all results was provided to the reference method with the following agreement.

Clinical + Challenge

	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA N	CA %	#R	min	maj	vmj
Clinical	**1805**	**1773**	**98.2**	**1081**	**1062**	**98.2**	**1775**	**98.3**	**38**	**28**	**0**	**2**
Challenge [1]	**208**	**206**	**99.0**	**127**	**125**	**98.4**	**178**	**85.6**	**84**	**30**	**0**	**0**
Combined	**2013**	**1979**	**98.3**	**1208**	**1187**	**98.3**	**1953**	**97.0**	**122**	**58**	**0**	**2**

[1] Challenge and Supplemental isolates

EA-Essential Agreement
CA-Category Agreement
R-resistant isolates
maj-major discrepancies
vmj-very major discrepancies
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. Evaluable (Eval) are results that are within the test range and on scale.

The test device had a growth rate of >95%.

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:

Ceftriaxone	**S**	**I**	**R**
Streptococcus pneumoniae (nonmeningitis)	≤ 1	2	≥ 4
Streptococcus pneumoniae (meningitis)	≤ 0.5	1	≥ 2
Streptococcus spp. Other than *Streptococcus pneumoniae*			
Beta hemolytic group*	≤ 0.5	---	---
Viridans group	≤ 1	2	≥ 4

* The absence of resistant strains precludes defining any results categories other than 'susceptible'. For strains yielding results suggestive of a 'nonsusceptible' category, organism identification and antimicrobial susceptibility test results should be confirmed."

N. Proposed Labeling:

The QC expected value range and interpretive criteria as recommended by CLSI for *Streptococcus spp*. are listed. All values will be included in the package insert.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.